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Scientific Highlights/Abstracts of Original Investigations

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SLEEP

EDITORIAL

In June of 1986, roughly 400 scientists and clinicians interested in sleep attended the first annual meeting of the Associated Professional Sleep Societies (APSS). This year we celebrate the 25th Anniversary Meeting of the APSS on June 11-15, 2011, in Minneapolis, Minnesota.

During this meeting, 1,003 abstracts will be presented – 196 as oral presentations and the remaining 807 as poster presentations. All of these abstracts are included in this special issue of *SLEEP*. The abstract supplement provides a glimpse into the new ideas and latest research taking place in the field of sleep.

The abstracts are divided between basic and clinical sleep science and then assigned to one of 27 subcategories. Each abstract has a unique four-digit number to facilitate identification and location both within this issue and at SLEEP 2011. The four-digit number in the abstract supplement matches the four-digit code published in the SLEEP 2011 final program.

Over the last 25 years, the SLEEP meeting has linked the bench to the bedside with a robust scientific program involving basic, translational and clinical sleep research, and practical studies on the care of patients with sleep disorders. SLEEP 2011 continues in this tradition, which is evident from this year's abstracts. We look forward to sharing in the success of this historic event.

David F. Dinges, PhD
Editor-in-Chief

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0001

DIFFERENTIAL EFFECTS OF SODIUM OXYBATE AND BACLOFEN ON EEG, SLEEP, NEUROBEHAVIORAL PERFORMANCE, AND MEMORY

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Introduction: Sodium oxybate (SO, sodium salt of δ-hydroxybutyric acid) is used to treat the sleep disorder narcolepsy. SO was shown to increase EEG slow wave (delta) activity in non-rapid eye movement sleep (NREMS). We investigated whether SO affects the homeostatic process of sleep and thus induces physiological sleep. We also compared the effects of SO with those of baclofen (BAC), a high affinity GABAB receptor agonist, to assess the role of GABAB receptors in the response to SO.
Methods: We performed a randomized double-blind crossover study in thirteen young healthy volunteers. SO and BAC were administered before an afternoon nap and before the subsequent night sleep. Sleep and EEG were analyzed and neurobehavioral performance, subjective sleepiness and memory consolidation were assessed.
Results: Both SO and BAC counteracted the nap effects on the subsequent sleep by decreasing sleep latency and increasing total sleep time, deep sleep during the first NREMS episode, and EEG delta and theta power during NREMS. However, SO also increased EEG delta and theta power during REMS and a nap under SO although with high levels of delta power did not affect delta power the following night. BAC showed very similar effects on sleep and EEG, but with a delayed action. Both drugs induced sleep onset REMS periods and affected REMS with different dynamics. Except a slight and transient decrease of vigilance after naps under SO compared to placebo, psychomotor performance and subjective sleepiness were not affected by SO and BAC. Moreover, no general effect on declarative and motor memory was observed.
Conclusion: Our results suggest that even if SO induces EEG slow waves, these are not involved in the homeostatic regulation of sleep and thus SO does not induce physiological sleep. In addition, naps under SO did not generally affect cognitive performance. Finally, GABAB receptors seem to be strongly involved in SO response due to the fact that SO major effects on sleep and EEG are also seen with BAC.

0002

MUSCLE ACTIVITY DURING WAKE AND SLEEP IN NARCOLEPSY PATIENTS TREATED WITH SODIUM OXYBATE

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Introduction: Sodium oxybate (SO) is used for the treatment of narcolepsy. NREM and REM parasomnias are frequently associated with narcolepsy and sleepwalking is a reported side effect of SO. The aim of the study was to investigate the influence of SO during wake and all sleep stages on motor activity RBD in patients with narcolepsy based on data of recent multicenter studies.
Methods: Polysomnographies of 146 out of 300 narcoleptic from the international study group trials were newly scored for sleep stages and artefacts. Muscle tone (uV) and activity of m. mentalis was then analyzed by an automatic program and a comparison performed between baseline and medication with SO (baseline/placebo: 69 pts.; 4.5g: 30

pts.; 6g: 26 pts.; 9g: 21 pts.). Muscle activity was defined as short (<0.5 s) and long (>0.5s) lasting activity and indices per hour were calculated (short movement index SMI; long movement index LMI).
Results: Compared to baseline and placebo SO reduces mean muscle tone in all sleep stages except for the 4.5g dose that is nonsignificantly increased in stages NREM1, NREM 3 and wake. During all sleep stages and wake SMI is reduced dose dependently. The reduction is significant for 9g in light sleep (p<0.05). LMI is non-significantly increased at 4.5 g in REM and at 6 and 9 g in stages NREM 3/4. All other doses cause LMI reduction in sleep stages and wake. The reductions are significant for 6g in REM (p<0.01) and light sleep (p<0.05), and for 9g in NREM1/2 (p<0.05).
Conclusion: Our data indicate that in general SO can be efficacious in reducing muscle tone and muscle activity in sleep and wake in a dose dependant manner. The results imply that the occurrence as well as the suppression of REM and NREM parasomnias is dose dependent.

0003

ROLE OF THE HYPOCRETIN (OREXIN) 2 RECEPTOR: NO EFFECT OF CATAPLEXY ALTERING DRUGS ON HYPOCRETIN (HCRT) LEVELS IN HCRT-R2 MUTANT NARCOLEPTIC DOGS

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Introduction: Genetic narcoleptic dogs have nonfunctional Hcrt-2 receptors (HcrtR2), but intact Hcrt-1 receptors. They have normal levels of Hcrt in their CSF, yet have severe cataplexy. We now report that drugs shown to reduce or increase cataplexy in narcoleptic dogs and narcoleptic humans increase and decrease, respectively, Hcrt levels in normal dogs but not in HcrtR2 mutant narcoleptic dogs, despite strongly modulating their cataplexy.
Methods: Four narcoleptic Doberman pinschers and four breed matched normals were used. They were trained to stand quietly in a sling, in which the drug studies were undertaken. During each study, blood pressure, heart rate and respiration were measured continuously. Measurements for the first 30 min served as baseline. Then, atropine, methamphetamine, physostigmine, prazosin, phenylephrine or labetalol was given I.V. A second dose was given 45 min thereafter except in the case of prazosin, the effect of which persisted without supplementation. CSF was taken from the cisterna magna 1.5 h after the initial dose and assayed for Hcrt-1.
Results: In normal dogs, drugs changed Hcrt levels significantly and substantially in accord with their effects on cataplexy: those that have been shown to exacerbate cataplexy (physostigmine and prazosin), greatly decreased Hcrt level, while drugs that reduce cataplexy (methamphetamine, phenylephrine and labetalol) greatly increased Hcrt level. In striking contrast, none of the drugs tested altered the CSF Hcrt level in the narcoleptic dogs even though they strongly modulated symptoms.
Conclusion: These results suggest a vital role of HcrtR2 in feedback regulation of Hcrt release by drugs affecting cholinergic and aminergic systems. They also demonstrate that the symptoms of narcolepsy triggered and prevented by these drugs are not mediated by phasic changes in Hcrt level in the HcrtR2 mutant dog. We hypothesize that in normal animals, a positive feedback enhancement of Hcrt neuronal discharge, mediated by HcrtR2, reinforces Hcrt activity and the activity of locus coeruleus and other monoaminergic and glutamatergic cell groups receiving Hcrt input. The absence of HcrtR2 causes abnormal function of cholinergic and aminergic systems resulting in cataplexy without change in Hcrt level.

0004

PHARMACOLOGICAL CHARACTERIZATION OF OREXIN RECEPTOR ANTAGONISTS

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Introduction: Orexin/Hypocretin neuropeptides are responsible for regulating wakefulness, signaling through the activation of two receptors, Orexin 1 Receptor (OX1R) and Orexin 2 Receptor (OX2R). Genetic and pharmacological studies have indicated that antagonism of Orexin Receptors could provide benefit for insomnia and other disorders with disruptions of the sleep/wake cycle. Merck has engaged in the discovery and development of Dual Orexin Receptor Antagonists (DORAs) as a novel treatment for primary insomnia, with the lead compound MK-4305 currently in Phase III clinical studies.

Methods: The sleep promoting effects and detailed pharmacological characterization of a series of small molecule DORAs will be presented. MK-4305 and other DORAs were evaluated in vitro by determining potency across species and by assessment of downstream signaling pathways, and in vivo using microdialysis, receptor occupancy, locomotor, sleep and quantitative EEG (qEEG) assays in wild-type and transgenic animals.

Results: DORA compounds demonstrate similar affinity and potency for orexin receptors from mice, rats, rabbits, dogs, rhesus and humans, and show distinct effects on downstream signaling mechanisms. MK-4305 and DORAs from different structural classes dose-dependently occupy orexin receptors in vivo, decrease homecage locomotor activity and reduce wake activity across species, while proportionally increasing slow wave sleep and rapid eye movement sleep to increase total sleep time. These sleep effects fundamentally differ from sedating GABAergic drugs, and unlike zolpidem and diazepam, DORAs do not impair rotarod performance even when administered at >10-fold above sleep-promoting doses. DORA compounds also significantly attenuated histamine and dopamine efflux in the rat brain. Sleep architecture and qEEG patterns were consistent and dose-dependent across species, showing modulation of low and high frequency spectral power bands.

Conclusion: Modulation of orexin/hypocretin signaling with a dual orexin receptor antagonist effectively promotes sleep and provides a novel approach for the treatment of insomnia.

Support (If Any): This project was supported by Merck.

0005

CHEMICAL CHAPERONE MODULATION OF AGE-RELATED DECLINES IN RECOVERY SLEEP

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Introduction: Alterations in the quality, quantity and architecture of sleep and recovery sleep have been shown to occur during aging. The fruit fly *Drosophila melanogaster* displays a sleep-like state that shares several characteristics of mammalian sleep, including circadian and homeostatic regulation. Studies have shown that sleep deprivation can lead to an increase in misfolded/unfolded proteins, a process that is detrimental to cell survival. Three hours of sleep deprivation in *D. melanogaster* upregulates the unfolded protein response (UPR). This process reduces the accumulation of misfolded/unfolded proteins and shields the cell from injury. A key mechanism of the UPR involves increasing the levels of endogenous chaperones that bind to misfolded proteins. The effectiveness of this signaling pathway is diminished by the aging process. Our laboratory has shown that increasing endogenous chaperone levels enhances recovery sleep in *D. melanogaster*. These results lead to the hypothesis that application of an exogenous chaperone could rescue age-related recovery sleep dysfunctions.

Methods: We compared total sleep, sleep bout number and average bout duration in young (9 days) adult (8 week) and old (12 week) wild-type Canton-S flies at baseline and after 6 h of sleep deprivation during lights off from ZT18 to ZT24. Animals were treated with a chemical chaperone for 48 h followed by baseline sleep recordings. Recovery was recorded 24 h after sleep deprivation. Protein expression levels were quantified for all groups.

Results: Significant ($p<0.05$) daytime chaperone effects were primarily in the adult (8 week) flies indicating an overall increase in sleep time, sleep bouts, sleep bout duration and a decrease in wake bout duration. These sleep changes correlate to increasing endogenous chaperone levels in the adult.

Conclusion: We were able to rescue dysfunctions in recovery sleep by pharmacological intervention.

0006

STRAIN- AND STRESSOR-DEPENDENT DIFFERENCES IN EXTRACELLULAR GLUTAMATE AND GLUCOSE IN THE MOUSE PREFRONTAL CORTEX

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Introduction: While it is generally well understood that glutamate and glucose signaling pathways are critical for proper brain functioning and behavioral state at many levels, experiments to evaluate real-time, temporally-sensitive changes in these molecules when presented with a stressor are few and largely inconsistent. Herein, we have utilized implanted biosensors in the prefrontal cortex to perform side-by-side comparisons of concentration changes in glutamate and glucose in two inbred strains of mice during acute stress exposure.

Methods: Two intracerebral guide cannulas were stereotaxically implanted contralaterally in the brains of A/J and C57BL/6J mice. Following recovery, tether, and cage acclimation, glutamate and glucose biosensors (Pinnacle Technology, Inc.) were inserted into the guide cannulas and animals were divided into three groups: 1) emotional stress exposure through 1 hour of social defeat (n = 20/strain), 2) physical stress exposure through 15 minutes of restraint (n = 20/strain), and 3) an undisturbed, control group (n = 20/strain). Glutamate and glucose data was collected at one-second intervals for up to 48 hours and biosensors were immediately post-calibrated *in vitro* upon removal.

Results: Preliminary results demonstrate clear strain- and stress-dependent differences in extracellular glutamate and glucose levels during acute stress exposure. Physical restraint appears more stressful for A/J mice than social defeat; C57BL/6J animals display a greater stress response during the social defeat protocol than during restraint.

Conclusion: Preliminary evidence suggests differential regulation of glutamate and glucose in the prefrontal cortex of two inbred strains of mice at rest and in response to different stress protocols. Forthcoming experiments to synchronize these findings with scored electroencephalogram (EEG) and electromyogram (EMG) recordings will elucidate analyte concentration changes during sleep states, ultimately improving our understanding between physiological and behavioral changes during stress exposure and how these stress responses are influenced by genetic alterations.

Support (If Any): This work was supported by the Defense Advanced Research Projects Agency (DARPA) and the Army Research Office (ARO), award number W911NF-10-1-006.

0007

INHIBITION OF 5-HT2A RECEPTORS PREVENTS CO2-INDUCED AROUSAL IN MICE

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Introduction: Hypercapnia-induced arousal is an important mechanism in a number of diseases including obstructive sleep apnea, panic and sudden infant death syndrome. Serotonin (5-HT) neurons are required for hypercapnia to induce arousal from sleep. Several 5-HT receptor subtypes reside within targets of the ascending arousal system, including thalamus and cortex, and have been implicated in sleep-wake regulation. These receptors include 5-HT1A/B, 5-HT2A-C, 5-HT3, 5-HT6 and 5-HT7. Here we examined which 5-HT receptor subtype(s) mediate CO2-induced arousal.

Methods: Adult (3-6 mo; 22-36 g) male wild type littermates of our central 5-HT neuron deficient mice were implanted with EEG/EMG headmounts and temperature/activity telemeters. EEG, EMG, body temperature and breathing were recorded with the animals within a plethysmograph. After baseline recording for one hour, animals received an i.p. injection of either vehicle or a 5-HT receptor antagonist [doses in mg/kg; broad spectrum: methysergide (0.5-10), 5-HT2A/C: ketanserin (0.1-5), 5-HT2A: MDL-11,939 (0.5-10), 5-HT2C: RS102221 (0.2-10), 5-HT3: ondansetron (0.1-5), 5-HT6: Ro4368554 (0.3-10), 5-HT7: SB269970 (0.3-6)]. Thirty min after injection, animals received either a hypercapnic (7% CO_2/21% O_2/72% N_2; 10 min) or hypoxic (5% O_2/95% N_2; 2 min) challenge. Twenty min after the first challenge, animals were challenged with the other gas mixture. Each animal received 5 injections in conjunction with gas challenges spaced 4-7 days apart. In total 4 doses with the given ranges of each drug were tested.

Results: Vehicle injections had no effect on latency to arousal from hypercapnia or hypoxia. None of the drugs tested had any effect on hypoxia-induced arousal latency. Drugs targeting the 5-HT2A receptor subtype (i.e. methysergide, ketanserin and MDL-11,939) dose-dependently blocked hypercapnia-induced arousal. The other drugs had minimal or no effect on hypercapnia-induced arousal.

Conclusion: Hypercapnia induced arousal is mediated though the 5-HT2A receptor. Additional studies will be necessary to determine which subset of 5-HT neurons senses acidosis and initiates arousal, where the downstream targets are, what signaling mechanisms ultimately lead to the vigilance state transition and whether other 5-HT receptor subtypes not specifically tested here may play a role. These data may prove useful in developing future pharmacologic management strategies for the aforementioned diseases.

0008

EFFECTS OF CHRONIC GAMMAHYDROXYBUTYRATE AND R-BACLOFEN ON SLEEP AND CATAPLEXY IN HYPOCRETIN/ATAXIN-3 MICE

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Introduction: Gammahydroxybutyrate (GHB) is an effective therapeutic for the excessive sleepiness and sudden loss of muscle tone (cataplexy) associated with narcolepsy. The anti-narcoleptic effect of GHB is thought to be mediated by the promotion of sleep consolidation during the rest phase. Although the mechanism of action underlying the therapeutic efficacy of GHB is unknown, it has been hypothesized to be $GABA_B$ receptor-dependent. Here, the effects of chronic administration of GHB and the $GABA_B$ agonist R-baclofen (BAC) on arousal state and cataplexy were compared in the hypocretin/ataxin-3 transgenic mouse model of narcolepsy.

Methods: Hypocretin/ataxin-3 mice were prepared for EEG and EMG monitoring using abdominally-implanted telemetry units. After 3 weeks recovery, mice began a treatment paradigm designed to model the twice-nightly GHB dosing regimen used by human narcoleptics. Mice were dosed at ZT-2 and ZT-6 with GHB (100 mg/kg, n=7), BAC (2.8 mg/kg, n=8) or vehicle (n=7) every day for 15 days. Physiological and video-recorded behavioral data were simultaneously acquired and manually scored as wake, rapid-eye movement (REM) sleep, non-REM (NREM) sleep, or cataplexy. Drug effects on these states were assessed for 24 h on the baseline day prior to treatment and on the last day of treatment.

Results: BAC significantly reduced cataplexy time and bout number by 50% relative to baseline and vehicle controls without affecting the average bout length. Reduction in cataplexy was observed in 6 out of 8 mice after BAC and in 4 out of 7 mice after GHB, however, the mean reduction in cataplexy time and bout number after GHB did not reach statistical significance at the 100 mg/kg dose tested. Compared to vehicle, BAC and GHB significantly increased NREM time (171% and 149%, respectively), bout duration (4- and 3-fold increase, respectively) and delta power (128% and 137%, respectively) during the 1st h after dosing. A pharmacodynamic difference between BAC and GHB was evident in the 2nd h after dosing: NREM continued to be promoted by BAC, but wakefulness increased after GHB. NREM returned to vehicle levels by the 3rd h after dosing with either treatment. REM was significantly suppressed by 52% for the first 2 h after GHB and by 80% for the first 3 h after BAC.

Conclusion: At the doses tested, BAC consolidates sleep and suppresses cataplexy to a greater extent than GHB. Further studies using higher concentrations of GHB are needed to define the therapeutic dose in hypocretin/ataxin-3 mice.

0009

MICROINJECTION OF THE SELECTIVE EXTRASYNAPTIC GABA$_A$ RECEPTOR AGONIST GABOXADOL INTO RAT PONTINE RETICULAR FORMATION INCREASES WAKEFULNESS AND DECREASES SLEEP

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Introduction: GABA causes phasic inhibition via synaptic GABA$_A$ receptors, and tonic inhibition via extrasynaptic GABA$_A$ receptors (J Clin Sleep Med 15:12, 2006). Extrasynaptic receptors mediate volume transmission that can effectively modulate the excitability of widely distributed neuronal networks. GABAergic transmission in the pontine reticular formation (PRF) promotes wakefulness (J Neurophysiol 82:2015, 1999; Sleep 31:453, 2008; Anesthesiology 109:978, 2008; J Neuroscience 30:12301, 2010). Whether tonic inhibition by extrasynaptic GABA$_A$ receptors in the PRF is physiologically relevant for the control of sleep and wakefulness has not been determined. This study tested the hypothesis that microinjection of gaboxadol (THIP) into the PRF causes a concentration-dependent increase in wakefulness and decrease in sleep.

Methods: Adult male, Sprague-Dawley rats (n=10) were implanted with electrodes to record sleep and wakefulness, and with a microinjection guide cannula aimed for the rostral PRF. After recovery and conditioning, microinjections (100 nL) of gaboxadol hydrochloride (0, 0.1, 1, 10, 100 pmol; 0, 0.01766, 0.1766, 1.766, 17.66 ng, respectively) were made in random order during wakefulness. EEG and EMG were recorded continuously for 4 hours. Sleep and wakefulness were scored manually by two investigators, one of whom was blinded to the treatment condition. Agreement in sleep scoring was >91%.

Results: Gaboxadol significantly increased the amount of wakefulness (F=4.67; df=4,31; P=0.0046), and decreased NREM sleep (F=4.82; df=4,31; P=0.0039) and REM sleep (F=3.24; df=4,31; P=0.0247). Gaboxadol (100 pmol) significantly (P<0.05) increased wakefulness by

30%, decreased NREM sleep by 44%, and decreased REM sleep by 68%. Coefficients of determination demonstrated that the concentration of gaboxadol accounted for 96%, 94%, and 98% of the variance in the amount of wakefulness, NREM sleep, and REM sleep, respectively.

Conclusion: The results suggest that tonic inhibition of sleep-promoting neurons via extrasynaptic GABA$_A$ receptors is one mechanism by which GABA in rat PRF promotes wakefulness.

Support (If Any): J. Christian Gillin, MD Research Grant (GV), National Institutes of Health grants MH45361 (HAB), and the Department of Anesthesiology.

0010

GABAERGIC TRANSMISSION IN SPRAGUE-DAWLEY RAT PONTINE RETICULAR FORMATION (PRF) MODULATES TIME REQUIRED FOR THE GENERAL ANESTHETIC PROPOFOL TO CAUSE LOSS OF WAKEFULNESS

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Introduction: Most anesthetics potentiate GABAergic transmission but the mechanisms by which anesthetics cause unconsciousness remain unknown. Pharmacologically increasing or decreasing endogenous GABA levels in rat PRF increases or decreases, respectively, time needed for isoflurane to induce anesthesia (Anesthesiology 109:978, 2008). Similarly, increasing GABA levels in rat PRF increases the amount of time spent in wakefulness, whereas decreasing GABA levels in the PRF decreases time awake (Sleep 31:453, 2008). Propofol is an intravenous anesthetic that enhances transmission at GABA$_A$ receptors (Mol Pharmacol 65:68, 2004) and is used for induction and maintenance of anesthesia. This study is testing the hypothesis that microinjection of the GABA uptake inhibitor nipecotic acid (NPA) or GABA synthesis inhibitor 3-mercaptopropionic acid (3-MPA) into the PRF of rat increases or decreases, respectively, propofol induction time.

Methods: Adult, male rats (n=9) were implanted with jugular vein catheters (JVC) and microinjection guide tubes aimed for the PRF. Rats received randomized microinjections (100 nL) of Ringer's (vehicle) and NPA (1.29 µg; 10 nmol) or Ringer's and 3-MPA (1.6 µg; 10 nmol). Fifteen minutes after each microinjection, a continuous, intravenous infusion of propofol (800 µg/kg/min) was started and induction time was quantified as time to loss of righting response (LoRR).

Results: LoRR was significantly changed by injecting drugs that alter GABA levels into the PRF. LoRR was increased (30%, P=0.03) by NPA (n=5 rats) and decreased (17.7%, P=0.03) by 3-MPA (n=6).

Conclusion: This is the first demonstration that LoRR caused by an intravenous anesthetic was altered by GABAergic mechanisms in the PRF. The effects of NPA and 3-MPA on LoRR to propofol paralleled their effects on LoRR to the volatile anesthetic isoflurane (Anesthesiology 109:978, 2008). These findings suggest that altering GABAergic transmission in the PRF changes anesthesia induction time, and support the interpretation that GABA in the PRF promotes wakefulness.

Support (If Any): NIH grants HL40881, MH45361, HL65272, and the Department of Anesthesiology

0011

SYSTEMIC ADMINISTRATION OF DEXMEDETOMIDINE (DEX) DISRUPTS SLEEP ARCHITECTURE AND MICRODIALYSIS DELIVERY OF DEX TO RAT SUBSTANTIA INNOMINATA (SI) DOES NOT INCREASE ADENOSINE LEVELS

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Introduction: The alpha-2 adrenoceptor agonist DEX causes a state of sedation and analgesia (Anesthesiology 98:428, 2003) that is often described as sleep. We are conducting two sets of experiments to evaluate the homology between DEX-induced sedation and spontaneous sleep.

The first study is testing the hypothesis that there is no difference in sleep architecture between DEX-induced sedation and spontaneous sleep. SI adenosine levels decrease during sleep and the second study is testing the hypothesis that microdialysis delivery of DEX to the SI decreases adenosine levels in the SI.

Methods: Adult, male rats (n=4) were implanted with EEG and EMG recording electrodes. Following recovery and conditioning, rats received DEX (0.1, 0.3, 0.5 mg/kg) or saline followed by a 48-h recording of sleep and wakefulness. An experimenter blinded to drug condition scored each 10-s epoch of the recording. A second group of isoflurane-anesthetized rats (n=4) was used to quantify the effect of DEX on adenosine levels in the SI.

Results: DEX disrupted sleep architecture. During the first 24 h after injection, the percent of time spent in wakefulness, NREM sleep, and REM sleep was: 80.1, 16.0, and 3.9 (saline); 60.2, 36.9, and 2.9 (0.1 mg/kg DEX); 53.7, 43.9, and 2.4 (0.3 mg/kg DEX); and 65.1, 34.2, and 0.7 (0.5 mg/kg DEX). The DEX-induced (0.5 mg/kg) increase in NREM sleep was characterized by an 8.2% decrease in EEG delta power. During the second 24 h after DEX there was a rebound increase in REM sleep of 11.1% (0.3 mg/kg) and 374% (0.5 mg/kg) compared to the first 24 h. Microdialysis delivery of DEX to the SI did not alter adenosine levels in the SI.

Conclusion: DEX-induced sedation is not a faithful replicate of spontaneous sleep. Ongoing studies are quantifying the effect of systemically administered DEX on SI adenosine levels in behaving animals.

Support (If Any): NIH grants HL40881, MH45361, HL65272, and the Department of Anesthesiology

0012

INFLUENCE OF ESZOPICLONE ON POLYP FORMATION IN APC3MIN+/- MICE

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Introduction: Habitual use of sleeping pills has been associated with cancer-related mortality, and experimental studies have found carcinogenic effects of supraphysiological doses of hypnotics. On the other hand, disturbed sleep could potentially precipitate or exacerbate cancer development, and conversely sleep treatments might attenuate these effects. Further research is needed, particularly considering the high prevalence of hypnotic use among cancer patients. The aim of this study was to examine the effect of chronic administration of a normally-prescribed hypnotic dose on polyp development in APCMin+/- mice. Because all APCMin+/- mice develop colorectal cancer, progression of cancer in these mice can be studied in a small fraction of the number of animals that would be needed to establish cancer incidence in wild-type mice.

Methods: Twenty-seven 5-week old APCMin+/- mice were randomized to one of two 10-week treatments: (1) N=14 received a daily dose (0.30 mg/kg) of eszopiclone (Lunesta®), equivalent to approximately 2 mg/day in humans, adjusted for metabolism. (2) N=13 received a saline placebo. The mice were sacrificed and polyps were measured blindly in the intestine and colon.

Results: Mean total intestinal polyps count was about half as high following eszopiclone (10.8±13.1) vs. placebo (21.3±21.2). In the colon, few polyps were found, and the number was less following eszopiclone (0.4±0.9) vs. placebo (0.9±1.1). However, these differences were not statistically significant. Mice in the eszopiclone treatment had significantly less weight gain, but weight changes differed by only 1 gram between treatments, and were not correlated with polyp formation.

Conclusion: The data suggest that eszopiclone might have attenuated colorectal cancer development in APCMin+/- mice. The data were limited by small sample size and high variability in response. The data are not consistent with FDA trials indicating carcinogenic effects of eszopiclone. Further research is needed with more animals and more prolonged treatment, and with other hypnotic medications.

0013

PERIVASCULAR AND MENINGEAL MACROPHAGE AFFECT SLEEP

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Introduction: Perivascular and meningeal macrophages comprise a large population of resident macrophages within the brain. These macrophages are potent producers of pro-inflammatory cytokines including interleukin-1 beta and tumor necrosis factor-alpha, which regulate sleep. Perivascular and meningeal macrophages are involved with blood brain barrier functioning and are likely involved with modulating peripheral/CNS inflammatory interactions. Clodronate-treatment destroys these cells. The goal of this research was to determine whether clodronate affects sleep.

Methods: Male C57BL/6 mice were provided electroencephalogram (EEG) electrodes over the somatosensory cortices on each brain hemisphere and an electromyogram electrode in the nuchal muscles for polysomnographic sleep analyses. In addition, mice were implanted with a guide cannulae for intracerebroventricular (icv) injections. Mice were injected with liposomes and sleep responses were recorded for 2 days. Thereafter, mice were injected with clodronate encapsulated in liposomes to eliminate perivascular and meningeal macrophages. Sleep was recorded for 5 days. Sleep state and EEG slow-wave activity (SWA) during non-rapid-eye-movement sleep (NREMS) were analyzed by standard criteria.

Results: Mice injected with either liposomes, or clodronate encapsulated in liposomes, exhibited significant diurnal variations in NREMS, REMS, and NREMS EEG SWA. However, durations of NREMS and REMS were significantly reduced in clodronate/liposome-treated mice compared to liposome controls. These sleep reductions lasted for the 5 days of subsequent recording. In contrast, NREMS EEG SWA was significantly enhanced the second day after the clodronate/liposome treatment compared to liposome controls.

Conclusion: These results indicate that perivascular and meningeal macrophages are involved in sleep and EEG SWA regulation.

0014

URINARY NEUROTRANSMITTERS AS POTENTIAL BIOMARKERS OF POOR SLEEP QUALITY

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Introduction: Although insomnia is a major pathological factor in a number of diseases, limited data exists regarding the biochemistry of poor sleepers compared to good sleepers. In particular, neurotransmitters such as gamma-aminobutyric acid (GABA) and histamine are known to be correlated with sleep quality. The current investigation examined the relationships between validated sleep scores and urinary neurotransmitter levels as well as sleep scores and advancing age.

Methods: Data analysis was performed on specimens submitted to Pharmasan Labs, Inc. (Osceola, WI) for urinary neurotransmitters measurements. The study included adult patients (18-63 years old; n=75; 48 females, 27 males) that had collected urine specimens before bedtime and upon awakening, and had completed a Pittsburg Sleep Index (PSI) questionnaire to assess sleep quality. All data were de-identified but retained gender, age, and sleep index scores. PSI scores were compared to neurotransmitter and hormone levels as well as to age.

Results: Wilcoxon rank sum tests suggested that norepinephrine, epinephrine, GABA, glycine, phenylethylamine (PEA), serotonin and histamine levels were higher in subjects with poor sleep quality (n= 22) compared to subjects with good sleep quality (n= 53). In addition, simple linear regressions revealed a weak, positive relationship between the PSI scores and histamine, GABA, glutamate, glycine and 3,4-dihydroxyphenylacetic acid (DOPAC) levels. A multiple linear regressions indicated that, DOPAC, dopamine, epinephrine, GABA, glycine, norepinephrine, serotonin, 5-hydroxyindoleacetic acid (5-HIAA) and histamine have a moderate positive association to PSI scores suggesting that, when considered together, these biomarkers were better indicators of poor sleep than when considered individually. Finally, there was a positive relationship between PSI scores and advancing age.

Conclusion: These results indicate that subjects who have poor sleep quality possess the highest levels of neurotransmitters, specifically GABA and histamine. These neurotransmitters may function as predictive markers for sleep issues while providing potential targets for therapy.

0015

DIFFERENTIAL SLEEP EEG EFFECTS OF SLEEP RESTRICTION VERSUS TEMAZEPAM IN HEALTHY SUBJECTS AND PATIENTS WITH PSYCHOPHYSIOLOGICAL INSOMNIA

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Introduction: Drugs enhancing GABAa transmission, such as temazepam, and sleep restriction paradigms are both commonly used in the treatment of patients suffering from insomnia. However little is known about how the 2 treatments differ in terms of mechanism of action. The present study compares their acute sleep EEG effects in healthy subjects (HS) versus patients with psychophysiological insomnia (PI).

Methods: 10 female and 8 male subjects aged 36.3 +/9 years (9 HC and 9 PI) were included in a 3-way randomized cross-over study after a screening procedure comprising polysomnographic recordings. During each of the 3 study periods, sleep was recorded during three consecutive nights (baseline, treatment, and recovery). Treatment consisted either of temazepam 20mg, placebo or a 4-h sleep restriction.

Results: Comparison of the baseline nights revealed that, compared to HC, PI had lower sleep efficiency, total sleep time and increased wake percentage. A main treatment effect was evidenced for most parameter, mostly due to the sleep restriction treatment. However, latency to persistent sleep, wake after sleep onset, sleep efficiency, and wake percentage were significantly improved with sleep restriction in PI but not in HC. Temazepam significantly decreased latency to persistent sleep and increased stage 2 sleep in PI but not in HC, while it prolonged REM latency in HC but not in PI.

Conclusion: Sleep restriction and temazepam have different effect on visual sleep EEG parameter and these effects are not the same in HC vs PI. It suggests that the 2 treatments act through different mechanisms and that their different effects on HC vs PI relate to the fact that they impact normal (HC) versus hyperaroused sleep (PI).

0016

PHARMACODYNAMICS OF LOWER DOSE MODAFINIL FOR MAINTENANCE OF COGNITIVE FUNCTION IN SLEEP DEPRIVED CHINESE MALES

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Introduction: Modafinil is a psychostimulant used to maintain cognitive performance in sleep deprived people. We measured various pharmacodymanic parameters of cognitive performance in healthy Chinese male adults given standard and two lower doses of modafinil during sleep deprivation.

Methods: 80 healthy Chinese male subjects were randomized to four oral dose groups: (1) three doses of 50 mg modafinil; (2) three doses of 100 mg modafinil; (3) two doses of 200 mg modafinil plus one dose of placebo; or (4) three doses of placebo (each dose separated by 8 hours). Subjects were subjected to 40 hour sleep deprivation from 7 am. The first dose of the medications was administered at 10 pm. A battery of pharmacodynamic tests was conducted every 4 hours. This included the psychomotor vigilance test (PVT), Tetrax posturography, SPES computerized tests and the fitness for duty (FIT) pupilometer test. Data were analysed with generalized estimating equations and robust standard errors adjusted for clustering by subject ID, using Stata 10.1.

Results: PVT and posturography tests showed significant differences for all doses (50 mg, 100 mg, 200 mg) versus placebo in ameliorating the effect of sleep deprivation. The SPES Choice Reaction Time and FIT Velocity parameters showed significant differences for the 100 mg and 200 mg doses versus placebo. Persistent beneficial effects were seen post-sleep recovery for Tetrax posturography and FIT Velocity at the 100 mg dose.

Conclusion: Lower doses of modafinil (50 mg and 100 mg) are effective in maintaining some measures of cognitive function. Our studies show that 100 mg of modafinil, but not 50 mg, given 8-hourly for 3 doses, may be sufficient to maintain most cognitive function parameters in sleep deprived adults. Results should be confirmed in other populations.

0017

ALCOHOL, SMOKING, CAFFEINE AND DRUG USE ASSOCIATED WITH SLEEP DURATION AND SLEEP QUALITY

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Introduction: The effects of habitual substance use on self-reported habitual sleep are relatively unknown, despite clinical and laboratory data to suggest that even relatively small amounts of commonly-used substances could have effects on sleep.

Methods: Data from the 2007-2008 National Health and Nutrition Examination Survey (NHANES) were used. Analyses included adults(18+) who provided complete data (N=4717). Outcomes assessed with survey items included short sleep duration (SS:$\leq$6h), long sleep duration (LS:$\geq$9h), and sleep quality complaints (5+ days/month) of difficulty falling asleep(SL), frequent awakenings(AW), unrestful sleep(UN), and daytime sleepiness(DS). Predictors included alcohol (0,1-3,4-6,7-9,10+ drinks/day), smoking (cigarettes/day), caffeine (mg/day), and drug use (history of marijuana/cocaine/methamphetamine/opiates). Covariates included age, sex, race/ethnicity, education, income, marital status, exercise, BMI (objective), health insurance, physical health, mental health, depression, and anxiety. Sleep duration (continuous) was included as a covariate for all analyses of SL/AW/UN/DS outcomes. Binary and mul-tinomial logistic regression analyses included main effects and 2-way/3-way interactions.

Results: There were main effects for alcohol, with 7-9 drinks associated with decreased likelihood of LS(OR=0.15,p<.05) and 4-6 drinks with decreased likelihood of DS(OR=0.67,p<.05). Increased smoking was associated with greater likelihood of SS(OR=1.10,p<.05). Increased caffeine was associated with decreased likelihood of LS(OR=0.78,p<.01). Prior drug use was associated with increased likelihood of SL(OR=1.42,p<.01), AW(OR=1.56,p<.001), UN(OR=1.44,p<.001) and DS(OR=1.27,p<.05). There were no significant interactions for SS or SL, but there were significant interactions for LS (Alcohol*Smoking*Drug), AW (Alcohol*Smoking, Alcohol*Sleep Duration), UN (Alcohol*Drug, Alcohol*Smoking, Caffeine*Sleep Duration) and DS (Alcohol*Caffeine).

Conclusion: Habitual alcohol use, smoking, caffeine intake and drug use history were related to sleep duration and/or sleep quality, after adjusting for a number of demographic, socioeconomic and health factors. These relationships are complicated by a number of interactions among these predictors, such that the effects of one predictor often depend on levels another. Future research should continue to explore and better understand these interactions.

0018

ACTIVATION OF THE ERK KINASE IS AN IMPORTANT REGULATOR OF SLEEP IN DROSOPHILA MELANOGASTER

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Introduction: Recent evidence has shown that social enrichment increases sleep time in the fruit fly. This increase in sleep has been hypothesized to be related to plastic changes that occur during social enrichment. In rodents, activation of extracellular signal-regulated kinase (ERK) has been shown to be a critical regulator of synaptic plasticity and specifically in the synaptic changes associated with learning. The mechanism that regulates sleep with respect to social enrichment is poorly understood. We hypothesized that ERK may regulate sleep directly and may be a mechanism by which plasticity alters sleep need.
Methods: Sleep and sleep homeostasis following 12 h of sleep loss was evaluated in virgin female flies using Trikinetics monitors. Western blot analysis was employed to determine the effects of social enrichment on ppERK levels. Socially isolated flies (n=1) were compared to their socially enriched siblings (n=50). Genetic analysis of ERK was accomplished using the UAS-GAL4 system. Sleep, sleep homeostasis and the response to social enrichment were evaluated in Gain of function alleles (UAS-ERKact), the hypomorphic mutant for ERK, rolled (rl1), and following pharmacological agents that inhibit ERK.
Results: Both total sleep time and sleep homeostasis are increased when UAS-ERKact was expressed in the adult using the pan-neuronal GeneSwitch driver Gswelav-GAL4. Conversely, mutants and pharmacological disruption of ERK were associated with decreased baseline sleep time and attenuated the homeostatic response. In wild-type flies, ppERK levels were increased following social enrichment. Consistent with these results, disrupting ERK prevents the increase in sleep typically seen after social enrichment.
Conclusion: The mechanism by which social enrichment increases sleep in the fruit fly is poorly understood. Our data suggest that ERK may play a role in regulating normal sleep and may also serve as a signal to increase sleep after social enrichment.

0019

INCREASED PRESYNAPTIC SIZE AND POSTSYNAPTIC COMPLEXITY DURING WAKE AS COMPARED TO SLEEP IN DROSOPHILA MELANOGASTER

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Introduction: Molecular/electrophysiological markers of synaptic strength are higher after wake and lower after sleep in rodents. In flies, overall levels of synaptic proteins increase after wake and decrease after sleep, suggesting that maintaining synaptic homeostasis may be a conserved function of sleep. However, whether physiological sleep/wake can drive synaptic changes within specific neural circuits remains unknown. The synaptic homeostasis hypothesis predicts that increased wake-related plasticity in specific neural circuits should increase their synaptic strength and sleep need, and sleep should revert these changes, but these predictions have not been tested.
Methods: We studied 3 neural circuits: small ventral lateral neurons (s-LN$_v$s, important for arousal, circadian rhythms), mushroom bodies γ neurons (learning/memory), and visual interneurons (VS1; orientation during flight). Individual neurons expressing unique epitopes localized pre- or postsynaptically were compared using confocal microscopy in fixed brains harvested from sleeping, awake, or sleep deprived (SD) flies (Kruskal-Wallis and Mann-Whitney tests).
Results: Synaptotagmin-eGFP labels synaptic vesicles and was used to identify presynaptic puncta, which were larger in s-LN$_v$s and gamma neurons of wake and SD flies compared to sleeping flies (P<0.05, 9-34 flies/group). Structural changes were driven by behavior and not cir-

cadian time, because SD and sleeping flies were harvested at the same time during the dark period. Actin-GFP localizes to dendritic branches and synaptic spines and was used to study VS1 postsynaptic structural changes. Enriched flies spent 12 hrs in a large "mall" where flight was possible, and showed increased branch length and spine number relative to flies housed in small tubes where flight was not possible (P<0.05, 10-12 flies/group). This increased dendritic complexity decreased after sleep (P<0.05, n=12) but not after SD (P=0.8, n=11). After enrichment flies slept longer for 48 hrs relative to small-tube flies (P<0.05, 75 flies/group).
Conclusion: Sleep/wake in flies affect presynaptic size and postsynaptic complexity. These structural changes depend on wake "intensity", and the latter also affects sleep need.

0020

THE BARRIER SEPARATING BEHAVIORAL STATE TRANSITIONS INDUCED BY ISOFLURANE ANESTHESIA IS MODULATED BY THE SLEEPLESS GENE PRODUCT IN DISCRETE NEURONAL POPULATIONS

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Introduction: We have previously shown experimental evidence of a barrier separating behavioral state transitions induced by volatile anesthetics, which we have termed neural inertia. Using *Drosophila* as a model system, we now present evidence that neural inertia is markedly reduced in mutant flies that do not express the *Sleepless* gene product, which is thought to regulate the function of the *Shaker* potassium channel, and has been shown to be important for the regulation of normal *Drosophila* sleep. We also show, that selective neuronal rescue of *Sleepless* by using the *UAS-Gal4* system, can restore such a barrier to state transitions in flies with a mutant *Sleepless* background.
Methods: Flies were individually loaded into cylindrical tubes which were then placed into a Drosophila Activity Monitoring System (DAMS) monitor, in which a photobeam bisects each tube. Each minute, beam breaks were automatically recorded for subsequent analysis. During ZT10:20 to ZT12:55,flies were simultaneously exposed to progressive increasing (every 5 minutes) and then decreasing (every 5 minutes) concentrations of isoflurane. Air mixed with isoflurane, was introduced through a manifold with one limb of the manifold going to an agent analyzer and the rest of the limbs going to their respective DAMS monitors via a resistor. All fly lines used were outcrossed at least 6 times into an isogenized *white* background.
Results: Flies with the *sss*[P1] allele which have no detectable *sss* protein, have a markedly increased EC$_{50}$ for emergence from isoflurane anesthesia when compared to sibling controls (0.43% ± vs 0.27% p <0.05) Given that they are only mildly resistant to induction, this results in a reduction of neural inertia (6.3±1.7 vs. 30.4 ±3.6 p<00.05). Our rescue experiments show that depending on the neuronal driver used, either induction or emergence from anesthesia could be preferentially altered, with the drivers that restored the wild-type emergence phenotype being more effective in restoring wild type neural inertia.
Conclusion: *Sleepless* is an important genetic regulator of the barrier separating behavioral state changes induced by isoflurane anesthesia and rescue of *Sleepless* in discrete neuronal circuits of mutant flies can restore such a barrier. In addition, selective neuronal rescue of *Sleepless (sss)* function allows us to anatomically dissociate neuronal circuits

important for either induction or emergence from anesthesia, confirming that these are path dependent processes.

0021

BTBD9 EXPRESSION INFLUENCES BOTH DOPAMINE AND FERRITIN EXPRESSION

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Introduction: The roles of dopamine and iron in the pathophysiology of Restless Legs Syndrome (RLS) are poorly understood. Clinical observations of symptom relief have led to the use of dopamine agonists as a first-line therapy for RLS. Both clinical and epidemiological observations have identified an association between iron deficiency and both primary RLS symptoms and known causes of secondary RLS. More recently, low serum ferritin levels have been correlated with the at-risk variant of the BTBD9 gene. However the causal link remains unknown. We investigated the interplay between dopamine, iron, and BTBD9 expression using both a Drosophila model and mammalian cultured cells.

Methods: HPLC was used to measure dopamine levels in the head of Drosophila with deletion mutations in the fly homolog of BTBD9 (gene CG1826). Human embryonic kidney cells (HEK293) were grown in medium with altered iron concentrations and were transfected with human BTBD9 plasmids. Both immunoblot and immunocytochemical assays were used to measure resulting BTBD9 and ferritin expression.

Results: Deletion mutations of CG1826/BTBD9 yields viable animals that have significantly decreased dopamine levels. While growing HEK293 cells in either iron enriched or iron depleted media did not alter BTBD9 expression, overexpression of BTBD9 in HEK293 cells did result in increased ferritin expression. These results suggest that BTBD9 plays a role in regulation of both dopamine levels and ferritin levels.

Conclusion: Our results suggest that the roles of dopamine and iron in the pathophysiology of RLS are downstream of BTBD9 expression. However, the precise regulatory mechanisms remain unknown. Our ongoing efforts to determine the molecular function of CG1826 should continue to illuminate the roles of dopamine, iron, and BTBD9 in RLS and sleep regulation.

0022

DISRUPTION OF PERIPHERAL LIPID METABOLISM GENES ALTERS THE RESPONSE TO SLEEP DEPRIVATION

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Introduction: : Insufficient sleep results in adverse effects including increased adiposity and cognitive impairments. While it is clear that sleep loss can alter genes involved in lipid metabolism, recent studies indicate that mutations in lipid metabolism genes can, in turn, protect flies from the negative consequences of sleep deprivation. To further understand the relationship between lipids and sleep deprivation, we conducted a microarray experiment and identified genes involved in various aspects of lipid handling. Using genetics, we manipulated these genes and evaluated sleep homeostasis and short-term memory following 12 h of sleep deprivation.

Methods: Flies mutant for the clock gene *timeless* (tim^{01}) do not show a sleep rebound after 3 and 6 h of sleep deprivation but display a sleep rebound after 9 and 12 h of sleep loss. mRNA was collected from tim^{01} flies after 3, 6, 9 and 12 h of sleep deprivation. cDNA microarrays revealed several classes of lipid metabolism genes that were significantly modified by 9 and 12 h of sleep loss were identified. These genes were manipulated by expressing UAS-RNAi lines in a tissue and circuit dependent manner. Flies were subjected to 12 h of sleep deprivation using the SNAP and sleep homeostasis and short-term memory were evaluated as previously described.

Results: We found several classes of lipid metabolism genes, including acyl-CoA and lipases that significantly altered sleep rebound and prevented cognitive impairments as measured by Aversive Phototaxic Suppression. Interestingly, we identified mutants that reduced sleep homeostasis but that did not prevent the cognitive impairments. Finally, we show that lipid metabolism genes can alter sleep homeostasis when manipulated in peripheral tissues.

Conclusion: These data emphasize that while sleep loss may increase the risk for obesity and metabolic syndrome, genes involved in lipid metabolism can mitigate or attenuate negative consequences that accrue during waking.

0023

GENETIC ANALYSIS REVEALS A MOLECULAR LINK BETWEEN REGULATION OF SLEEP AND LIPID METABOLISM

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Introduction: Epidemiological studies show that short sleep is related to increased mortality and metabolic diseases that manifest pathological blood lipid levels. In addition, genome-wide association studies on T2DM and obesity have identified genes that link to regulation of sleep. Lipid metabolism is also involved in recovery from sleep loss. However, the role of genetic variants relevant to lipid metabolism has not been examined previously in regulation of sleep.

Methods: Here we examined (i) association of blood lipid profiles with total sleep time at population level and (ii) association of 60 genetic variants previously associated with lipid traits with TST. The analyses were performed in Finnish samples comprising 12524 participants and genetic analysis with 6334 participants and replicated in 2189 twins. Finally we studied the RNA expression in sleep restriction study (4 hours of sleep for five nights) of nineteen healthy men.

Results: We found that both short and long sleepers had increased triglyceride levels. In the genetic analysis we identified two variants that independently contributed to blood lipid levels and to sleep duration (P<0.0005, P corrected <0.05, β>0.07). The allelic variants previously related to a beneficial lipid profile associated here with longer sleep, reduced fatigue and reduced eveningness chronotype. The finding was replicated and meta-analysis further strengthened the association. Finally, we demonstrated that the expression of these variants also increased after sleep deprivation (P=0.006).

Conclusion: These results indicate that some of the common genetic variants primarily identified for lipid regulation may have a role in normal regulation of sleep, evidencing for a genetic link between regulation of sleep and metabolism. We suggest the currently discovered variants to be one of the lipid metabolism genes that also participates in sleep regulation.

0024

COMMON VARIANT IN THE P2Y11 RECEPTOR GENE IS ASSOCIATED WITH NARCOLEPSY AND WITH HIGHER SUSCEPTIBILITY TO ATP INDUCED CELL DEATH IN T LYMPHOCYTES

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Introduction: The human sleep disorder narcolepsy-cataplexy affects 1 in 2,000 individuals. Narcolepsy symptoms are primarily caused by the loss of approximately 70,000 hypocretin producing neurons located in the hypothalamus, and growing evidence supports the hypothesis that narcolepsy with cataplexy is an autoimmune disease targeting these neurons.

Methods: Following on a recently published GWAS of narcolepsy, we conducted replication of 10 additional loci in 1,525 Caucasians. Of these, only one loci replicated strongly (rs4804122, p= 5.42x10-4; odds ratio 0.77), but this association was not seen in other ethnic groups. Based on differential LD patterns for this marker across ethnic groups 6 SNPs were then genotyped in 3,406 Caucasians, 2,414 Asians, and 302 African Americans. Based on a hit in *P2RY11*, we determined P2Y11 expression levels in white blood cells of different genotypes. We further examined the effect of P2Y11 stimulation on ATP induced cell death in different white blood cell types.

Results: Rs2305795, a SNP located in the 3'untranslated region of the *P2RY11* gene, is highly associated with narcolepsy across all ethnic groups (p= 6.1x10-10; odds ratio 1.28). Additional experiments indicate rs2305795 effects on P2Y11 expression in white blood cells, most notably CD8+ T cells and NK cells where the disease associated allele show a significantly lower expression. ATP induces cell death via the P2X7 receptor, and we find that co-stimulation of P2Y11 rescues the cells. Further, lymphocytes with the narcolepsy associated genotype show a lower response to P2Y11 stimulation in our cell death assay.

Conclusion: We have identified a novel narcolepsy susceptibility locus on chromosome 19 with a highly significant association to rs2305795, a SNP in the 3'UTR of *P2RY11*. This receptor is highly expressed in CD8+ T cells and NK cells, and modulates ATP induced cell death. This association may reflect the importance of immune system regulation in the etiology of narcolepsy.

0025

GENOME-WIDE ASSOCIATION STUDY OF INSOMNIA PHENOTYPES

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Introduction: Insomnia phenotypes assessed by self-report have demonstrated evidence of heritability, yet little is known about specific genes that may confer risk for these phenotypes. This is surprising given that insomnia is the most prevalent sleep disorder and is associated with negative sequelae. Here we present the results of the first genome-wide association study (GWAS) of insomnia phenotypes.

Methods: A Health and Lifestyle Questionnaire was completed by 2,323 Australian twins and their siblings who subsequently provided blood samples for DNA analysis. There were a series of questions assessing insomnia-related phenotypes including sleep latency, sleep duration, sleep quality, and bedtime. Genotypes were assessed for 274,604 SNPs and imputation based on the HapMap project yielded a total of 2,380,486 SNPs. GWAS analyses were performed in Merlin with each SNP tested in a singlepoint analysis.

Results: Although no SNPs passed the genome-wide significance threshold (p<5x10-8), there were a number of suggestive findings. Sleep duration was associated with several SNPs from the ATP8A1 gene (p=7.9x10-7), which is involved in ion transport across the membrane. Sleep latency was associated with a set of SNPs in perfect LD (p=1.3x10-6) with minor allele frequency ~0.014 from CACNA1C, a calcium channel gene that has shown association with bipolar disorder. There were weaker associations (p<10-5) between bedtime and SNPs in the L3MBTL4, EBF3, and NPSR1 genes.

Conclusion: This GWAS found associations between insomnia phenotypes and individual SNPs, although none reached genome-wide significance. The sleep latency results suggest a genetic link in a rare variant between insomnia and bipolar disorder that may underlie some of the sleep disturbance commonly found in this disorder. SNPs associated with sleep duration are more difficult to interpret but suggest that cellular ion transport may impact sleep/wake characteristics. The association between bedtime and neuropeptide S provides further evidence its role in sleep regulation.

0026

IDENTIFICATION OF NOVEL CORE CLOCK GENES BY BAYESIAN INTEGRATION

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Introduction: After two decades of research, a set of core clock genes has been identified that plays a key role in regulating circadian rhythms. However, more remain undiscovered. To accelerate the process of clock component discovery, we used a naive Bayesian strategy to integrate publicly available data sets and identify the genes most likely to have core circadian functions.

Methods: We constructed a list of functional properties that characterize core clock genes. For each property we developed a simple, quantifiable metric that encapsulates it. We used previously published data sets to determine how that metric was distributed among known clock genes and within the genome at large. These distributions were used to calculate Bayes factors that describe level of evidentiary support provided by each data set that a given gene is a core clock component. After combining the results for each feature and data set, genes were rank ordered by the probability that they have a core clock function. To demonstrate the utility of this method, we performed several experiments to better characterize Gm129, a high probability candidate.

Results: The output of this analysis, a ranking of genes by the probability that they play a role in the clock, was, as expected, greatly enriched for known core clock genes. However several novel candidates were identified. Gm129 was found to have many core clock properties. Overexpression studies demonstrate that it functions as a Cry1/Cry2 independent repressor of Clock/Bmal1 mediated transcription. Additional data from a mammalian 2 hybrid screen shows direct physical interactions between Gm129 and the clock genes Bmal1 and Per2.

Conclusion: Bayesian integration of genome-wide data sources may accelerate discovery of core clock genes and the understanding of how they influence physiology and behavior.

0027

A NOVEL TECHNIQUE TO IDENTIFY THE TARGETS OF CIRCADIAN MODIFIERS

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Introduction: A recent genome-wide RNAi screen identified hundreds of genes that influence circadian rhythms in the U2OS model system. Core clock genes form a highly interconnected network and most modifiers impact the expression of many clock genes. We have developed a strategy to distinguish directly mediated changes in clock gene expression from changes mediated by circadian network interactions. We demonstrate the application of this strategy in identifying likely targets of these circadian modifiers.

Methods: Using the U2OS model system, we knocked down each core clock gene in a dose dependent fashion. The expression of all clock genes was measured in every sample by quantitative PCR. For each clock gene, we collected the data from all samples in which RNAi was not targeted against the gene in question. The pooled data was fit using singular value regression. The resulting equation is used to predict the expression of the specified clock gene in new samples, given the expression of all other core clock components. PCR was then performed to measure clock gene expression in samples transfected by the recently identified circadian modifiers. Changes in core clock gene expression that are well predicted by the changes in the other core clock genes are taken to represent network effects. Poorly predicted changes are taken to represent influences not mediated by other core clock genes. In order to test the utility of this approach, we applied this methodology to genes with known core clock interactions

Results: The expression of each core clock gene was found to depend strongly on the expression of others. Singular value regression was able to describe a significant fraction of this variance and allows predictions of clock gene expression.

Conclusion: This methodology permits rapid, preliminary determination of the molecular targets of circadian modifiers and will improve our understanding of the inputs influencing the circadian network.

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0028

THE ROLE OF A SYNAPTIC ADHESION MOLECULE IN SLEEP REGULATION

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Introduction: Sleep need builds up during wakefulness and decays during sleep and this has been linked to changes in synaptic strength. Accordingly, sleep deprivation was shown to decrease NMDA receptors (NMDAr) functioning in different brain areas. NMDAr functioning is regulated by synaptic adhesion molecules (SAM), and one of these was shown to determine NMDAr synaptic localization. Here, we assessed the effect of sleep pressure on the expression of this SAM and its role in sleep regulation.

Methods: 1) Male mice from 3 inbred strains were submitted or not to a 6h sleep deprivation (SD) by gentle handling starting at ZT0 (Zeitgeber time 0: lights on), and sacrificed at ZT6 for brain sampling. Total RNA was extracted and expression levels measured by microarray or qPCR. 2) AKR/J male mice were submitted to a 6h SD at ZT0, followed by protein extraction of brain cortical tissue and Western blot. 3) The EEG of mutant male mice not expressing the targeted SAM was recorded during 24h of baseline, during a 6h SD starting at ZT0 and 18h of recovery.

Results: We observed that the mRNA expression of the targeted SAM was consistently decreased by SD in all inbred strains, whereas the SD-dependent decrease in its protein level was not significant for total cortical protein samples. Preliminary observations indicate that mice homozygote for the SAM mutation are much more difficult to keep awake during SD. Also, mutant and heterozygote mice had increased non-rapid eye movement sleep time during baseline compared to wild-type littermates. A similar trend was observed for recovery.

Conclusion: Additional analyses are underway to assess the effect of this SAM on the dynamics of EEG markers of sleep pressure. Our preliminary data suggest a role for this SAM in sleep regulation.

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0029

HIPPOCAMPAL GENE EXPRESSION DURING PARADOXICAL SLEEP AS REVEALED BY CDNA MICROARRAY, QPCR AND IMMUNOHISTOCHEMISTRY

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Introduction: Paradoxical sleep (PS), the state during which dreams occurs is present in mammals and birds. Its function remains unknown although several studies indicate that it might play a role in learning and memory. It has been named PS because the EEG shows a cortical activity similar to that of waking while the muscle tone is completely abolished. To investigate what modifications PS induces at molecular level in the neurons of the hippocampal formation, we profiled gene expression by cDNA microarrays approach in the hippocampal formation of rats displaying different quantities of PS and then localized the neurons with a modification in gene expresson.

Methods: A first group of rats (n=12) was deprived of PS (PSD rats) by the multiple platform method during 78h. A second group of rats was allowed to recover from this deprivation (PSR) during 6 hours (n=12). A third group of rats remained in their home cage during all the protocol (PSC, n=12). All animals were sacrificed at the same time of the day. Total mRNA was extracted from the hippocampal formation and hybridized on Affymetrix cDNA microarrays. Quantitative PCRs were then made to validate the results of the microarrays. Then, we used immunohistochemistry to localize neurons that express the proteins of interest in the hippocampal formation of another set of 3 group of rat (PSC, PSD, PSR, n=12).

Results: The expression of 83 transcripts was modified in the hippocampal formation by the protocol. 32 of these transcripts increased their expression level after PS recovery. The majority of them are implicated in synaptic plasticity, learning and memory (Homer1a, Arc, c-Fos, Zif-268, Cox2) and others are implicated in the nervous system development (Bdnf, Nptx2, Mas1). 24 transcripts increased their expression level after PS deprivation and are mainly implicated in metabolism regulation. In the PSR animals, the number of Fos and Arc immunoreactive granular cells in the dentate gyrus was 10 time higher than in the other groups. The number of Cox2+ cells in the dentate gyrus and CA3 was 2 time greater than in the other groups. We have also verified if theses IEG+ neurons were young cells. No double labelled cells Fos+ or Arc+/doublecortin were observed. Morever we injected BrdU 3, 6 and 12 weeks before the protocol of privation/recovery of PS and no Fos or Arc neurons expressed BrdU+.

Conclusion: Our results indicate that a subpopulation of the granular dentate gyrus neurons shows a strong activation and plasticity process during PS.

0030

OPTOGENETIC STIMULATION ENHANCES C-FOS AND INTERLEUKIN-1β LEVELS IN CULTURED NEURONS

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Introduction: The pro-inflammatory cytokine interleukin-1β (IL-1) has a role in sleep regulation in health and disease states including the chronic inflammation associated sleep disorders. Yet a mechanistic connection between specific activity at the cellular level and IL-1 expression remains to be established. We have recently developed the methods for optogenetic stimulation of cultured networks of neurons and glial cells. Using that *in vitro* tool, here we test the hypothesis that enhanced level of induced activity in neurons elevates IL-1 production in cultured neurons.

Methods: Cortices from newborn mouse (C57BL/6) brains were dissected in ice-cold Hibernate-E solution, digested in 2mg/mL papain, and then mechanically dissociated. The cells were transfected, using nucleofection technique, with YFP-tagged Syn-Channelrhodopsin-2 (SynChR2-YFP). The transfected cells were grown on poly-D-lysine coated coverslips in a 5% CO_2 incubator at 37°C in serum free NbActiv4 medium. Within about 4 days, cells form complex neuronal/glial networks. On day 8 *in vitro* (DIV8), these networks were stimulated using a train of light pulses (random, frequency 10 Hz) from light emitting diodes (470nm) under ambient growth conditions. After stimulation the cells were fixed and probed for c-Fos and IL-1 expression using immunofluorescence techniques, and imaged using a confocal microscope.

Results: Stimulation for 90 minutes shows increase in c-Fos (in nuclei) and IL-1 (in cytoplasm) expression for most neurons. The extent of c-Fos and IL-1 expression depended on the duration of stimulation.

Conclusion: Optogenetic stimulation increases the expression levels of c-Fos confirming cell activation. The elevated level of IL-1 in neurons indicates that the expression of IL-1 is dependent, at least in part, on neuronal activation. Neuron activation-induced IL1 expression may provide a mechanism linking cell activity to sleep regulation.

0031

EXPRESSION OF CHANNELRHODOPSINS IN PARVALBUMIN-POSITIVE BASAL FOREBRAIN NEURONS

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Introduction: The basal forebrain (BF) plays an important role in the modulation of cortical activity across sleep-wake cycles via corticopetal projections of cholinergic and non-cholinergic neurons. Among non-cholinergic neurons, an important component consists of parvalbumin (PV)-containing, γ-aminobutyric acid (GABA)ergic neurons whose firing rates increase during electroencephalographic (EEG) low-voltage fast activity. However, their precise contribution to cortical activation and sleep-wake regulation is not well understood. Therefore, we sought to selectively incorporate channelrhodopsins (light-activated ion channels) into PV-positive neurons in BF in order to investigate the effect on sleep and wakefulness.

Methods: Adeno-associated virus with double-floxed Channelrhodopsin2 (ChR2)-eYFP was injected stereotactically into BF of two types of transgenic mice (n=2/each). In both transgenic mice, Cre recombinase expression was under the control of the PV promoter, thus ChR2-eYFP should be expressed specifically in PV neurons. In homozygous PV-Cre mice, colocalization of ChR2-eYFP with PV protein was confirmed by immunohistochemistry. The second strain of transgenic mice (PV-Tomato) was generated by crossing PV-Cre mice with Cre-reporter Rosa/Tomato mice, creating heterozygous PV-Cre mice with Cre-dependent expression of Tomato (red fluorescence), allowing confirmation that viral expression was Cre-dependent without the need for immunohistochemistry. Following viral injection, co-expression of ChR2-eYFP and Tomato was compared.

Results: Preliminary data showed that >90% of ChR2-eYFP-positive BF neurons expressed PV and ~75% of the BF PV-positive neurons expressed ChR2-eYFP in PV-Cre mouse. In the second condition of PV-Tomato mice >90% of ChR2-eYFP-positive BF neurons expressed Tomato, and >90% of Tomato-positive BF neurons expressed ChR2-eYFP.

Conclusion: Our results confirm that ChR2-eYFP expression was exclusively dependent on Cre recombinase under the control of the PV promoter. These results suggest that the Cre-dependent AAV expression system will be a useful tool to enable selective stimulation of BF PV neurons in order to examine their role in cortical arousal.

0032

CD73 IN SLEEP REGULATION

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Introduction: Adenosine and extracellular ATP have multiple physiological actions including sleep and cerebral blood flow regulation. However, the exact mechanisms of adenosine-modulated sleep remain unknown. Extracellular ATP and ADP are converted to AMP by the enzyme CD39. Extracellular AMP is in turn converted to adenosine by the enzyme CD73. Here, we investigate the role of CD73 in sleep regulation.

Methods: Male CD73KO mice (provided by Thompson LF, Oklahoma Medical Research Foundation, Oklahoma City, OK) and C57BL/6 control mice were implanted with cortical EEG and EMG electrodes. Spontaneous sleep and sleep responses to 6 h of sleep deprivation (SD) were determined by established criteria. Power spectral analyses were also performed. Adenosine-related molecules in the somatosensory cortex following SD were analyzed by real-time PCR. Further, CD73 expression was analyzed in male rats throughout the time-of-day and following 6 h of SD.

Results: Spontaneous NREMS was enhanced in CD73KO mice compared to controls (P = 0.046). REMS did not differ between strains. NREMS following SD was enhanced in controls (P = 0.004). In contrast, SD failed to affect NREMS duration in CD73KO mice. EEG SWA during NREMS following SD was enhanced in both strains (P = 0.044). CD39, adenosine deaminase, adenosine kinase, and adenosine A2a receptor expression did not differ between strains or in their responses to SD. Adenosine A1 receptor expression was significantly lower in CD73 mice compared to controls (P = 0.004) but enhanced following SD only in CD73KOs (P = 0.003). In rats, CD73 expression was elevated following SD and with time-of-day dependent increases in sleep propensity (P = 0.012 and P < 0.001, respectively).

Conclusion: These data indicate that CD73 is involved with sleep regulation. Further, these data suggest that mechanisms upstream of adenosine and CD73, such as extracellular ATP, are involved in regulating sleep.

0033

NEUROTENSIN RECEPTOR 1 (NTSR1) IS INVOLVED IN BOTH AFFECT AND SLEEP

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Introduction: Neurotensin, a neuropeptide that interacts with the dopaminergic system, has been previously associated with many psychiatric illnesses such as anxiety, addiction, and schizophrenia. Based on results from a large-scale sleep-wake phenotype and genotype analysis of 269 adult male mice from a [C57BL/6J X (BALB/cByJ X C57BL/6J F1)] N2 segregating cross, we identified neurotensin receptor 1 (NTSR1) as a candidate gene for affect and sleep through quantitative trait loci (QTL) and expression QTL (eQTL) analyses.

Methods: 10 control C57BL/6 mice and 10 NTSR1 knockout mice were behaviorally tested in the open field, elevated plus maze, tail suspension, and forced swim tests. The same animals were used to record baseline sleep, sleep deprivation, and subsequent recovery, of which 8 knockout animals and 9 wild type controls successfully completed the protocol.

Results: NTSR1 knockouts showed increased anxious behavior as compared to the wild types in the open field test, with significant differences in distance traveled, percent of time spent in the center, and percent of time spent in the corners. NTSR1 knockouts also showed an increase in despair behavior in the tail suspension test, with significant differences in bouts of immobility. NTSR1 knockouts also displayed a lower percentage of sleep time spent in REM sleep in the dark phase, and larger diurnal variation of REM minutes than the wild type controls in baseline conditions. In the recovery period following sleep deprivation, the NTSR1 knockout animals presented with more wake and less non-REM rebound sleep.

Conclusion: Anxiety and depression have long been associated with alterations in sleep. Despite a wealth of evidence for a genetic component for depression and anxiety, the specific genes and gene networks associated with these affective disorders remain largely unknown. Here we present that a knockout of a candidate gene in the region of a mouse QTL for sleep characteristics, known to have comorbidity in humans with affective disorders, shows similar behavioral characteristics associated with affective disorders in humans.

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0034

TOLL-LIKE RECEPTOR 4 IS A REGULATOR OF MONOCYTE AND ELECTROENCEPHALOGRAPHIC RESPONSES TO SLEEP LOSS

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Introduction: Sleep loss triggers changes in inflammatory signaling pathways in the brain and periphery. The mechanisms that underlie these changes are ill-defined. The Toll-like receptor 4 (TLR4) activates inflammatory signaling cascades in response to endogenous and pathogen-associated ligands known to be elevated in association with sleep loss. TLR4 is therefore a possible mediator of some of the inflammation-related effects of sleep loss. Here we describe the baseline electroencephalographic sleep phenotype and the biochemical and electroencephalographic responses to sleep loss in TLR4-deficient mice.

Methods: : TLR4-deficient mice and wild type controls were subjected to electroencephalographic and electromyographic recordings during spontaneous sleep/wake cycles and during and after sleep deprivation sessions of 3, 6 and 24-hr duration.

Results: Relative to wild type control mice, TLR4-deficient mice exhibited an increase in the duration of the primary daily waking bout occurring at dark onset in a light/dark cycle. The amount of time spent in non-rapid eye movement sleep by TLR4-deficient mice was reduced in proportion to increased wakefulness in the hours immediately after dark onset. Subsequent to sleep deprivation, EEG measures of increased sleep drive were attenuated in TLR4-deficient mice relative to wild type mice. TLR4 was enriched 10-fold in brain cells positive for the cell surface marker CD11b (cells of the monocyte lineage) relative to CD11b-negative cells in wild type mouse brains. To assess whether this population was affected selectively by TLR4 knockout, flow cytometry was used to count F4/80- and CD45-positive cells in the brains of sleep-deprived and time of day control mice. While wild type mice exhibited a significant reduction in the number of CD11b-positive cells in the brain after 24-hr sleep deprivation, TLR4-deficient mice did not.

Conclusion: These data demonstrate that innate immune signaling pathways active in the monocyte lineage, including presumably microglia, detect and mediate in part the cerebral reaction to sleep loss.

Support (If Any): These experiments were supported by a Washington State University, Spokane Faculty Seed grant and a Washington State University New Faculty Seed grant.

0035

GENE EXPRESSION IN SLEEP-DEPRIVED PURINE TYPE 2X7 RECEPTOR KNOCKOUT MICE

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Introduction: The purine type 2X7 receptor (P2X7R) is involved in cytokine release and sleep regulation. ATP is released during neurotransmission. Further, P2X7R expression changes with sleep loss and time of day. Mice lacking the P2X7R have reduced duration of NREMS and electroencephalography (EEG) slow wave activity (SWA) during NREMS following sleep deprivation (SD) as compared with wildtype mice (WT). We posit that the attenuated sleep responses to sleep loss observed in the P2X7R knockout (KO) mice is accompanied by changes in mRNAs previously linked to sleep regulation.

Methods: Levels of mRNAs previously linked to sleep were determined using reverse transcriptase polymerase chain reaction (PCR). Two strains of mice were used, control C57BL6 and P2X7RKO mice. For each strain, one group of mice (N=8) was deprived of sleep by gentle handling during the last 6h of daylight and the control groups (N=8 each) were allowed to sleep undisturbed. All mice were sacrificed at dark onset. The hypothalamus and the somatosensory cortex were harvested, RNA extracted, cDNA prepared and PCR performed by standard methods.

Results: SD enhanced brain-derived neurotrophic factor (BDNF), the P2X4 receptor (P2X4R), and adenosine deaminase (Ada) mRNAs in the cortices of both strains. In the hypothalamus of WT mice, BDNF, P2X4R, and Ada mRNAs also increased, but in this tissue these mRNAs failed to change in the P2X7RKO mice. SD enhanced tumor necrosis factor alpha (TNF) mRNA in WT cortices but not in P2X7RKO cortices. In contrast, in the hypothalamus, SD failed to alter TNF mRNA expression in WT mice but decreased it in the P2X7RKO mice.

Conclusion: Differential brain expression in WT and P2X7RKO mice of BDNF, P2X4R, Ada and TNF mRNAs may be involved in the biochemical causal pathways that lead to the differential sleep responses to sleep loss exhibited by these two strains of mice.

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0036

NADPH OXIDASE 2 ACTIVATION IN MOUSE BRAIN DURING INTERMITTENT HYPOXIA PROMOTES EXCESSIVE MITOCHONDRIAL ROS PRODUCTION AND DYSFUNCTION

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Introduction: We recently showed that intermittent hypoxia during sleep (IH)-induced neuronal oxidative stress and neurocognitive deficits in mice were closely related to increased reactive oxygen species (ROS) content and impaired respiratory function in cortical and hippocampal mitochondria. On the other hand, these IH-induced pathological changes were shown to be abolished or attenuated in mice in which NADPH oxidase was genetically inactivated or pharmacologically inhibited. The interaction between the NADPH oxidase pathway and pathways underlying excessive mitochondrial ROS production is however unclear.
Methods: C57BL/6 and gp91phox-/- mice were exposed to IH (alternating 5.7% and 21% O2 every 90 seconds 12 hours/day for 2 months). Cortical mitochondria were isolated for assessment of ROS content, membrane potential, and electron transport chain complex activities.
Results: IH elicited significant increases in ROS content in cortical mitochondria isolated from C57BL/6 mice, especially when respiration was supported by a complex II substrate. Addition of ADP reduced mitochondrial ROS content in both control and IH-treated animals and completely abolished the difference between the two groups. Cortical mitochondria from IH-treated C57BL/6 mice were also characterized by decreased complex I activity and reduced inner mitochondrial membrane potential. In contrast, IH-induced increases in cortical mitochondrial ROS content were significantly attenuated in gp91phox-/- mice lacking NADPH oxidase 2 activities due to disruption of the gene encoding the catalytic subunit of the enzyme. Furthermore, IH-induced impairment of complex I activity and inner mitochondrial membrane potential were abrogated in gp91phox-/- mice.
Conclusion: Our findings suggest the presence of a cross-talk between the NADPH oxidase 2 and mitochondrial ROS production pathways, in which the former triggers the latter to generate excessive amounts of ROS. Excess ROS production in turn, leads to mitochondrial oxidative stress and dysfunction in cortical mitochondria of mice exposed to IH, promoting apoptosis and cellular dysfunction.
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0037

CORTICAL WHITE MATTER IS VULNERABLE TO INTERMITTENT HYPOXIA IN NKX6.2 NULL MICE

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Introduction: Recent studies demonstrate that white matter is extensively affected in brains of obstructive sleep apnea (OSA) patients. We hypothesize that developmental myelin defect or breakdown underlies the vulnerability of brain white matter to sleep apnea-associated IH. To test this hypothesis, we examined the molecules relevant to myelin architecture and oligodendrocytes in the mouse model of sleep apnea-associated intermittent hypoxia (IH) using Nkx6.2-null mutant mice with characteristics of mild abnormal paranodes and slight hypomyelination.
Methods: 12-week C57BL wild-type and Nkx6.2-null mice were exposed to intermittent hypoxia (IH, 8% / 20.9% O2 /120s each cycle/12hrs) or intermittent air (IA) during the light phase. After two-week IA or IH exposure, prefrontal cortex, cortex, CA1 region and cerebellum were dissected and collected. Myelin-related proteins, structural molecules of paranode/node of Ranvier, and adult oligodendrocyte progenitor cells (aOPCs) were examined in different brain regions between IA- and IH-treated young adult wild-type or Nkx6.2 null mice.
Results: The expressions of myelin-relevant molecules including MBP and CNPase were significant decreased in cortex, especially in prefrontal area, in Nkx6.2-null brains after 2-week IH exposure. The NG2+/pdgfrα+ aOPCs proliferated in response to IH insult. However, no obvious phenotype of myelin was observed in IH-insulted wild-type brains.
Conclusion: The white matter in region of cortex with myelin deficiency is vulnerable and sensitive to short-term IH insult, which may further lead to neurological disorders. Intact and compact myelin laminate may protect axons against short-term IH insult.
Support (If Any): Sleep Research Society Foundation/J. Christian Gillin M.D. Research Grant (J.C.), University of Louisville SOM Basic Grant (J.C.), and NIH HL-086662 (D.G.)

0038

EFFECTS OF STRESSOR CONTROLLABILITY ON NEURAL PLASTICITY ASSOCIATED MRNA LEVELS IN MOUSE AMYGDALA AND MEDIAL PREFRONTAL CORTEX (MPFC)

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Introduction: Controllable and uncontrollable stress, modeled by escapable and inescapable shock (ES and IS), produce different alterations in post-stress rapid eye movement sleep (REM; ES increases whereas IS decreases). Conditioned reminders of ES and IS also produce increases and decreases in REM similar to those seen with the original stressors. The mPFC assesses stressor controllability and interacts with the amygdala which regulates post-stress sleep and conditioned changes in sleep. We examined the expression of genes linked to neural plasticity in the mPFC and amygdala after training with ES and IS.
Methods: Male BALB/cJ mice were trained in a shuttlebox using a yoked design such that pairs of ES and IS mice received identical amounts of shock (20 shocks: 0.5 mA, 5.0 sec maximum duration, 1.0 min intervals), but only ES mice could terminate shock. Control animals (NS) were treated identically, but did not receive shock. Immediately or 2 hour after training, animals were sacrificed, total RNA was isolated, then reverse transcription and real-time quantitative PCR (RT^2 qPCR) was performed to assess mRNA levels of RIM1, BDNF, NGF-β, TNFα, FGF-2, Arc, c-Fos, zif268, GRPR, spinophilin and GluR1 genes in the amygdala, mPFC and somatosensory cortex, a control region. Corticosterone was examined at each time point as an index of the stress response.
Results: ES produced a significant up-regulation of BDNF mRNA levels at 2 hour post-training in both regions. ES also significantly elevated zif268 and GluR1 mRNA levels in mPFC whereas IS significantly elevated Arc and GRPR mRNA levels in the amygdala. ES and IS did not differentially alter mRNA levels in the somatosensory cortex. Corticosterone was similarly increased by ES and IS compared to NS.
Conclusion: The observed differences in zif268, GluR1, Arc, and GRPR mRNA levels after ES and IS may be due to differential expression of neuronal plasticity related genes in the mPFC and amygdala. Activation of divergent cellular pathways may underlie differences in behavior and sleep produced by controllable and uncontrollable stress and their associated memories.
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0039

IN VIVO MICRORNA-138 INHIBITION SUPRESSES SLEEP AND DELTA POWER DURING THE LIGHT PHASE

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Introduction: MicroRNAs (miRNAs) are regulators of mRNA stability. They are small (~22 nucleotide) strands with the capacity to hybridize with the RNA-induced silencing complex and target mRNA for degradation or by inhibiting their translation. MiRNA regulation is involved in virtually every biological process studied. Previously we showed that miRNAs in the brain change with sleep propensity. We hypothesize that manipulating miRNA levels in the brain affects sleep.
Methods: Male Sprague-Dawley rats 275-325 g were maintained on a 12 hr light/dark cycle and instrumented with intracerebroventricular cannula and differential EEG electrodes. At light onset, negative control sequence was injected and after 24 h, miR-138 inhibitor sequence (4 pmoles; Ambion) was delivered. EEG was recorded for 4 post-injection days and manually scored offline as wake, rapid eye movement sleep (REMS) or non-REMS (NREMS). Power analyses of NREM sleep from treatment days were performed using two hour time blocks and compared with recordings from control days.
Results: miR-138 inhibitor sequence state-specifically decreased NREMS duration and NREMS EEG slow-wave amplitude during post-injection days 2 and 3 as compared with negative control sequence. These effects were primarily confined to the light phase on both days.
Conclusion: These findings indicate that in vivo manipulations of miR-NAs alter sleep phenotypes and are the first demonstration of miRNAs causing changes in sleep phenotypes. It seems likely that miRNAs acting on sleep regulatory substance mRNAs are important components in the regulation of sleep.

0040

SLEEP AFFECTS BRAIN-SPECIFIC INTERLEUKIN-1 (IL1) RECEPTOR ACCESSORY PROTEIN (ACPB) MRNA EXPRESSION IN RAT SSCTX

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Introduction: IL-1 is involved in physiological sleep regulation. The IL-1 receptor accessory protein (IL1RAcP) is an essential component for IL-1 signaling. AcPb, initially characterized by one of us (DES), is an alternatively processed IL1RAcP mRNA product. Its role in the brain is incompletely understood although it affects IL1-induced neuronal gene expression in vitro. Herein we report the sequence of the rat AcPb nucleotide and AcPb mRNA responses to spontaneous sleep, sleep deprivation (SD) and IL1β treatment using real-time RT-PCR.
Methods: Male Sprague-Dawley rats were used. AcPb cDNA sequence: 5' RACE and PCR were used to clone full-length AcPb cDNA sequence from four rat brains. For the next three experiments, groups of rats (n=8/group) were used. 1).Two groups, control, and SD for 6h by gentle handling, were killed 6h after lights were on; 2).Six groups were sacrificed at 4h intervals for 24h; 3).Six groups received either human recombinant IL1 (0, 2.5 and 25ng) intraventricularlly at 1h before dark onset and were sacrificed 2 or 5h later. The somatosensory cortices (SSctx) were harvested. Total RNA was extracted and analyzed for AcPb mRNA expression using real-time PCR.
Results: The rat AcPb exon 12 genomic sequence was 96% identical to the mouse exon at the amino acid level (Gene bank #: GU123169).

AcPb mRNA in the rat SSctx was significantly increased after SD compared with the control group and during the daily cycle was highest (2 fold) 4h after dark onset and lowest values were observed 8h after light onset (p<0.05). Finally, SSctx AcPb mRNA levels were significantly increased 5 h after 2.5 ng IL1 treatment but not under other conditions.
Conclusion: AcPb is conserved in the rat and closely related to murine AcPb. Brain AcPb mRNA levels are sensitive to changes in sleep and IL1 treatment. AcPb may be involved in IL1-altered sleep.

0041

PRIOR IMMUNIZATION DOES NOT PREVENT HUMAN H1N1 INFLUENZA INVASION INTO THE OLFACTORY BULB OF MICE

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Introduction: Influenza induces changes in sleep during the acute phase response (APR) after infection. The mouse adapted HIN1 influenza strain (PR8) invades the olfactory bulb (OB) within 4h of intranasal infection and alters sleep. We investigated whether immunization could prevent OB viral invasion. We hypothesized that immunization would inhibit OB influenza invasion and virus-induced APR and cytokine expression.
Methods: C57BL/6J mice were intranasally inoculated at light onset with an immunizing dose (1:100,000) of heat-killed or live PR8, five weeks prior to a lethal PR8 dose (1:200). OBs and lungs were collected 24h post-infection. Viral RNA (vRNA) was detected by amplification of viral cDNA with nested PCR. Virus-and sleep-linked cytokines were quantified with real-time PCR. Additional groups of mice were implanted with transponders to monitor the APR up to 14 days post-infection.
Results: In naïve mice, 1:200 PR8 treatment reduced body temperatures and weights; these mice died within 7 days following infection. In contrast, both immunized groups had attenuated APRs compared to infected naïve mice. Genomic vRNA was detected in the OB in 7/10 live virus and 9/10 heat-killed virus immunized mice. In the OB and lungs of naive mice, but not immunized mice, the toll-like receptor 7 (TLR7) (an intracellular receptor that binds viral single-stranded RNA) mRNA, was upregulated following viral challenge. In lungs, prior immunization with live or dead virus significantly attenuated virus (1:200)-induced expression of IL1-beta mRNA compared to non-immunized virus-challenged mice.
Conclusion: Immunization was unable to prevent influenza OB invasion, but attenuated the APR. The attenuated APR in immunized mice may be mediated, in part, by lung IL1 and OB TLR7.

0042

INFLUENZA-INDUCED RESPONSES IN MICE WITH A FUNCTIONAL MX1 GENE

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Introduction: Influenza infection enhances sleep for days in mice; these responses are related to expression of host interferon-inducible proteins and cytokines. Most inbred mice carry a dysfunctional antiviral gene, myxovirus resistance-1 GTPase (dMx1). In this study, we compared the responses at 15 and 96 h after influenza virus challenge in mice bearing the dMx1 gene to mice with a functional (fMx1) gene that blocks viral transcription.
Methods: The mice expressing the fMx1 protein were a gift from Peter Staeheli (Freiburg, Germany). Purified influenza virus (PR8) was inoculated intranasally and total RNA, cDNA, nPCR and real-time PCR were done according to manufacturer's instructions.

Results: Viral nucleoprotein (NP) negative and positive sense RNA was found in the olfactory bulb (OB) of both fMx1 and dMx1 mice that received live virus at both time points although more was present at 96 h post-inoculation. In contrast, in lungs by 96 h post-inoculation significantly more viral NP - and + sense RNA was found in the dMx1 mice. Further, in lungs TNFα and IL1β mRNAs were higher in the fMx1 whereas the anti-inflammatory type I interferons were higher in the dMx1strain at 15 h post infection. By 96 h, only dMx1 had elevated TNFα mRNA in the OB. In the lungs, dMx1 mice had elevated IFNβ, IL1β and TNFα mRNAs. The fMx1 strain also showed elevation of the same genes but at significantly lower levels.

Conclusion: Influenza virus invaded the OB of both dMx1 and fMx1 mouse strains and there was little difference in viral levels between the strains. In contrast, the lungs of the fMx1 mice had a much lower response of innate immune mediators than the dMx1 mice. Data suggest that the recovery of the fMx1 mice is likely due to what is happening in the lung and not the OB.

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0043

THE EFFECT OF PRO-INFLAMMATORY MEDIATORS ON HYPOCRETIN/OREXIN RECEPTOR EXPRESSION

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Introduction: The important role of the Hypocretin/Orexin system in regulation of the pattern of sleep and wakefulness, as well as the related disorders, is recognized. Also, autoimmune diseases or/and enhanced inflammatory mediators are found in patients with sleep and wakefulness disorders. Thus, the crosstalk between neuroinflammation and regulators of sleep and wakefulness needs to be further investigated. Here, we present our research studies on the effect of pro-inflammation mediators on expression of the Hypocretin/Orexin receptors.

Methods: Hypocretin/Orexin receptor 2 (HcrtR2) was inserted into the MSCV vectors between the polylinker located within the multiple cloning sites of the MSCV vector. Then, the MSCV- HcrtR2 vector was transfected into the packaging cells by lipid-mediated transfection, to produce retroviral particles, and the collected rtroviral vectors are used to transfect the primary neuron cells. Cells then were treated with vehicle only or pro-inflammation mediators, tumor necrosis factor alpha (TNF-α) and IL-1. The expression of HcrtR2 was examined after cells treated with or without TNF-α and IL-1.

Results: HcrtR2 expression in cells treated with TNF-α was decreased, and the downregulation of HcrtR2 is in one persistent pattern. In contrast, HcrtR2 expression in cells treated with IL-1 was in a slow-wave pattern, and the effect of IL-1 on HcrtR2 expression is not persistent.

Conclusion: These results demonstrate that TNF-α and IL-1 can be involved in regulation of the Hypocretin/Orexin system through manipulation of the HcrtR2 expression. These results also suggest that pro-inflammatory mediators may be involved in sleep and wakefulness disorders through regulation of the Hypocretin/Orexin system.

0044

TEMPORAL CHANGES IN THE BRAIN CORTICAL UNFOLDED PROTEIN RESPONSE (UPR) FOLLOWING SLEEP FRAGMENTATION (SF) IN THE MOUSE

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Introduction: The activation of the UPR is a critically important component of the molecular response to stressful conditions such as ischemia/reperfusion, hypoxia, trauma, and sleep deprivation. The UPR occurs as the result of accumulation of misfolded proteins in the ER lumen, which in turn activates the molecular events leading to either cell survival or apoptosis. However, the effect on the UPR of conditions such as sleep fragmentation, a frequent occurrence in many sleep disorders, is unknown.

Methods: C57BL/6 mice (n=40; 6 week-old) were purchased from Jackson Laboratories and were exposed to SF for different time periods using a custom designed and validated device that does not require social isolation, restricted access to food, increased physical activity or increases corticosterone levels. . SF or control mice were sacrificed after 3 hrs, 6 hrs, 9 hrs, 12 hrs, 36 hrs, 60 hrs, and 1 week of exposure. The SF paradigm was implemented during daylight hours from 7 am to 7 pm. The cortex was rapidly harvested, snap frozen, and subsequently processed for protein extraction. Equal amounts of cortical lysate proteins were run on 15% SDS gels and immunoblotted for detection of phosphorylated eIF2(alpha) and CHOP using previously validated antibodies.

Results: An increase in eIF2(alpha) phosphorylation occurred at 6 hrs of SF, persisted for 48 hours, and subsequently gradually returned to basal levels at 1 week of SF. CHOP was not expressed in control conditions, and became detectable at 2 days of SF, progressively decreasing thereafter to basal levels after 1 week of SF.

Conclusion: Sleep fragmentation elicits transient and distinct activation of the UPR in the brain cortex. We postulate that the UPR triggered by SF may reflect induction of protective mechanisms aiming to minimize neuronal cell dysfunction and initiation of apoptotic processes.

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0045

SLEEP FRAGMENTATION REDUCES VISCERAL FAT INSULIN SENSITIVITY IN MICE

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Introduction: Sleep fragmentation (SF) is one of the hallmarks of sleep apnea (SA), which is associated with metabolic dysregulation independently of obesity. SF has been proposed as contributing to the putative adverse metabolic conse¬quences of SA via disruption of visceral adipose tissue (VAT) homeostasis, and altered insulin sensitivity. We hypothesized that chronic experimental SF in mice will lead to changes in insulin signaling in visceral fat

Methods: Adult young male C57BL/6J mice were exposed to SF or control sleep conditions (CO) for 7 days, after which visceral fat tissues were harvested and treated with a series of incremental insulin concentrations for 10 min. SF was performed for 12 hrs during daylight and consisted of gentle, mechanically-induced arousals at 2 min intervals using a custom developed automated device. Protein lysates were separated by electrophoresis and probed with anti-phosphorylated-Akt (pAkt) and total Akt antibodies. Antibodies to phosphorylated tyrosine residues, insulin receptor substrate 1 (IRS1), and insulin receptor beta (IRb) were also used. Serum lipid profiles were measured.

Results: A dose-response of insulin sensitivity emerged in CO intact visceral fat in vitro. However, pAkt was decreased in mice exposed to SF at lower doses of insulin compared to CO, indicating the presence of insulin resistance. In addition, serum triglycerides were increased and HDL levels were reduced in SF-exposed mice. Phosphorylated tyrosine in the lysates, IRS1, and IRb proteins showed no changes in SF compared to CO.

Conclusion: SF induces development of insulin resistance in mouse visceral fat, and is also accompanied by dyslipidemia. Further delineation of the pivotal molecular components that coordinate insulin action in visceral fat, and the perturbations in these pathways that are associated with SF, will be essential for further understanding of the mechanisms underlying insulin resistance and metabolic dysfunction in sleep apnea.

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0046

INFLAMMATORY CYTOKINES ARE INDUCED IN THE BRAIN CORTEX OF SLEEP FRAGMENTED MICE

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Introduction: Inflammatory cytokines are involved in the regulation of sleep, and have been assigned modulatory roles in physiological and pathophysiological aspects of sleep cycle dynamics. Sleep fragmentation (SF) is an important feature of many sleep disorders, and may lead to excessive sleepiness. We hypothesized that inflammatory cytokine expression in brain will be altered by SF.

Methods: Adult male C57/b6 mice were exposed to SF during the light period (from 7:00am to7:00pm) using a custom-designed apparatus that elicits minimal stress from periods ranging from 1 day to 14 days of SF, along with time-matched controls (CO). Frontal cortical samples were harvested on dry ice, total RNA was purified, 1μg of RNA was transcribed to CDNA, and gene expression of TNF-α, TNFR1a, TNFR1b, IL-6 and IL-1B was quantified by RT- PCR using β-actin as the housekeeping gene .The relative fold increase was calculated by the ΔΔCt method.

Results: TNF-α expression progressively increased over time during exposure to SF, particularly at days 7 ($p<0.004$), and day 14 ($p<0.003$). Expression of TNF receptors was also enhanced by SF, but starting at day 1 and remaining stable but elevated thereafter ($p<0.04$). IL1-β and IL-6 gene expression did not change during SF, although a slight trend was observed for IL1-β.

Conclusion: The expression of both TNF-α and TNF-α receptors is upregulated by sleep fragmentation, and may play a role in the altered sleep homeostasis and cognitive dysfunction associated with such frequent perturbation of sleep integrity.

0047

BIP/GRP78 IMMUNOREACTIVITY IN SLEEP/WAKE AND CIRCADIAN NEURAL AREAS OF AGED MICE

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Introduction: Advanced age is associated with a reduction in sleep/wake quality and disrupted circadian rhythms. Many individuals experience increased nighttime awakenings and have difficulty staying awake during the day. This is likely attributed to age related neuronal dysfunction. Recently we have shown a reduction in the neural activity of wake active neurons in aged mice. Expression of BiP/GRP78, an ER molecular chaperone is also reduced in wake-active neurons. BiP ensures proper protein folding and helps to alleviate cellular and endoplasmic reticulum stress. A decrease in BiP yields accumulation of misfolded proteins and an increase in apoptotic factors. It is likely that BiP is reduced in other areas of sleep/wake or circadian function. We predicted that a reduction in BiP in sleep/wake and circadian areas would be associated with sleep/wake function in aged mice.

Methods: We compared 2 month and 24 month old c57 BL6 mice. We used fluorescence immunohistochemistry to compare fluorescent intensity of several neural areas associated with sleep/wake or circadian function. We used NIH Image J software to analyze intensity.

Results: Aged 24 month mice show less BiP-immunoreactive intensity in several areas including the lateral habenula when compared to 2 months of age ($p<0.05$). In the suprachiasmatic nucleus BiP immunoreactive intensity also shows a trend in reduction in aged mice.

Conclusion: BiP levels decline in several circadian and sleep/wake neuronal areas in aged animals and this reduction may contribute to the dysregulation of sleep and wakefulness.

0048

IDENTIFYING PHENOTYPIC DIFFERENCES IN SLEEP USING WILD-DERIVED INBRED MICE

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Introduction: Electroencephalograph (EEG) was analyzed to compare various sleep phenotypes in seven inbred mouse strains from different Mus musculus subspecies including, Mus. m. domesticus, musculus, castaneus, and molossinus, in the idea that the identified strain differences in sleep phenotypes are attributable to the differences in genotypes. Wild-derived inbred mice have far more diverse genetic background than laboratory mice, increasing the opportunity of identifying phenomenal sleep phenotypes.

Methods: The inbred mice used in this study were C57BL/6J (B6), a commonly used laboratory mouse strain, and six wild-derived mice strains, namely, PGN2/Ms (PGN), NJL/Ms (NJL), BLG2/Ms (BLG), KJR/Ms (KJR), MSM/Ms (MSM), and HMI/Ms (HMI). These mice were chronically implanted with EEG and electromyogram (EMG) electrodes for polysomnographic recording of sleep-wake states. The vigilance states were automatically classified by SleepSign ver.3 software.

Results: Four phenomenal strain differences were found in sleep phenotypes: 1) A block of 'high levels of wakefulness with less than 10% of sleep per hour' was observed immediately after the dark onset in PGN, NJL, BLG, and KJR. In particular, the duration of this period reached four hours in BLG and KJR; 2) The amount of NREM sleep, REM sleep, and wakefulness were varied significantly among strains. The largest difference was observed in REM sleep during the dark period. HMI had the most REM sleep, 3.2-fold more than that of BLG; 3) HMI had the significantly lowest delta peak frequency (DPF) during NREM sleep among the seven inbred mouse strains. The other five wild-derived mice strains had similar DPF to B6; 4) KJR had clear alpha oscillations in addition to theta oscillations during REM sleep, which made it unique to this strain.

Conclusion: Since these four phenomenal sleep phenotypes identified are potentially under strong genetic control, this study provides an avenue for pursuing responsible genes involved in sleep regulation by genetic approach.

0049

GENETIC ANALYSIS OF SLEEP DURATION

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Introduction: Sleep duration in the adult human population is normally distributed with a mean of ~ 7-8 hours. Short or long sleep (<6h or >9h) has been associated with changes in cognition, personality, disease susceptibility and mortality. Twin studies suggest that variation in sleep duration is a heritable trait (h=0.44 in MZ twins and 0.22 in DZ twins). Using sleep questionnaires, previous studies have identified specific gene candidates that are associated with variation in sleep duration. These include variations in CLOCK genes involved in the molecular regulation of the circadian cycle. In this study, we will determine

whether these genetic findings can be replicated using total sleep period measured by EEG in the Wisconsin Sleep Cohort (WSC).

Methods: We assess 1,876 polysomnographs (PSGs) in 1,300 adult individuals from the WSC. Sleep onset is defined as the first occurrence of stage 1 sleep, and sleep cessation is the final epoch of sleep prior to morning awakening. Six hundred and sixty-nine individuals had more than two PSGs separated by 4 years, so we could assess the reliability of the EEG total sleep period within an individual over time. Genotyping in this cohort was performed using Affymetrix 6.0 genechip and direct Taqman genotyping. Bonferroni corrected genetic association is determined using an additive genetic model and linear regression with subject age, sex, BMI, and medications as potential covariates.

Results: We report whether variations in candidate genes are associated with sleep duration. This includes known polymorphisms in ABCC9/SUR2, COMT, HLA DQB1*0602, PER3, PER2, PER1 and CLOCK, DEC2, MYRIP, OR10K1/2 and TSHZ2.

Conclusion: Results reveal support for the genetic control of sleep duration in humans. Further studies are needed to examine gene-gene and gene-environment interactions on this basic sleep phenotype.

0050

THE CATECHOL-O-METHYLTRANSFERASE (COMT) GENE RELATES TO RESPIRATORY AROUSALS IN CHILDREN WITH DOWN SYNDROME

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Introduction: In previous studies, the homozygous Val polymorphism of the COMT (catechol-O-methyltransferase) gene, which is involved in the degradation of dopamine and norepinephrine, has been associated with poor sleep continuity in children with ADHD (Gruber et al, 2006). Specifically, children with ADHD have been shown to have more snoring and respiratory arousals than typically developing children (Goroya et al., 2009). Children with Down syndrome (DS) have been shown to have attention deficits (Clark & Wilson, 2003) as well as poor sleep, including symptoms of obstructive sleep apnea (Ng et al., 2006). Our goal was to examine the relationship between COMT and respiratory arousals in children with DS.

Methods: Seventeen children with DS (age range: 7-18 years, mean age= 11.79; 18 girls) participated in this study. Nocturnal sleep was assessed with ambulatory in-home polysomnography (PSG). ADHD symptoms were assessed with the Conners Parent Rating Scales (CPRS-3), and the ADHD Probability Index Score was calculated. Gene data were collected via saliva samples in Oragene DNA kits (DNA Genotek) and the Val/Met polymorphism of the COMT gene was genotyped using a Taqman assay with a polymerase chain reaction (PCR)-based method.

Results: Eighty-two percent of our sample (n = 14) met criteria for pediatric obstructive sleep apnea (AHI > 1.5) and twenty-nine percent (n = 5) met criteria for ADHD. We found that there was a trend for children who were Met allele carriers (n = 10) to have a lower respiratory arousal index compared to children with the Val-Val genotype (n = 7) (F (1,15) = 3.802, p = 0.07), but we did not find a difference in AHI between the two groups.

Conclusion: These findings lend support to the idea that COMT is involved in the regulation of sleep in Down syndrome.

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0051

OBSTRUCTIVE SLEEP APNEA AND ADIPOSE TISSUE GENE EXPRESSION

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Introduction: Obstructive sleep apnea (OSA) is associated with increased levels of circulating inflammatory markers and a state of insulin resistance. The tissues responsible for these effects are unclear. We hypothesized that OSA may induce a pro-inflammatory and insulin resistant state in adipose tissue.

Methods: 18 patients scheduled to undergo ventral hernia repair surgery were recruited. Subjects wore a portable sleep monitor two nights prior to surgery. The respiratory disturbance index (RDI) was obtained across both nights and averaged. Biopsies from abdominal subcutaneous and visceral fat depots were obtained intra-operatively. RNA was isolated using a commercial kit. Expression of a set of 8 genes related to inflammation and insulin resistance were measured using real time PCR, normalizing for amount of the 18S component of ribosomal RNA. Expression levels were compared between those with and without OSA as defined by an RDI > 5.

Results: The OSA group (n=10) had a mean RDI of 19.2 ± 25.9 versus 0.6 ± 0.5 in the control group (n=8). Groups had similar age (56.1 ± 10.8 y versus 54.5 ± 12.2 y; p=0.8) and body mass index (36.1 ± 9.3 kg/m2 versus 35.2 ± 5.6 kg/m2; p=0.8). In subcutaneous fat, mean expression levels of TNF-α, MCP-1, and IL-8 were 56%, 76%, and 95% greater in those with OSA though none met criteria for statistical significance. In visceral fat, PAI-1 expression was 3.1 fold greater in OSA though again, this was not statistically significant (p=0.4). In contrast, adiponectin expression was 54% less (p=0.0005) and PPAR-gamma expression was 31% less (p=0.05) in the visceral fat of those with OSA.

Conclusion: Decreased expression of adiponectin and PPAR-gamma in visceral adipose tissue of apneics may provide a mechanism by which insulin resistance may occur. A trend towards greater inflammation was observed in subcutaneous fat, though the differences were not statistically significant.

Support (If Any): This work was supported by NIH HL081385, CA116867, and the ATS.

0052

POLYMORPHISMS OF THE MACROPHAGE MIGRATION INHIBITORY FACTOR (MIF) GENE IN CHILDREN WITH AND WITHOUT OBSTRUCTIVE SLEEP APNEA (OSA)

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Introduction: OSA is currently viewed as a systemic inflammatory disorder. Furthermore, it has become apparent that genetic and environmental factors modulate the occurrence and magnitude of morbid consequences in pediatric OSA. MIF is a potent pro-inflammatory cytokine and a key modulator of immune, inflammatory responses, and is associated with cardiovascular disease. This study compares the frequency of 28 nucleotide polymorphisms (SNPs) in the MIF gene of children with OSA and matched controls.

Methods: Children (ages 5-10 years) prospectively underwent a standard overnight multichannel polysomnographic evaluation and a fasting morning blood draw. The diagnostic criteria for OSA were an obstructive AHI ≥2/h TST, snoring during the night, and a nadir oxyhemoglobin saturation <92%. Control children were defined as non-snoring children with AHI <1/h TST. Genomic DNA from peripheral blood was extracted and genotyping allele frequencies for MIF SNPs were determined using the polymerase chain reaction/restriction fragment length polymorphism method.

Results: The relative frequencies of MIF genotypes was evaluated in 401 subjects, 131 with OSA and 270 without OSA. Of 28 SNPS studied, the frequencies of 27-MIF SNPs polymorphisms were similar between OSA and control children. However, the frequency of rs2070767 (C/T) was significantly higher in children with OSA, even after correction for multiple comparisons and for haplotype distribution (the population diversity of rs2070767 C/C SNP frequency is: Europeans is 71%, African American is 65% and Asian is 39%).

Conclusion: The MIF polymorphism rs2070767 (C/T) is associated with OSA in children, and may operate as a disease-modifying gene. Analysis of MIF genotype-phenotype interaction in snoring children may assist in categorical risk estimates of end-organ morbidities associated with OSA.

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0053

NOVEL CANDIDATE GENES OF SLEEP APNEA: INSIGHTS FROM ANIMAL MODELS TO THE SLEEP CLINICAL RESEARCH

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Introduction: This study tested the hypotheses that hypoxia per se modulates gene expression in animal model of sleep apnea and these results may be translated with alterations that occur in apneic patients. Thus, we aimed to integrate basic and clinical research to shed light on novel candidate genes involved in sleep apnea.

Methods: Twenty-four male rats were exposed to chronic intermittent hypoxia (CIH - 5% O_2) or normoxia for 6 wks. Following CIH, a group of 8 rats were removed from the CIH protocol and allowed to normoxic conditions over a period of 2 wks. For the human protocol, the AHI measured by overnight polysomnography was used to select individuals with sleep-related breathing disorders, and controls (35 age-matched men). After standard CPAP titration, 14 men with severe OSA were assigned for the CPAP protocol for future assessment of the influence of 6 m OSA treatment. A total of 84 genes were evaluated using the Hypoxia Signaling Pathway PCR Array (SA Biosciences, EUA).

Results: For rats exposed to CIH, only the Cystatin B gene showed increased expression. A down-regulation of 4 other genes related to immune response, metabolism and protein biosynthesis was also identified. For the animals exposed to normoxia condition for 2 wks after CIH, a range of different genes showed altered expression. In the human protocol, the mild to moderate OSA patients had down-regulation of genes associated to apoptosis, cardiac E-C coupling, and transcription factors. A total of 14 genes (apoptosis, cardiac E-C coupling, metabolism, transcription factors, cell growth and immune response) were down-regulated in severe OSA patients. Interestingly, the rats exposed to CIH as well as the severe OSA patients showed reduced expression of a common gene responsible for encoding ribosomal proteins.

Conclusion: This translational research protocol led to the development of novel drugs and alternative diagnostic methods.

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0054

ADORA2A POLYMORPHISM REGULATES NEUROBEHAVIORAL PERFORMANCE RESPONSE TO CHRONIC SLEEP RESTRICTION

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Introduction: Polymorphisms in adenosine A2A receptor genes (ADORA2A) have been shown to regulate sensitivity to caffeine: individuals homozygous for the T allele are less sensitive to caffeine than are individuals homozygous for the C allele (the C/T genotype is roughly equally distributed between sensitive v. insensitive subjects). As the adenosinergic system also plays a role in sleep homeostasis, we investigated whether ADORA2A polymorphisms are associated with neurobehavioral performance vulnerability to chronic sleep restriction.

Methods: Nineteen volunteers (11 males and 8 females; mean age [SD] = 28.1 [4.7]) underwent chronic sleep restriction consisting of 7 nights of 3 hours time in bed (TIB) per night, preceded by a baseline night (10 hour TIB) and followed by 3 recovery nights (8 hours TIB per night). Volunteers were genotyped for the ADORA2A polymorphisms (ADORA2A$^{C/T}$ n = 9; ADORA2A$^{T/T}$ n = 9; ADORA2A$^{C/C}$ n = 1; ADORA2A$^{C/C}$ not included in analyses due to small sample size). A 10-min Psychomotor Vigilance Task (PVT) was administered bi-hourly daily on baseline (B), sleep restriction (SR1 - SR7) and recovery (R1 - R3) from 08:00 to 20:00 and analyzed for speed (1/RT*1000) and lapses (reaction times >500 msec). Mixed-model ANOVAs with repeated factors day and time of day and between-subjects factor ADORA2A genotype (ADORA2A$^{C/T}$ or ADORA2A$^{T/T}$) were performed and followed by post-hoc t-tests (Bonferroni corrected).

Results: Compared to ADORA2A$^{C/T}$ individuals, ADORA2A$^{T/T}$ (associated with caffeine insensitivity) individuals displayed more lapsing during chronic sleep restriction (Day X ADORA2A interaction, p = 0.002); significant differences were found on SR6 (4.06 v. 10.10 lapses for C/T v T/T, respectively, p < 0.05); differences on SR5 (3.70 v 8.08, respectively) and SR7 (4.38 v. 8.83) were marginal (p < 0.10).

Conclusion: To our knowledge, this is the first report that the ADORA2A$^{T/T}$ polymorphism is associated with greater vulnerability to chronic sleep restriction. We speculate that potentially increased adenosine receptor sensitivity in individuals homozygous for the T allele could underlie both their increased sensitivity to sleep restriction and insensitivity to caffeine. Research is underway to determine the role of ADORA2A polymorphisms and adenosine receptor density on neurobehavioral performance changes during sleep loss.

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0055

PER3 POLYMORPHISMS IMPACT NEUROBEHAVIORAL PERFORMANCE DURING CHRONIC SLEEP RESTRICTION

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Introduction: The 4-repeat allele of the PER3 VNTR polymorphism has been associated with greater neurobehavioral resistance to acute, total sleep loss; however, in one previous study of chronic sleep restriction(4 hours TIB for 5 nights), no association was found. We hypothesized that neurobehavioral manifestation of the PER3 VNTR polymorphisms may only occur during relatively severe sleep loss/restriction. In the present

study, we assessed the effects of restricting sleep to 3 hours TIB on neurobehavioral performance as a function of polymorphism.

Methods: Nineteen volunteers (11 males and 8 females; mean age [SD] = 28.1 [4.7]) underwent 7 nights of sleep restricted to 3 hours TIB per night. Volunteers were genotyped for the PER3 VNTR polymorphism (PER3[4/4] n = 7; PER3[4/5] n = 10; PER3[5/5] n = 2 [PER3[5/5] not included in the analyses due to small sample size]). The 10-min Psychomotor Vigilance Task (PVT) was administered bi-hourly from 08:00 to 20:00 on baseline (B) sleep restriction (SR1 - SR7) and recovery (R1 - R3) nights and analyzed for number of lapses (reaction times >500 msec). Mixed-model ANOVAs with repeated factors day and time of day and between-subjects factor PER3 genotype (PER3[4/4] or PER3[4/5]) were performed and followed by post-hoc t-tests (Bonferroni corrected). Results for the Recovery days are presented in a companion abstract (this volume).

Results: Compared to PER3[4/5] individuals, PER3[4/4] individuals displayed significantly less lapsing on SR4 - SR7 (DAY X PER3, $p < 0.05$; post-hoc t-tests, p's < 0.05; mean lapses = 1.95 v 7.90, 3.22 v 8.43, 3.47 v 11.44, and 1.84 v 10.73, respectively) and marginally less lapsing on SR2 and SR3 (ps < 0.10; mean lapses = 1.20 v 5.46 and 1.47 v 5.77, respectively). A TIME X PER3 interaction ($p < 0.05$) indicated significantly less lapsing in the PER3[4/4] group at 08:00, 14:00, and 16:00 (post-hoc p's < 0.05) and marginally less lapsing in the PER3[4/4] group at 10:00, 12:00 and 20:00 (ps < 0.10).

Conclusion: Consistent with findings from studies of total sleep deprivation, PER3[4/4] individuals were less vulnerable to chronic sleep restriction compared to PER3[4/5] individuals. These findings contrast with the previous study of 4 hrs TIB, suggesting that mild perturbations in EEG spectral density (in particular, buildup and dissipation of SWA) associated with PER3 VNTR polymorphisms may only become behaviorally relevant under substantial sleep loss challenges.

0056

PER3 4-REPEAT ALLELE IS ASSOCIATED WITH FASTER RECOVERY OF NEUROBEHAVIORAL PERFORMANCE FOLLOWING CHRONIC SLEEP RESTRICTION

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Introduction: The PER3 VNTR polymorphism has been associated with individual differences in decrements in neurobehavioral performance during total sleep deprivation. In a companion abstract (this volume) we report that PER3[4/4] individuals display greater resistance to chronic sleep restriction compared to PER3[4/5] individuals. Here we examine differences in rates of recovery from chronic sleep restriction.

Methods: Immediately following 7 nights of restricted sleep (3 hours TIB per night), 19 volunteers (11 males and 8 females; mean age [SD] = 28.1 [4.7]) underwent 3 Recovery (R1—R3) nights (8 hours time in bed per night). Volunteers were genotyped for the PER3 VNTR polymorphism (PER3[4/4] n = 7; PER3[4/5] n = 10; PER3[5/5] n = 2 [PER3[5/5] not included in the analyses due to small sample size]). The 10-min Psychomotor Vigilance Task (PVT) was administered bi-hourly between 08:00 and 20:00 on baseline (B), sleep restriction (SR1 - SR7 - see companion abstract, this volume), and recovery (R1 - R3) nights and analyzed for number of lapses (reaction times >500 msec). Mixed-model ANOVAs with repeated factors day and time of day and between-subjects factor PER3 genotype (PER3[4/4] or PER3[4/5]) were performed, followed by post-hoc t-tests (Bonferroni corrected).

Results: Compared to PER3[4/5] individuals, PER3[4/4] individuals displayed significantly less lapsing on R1 and R2 (DAY X PER3, $p < 0.05$;

post-hoc t-tests, p's < 0.05; mean lapses = 0.5 v. 5.8 and 0.5 v. 5.7 respectively).

Conclusion: To our knowledge, this is the first report that the PER3[4/4] polymorphism is associated with faster neurobehavioral recovery from chronic sleep restriction. These findings suggest that the neurobiologic mechanisms underlying the long time constant that characterizes recovery from sleep restriction are mediated in part by the PER3 VNTR polymorphism.

0057

CLINICAL AND GENETIC STUDIES IN KLEINE-LEVIN SYNDROME

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Introduction: Kleine-Levin Syndrome (KLS) is a very rare disorder (quoted prevalence~1 for 1M) characterized by relapsing-remitting episodes of profound hypersomnia accompanied by specific cognitive and behavioral disturbances. Episodes typically last 1-3 weeks and recur every few weeks to few months with no symptomatology between episodes. The disease affects primarily adolescent males, with onset in the teens, and subsides within 8-12 years (median duration). A viral prodrome frequently precedes episodes, but no specific infectious trigger has ever been identified. An increased risk in first and second degree relatives of KLS cases (5 of 105 cases had an affected family member), and increased prevalence in the Ashkenazi Jewish population suggest the implication of genetic risk factors. We hypothesize that KLS results from an abnormal response to a pathogenic trigger acting on a susceptible genetic background.

Methods: We performed a pilot genome-wide association study (GWAS) in 225 KLS patients of various ethnic backgrounds and 617 matched controls genotyped on the Affymetrix 6.0 array.

Results: We identified SNP variations in three genomic regions (Chromosomes 8, 10, and 14) with genome-wide significant associations. These findings are currently being replicated in additional patients. To date, we have an additional 134 patients of various ethnic backgrounds pending analysis. To increase this number, we are currently recruiting and forming collaborations. Results of genotyping will direct our follow up of susceptibility loci, versus extending our GWAS with the larger and more statistically powerful overall cohort.

Conclusion: We are currently replicating SNP variations in these three genomic regions reaching genome-wide significance. Due to the rarity of the disease, recruitment is a significant challenge, and we are continuously collecting samples. In addition to blood samples, nasal and throat swabs are being collected from controls and patients both during and between episodes to identify potential pathogenic triggers or other factors associated with episode onset.

0058

INTERMITTENT HYPOXIA-INDUCED WHITE MATTER LESIONS IN NEONATAL MICE

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Introduction: Recent studies from both clinical and animal research suggest that diffuse structural changes in brain white Recent studies from both clinical and animal research suggest that diffuse structural changes in brain white matter are a positive predictor of poor cognitive outcomes. We hypothesize that infantile apnea could lead to and/or ex-aggerate white matter impairment. To test this hypothesis, oligodendroglia and axon development were investigated in neonatal mouse model of intermittent hypoxia (IH) between postnatal days 2 to 10.

Methods: P2 C57BL/6 pups were exposed to either 4 to 8 days of intermittent hypoxia (IH, 8% or 5.7% O2 / 20.9% O2 /120s or 140s each cycle/6hrs) or intermittent air (IA) with pseudo dam during the light phase. After IA or IH exposure, all pups were restituted to their lactating dam in room air. The brains were collected at 4 and 8 post-exposure days. Oligodendrocyte-specific proteins, neurocytoskeletal and synapse-relevant molecules, ultra-structure of myelinated axons, and electrophysiological function were examined at different post-exposure days in IA- and IH-treated developing mice.

Results: Short-term neonatal IH exposure induced hypomyelination in brain regions, including corpus callosum, striatum, fornix and cerebellum, but not pons or spinal cord. Myelin-forming process was disturbed by lack of myelin proteins due to arresting the maturation of oligodendrocytes. Immature oligodendrocytes were more vulnerable to neonatal IH exposure than developing axons. Insufficient neurofilament (NF) synthesis with anomalous components of NF subunits, β-tubulin and MAP2 isoforms indicated immaturity of axons in IH-exposed mouse brains. In addition, down-regulation of Synapsin I, Synaptophysin and Gap-43 phosphorylation suggested a potential stunt in axonogensis and synaptogensis. This region-selective and complex white matter impairment was further associated with electromicroscopic abnormalities and electrophysiological changes.

Conclusion: These findings suggest that IH insult during sleep in neonates, as occurs in apnea of prematurity, may couple disturbance of myelinogenesis and axonal immaturation within a critical window of CNS development, which could in turn cause long-term neurobehavioral sequelae.

0059

LONGITUDINAL ASSOCIATION BETWEEN SHORT SLEEP AND BODY WEIGHT, ANXIOUS/DEPRESSED, AND LEARNING IN HISPANIC AND CAUCASIAN CHILDREN

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Introduction: Cross-sectional studies have reported associations between shorter sleep and high body mass index (BMI). However, few longitudinal studies have assessed this relationship from childhood to young adulthood, and none has assessed sleep using polysomnography (PSG). This study aimed to determine the impact of lower amounts of childhood sleep determined by PSG on development of obesity, being anxious or depressed, or having learning problems five years after.

Methods: A prospective cohort included 304 community participants from the Tucson Children's Assessment of Sleep Apnea study, aged 6-10 years old at baseline. Children were classified according to baseline sleep as *normal sleepers* (slept ≥ 9 hours/day), *short sleepers* (slept > 7.5 - < 9 hours/day), and *very short sleepers* (slept ≤ 7.5 hours/day). Odds of overweight/obese (≥85th BMI percentile), obese (≥95th percentile), anxious or depressed, and learning problems at follow-up were assessed according to baseline sleep categories.

Results: Children with *very short sleep* had higher odds of being obese (OR = 3.3, P=0.03) and anxious or depressed (OR = 4.2, P=0.03) at follow-up compared to children with *normal sleep*. Hispanic children had higher odds for obesity (OR = 2.4, P = 0.01) than Caucasian children. Borderline significance for overweight/obese (OR = 2.2, P=0.06) and having learning problems (OR = 7.1, P=0.08) were seen for children with *very short sleep*. A mean increase in BMI of 1.7 kg/m2 over the 5 years of follow-up (P=0.01) was seen for *very short sleepers* compared to *normal sleepers*.

Conclusion: Children with very short sleep (< 7.5 hours/day) had an increased risk for higher body weight in early adolescence; this risk was higher for Hispanic than Caucasian children. Children with very short sleep also had higher risk of being anxious or depressed or having learning problems in early adolescence.

0060

HIPPOCAMPAL VOLUME AND SLEEP IN CHILDREN OF ALCOHOLICS

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Introduction: Mounting evidence suggests that sleep plays a role in neural plasticity, especially of the hippocampus, which is sensitive to neurotrophic or stressful signals. Although not a universal finding, several studies report that insomnia and sleep-related disordered breathing, in adults, is associated with smaller hippocampal volume. Similarly, evidence from animal studies suggests that sleep is involved in hippocampal neurogenesis and synaptic density, in both adult and developing brains. In this study we assessed the relationship between subjective and objective sleep measurements, behavioural problems, and gray matter volume in children of alcoholic (COA) parents, hypothesizing that sleep disruption will be associated with cortical and hippocampal development, reflected by gray matter volumes.

Methods: 31 children of alcoholic parents, ages 8-12 (15 girls, 16 boys), wore actiwatches and completed sleep diaries for one week, and their parents completed the Paediatric Sleep Questionnaire (PSQ). T1-weighted, high-resolution, magnetic resonance images were obtained from each child. Cortical volume analysis was performed using Free-Surfer software. Teacher-rated internalizing (In) and externalizing (Ex) problem scores were obtained. Sleep variables and behaviour variables were correlated with the total cortical and white matter volume, and with hippocampal and amygdala volumes.

Results: Younger children reported more wake after sleep onset (WASO: p=.035), which coincided with an age-dependent decline in parent-reported insomnia (p=.046). Age and gender were not associated with actigraphy measures. Actigraphy total sleep time (TST) and sleep efficiency correlated with Ex scores (R2=-.505, R2=-.505), with no cor-

relations with diary or PSQ scales. Total intracranial, cortical, and white matter volumes did not vary with age and gender. The hippocampus was bilaterally correlated with Ex (Right: R2=-.703, Left: R2=-.661), and the left hippocampus correlated with In (R2=-.575). Actigraphy and diary-reported TST correlated with right hippocampal volume (R2=.523, R2=.505, respectively), with no correlation with PSQ scales. Hierarchical regression analyses revealed that actigraphy TST partially mediated the relationship between Ex and hippocampal volume.

Conclusion: Sleep measures are associated with hippocampal volumes, suggesting that it may mediate, or at least contribute to the relationship between behavioral problems and hippocampal function, in at-risk children.

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0061

AGE-RELATED DIFFERENCES IN THE EFFECT OF CHRONIC SLEEP RESTRICTION ON SLEEP QUALITY

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Introduction: Changes in the interaction of circadian and sleep-wake homeostatic regulatory processes have been reported to result in increased vulnerability to sleep disruption in older adults, suggesting chronic sleep deficiency associated with aging may in part be due to circadian misalignment. We tested the hypothesis that under conditions of chronic sleep restriction (CSR), the sleep of older adults will be disrupted when scheduled at adverse circadian phases, while that of young adults will remain consolidated.

Methods: 12 healthy older (mean±sd 59.6±4.5 yrs; 6f) and 12 healthy young (22.8±2.3; 6f) adults participated in a 39-day study. After spending 10h/night time in bed (TIB) at home for 3 weeks, the inpatient study began with six 24h baseline days (10-16h TIB/day), followed by 3 weeks of CSR-forced desynchrony, during which subjects lived on 28h "days" (6.53h TIB/28h, equivalent to 5.6h TIB/24h) with sleep episodes beginning 4h later each CSR-day. Core body temperature data were collected throughout to assess circadian phase. Polysomnography data were recorded throughout and scored in 30-sec epochs. Sleep data were binned into 60° circadian phase bins. Sleep efficiency (SE, total sleep time/TIB) during CSR was analyzed via mixed model analysis with fixed effects for AGE and PHASE.

Results: There was a significant effect of AGE ($p<0.0001$), with older adults having lower overall SE during CSR than young adults (mean±sd 86%±13 vs. 95%±05). There was a significant effect of PHASE ($p<0.0001$), with lowest overall SEs observed when sleep occurred during the biological day (circadian phase bins 120°, 180°, 240°). There was also a significant AGE x PHASE interaction ($p<0.0001$); tests of simple main effects revealed that older adults had significantly lower SEs than young adults when sleep occurred during the biological day ($p<0.0001$ for circadian phase bins 120°, 180°, 240°).

Conclusion: Despite increased homeostatic sleep pressure induced by CSR, the sleep of these healthy older adults was significantly more disrupted than that of young adults when scheduled at adverse circadian phases. Our findings have implications for cognitive behavioral therapy, which often relies on CSR to improve sleep consolidation. These data indicate that age-related changes in the interaction of circadian and homeostatic processes adversely influence sleep quality in healthy older adults even under conditions of CSR, when the sleep of older adults remains particularly sensitive to misalignment of circadian phase.

0062

SLEEP AND WAKE MODULATE SPINE TURNOVER IN THE ADOLESCENT MOUSE CORTEX

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Introduction: In both mice and men the maturation of the cerebral cortex is characterized by an initial overproduction of synapses, followed during adolescence by net synaptic elimination (pruning). It is believed that synaptogenesis and pruning happen concurrently, but this has never been formally tested.

Methods: After skull thinning, branches of apical dendrites of layer V pyramidal neurons in barrel cortex were imaged using a two-photon microscope in adolescent yellow fluorescent protein (YFP)-H-expressing mice (mean age SD, 29 days ±4, n=35). One month-old YFP-H mice show consolidated sleep/wake patterns, with most sleep occurring during the day and wake mainly at night. Each animal was imaged in the same area twice within 12-18h. W1S2 mice (n = 11) were spontaneously awake for at least 75% of the previous night, imaged, allowed to sleep for 6-8h during the day, and then imaged again. S1W2 mice (n=11) were imaged first after sleep during the day and then after mainly wake at night. W1SD2 mice (n=13) were imaged first after wake at night and then after 6-7h sleep deprivation (SD) during the day.

Results: Mean number of imaged spines/mouse was 227 ±127 (mean ±SD). Overall spine turnover (spines lost + spines gained, expressed as % of all spines imaged in the first session) was ~ 3.3% and did not differ across groups. Relative to the sleep group (W1S2), the wake groups (S1W2+W1SD2) showed lower spine loss and higher spine gain. As a result, overall spine density showed a net increase when spontaneous wake or SD followed sleep, and a net decrease when sleep followed wake ($P<0.01$, Kruskal-Wallis). Filopodia (2.6% of all dendritic protrusions) showed higher turnover than spines (24.3%, mean ±SD, no differences across groups) but no consistent sleep/wake dependent changes.

Conclusion: Sleep/wake, independent of light or circadian time, can modulate spine turnover and sleep may be more conducive to pruning.

0063

SLEEP CHANGES ACROSS ADOLESCENCE IN MICE

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Introduction: Recent studies in humans suggest that changes in absolute levels of sleep slow wave activity may reflect neurodevelopmental changes in cortical synaptic density. To test this directly, we will combine EEG recordings and in vivo imaging of dendritic spines in YFP-H mice. As a first part of this study, in this transgenic line we characterize developmental changes in sleep patterns and in the response to sleep deprivation across adolescence (from postnatal day P20 to P60).

Methods: Male transgenic YFP-H mice were kept in a 12:12 light/dark cycle and implanted with miniature screw electrodes over frontal and parietal cortices at different ages starting from P15 through adulthood (>P60, overall n=60). EEG and EMG signals were collected continuously and visually scored offline with a 4-sec resolution as early as P23 (sampling rate: 256 Hz, HPF 0.1 - LPF 100 Hz). Sleep deprivation by exposure to novel objects was performed once in each mouse at least 5 days after surgery.

Results: Overall total sleep duration (598 +4.9 minutes, mean ±SEM) did not change from early adolescence to adults. Nevertheless, during early adolescence, NREM sleep duration increased from P23 (449 ±12.9) to P29 (485 ±10.7, P=0.04) while REM sleep duration decreased (130 ±5.2 to 106 ±3.3, P<0.001). After P29, NREM/REM durations remained stable. At all ages, recovery sleep following 4h sleep deprivation starting at light onset was characterized by an increase in the percentage of time spent in NREM and an increase in the mean sleep episode length (P<0.05, paired t-tests).

Conclusion: In YFP-H mice, NREM and REM duration reach adult levels by P29. The increase in NREM duration following sleep deprivation indicates that homeostatic sleep regulation is already present during early adolescence.

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0064
DEVELOPMENTAL CHANGES IN SLEEP SLOW WAVE ACTIVITY (SWA) IN MICE

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Introduction: Adolescence is a sensitive period for synaptic pruning and it is a crucial time in the pathophysiology of many psychiatric disorders. New evidence in humans suggests that changes in absolute levels of sleep SWA may parallel neurodevelopmental changes in cortical synaptic density. The relation between SWA and synaptic remodeling can be directly tested in transgenic animals, in which EEG recordings and repeated in vivo imaging of dendritic spines with two-photon microscopy can be combined. As a first part of a wider study, we characterize here SWA developmental changes in YFP-H mice across adolescence (from postnatal day P20 to P60).

Methods: Male transgenic YFP-H mice, kept in a 12:12 light/dark cycle, were implanted with screw electrodes over frontal and parietal cortices at different ages starting from P15 through adulthood (>P60, overall n=60). EEG and EMG signals were collected continuously and analyzed as early as P23 for 7-10 days per animal (sampling rate: 256 Hz, HPF 0.1 - LPF 100 Hz). EEG power spectra (0.5-30 Hz) of consecutive, visually scored 4-sec epochs (FFT routine, Hanning window) were calculated for the frontal derivations. To address potential technical variability across development, both mean absolute and relative NREM SWA over 24 hr were computed.

Results: Absolute SWA showed a progressive decline from P23 (489 ±74 µV^2/0.25 Hz, mean ±SE) to P29 (165 ±11; p<0.01 t-test). SWA then increased between p29 and p48 (363 ±80) and dropped to lower and stable adulthood levels by P55 (146 ±13). No developmental differences could be detected during waking. Relative SWA, normalized for NREM total power or for SWA across all behavioral states, showed a similar trend.

Conclusion: SWA showed a developmental modulation in YFP transgenic mice. Future work will directly examine whether developmental changes in synaptic density are reflected in NREM sleep SWA, which could be used as a biomarker of brain maturation.

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0065
EARLY-LIFE REM SLEEP DEPRIVATION REDUCES MRNA, HIPPOCAMPAL SYNAPTIC PLASTICITY AND SWS SPINDLE AND THETA FREQUECIES IN YOUNG ADULT RATS

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Introduction: In early life, synaptic plasticity participates in correct development of the CNS. Synaptic plasticity can be compromised during development, however, by insults such as hypoxia, drugs and deficiencies of sleep. REM sleep has a significant role in brain development, and its restriction during early life leads to: altered size of cells in the lateral geniculate nucleus, extension of visual cortical plasticity beyond the usual developmental phase, and delayed maturation of LTP-stability and glutamatergic signaling proteins in hippocampus. The latter changes were observed in rats that were REMS-deprived when very young and allowed up to a week of recovery before LTP-stability was examined. The present study attempted to determine whether early-life REM sleep restriction affects gene expression, sleep spindles and hippocampal synaptic plasticity in adults.

Methods: Rats were REM sleep-deprived for 4 h (9:00 - 13:00 h) each day between postnatal day (P) 16 and P19. The animals survived until P45 when 24h of undisturbed sleep/wake data was obtained. Between P50 and P54, one rat was killed each day, and coronal hippocampus slices were obtained. Following published protocols, slices were maintained in a brain interface chamber for at least 2h before LTP induction in the CA1 region was undertaken with CA3 stimulation. The opposite hippocampus was harvested in every case and prepared for gene expression studies.

Results: In normal and control animals, LTP was produced in 14 of 16 attempts. In contrast, animals deprived of REM sleep just after the second week of life were less likely to produce LTP (4 / 11 attempts, Fisher's Exact, two-tailed, P = 0.0115). Further, the level of LTP, when exhibited in the deprived group, was much lower (129 vs 148% increase over baseline). Whereas SWS amounts were not affected, REMS- deprived rats showed reduced power in delta and spindle frequencies compared to control and normal rats (p<0.05). Also, expression of several plasticity related genes were reduced in the REMS-deprived hippocampus compared to the other two groups.

Conclusion: These preliminary data extend into adulthood our previous findings that early REM sleep deprivation has persistent effects on sleep, gene expression and hippocampal synaptic plasticity. The hippocampus is involved in memory, learning and major depression. Unperturbed REM sleep in the first weeks of life appears to be essential for correct brain development.

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0066
RECOVERY SLEEP RESPONSES TO MILD CHRONIC PARTIAL SLEEP RESTRICTION IN YOUNG, MIDDLE-AGED AND OLD RATS

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Introduction: Recent studies have suggested that the homeostatic regulation of sleep is altered under conditions of chronic partial sleep restriction (CPSR), however several investigators have challenged this hypothesis. Furthermore, although sleep-wake characteristics are known to change with aging, the effects of repeated sleep restriction on old animals are not well-understood. Thus, the dynamic regulatory responses to chronic sleep loss and the influence of aging in maintaining homeostasis

remain important areas of investigation. Here we report the effects of a mild CPSR protocol on young (4-month), middle-aged (12-month) and old (18-month) rats.

Methods: Young, middle-aged and old male Fischer-344 rats had electroencephalogram (EEG) and electromyogram (EMG) recording electrodes surgically implanted. After recovery and acclimation to sleep chambers, rats were subjected to a mild CPSR protocol using an automated system that records EEG/EMG in real-time and uses an autoscoring program to start a slowly rotating bar in the animal's cage upon detection of sleep onset (Pinnacle Technology, Inc.). EEG/EMG were visually scored in ten-second epochs as belonging to one of the following vigilance states: wake, rapid eye movement (REM) and non-REM (NREM) sleep.

Results: The mild CPSR protocol utilized in this study consistently resulted in an approximately 25% reduction in daily sleep amount during CPSR in the different age groups. REM sleep was particularly reduced when wakefulness was enforced. Preliminary EEG analyses suggest that age-dependent differences in homeostatic processes during recovery sleep and wake exist.

Conclusion: Young, middle-aged and old rats exhibit similar sleep-state responses to mild CPSR, including a failure to elicit increased recovery sleep in spite of accumulating sleep debt. EEG spectral analysis is expected to reveal the dynamics of homeostatic sleep regulation in animals of different age groups, which may yield insight into how the regulation of sleep is affected by CPSR and influenced by aging.

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0067

AGE-RELATED CHANGES OF EEG POWER AND COHERENCE IN THE SLEEP SLOW-WAVE FREQUENCY RANGE

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Introduction: EEG power in the slow-wave (SW) frequency range (1-4.5 Hz) is a well established electrophysiological marker of sleep homeostasis. Moreover, SW-power was suggested to mirror cortical maturation. EEG coherence, in waking and sleep, is thought to reflect connectivity of underlying brain regions. Thus, the combination of the two EEG measures may reflect the maturation of basic cognitive functions. We therefore assessed SW-power and SW-coherence in developing human subjects.

Methods: High-density sleep EEG (128 channels) was assessed in 63 subjects (2-26 years). The first 60 min of sleep stage N2 and N3 were analyzed. For the SW-range EEG power was calculated for all channels and EEG coherence for a selection of channels (Fp1F3-F3C3, Fp2F4-F4C4, F3C3-C3P3, F4C4-C4P4, C3P3-P3O1, C4P4-P4O2, Fp1F3-P3O1, Fp2F4-P4O2).

Results: SW-power exhibited an initial increase, a peak in late childhood and a decrease thereafter (cubic fit for C4A1 R^2=.73, p<.001). The age of peak SW-power was determined for all electrodes (peak at 4.9-8.6 years). We found that posterior electrodes reached this peak early, and frontal electrodes late. All coherence measures correlated positively with age (R^2= .14- .72, p<.005). To quantify the change in coherence across age, we calculated the slope of the regression line for each coherence measure. This slope was highest over parietal and lowest over frontal regions.

Conclusion: The maturation of SW-power followed an inverted U-shape time course across age, which parallels the development of gray matter (thickness, volume). In contrast, the linear increase of SW-coherence mirrors the development of white matter (volume, fibre tract length).

Moreover, we found regional differences in the maturation of both EEG measures along the postero-anterior axis, which may be related to the maturation of basic cognitive functions. How much each of the sleep EEG measures accounts for the maturation of such basic cognitive functions remains to be established.

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0068

HOMEOSTATIC SLEEP REGULATION IN ADOLESCENTS: LONGITUDINAL PERSPECTIVES

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Introduction: Two independent processes influence the timing and duration of sleep: a homeostatic (Process S) and a circadian (Process C) process. Cross-sectional studies of Process S in adolescent humans have shown that the rate of dissipation of sleep pressure across the night does not change between pre- and post-pubertal adolescents. The aim of the current study was to examine sleep homeostasis across adolescent development with longitudinal data.

Methods: Twenty children and twenty-five teens underwent polysomnographic recordings when they were ages 9/10 and 15/16 years and again 1.5 to 3 years later. Sleep EEG was recorded from C3/A2, C4/A1, O2/A1, and O1/A2. At each assessment, the dissipation of slow wave activity (SWA) during sleep was modeled for each individual using $S(t) = (So - LA)*exp(-t/Td)+LA$. In this equation, So is SWA at sleep onset, LA is the lower asymptote and Td is the time constant of the decay. Time constants were limited to a physiological range. Statistical analysis was performed within a cohort using a paired t-test.

Results: In the children cohort there was no change in any of the parameters of Process S from the initial to the follow-up session for any derivation. For teens, there was no change in the occipital leads and an increase in Td from the initial to the follow-up sessions for C3/A2 (Initial Td = 2.54; Follow-up Td = 3.34; p = 0.005) and C4/A1 (Initial Td = 2.55; Follow-up Td = 3.14; p = 0.032) derivations. There was no change in So or LA for any derivation.

Conclusion: We found a region-specific change in late, but not early adolescents. If SWA decay reflects sleeps recovery function, these data indicate that certain brain regions in older adolescents require longer to achieve the same degree of recovery than they did before.

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0069

CHANGES IN THE AWAKENING CORTISOL RESPONSE (ACR) AS CHILDREN TRANSITION FROM PRESCHOOL TO KINDERGARTEN

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Introduction: The start of kindergarten (K) is the first major life transition for many children due to parental separation and increases in academic and social demands. In an earlier paper, we presented that

Napping (N) and Non-Napping children (NN; per caregiver report at baseline) lost equal amounts of sleep (~3 hours over the week per actigraphy) as they transitioned to all-day K where napping was reduced or eliminated; however NN lost nocturnal sleep and N lost diurnal sleep. The current analyses focus on endocrine changes (ACR) in the same cohort. Very little is known about the ACR during childhood. Research in adults suggests that the ACR is associated with a variety of psychological and health variables including sleep.

Methods: Data were collected from 34 children (44% female) recruited from the community. Caregivers collected saliva at 0, 15, and 30 minutes post wake on one day at each of the following: the summer prior to K, within two weeks of K, and after one month of K. Accuracy of wake saliva sampling was confirmed by comparing actigraphically-assessed wake time with caregiver-reported sampling time. Dynamic (increase) of the ACR was computed using area under the curve (AUC) increase and % change. Overall cortisol production post wake was calculated using AUC ground. Participants were excluded if they did not have complete sleep or cortisol data (n = 4).

Results: The ACR was evident in this sample of children and had significant linear $\eta2 = .71$ and quadratic $\eta2=.73$ trends. On average, cortisol rose 69.2% fifteen minutes (p<.001) and 76.5% thirty minutes (p<.001) post wake. Average waking, 15, and 30 minute cortisol values were (μg/dl +/- SD) 7.9 +/- 1.9, 13.3+/- 3.3, and 13.8 +/- 4.2, respectively. A dampened ACR dynamic (AUC increase) was observed after the start of K; $\eta2=.10$. Overall cortisol production (AUC ground) was reduced for NN as they transitioned to K; $\eta2 = .23$.

Conclusion: ACR values in this sample of children were similar to those found in adults (typically ~50-75% increase post wake). A dampened ACR with the transition to kindergarten may indicate less biological preparedness during waking hours as a function of sleep loss and/or circadian misalignment. The finding that NN had a reduction in overall cortisol production may implicate the importance of nocturnal sleep in overall morning cortisol production. These exploratory findings on sleep/endocrine changes at the start of school indicate the need for further research.

0070

AGE DIFFERENCES IN EXECUTIVE FUNCTIONS UNDER DIFFERENTIAL SLEEP PRESSURE CONDITIONS

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Introduction: Executive functions are necessary when unexpected changes in the environment require the suppression of current or planned actions to afford adapted behavioural responses. We designed a protocol to analyse the effects of age, circadian system and sleep pressure on executive functions. Recent findings show that age-related differences in basic cognitive performance rely more on a reduced circadian influence rather than a reduced homeostatic sleep pressure. No data confirm these findings in executive functions.

Methods: We compared executive performance (Go/No Go task and Stop Signal task every 3H45) in 14 young healthy males (mean age = 23 ± 2.7; 20-29 years) and 8 elderly healthy males (mean age = 67 ± 1.3; 66-70 years) during a 40-h extended wakefulness condition ("high sleep pressure condition") and a 40-h multiple sleep nap condition ("low sleep pressure condition"). The volunteers were kept awake in the sleep deprivation condition and adopted a short wake/sleep cycle (150/75 minutes) in the multiple nap condition to examine the circadian influence in constant experimental conditions of confinement.

Results: In the extended wakefulness condition, executive performance during the biological night were more affected in the young than in the elderly volunteers in both tasks (P<.05 and tendency P<.07, respectively). In the multiple nap condition, whereas performance were stable in the older subjects, a decline of performance were found in the young subjects during the biological night in the Stop Signal task (P<.05).

Conclusion: Older volunteers' executive functions are more resilient to extended wakefulness than the ones of the young volunteers. This can be explained by an attenuated circadian influence on executive functions in the older people.

0071

PUPIL LIGHT REFLEX IN RESPONSE TO MONOCHROMATIC LIGHT STIMULI IN YOUNGER AND OLDER SUBJECTS

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Introduction: Aging induces changes in the circadian regulatory process which may be associated with impaired photic input. Changes in pupil light reflex (PLR) during aging may alter retinal photic input and consequently affect the impact of light on non-visual functions. Circadian entrainment and other non-visual functions are regulated by a non-visual photoreceptive system that shows peak sensitivity to blue light, in contrast to the photopic visual system, maximally sensitive to green light. Here, we assessed whether PLR to green and blue light of different irradiance levels changes with aging.

Methods: PLR was measured in 16 young (23±3.9y) and 14 older (61.1±4.4y) healthy subjects, in response to blue (480nm, hbw=10nm) and green (550nm, hbw=10nm) monochromatic light presented at low (7x1012 ph/cm2/s), medium (3x1013ph/cm2/s), and high (1014ph/cm2/s) irradiance levels. Subjects were first dark adapted before light exposure. Light exposures lasted 45s and were separated by 60s of darkness. Pupil constriction was normalized according to pupil size at the end of dark adaptation.

Results: Analysis of raw data showed that young subjects had larger pupils than older subjects at the end of dark adaptation (young: 0.39±0.01, arbitrary unit, mean±SEM, older: 0.33±0.02; p=0.008) and during light exposure (young: 0.232±0.01, older: 0.185±0.01; p=0.002). Analysis of normalized sustained pupil constriction (6-45s) revealed that blue light induced more constriction than green light (blue: 57.7±2%, mean±SEM; green: 59.4±2%; p<0.05), and constriction was greater with higher irradiances (low: 64.9±19%; medium: 57.8±15%; high: 52.9±16%; p<0.01).

Conclusion: Pupillary constriction is greater with blue than green light and varies with irradiance level. Although the degree of pupil constriction is not significantly affected by age, absolute pupil size is smaller in older individuals both in darkness and during light exposure. This may reduce retinal illumination and affect other non-visual responses to light such as circadian entrainment.

0072

AGING AFFECTS THE IMPACT OF LIGHT ON NON-VISUAL COGNITIVE BRAIN FUNCTIONS

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Introduction: Age-related change in non-visual cerebral light sensitivity may underlie modifications in sleep-wake cycle and circadian rhythms. Here, we investigated the acute impact of blue light exposure on non-visual cognitive brain activity as a function of age.

Methods: 16 young (22.8 ± 4 y.o.) and 14 older (60.9 ± 4.5 y.o.) individuals were alternatively maintained in complete darkness or exposed to short (45s) monochromatic blue (480nm) illuminations of three irradiance levels while performing an auditory working memory task in fMRI. Blue light irradiance levels were 7×10^{12}, 3×10^{13} and 10^{14} photons/cm^2/s and pupil constriction was not inhibited. Data acquisition took place 1h after habitual sleep time. Data were normalized using state of the art techniques (Dartel in SPM8) to take into account morphological changes with age.

Results: Performance to the task was equally high in both age groups (> 87%), was not significantly difference between light conditions, and showed no significant age x light intensity interaction (p > 0.05), preventing behavioural bias of fMRI results. fMRI analyses revealed that, taking into account age-related differences in brain activity independent of the light condition, increasing irradiance enhanced brain responses to the task more strongly in younger than older individuals (p corrected < 0.05). These age-related differences in the impact of light irradiance on brain responses to the task were found in the thalamus, prefrontal cortex, hippocampus, and cerebellum.

Conclusion: These results show that the stimulating effect of blue light on non-visual cognitive brain function decreases with age in regions important for cognition (prefrontal cortex, hippocampus, thalamus) and alertness regulation (thalamus). Future research will determine if this decrease reflects age-related changes at the level of the brain, of the eye, or both.

Support (If Any): IRSC, CRSNG, FRSQ

0073

OBJECTIVE SLEEP BY AGE AND SEX IN A LARGE AT-HOME SAMPLE

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Introduction: It may be concluded from previous research that objective sleep quality depends, in part, on both age and biological sex. However, there is very little information available about the interacting effects of age and sex on sleep. This is especially true of objective measures of sleep taken in home settings.

Methods: The DOZER sleep registry is an IRB approved database of de-identified, objectively measured sleep (via the Zeo) in the home. Participants use the instrument and upload data to the registry as they see fit. Measures include Total Sleep Time (TST), Time in REM (REM), Time in Light (Light, stages 1 and 2), and Time in Deep (Deep, stages 3 and 4). Age groups were categorized by decade and sleep measures were averaged for each subject who contributed more than one night of data. Two-way factorial ANOVAs were run to look for the effects of age and sex on these measures. An alpha level of 0.001 was set to account for the large sample size and the number of tests run in the analysis.

Results: 7,473 subjects (ages 17-89, 25% female) contributed 298,500 nights of data for analysis. A significant (p<0.001) main effect of age was found for TST (decrease across age), REM (decrease), Light (increase), and Deep (decrease), while a significant (p<0.001) main effect for sex was found for REM (more for males), and Light (less for males), but not for TST (p=0.6261) or Deep (p=0.0016). Significant interactions (p<0.001) between age and sex were found for Light, and Deep, but not for TST (p=0.0325) or REM (p=0.2332).

Conclusion: The age related effects on sleep architecture (reduced TST, REM and Deep, increased Light) are consistent with previous reports. However, the persistent sex-related difference in REM sleep has not been noted in previous studies and warrants further exploration.

Support (If Any): Support for this study was provided by Zeo, Inc.

0074

INDUCING SLEEP BY REMOTE CONTROL FACILITATES MEMORY CONSOLIDATION IN DROSOPHILA

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Introduction: Historically, the importance of sleep has been most convincingly established by demonstrating negative consequences that accrue in its absence. One reason that sleep deprivation is an effective strategy is that the experimenter controls the exact timing and duration of sleep loss. In contrast, methods allowing an experimenter to induce sleep on demand, especially in animal models, are lacking. In the current studies, we identify a novel cluster of ~20 neurons in the Drosophila brain that can be acutely activated to induce sleep on demand and characterize beneficial effects of sleep induction on memory formation.

Methods: Sleep was recorded in Drosophila using the Trikinetics locomotor activity system. Long-term memory (LTM) was tested using a Courtship Conditioning assay.

Results: To identify novel sleep regulatory centers in Drosophila, the bacterial sodium channel NaChBac was constitutively expressed using a variety of GAL4 drivers. Using this strategy, we identify a cluster of ~20 neurons which, when activated, induce a dramatic increase in sleep time and consolidation. During sleep induction, flies enter a quiescent state that meet the criteria for identifying sleep, including increased arousal thresholds, rapid reversibility and homeostatic regulation. When sleep is induced for 4 h following a massed-training protocol for courtship conditioning that is not capable of inducing LTM by itself, flies develop an LTM. Importantly, activating these neurons in the absence of sleep does not result in the formation of LTM following massed training. Together these data support an active role for sleep in the consolidation of LTM.

Conclusion: We identify a cluster of ~20 neurons that plays an important role in sleep regulation. These neurons can be activated on-demand to precisely control the timing and duration of sleep. Importantly, our data complement previous sleep deprivation experiments by demonstrating that sleep plays a positive role in both synaptic homeostasis and memory consolidation.

0075

STRUCTURAL BRAIN CORRELATES OF HUMAN NREM SLEEP OSCILLATIONS

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Introduction: The morphology of the nervous system is a powerful determinant of its function, evidenced in circumstances of development, brain damage and disease. Despite the importance of this relationship, the structural brain correlates of human sleep physiology remain largely unknown. Using EEG and high-resolution structural MRI, here we characterize the underlying neuroanatomical correlates of human NREM oscillations.

Methods: 22 healthy adults (21.2±2.25 yrs, 10 males) independently obtained a night of polysomnography (19-channel-EEG), together with high-resolution structural MRI scans. NREM EEG sleep-spindle and slow-wave oscillations were analyzed topographically, together with corresponding EEG current-source analysis, and entered into regression models with high-resolution MRI grey-matter maps.

Results: Both the amplitude and slope of slow-waves demonstrated highly significant positive correlations with grey-matter in frontal cortex, specifically middle cingulate and orbitofrontal cortices. Moreover, EEG source-analysis of slow-waves revealed convergent, homologous source foci in these same cingulate and orbitofrontal locations. In addition, the time-course of SWA decay, related to Process-S and slow-wave generation, also correlated with grey-matter density in medial and lateral prefrontal cortex. In contrast, sleep-spindle parameters, especially amplitude, correlated with grey-matter density in memory-related bilateral hippocampus, and cerebellum. Relevant to classical theories of protection against sensory interference, fast sleep-spindle power further correlated with grey-matter density in bilateral auditory cortex.

Conclusion: Here we demonstrate that NREM oscillations, both spindles and slow-waves, are differentially predicted by gross structural morphology of the human brain. Specifically, grey-matter in frontal cortex was proportional to slow-wave oscillatory features, while grey-matter in hippocampus, cerebellum and auditory cortex predicted sleep-spindle characteristics. These associations offer insights into the neural networks generating human NREM oscillations, and the potential cognitive functions they support. More generally, this methodology may represent a novel tool for understanding the mechanistic relationship between brain structure and sleep physiology across the lifespan, from early development to old age, and in diseases and disorders.

0076

THE EXTRACELLULAR CONCENTRATIONS OF LACTATE AND OXYGEN EXHIBIT SLEEP/WAKE DEPENDENT CHANGES IN RAT CEREBRAL CORTEX

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Introduction: The brain utilizes a disproportionate amount of the body's energy, primarily to satisfy the metabolic demands of excitatory neuronal activity. The levels and patterns of neuronal activity change considerably across behavioral states and are affected by sleep pressure. It remains unclear, however, how glycolysis and oxidative phosphorylation respond to meet the energy demands associated with changes in neuronal activity across the sleep/wake cycle.

Methods: Fixed potential amperometry was used to chronically record extracellular lactate and oxygen concentrations in the motor cortex (frontal: AP(+2), ML(-3), DV(-1.5) or prefrontal: AP(+3.2), ML(-.8), DV(-4.5)) of freely behaving rats (N=10 rats each). Over several days, we assessed at high (1-sec) resolution how the concentrations of these metabolites were affected by behavioral state (as determined by simultaneous EEG and EMG recordings) and sleep pressure (including the response to 3h sleep deprivation).

Results: Both lactate and oxygen concentrations increased during waking and REM sleep, states in which neuronal activity is elevated, and decreased during NREM sleep. Oxygen, but not lactate, concentrations were affected by acute activity changes: during waking oxygen concentrations increased most when 1) locomotion and/or 2) high frequency EEG power were high. In contrast, lactate, but not oxygen, concentrations were affected by sleep pressure: 1) during NREM sleep the rate of decline in lactate concentration was correlated with slow wave activity and 2) lactate concentrations progressively increased during sleep deprivation and declined more rapidly during recovery sleep than during spontaneous sleep.

Conclusion: The observed state-dependent changes in lactate and oxygen concentrations are consistent with increased metabolic load during waking and REM sleep as compared to NREM sleep. While oxygen levels were sensitive to acute changes in cortical activity, lactate responded to chronic changes in sleep pressure, suggesting that glycolytic activity may play an important role in responding to energetic demands associated with sleep homeostasis.

0077

ROLE OF THE BASAL FOREBRAIN CHOLINERGIC NEURONS IN THE NITRIC OXIDE-MEDIATED REGULATION OF SLEEP HOMEOSTASIS

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Introduction: Sleep deprivation (SD) leads to selective increases in extracellular adenosine (AD) and inducible nitric oxide synthase (iNOS)-mediated nitric oxide (NO) in the BF. NO donor (DETA NONOate) infusion increases AD and sleep, while the inhibition of iNOS prevent SD-induced AD increase suggesting that iNOS/NO stimulates AD increase (Kalinchuk et al., 2006). iNOS induction during SD occurs in wake-active neurons (Kalinchuk et al., 2010), however, neurotransmitter specificity of these cells was not characterized. As the lesion of cholinergic cells attenuates both SD-induced AD increase and recovery sleep response (Kalinchuk et al., 2008), we decided to test the role of cholinergic versus non-cholinergic neurons in iNOS-dependent NO release and homeostatic sleep response.

Methods: Male rats were implanted with electrodes for EEG/EMG recording. In the first experiment, iNOS induction in cholinergic cells was detected by double-labeling immunohistochemistry for iNOS and acetylcholinetransferase (ChAT) in sleep deprived rats and compared with their time-matched controls. In the second experiment, rats were also implanted with guide cannula for microdialysis probes targeting BF. In these rats the effects of SD on iNOS/NO production and the effect of DETA NONOate infusion on sleep-wake EEG was investigated before and 2 weeks after the destruction of BF cholinergic cells using 192 IgG-saporin.

Results: Experiment 1. SD lead to significant increases in the number of BF iNOS+ cells and intensity of iNOS+ staining. In the SD group, 96% of ChAT+ cells were also iNOS+, while in control group only 3% of ChAT+ neurons had weak iNOS+ staining. In control group, 15% of iNOS+ cells were ChAT-; the number of ChAT-/iNOS+ cells only slightly increased after SD. Numbers of iNOS+/ChAT+ cells positively correlated with increase in theta power during SD. Experiment 2. Before saporin injection, both SD and infusion of DETA NONOate induced significant increases in NREM sleep (by 33 and 38%) and NREM delta power (by 43 and 45%, respectively) as compared to baseline. After saporin injection, both recovery NREM sleep after SD and DETA NONOate-induced sleep were significantly attenuated and increases in delta power were totally blocked. Also, SD-induced increase in NO metabolites, nitrate and nitrite, observed in the BF before saporin injection, were abolished after the saporin lesion.

Conclusion: We conclude that cholinergic neurons of the BF play an important role in iNOS/NO-mediated homeostatic sleep control.

0078

HOMEOSTATIC SLEEP REGULATION IS DISRUPTED IN nNOS KNOCKOUT MICE

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Introduction: We have previously shown that cortical nNOS neurons are activated during spontaneous sleep and during recovery sleep (RS) after sleep deprivation (SD). Furthermore, the % Fos+/nNOS neurons in the mouse brain was highly correlated with NR delta energy. These observations indicate that cortical nNOS neurons may play a role in homeostatic sleep regulation. Previous studies suggested a defect in the homeostatic sleep response in nNOS KO mice since they fail to show increased NR after systemic administration of TNF-α or after exposure to influenza virus. In the present study, we evaluated the response of nNOS KO mice to SD.

Methods: Fifteen male nNOS knockout (KO) mice (B6;129S4-Nos[1tm-1Plh]) and 20 control mice (B6129SF2/J) aged 8-12 weeks were implanted for EEG and EMG recordings using either telemetry (n= 9 KO and 14 WT) or tethered (n= 6 KO and 6 WT) techniques. Following a baseline recording, all mice were sleep deprived for 2, 4, or 6 h in balanced order. All SD periods ended ZT6 (6 h after lights on). Mice also underwent a multiple sleep latency test (MSLT) consisting of five 20 min sessions of forced waking followed by a 20 min nap opportunity within a continuous 200 min time interval. Sleep onsets were identified during each of the five nap opportunities.

Results: During baseline, W was increased and NR decreased in KO mice during both the light and dark periods compared to controls (for W, 44% vs. 33% in light, 57% vs. 47% in dark). The decreased time in NR was due to a decrease in the number of NR bouts without affecting the average NR bout duration. REM time was not different in the KO mice but REM bout duration was increased and the number of REM bouts decreased in both the light and dark periods. NR delta power in KO mice was half that of control mice across the 24 h period. The latency to sleep onset following SD and during the MSLT was significantly decreased in KO versus control mice. In addition, control mice did not sleep during 36% of the nap opportunities while KO mice only missed nap opportunities 10% of the time. Although delta power during RS increased in KO mice, this response was reduced relative to control mice.

Conclusion: While nNOS KO mice have less NR under baseline conditions, they appear more "sleepy" in response to both short (20 min) and longer (2-6 h) SD. However, NR delta power is significantly reduced in KO mice under all conditions tested compared to control mice. Together, these data show impaired homeostatic sleep regulation in nNOS KO mice.

0079

INHIBITION OF PROTEIN SYNTHESIS IN BASOLATERAL AMYGDALA PREVENTS FEAR CONDITIONED CHANGES IN SLEEP

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Introduction: Contextual fear significantly reduces rapid eye movement sleep (REM) during post-exposure sleep in mice and rats. The amygdala, has long been recognized as having a significant role in mediating conditioned fear responses (specifically the central amygdala) and in storing fearful memories (specifically the basolateral amygdala (BLA)). Several lines of research also demonstrate that the amygdala plays a significant role in regulating sleep and arousal and we have demonstrated that it plays a role in regulating changes in arousal induced by stress. However, it is unknown whether the BLA is critical for the role fear memory plays in fear-induced alterations in sleep. Here, we examined the influence of microinjections of anisomycin (ANI), a protein synthesis inhibitor, into the BLA following fear conditioning on subsequent exposure to a fearful context in the reactive BALB/c mouse strain.

Methods: Ten mice were implanted for recording sleep via telemetry and with cannulae for bilateral microinjections into BLA. After recovery, the mice were exposed to shock training (ST; 20 shocks, 0.5 mA, 0.5 sec duration, 1.0 min intervals). Immediately after training, five mice received microinjections of ANI (8.0μg/0.2μl) into BLA and five mice received microinjections of vehicle alone (saline) into BLA. They were then returned to their home cages. One week later, the mice were placed back in the fearful context (FC) for 30 min without shock. During both

ST & FC, animals were video recorded to analyze freezing behavior. Sleep was recorded for 20 h after each training or test session.

Results: Compared to baseline, training with ST significantly reduced REM in both ANI and vehicle treated mice during the first 2h. However, only vehicle treated mice showed reduced REM following FC whereas ANI treated mice exhibited REM levels similar to that of baseline. Moreover, compared to vehicle, the ANI showed significantly reduced FT% during FC.

Conclusion: Inhibiting protein synthesis in BLA after ST attenuates contextual freezing and fear-induced reductions in REM.

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0080

GLUTAMATERGIC NEURONS IN PARABRACHIAL NUCLEUS AND THEIR ROLE IN AWAKENING FROM SLEEP DURING HYPERCAPNIA

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Introduction: The mechanisms of arousal from sleep in patients suffering from obstructive sleep apnea are not well understood. We hypothesize that chemosensory pathways, coalesce on nucleus of solitary tract which mediates awakening by dense inputs to the parabrachial nucleus (PB). The PB shows activation in response to RCA and sends glutamatergic projections to a variety of forebrain structures critical to arousal including the basal forebrain, midline thalamus, and cerebral cortex.

Methods: We developed a mouse model, repetitive CO_2 arousal (RCA), to examine the mechanisms that cause arousal from sleep. Mice slept in a plethysmograph chamber for 6-7 hours during the early light phase and received 10-30 sec pulses of elevated CO_2 every 100-300 s, to mimic the cyclic hypercarbia of sleep apnea. To test whether glutamatergic projections from the PB are necessary for CO_2 arousal, we used mice in which loxP sequences flanked exon2 of the vescicular glutamate transporter 2 (VGLUT2) gene. Adeno-associated viral vectors containing genes encoding Cre recombinase and green fluorescent protein were microinjected into the PB to permanently and selectively disrupt VGLUT2 expression.

Results: At 5 weeks post injection; we recorded baseline sleep in these mice and then investigated the sleep during RCA. Loss of VGLUT2 was verified by in situ hybridization and examination of VGLUT2 immunoreactivity in terminals from GFP-labeled neurons. Selective ablation of VGLUT2 expression in the cells of PB region significantly prolonged the latency to arousal (> 30s) (F 2, 19= 8.19; P= 0.003 for 10s stimulus; and F1,5= 10.38, P= 0.02 for 30 s stimulus) and in a substantial proportion of trials (20-50%) animals fail to arouse at all during the CO_2 stimulus (F2, 19= 20.28, P=<0.001 for 10s and F1,5= 9.21, P= 0.03 for 30s stimulus).

Conclusion: Our results suggest that glutamatergic projections from the lateral PB region are necessary for arousals from sleep in response to CO_2.

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0081

EXCITATORY INPUTS TO HYPOGLOSSAL MOTONEURONS ARE DIFFERENTIALLY DEPRESSED DURING REM SLEEP IN RATS

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Introduction: Hypoglossal motoneurons innervate the genioglossus muscle which is important in maintaining upper airway patency in individuals with Obstructive Sleep Apnea. Since many inputs modulate the activity of hypoglossal motoneurons, it is important to determine the manner in which they control the excitability of hypoglossal motoneurons during particular experimental conditions and states of sleep and wakefulness. In the present study, we examined excitatory inputs to hypoglossal motoneurons in rats during natural sleep and waking states.

Methods: Two adult Sprague-Dawley rats were prepared for chronic experimentation and to record the EEG, neck EMG and activity of the hypoglossal nerve. Non-arousing monopolar electrical stimulation (0.2 ms, 50-75 µA, 0.2 Hz) in regions surrounding the hypoglossal nucleus induced compound action potentials in the hypoglossal nerve. The integral of the nerve potential was determined during sequential episodes of NREM and REM sleep.

Results: After the animals were adapted to head-restraint, no spontaneous activity was recorded from the hypoglossal nerve, except in conjunction with twitches during REM sleep or grooming during wakefulness. Stimulation of three areas adjacent to the hypoglossal nucleus elicited nerve potentials with latencies of 1.2-2.0 ms. Stimulation of a site ventral to the hypoglossal nucleus elicited potentials which were depressed during REM sleep by 29% compared to NREM sleep. Stimulation of sites located laterally to the hypoglossal nucleus yielded potentials which were depressed during REM sleep by 67-86% compared to NREM sleep. Stimulation in a dorsal region elicited potentials whose integrals were similar to those recorded from the preceding two areas during NREM sleep; however, these potentials were not depressed during REM sleep.

Conclusion: The present data provide important insight into the organization of the state-dependent control of hypoglossal motoneurons. Our findings suggest that excitatory inputs to hypoglossal motoneurons are differentially suppressed during REM sleep. These results may be explained by the presence of various patterns of pre- and postsynaptic control of specific populations of hypoglossal motoneurons.

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0082

INSPIRATORY MODULATION OF LINGUAL EMG IS RARE IN RATS AND OCCURS PREDOMINANTLY DURING SLOW-WAVE SLEEP

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Introduction: In obstructive sleep apnea (OSA) patients, lingual muscles are hyperactive and frequently exhibit inspiratory modulation in wakefulness and slow-wave sleep (SWS). We previously reported that, in rats, unlike OSA patients, lingual EMG is very low or absent during SWS (<8% of the mean during wakefulness) and rarely exhibits respiratory modulation. Our present goal was to determine the conditions under which lingual EMG is respiratory-modulated.

Methods: Seven male Sprague-Dawley rats were instrumented for recording of cortical EEG and nuchal, lingual and diaphragmatic EMGs. Lingual recording sites were localized near the base of the tongue. Sleep-wake states were scored in 10 s epochs over 2 h periods. Respiratory modulation of lingual EMG was assessed by comparing integrated records of diaphragmatic and lingual EMGs and was deemed genuine when the two signals had a stable phase relationship over at least 5 successive respiratory cycles.

Results: In 3 of the 7 rats, multiple segments of records were identified in which lingual EMG was respiratory-modulated. The duration of these segments varied from 2.4 to 312 s (5-513 respiratory cycles). In another 2 rats, less than 4 instances of respiratory modulation were found, and in the remaining 2 none was present. In the 3 rats with relatively frequent modulation, it was always of inspiratory type. 98% of these cases occurred during SWS as one or multiple clusters found in 37 out of 167 separate SWS episodes analyzed (22%). When present, inspiratory modulation started 0-310 s after SWS episode onset (median: 50 s, interquartile range: 30-80 s) and ended either before the end of the episode (62% of episodes) or during its last 10 s (38%). The amplitude

of inspiratory modulation of lingual EMG tended to be proportional to the amplitude of diaphragmatic activity and inversely proportional to the respiratory rate.

Conclusion: In rats, inspiratory modulation of lingual EMG is rare, of low amplitude, and preferentially occurs during SWS. This suggests that removal of wake- and REM sleep-related inputs to lingual motor output facilitates transmission of inspiratory drive to hypoglossal motoneurons.

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0083

RATS SUBJECTED TO CHRONIC-INTERMITTENT HYPOXIA (CIH) HAVE INCREASED DENSITY OF NORADRENERGIC TERMINALS IN THE TRIGEMINAL SENSORY (SP5) AND MOTOR (MO5) NUCLEI

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Introduction: Rodents subjected to CIH are used to investigate cardio-respiratory and other consequences of obstructive sleep apnea (OSA). We recently determined that rats subjected to CIH have increased density of noradrenergic terminals in the hypoglossal nucleus (Mo12) which innervates the muscles of the tongue that, in OSA patients, are hyper-active and help maintain airway patency. Noradrenergic terminals in the ventromedial Mo12 were nearly 40% more numerous in CIH than sham-treated rats. We now investigated whether increased noradrenergic innervation following CIH also occurs in other motor and sensory nuclei of the brainstem.

Methods: CIH was administered for 10 h/day for 35 days, with oxygen levels oscillating between 24% and 7% every 180 s. Six pairs of male Sprague-Dawley rats were exposed to CIH or identically timed air exchanges. Brainstems were cut into 35 μm transverse sections and immunohistochemically processed for dopamine-β-hydroxylase. For each rat in each pair, noradrenergic varicosities were counted in three sections in 100x100 μm counting boxes positioned at matching anteroposterior levels in the center of Mo5 and three counting boxes placed at the nucleus ambiguus level dorsoventrally and 100 μm medial to the lateral margin of the interpolar part of Sp5.

Results: The average numbers of noradrenergic varicosities were much higher in Mo5 than Sp5. In both locations, they were higher in CIH than sham-treated rats (Mo5: 258±11(SE) in CIH and 236±10 in sham-treated rats; n=18 section pairs, p=0.067, paired t-test; Sp5: 184±9 in CIH and 156±8 in sham-treated rats; n=18, p=0.029).

Conclusion: Exposure to CIH results in 9-18% increased density of noradrenergic terminals in the Mo5 and Sp5, suggesting that the effect occurs in multiple functionally distinct nuclei. The increases in Mo5 were less prominent than those in Mo12, a difference possibly related to stronger hypoxic stimulation of Mo12 than Mo5.

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0084

ROLE OF HYPOTHALAMIC GLUTAMATE AND GABA RELEASE IN THE EFFECTS OF CAFFEINE ON HISTAMINE NEURONS

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Introduction: We hypothesized that the adenosine receptor antagonist caffeine, the most widely used stimulant, increases glutamate release and reduces GABA level in the tuberomammillary region and that this underlies an activation of histamine (HA) neurons, thereby suppressing sleep and promoting waking.

Methods: Male Sprague-Dawley rats were chronically implanted with sleep-wake recording electrodes and cannulae for microdialysis probes. After a one-week recovery period, microdialysis probes were inserted through the guide cannulae to the PH-TMN. Microdialysis experiments were performed between 10:00AM to 6.00PM (09:00AM lights-on: 09.00PM light-off) and were continuously perfused with aCSF at a flow rate of 2μl/ min. We collected 10-minute samples starting two hours after the beginning of the aCSF perfusion. Rats were given caffeine intra-peritoneally (25 mg/kg) and samples were collected from the PH-TMN for 120 minutes after caffeine administration.

Results: HPLC analysis of the samples showed a significant increase in glutamate levels after the caffeine treatment. Glutamate levels were significantly elevated 30 min after caffeine administration and remained high for an additional 90 minute period compared to pre-injection (F4,25 =10.9, P<0.0001; ANOVA). However, GABA levels during the waking periods following the caffeine administration were not significantly different from pre-injection levels. HA level significantly increased after 30 min and remain elevated for 120 minutes after caffeine treatment (F6, 133=3.7; P<0.0001; ANOVA). Double labeling for adenosine de-aminase (ADA) immunostaining for HA neurons and c-fos showed a significant increase in double labeled cells in caffeine treated rats compared to saline treated controls.

Conclusion: Glutamate levels were elevated but GABA levels were not altered, in the tuberomammillary region during the period of increased arousal. Induced increases in glutamate level, rather than reductions in GABA level are likely responsible for increased histamine activity after caffeine administration

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0085

DISTRIBUTION AND INTERACTION BETWEEN CORTICALLY PROJECTING BASAL FOREBRAIN NEURONS INVESTIGATED USING MUTANT MOUSE STRAINS EXPRESSING FLUORESCENT PROTEINS IN GABAERGIC AND PARVALBUMIN NEURONS

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Introduction: The ventral ascending arousal pathway includes projections from the brainstem reticular formation to the basal forebrain (BF) and posterior hypothalamus, which influence cortical EEG activation by means of projections to the neocortex. Here we investigated the distribution and interaction between two cortically projecting subpopulations, cholinergic and parvalbumin (PV)-positive GABA neurons.

Methods: We used two mutant mouse strains expressing fluorescent proteins: (i) GAD67-GFP knock-in mice, in which green fluorescent protein (GFP) is expressed under control of the promoter region of the Gad1(GAD67) gene; (ii) mice expressing red fluorescence in PV neurons (PV-Tomato), generated by crossing PV-Cre and Cre reporter red fluorescent mice. In both mouse models, BF was immunohistochemically stained for choline acetyltransferase (ChAT, cholinergic neurons) or PV. We also labeled vesicular acetylcholine transporter (VAChT) and PV in the GAD67-GFP mouse, to investigate cholinergic innervation of GFP(GABAergic)-PV positive cells. Labeled cells were mapped onto mouse atlas templates using Neurolucida. We characterized the size of these different BF neuronal phenotypes, including sub-nuclei differentiation.

Results: GFP-pos neurons were located throughout the BF, and GFP was not co-localized with ChAT. Most GFP-Pos neurons were of relatively small size (average ~15-16 microns) when compared to ChAT-pos

(average ~21-22 microns). However, a subpopulation of mainly large (average ~21-22 microns) GFP-positive neurons were PV-positive. In both mouse strains PV neurons were located medially, close to the cholinergic neurons in the horizontal limb of the diagonal band and laterally in the magnocellular preoptic area. GFP(GABAergic)-PV-positive BF neurons were surrounded by VAChT staining.

Conclusion: In these mutant mouse strains the distribution and size of cholinergic, GABAergic, and GABAergic-PV-positive neurons was broadly similar to that previously reported in the rat. GABAergic, PV-positive neuronal activity during waking and REM sleep may be modulated by input from neighboring BF and/or brainstem cholinergic neurons.

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0086

MECHANISM BEHIND GAMMA BAND SINGLE CELL ACTIVITY IN THE PARAFASCICULAR NUCLEUS

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Introduction: The parafascicular nucleus (Pf) is part of the "non-specific" intralaminar thalamus involved in waking and REM sleep, during which the EEG shows activity at gamma frequencies (~20-80Hz). Gamma oscillations appear to participate in sensory perception, problem solving, and memory, and this coherence may occur at cortical or subcortical levels. We previously reported that Pf neurons fired maximally in the gamma range (20-60Hz). The present studies tested the hypothesis that P/Q- and N-type calcium channels are responsible for generating the rising phase of gamma band oscillations in Pf neurons.

Methods: Single cell responses were recorded using whole-cell patch clamp electrodes in an immersion chamber using 9-18 day old rat brainstem slices. Recordings were made at 37°C while perfusing aCSF containing the GABAA receptor antagonist gabazine (10 μM), the glycine receptor antagonist strychnine (10 μM), and the glutamate receptor antagonists CNQX (10 μM) and APV (40 μM) to block fast synaptic transmission. Tetrodotoxin (TTX) was used to block sodium channels while the specific calcium channel blockers, ω-agatoxin-IVA (100-200 nM) and ω-conotoxin-GVIA (1-3 μM), were used to block P/Q- and N-type calcium channels, respectively.

Results: Gamma band oscillations were induced in all Pf cells (n=31) at higher amplitudes using ramps than steps (p<0.01), and at potentials above -30 mV, suggesting a dendritic origin beyond voltage clamp control. Pf cells showed an increase in oscillation frequency with age (p<0.01). ω-agatoxin-IVA completely blocked high frequency oscillations (~20-60Hz) during current ramp protocols (n=3). ω-conotoxin-GVIA only partially decreased the amplitude of gamma frequency oscillations (n=2).

Conclusion: Gamma band activity appears to be an intrinsic membrane property of Pf neurons, and we suggest that high voltage-dependent P/Q- and N-type calcium channels mediate the rising phase of high frequency oscillations. We hypothesize that Pf neurons, given sufficient excitation, may impart gamma band activation on its targets.

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0087

MODULATION OF GAMMA BAND ACTIVITY IN THE PEDUNCULOPONTINE NUCLEUS

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Introduction: We previously reported that gamma band activity is generated by intrinsic membrane properties of pedunculopontine (PPN) neurons, and other studies at this meeting suggest that high threshold voltage-gated calcium channels are responsible for this activity. Previous studies on the mechanisms behind gamma band activity in the cortex used slice recordings at 36-38oC instead of 30oC. These studies tested the a) temperature dependence of gamma band activity, and b) mechanism behind gamma band activity, in the PPN.

Methods: Population responses were recorded using extracellular microelectrodes in an interface chamber in 9-16 days old rat brainstem slices. Recordings of activity were taken at 30, 32, 34, 36, and 38oC in each slice. In another experiment, carbachol (CAR), along with the GABAA receptor antagonist gabazine (10 μM), the glycine receptor antagonist strychnine (10 μM), and the glutamate receptor antagonists CNQX (10 μM) and APV (40 μM) were used to block fast synaptic transmission. These recordings manifested CAR-induced gamma oscillations. Either ω-agatoxin-IVA (100-200 nM), a P/Q-type calcium channel blocker, or ω-conotoxin-GVIA (1-3 μM), a N-type calcium channel blocker, was then applied. After 20 minutes, CAR was reapplied with synaptic blockers.

Results: Population recordings showed a significant increase in response at theta, beta, and gamma frequencies as the temperature increased from 30-38oC (n=4, p<0.01). ω-agatoxin-IVA exponentially (r=0.85) blocked the CAR-induced responses at gamma frequencies (n=4, p<0.01), while ω-conotoxin-GVIA linearly (r=0.64) blocked the CAR-induced responses at lower (theta and beta) frequencies (n=4, p<0.01), and only partially blocked activity at higher (gamma) frequencies (p<0.05).

Conclusion: CAR-induced gamma band activity in populations of PPN neurons can be potentiated by increasing the temperature of the slice. P/Q-type calcium channels appear to be necessary to generate this gamma band activity, while N-type calcium channels modulate this activity to a lesser extent, but have greater effects on lower frequency activity.

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0088

GAMMA BAND SODIUM-DEPENDENT SUBTHRESHOLD OSCILLATIONS IN THE SUBCOERULEUS NUCLEUS

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Introduction: The subcoeruleus nucleus (SubC) is most active during rapid eye movement (REM) sleep and is involved in the generation of muscle atonia and ponto-geniculo-occipital (PGO) waves during REM sleep. Previously, we found that SubC neurons fired action potentials maximally in the gamma range (20-100 Hz). The SubC receives input from the pedunculopontine nucleus (PPN), a region in which we also described the presence of gamma band activity. High-threshold calcium channel mediated oscillations underlie the firing of PPN neurons, as shown at this meeting. These studies tested the hypothesis that SubC neurons have sodium dependent, gamma frequency subthreshold oscillations, which underlie their maximal firing at gamma frequencies.

Methods: Sagittal brainstem slices from 9-15 day old rats were cut and placed in an immersion chamber for recordings at 37° C. Slices were bathed with artificial cerebrospinal fluid (aCSF) containing the GABAA receptor antagonist gabazine (10 μM), the glycine receptor antagonist strychnine (10 μM), and the glutamate receptor antagonists CNQX (10

μM) and APV (40 μM) to block fast synaptic transmission. Whole-cell patch clamp was used to record subthreshold oscillations in SubC neurons in current clamp mode before and after application of the sodium channel blocker tetrodotoxin (TTX, 1-10 μM).

Results: Subthreshold oscillations in the gamma frequency range were observed using ramp and various membrane holding potential protocols in all SubC cells (n=12) in the presence of fast synaptic blockers. These oscillations were blocked by application of TTX (n=8, p<0.01).

Conclusion: SubC neurons manifest sodium-dependent, gamma frequency subthreshold oscillations. These subthreshold oscillations may underlie the maximal firing of SubC neurons at gamma frequencies. Gamma band activity appears to be due to intrinsic membrane properties of SubC neurons and, given sufficient excitation, the SubC may impart gamma band activation on its targets.

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0089

MECHANISM BEHIND GAMMA BAND ACTIVITY IN PEDUNCULOPONTINE NUCLEUS

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Introduction: The pedunculopontine nucleus (PPN) modulates waking and paradoxical sleep, during which the EEG shows activity at gamma frequencies (~20-80 Hz). Gamma oscillations appear to participate in sensory perception, problem solving, and memory, and this coherence may occur at cortical or subcortical levels. We previously reported that PPN neurons fired maximally in the gamma range (20-60 Hz). The present studies tested the hypothesis that P/Q- and N-type calcium channels are responsible for generating the rising phase of gamma band oscillations in PPN neurons.

Methods: Whole-cell patch-clamp responses were recorded using 9-14 day old rat brainstem slices at 370C while perfused with oxygenated aCSF in an immersion chamber containing the GABAA receptor antagonist gabazine (10 μM), the glycine receptor antagonist strychnine (10 μM), and the glutamate receptor antagonists CNQX (10 μM) and APV (40 μM) to block fast synaptic transmission. Tetrodotoxin (TTX) was used to block sodium channels, while the specific calcium channel blockers ω-agatoxin-IVA (100-200 nM), and ω-conotoxin-GVIA (1-3 μM) were used to block P/Q- and N-type calcium channels, respectively.

Results: Gamma band oscillations were induced in all 3 types of PPN cells (n=103) at higher amplitudes using ramps compared to steps (p<0.01), and at potentials above -30 mV (n=6), indicating an origin beyond voltage clamp control. ω-agatoxin completely blocked high frequency oscillations (20-60 Hz) during current ramp protocols (n=4). ω-conotoxin partially decreased the amplitude of gamma frequency oscillations (n=4).

Conclusion: Gamma band activity appears to be an intrinsic membrane property of all PPN neurons, and we suggest that high voltage-dependent P/Q- and N-type calcium channels mediate the rising phase of gamma oscillations. We hypothesize that, rather than participating in the temporal binding of sensory events, gamma band activity generated in the PPN may help stabilize coherence related to arousal, providing a stable activation state during waking and paradoxical sleep.

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0090

ACETYLCHOLINE DIRECTLY AND INDIRECTLY INCREASES THE EXCITABILITY OF PARVALBUMIN-POSITIVE GABAERGIC NEURONS IN MOUSE BASAL FOREBRAIN

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Introduction: The basal forebrain (BF) constitutes the ventral extra-thalamic relay from the brainstem activating system to the cortex. While cholinergic neurons projecting to the cortex have been extensively investigated, little is known about neighboring, cortically-projecting, parvalbumin (PV)-positive GABAergic neurons and their interaction with cholinergic neurons.

Methods: Coronal brain slices were prepared from young (14-22 d) heterozygous GAD67-GFP knock-in mice or mice expressing red (Tomato) fluorescence in PV neurons. Whole-cell patch-clamp recordings were made using a Multiclamp 700B amplifier. BF neuronal subtypes were identified prior to recording based on their expression of green fluorescent protein (GFP) or Tomato. The cholinergic agonist, carbachol, was bath-applied.

Results: Two types of PV-positive BF GABAergic neurons were identified which differed in the amplitude and kinetics of hyperpolarization-activated cation current (Ih) and in the receptor subtype mediating the response to carbachol. Both types responded to carbachol (50 μM) with a significant increase in spontaneous firing frequency (*p*<0.05, n=9/type). However, the carbachol response in one type (large Ih) was blocked by the M1 muscarinic receptor antagonist pirenzepine dihydrochloride (10 μM, n=7/10) while the response in the other type (small Ih) was blocked by the M3 muscarinic receptor antagonist 4-DAMP (3 μM, n=5/5). Under voltage-clamp, carbachol induced an inward current in both types in the presence of 500 nM TTX (*p*>0.05, n=8-14/group), suggesting a direct postsynaptic effect. Reversal potential measurements and ion substitution experiments revealed that in both types the carbachol-induced current was mainly due to opening of sodium-permeable cation channels. Carbachol also significantly increased the frequency and amplitudes of spontaneous EPSCs and sIPSCs (*p*<0.05, paired-t-test, n=6-10/group).

Conclusion: The increased firing of cortically projecting, PV-Positive, BF GABAergic neurons during waking and REM sleep may be mediated by input from neighboring basal forebrain and/or brainstem cholinergic neurons.

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0091

INTERACTIONS BETWEEN PROJECTIONS FROM THE AMYGDALA AND THE PEDUNCULOPONTINE TEGMENTAL NUCLEUS IN THE CONTROL OF ACTIVITY OF NEURONS IN THE NUCLEUS PONTIS ORALIS

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Introduction: We recently reported that there are direct, excitatory (glutamatergic) projections from the central nucleus of the amygdala (CNA) to the nucleus pontis oralis (NPO). We therefore hypothesize that the CNA acts in concert with projections from the pedunculopontine tegmental nucleus (PPT) to promote active (REM) sleep by increasing the discharge of active sleep-on neurons in the NPO. To test this hypothesis,

the interactive effects of stimulation of the CNA and the PPT on the intracellularly recorded activity of NPO neurons were examined.

Methods: Experiments were performed on urethane-anesthetized, adult male Sprague-Dawley rats. NPO neurons were recorded with glass micropipettes filled with 3 M KCl in conjunction with ipsilateral electrical stimulation of the CNA (100 to 400 µA) and the PPT (10 to 50 µA).

Results: Stimulation of either the CNA or the PPT evoked short-latency EPSPs in neurons within the NPO. Concurrent stimulation of the CNA and the PPT potentiated the effects of stimulation of either site by itself. The amplitude of PPT-evoked EPSPs in NPO neurons increased by 20 to 58% when stimulation of the PPT was preceded by stimulation of the CNA at an interval of 3 to 15 ms, and vice-versa. Maximal facilitation occurred when the CNA and PPT were stimulated with an interval of 8 to 10 ms. Simultaneous subthreshold stimuli of the CNA and the PPT resulted in the discharge of NPO neurons.

Conclusion: The present data provide evidence that there are converging excitatory synaptic inputs from the amygdala and the PPT that facilitate the discharge of neurons in the NPO. Therefore, we suggest that the amygdala is capable of inducing active sleep by promoting the discharge of active sleep-on neurons in the NPO and by its interactions with projections from the PPT.

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0092

ELECTROPHYSIOLOGICAL IDENTIFICATION OF SLEEP ACTIVE NEURONS IN RAT BASAL FOREBRAIN

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Introduction: Inhibitory neurons in the preoptic area are important for induction of non-rapid eye movement (NREM) sleep in many species. Cholinergic neurons in the brainstem and basal forebrain mediate rapid eye movement (REM) sleep induction. Sleep-active neurons have also been found by electrophysiological recordings in the medial basal forebrain of cat - specifically the horizontal limb of the diagonal band of Broca (hDB). Electrical stimulation of this area in the cat induces sleep, suggesting that these neurons are involved in sleep induction. However, no one has identified sleep active cells in the corresponding area of the hDB in rodents. Therefore, this study investigated the sleep state dependent firing patterns of neurons in the hDB of rat.

Methods: Adult male Sprague-Dawley rats were implanted with microdrives containing movable tetrodes aimed for the hDB and electroencephalogram (EEG) and electromyogram (EMG) recording electrodes. The tetrodes were adjusted to yield single unit isolation across the hDB. Spikes, EEG, and EMG were recorded across multiple spontaneous sleep wake cycles. Single neurons were clustered offline using M-Clust in Matlab and sleep was scored visually using Spike2.

Results: Four main categories of neurons were identified that demonstrated state dependent firing. There were 5 Wake-on neurons, 5 Wake/REM-on neurons, 14 NREM/REM-on neurons, and 14 REM-on neurons. Significant differences in firing rate between states were determined using 95% confidence intervals computed with a non-parametric bootstrap.

Conclusion: While much of the cholinergic basal forebrain is involved in arousal and REM sleep generation, approximately 37% of recorded cells in the hDB showed an increased firing rate during both NREM and REM sleep compared to wakefulness. These data suggest that in addition to cholinergic arousal promoting neurons in the rat basal fore-

brain, a non-cholinergically mediated sleep induction mechanism may also exist.

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0093

STATE-SPECIFIC ACTIVITY OF CORTICAL SLEEP-ACTIVE NEURONS DOES NOT REQUIRE PRESENCE OF NEURONAL NITRIC OXIDE SYNTHASE

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Introduction: Recently, our lab identified a population of sleep-active cortical neurons. These neurons express Fos during sleep but not during wake and can be readily identified histochemically because they express the enzyme neuronal nitric oxide synthase (nNOS). However, it is unclear what functions cortical nNOS neurons have in sleep and whether the nitric oxide produced feeds back (directly or indirectly) on the activation of this neuronal population. In the present study, we asked whether the enzymatic activity of nNOS is critical for the regulation of the state-specific activity of cortical sleep-active neurons.

Methods: Of the 15 male nNOS knockout (KO) mice (B6;129S4-Nos-1tm1Plh) and 20 nNOS control mice (B6129SF2/J) implanted for EEG and EMG recordings using either telemetry or conventional techniques described in the accompanying abstract by Morairty et al., 13 nNOS KO and 15 controls were sleep deprived (SD) for 6 h by gentle handling. 5 nNOS KO and 6 controls were perfused immediately following SD, 8 nNOS KO and 9 controls mice were allowed 2.5 h recovery sleep (RS) before perfusion (ZT 8.5 for all animals). In the absence of nNOS, the sleep-active cortical neurons were identified by immunoreactivity for NK1, the cortical expression of which occurs almost exclusively in nNOS-immunoreactive neurons in wild type mice. Neuronal activity was assessed by double-labeling with Fos.

Results: The proportion of Fos-positive cells among the cortical NK1-immunoreactive neuronal population was greater during RS than during SD in both controls and nNOS KO mice. The proportion of Fos-positive cells did not differ between the genotypes.

Conclusion: These results indicate that nNOS is not necessary for the activation of cortical interneurons during sleep.

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0094

SLEEP ACTIVE NEURONS IN THE CAUDAL BRAIN STEM

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Introduction: Early brainstem transection studies indicated the existence of a sleep promoting system in the medullary brainstem although its precise location has been never identified. Electrical stimulation of the solitary tract nucleus (NTS) and dorsal reticular formation produced cortical EEG synchronization suggestive of inducing NREM sleep. Although the nucleus of solitary tract (NTS) in the caudal medulla has been proposed to be a potential candidate for the medullary sleep system, the evidence for this claim has been not substantiated. A recent observations from our lab showed that cell specific lesions using orexin-saporin of NTS had no affect on the sleep-wake percentages, but, lesion of the structure rostral to NTS; dorsal and lateral to facial nerve (referred to as parafacial zone; PZ) showed about 50% increase in wakefulness. Interestingly, the PZ also corresponds to the region where stroke caused severe insomnia in a human case. In order to get a direct evidence for the presence of the sleep active neurons in this area, we did extracellular single-unit recordings of the neurons in PZ in the freely behaving animals.

Methods: Male Sprague-Dawley rats were implanted with electrodes to record sleep-wake behavior and a microwire assembly to record single neurons from the parafacial zone (PZ). After post-surgical recovery and

habituation, activity of single neurons (3:1 signal: noise) was recorded in freely-behaving rats over multiple episodes of sleep-wake.

Results: Eleven neurons in the PZ region, all of which showed either tonic/sustained activity or phasic/burst activity during sleep and firing rate higher than wake and REM sleep. This indicates that the PZ contains high density of sleep active neurons. The firing frequency for these neurons ranged from 0.2 to 2.3 Hz.

Conclusion: This study for first time has identified a sleep active area in parafacial zone of the caudal brain stem.

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0095

BOOSTING SK2-TYPE K+ CHANNEL ACTIVITY IN THE NUCLEUS RETICULARIS THALAMI CONSOLIDATES NREM SLEEP

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Introduction: The *nucleus reticularis thalami* (nRT) is known for its pacemaking function during oscillatory brain activity related to non-rapid-eye-movement sleep (NREMS). Small conductance type-2 (SK2) K+ channels are crucial for oscillatory bursting in nRT neurons and a loss of SK2 channels increased NREMS fragmentation and reduced EEG delta (1-4Hz) power during NREMS. We tested whether over-expressing SK2 channels (SK2-OE) potentiates nRT oscillatory capacity and stabilizes NREMS.

Methods: Whole-cell patch-clamp recordings in horizontal brain slices (300μm) were obtained from nRT and thalamocortical (TC) neurons of SK2-OE and wild-type (WT) littermates (C57Bl/6J background, P25-34). At P56-63, mice were implanted with EEG and EMG electrodes. After 8-12 days of recovery, spontaneous sleep and waking behavior was recorded for 48h.

Results: SK2-current amplitudes were >2-fold greater and oscillatory bursting was strengthened in SK2-OE compared to WT nRT cells (p<0.01). T-type Ca^{2+} currents, main triggers for SK2-currents, were unaltered (p>0.05). However, SK2 channel over-expression reduced action potential (AP) number per nRT burst and attenuated the efficacy of unitary burst-induced inhibitory postsynaptic currents in rebound AP generation in TC neurons (p<0.002). Nonetheless, synchronized multiunit activity in nRT-TC circuits at ~10 Hz was strengthened in thalamic slices (p<0.01), indicating that synchronously bursting SK2-OE nRT cells facilitated oscillatory network activity related to sleep oscillations. During light periods, SK2-OE mice spent less time in REMS (p<0.05) and more time in longer (>2min) NREMS episodes (p<0.05). At the NREMS-REMS transition, SK2-OE mice showed a delayed decline in delta and a smaller peak in sigma (11-15Hz; p<0.05) power.

Conclusion: SK2-OE increased oscillatory capacity of nRT cells, while compromising single-cell inhibitory output. However, synchronized network activity seemed to be strengthened, which might have impeded the exit from nRT oscillatory bursting at NREMS-REMS transitions resulting in a consolidation of NREMS at the expense of REMS.

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0096

NOISE INDUCED TRANSITIONS REPRODUCE REALISTIC SLEEP/WAKE ARCHITECTURE IN A MATHEMATICAL MODEL OF HUMAN SLEEP

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Introduction: On the macroscale, human sleep occurs in consolidated daily blocks, characterized by an ultradian REM/NREM rhythm. On the microscale, sleep is punctuated by many brief arousals, even in healthy subjects. Previous studies have concluded that the durations of these arousal events have power law or multi-exponential distributions, while sleep bouts have single or multi-exponential distributions. However, the physiological basis for these dynamics remains poorly understood. To bridge the gap from the common flip-flop sleep models (which are deterministic and therefore have no "noise") to realistic sleep architecture, we explore the effects of model stochasticity on simulated hypnograms.

Methods: Our model includes the mutually inhibitory sleep/wake switch nuclei: wake-active monoaminergic nuclei (MA), and sleep-active ventrolateral preoptic area (VLPO). We introduce noisy inputs to both nuclei. Since it is not known what type of noise might occur physiologically, we test three plausible types: Gaussian white noise, Poisson white noise, and correlated 1/f (pink) noise. In each case, the relative effects of noise on the MA and VLPO are explored, and noise amplitude is chosen to generate a realistic frequency of sleep/wake transitions.

Results: Without noise, the distributions of simulations produced by the model were deterministic and invariant from night to night. All noise types generate monotonic probability distributions for wake and sleep bouts, with shorter bouts being more probable than longer bouts, consistent with experimental data. Gaussian and Poisson distributed white noise result in both events following a mono-exponential distribution, while pink noise results in distributions that are neither mono-exponential nor power law.

Conclusion: These results help shed light on how the sleep/wake switch responds to biological noise, which may contribute to the complex observed architecture of sleep/wake transitions. Determining the biological basis for short timescale transitions could potentially also improve understanding of pathological sleep fragmentation.

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0097

NETWORKS OF CULTURED NEURONS SHOW OSCILLATORY DYNAMICS

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Introduction: Sleep is a fundamental property of all animals with nervous systems. Yet, what actually sleeps or even what triggers sleep remains debatable. We hypothesize that sleep is a local phenomenon; an emergent property resulting from the interactions of neurons within networks; and an inherent property of those networks determined by prior network activity and gene expression. We hypothesized that any viable neuronal/glial network oscillates between two or more states. Based on this hypothesis we set out to generate an *in vitro* model system for measuring state oscillations.

Methods: Somatosensory cortices (Sctx) from embryonic day 18 (E18) Sprague-Dawley rat fetuses were dissected in ice-cold Hibernate-E solution, digested in 2mg/mL papain and then mechanically dissociated. Cells were grown on 8×8 multi-electrode array (MEA) in a 5% CO_2 incubator at 37°C in serum free NbActiv4 medium. After 4 days, neurons exhibit multiple projections that form intricate networks. Electrical activities from neuronal cultures were recorded on day 12 *in vitro* at all electrodes using a commercial MEA recording setup (Multi Channel Systems, Germany). MatLab and MC_Rack analysis routines were used for data processing.

Results: The recorded signal at each electrode shows rich temporal structure, consisting of intermittent bursts of action potentials with quiescent periods in between. The recordings from neighboring channels display strong temporal and spatial correlation. The patterns of action potentials varied across the 24 hour recording period. These patterns were evident in the different nodes although the exact pattern was node-specific. Fast Fourier analyses indicated a complex frequency pattern including some periodicities between bursts.

Conclusion: Networks of Neuron/glia in culture oscillate between functional states as defined by bursts of action potential patterns.

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0098

TWO WEEKS DELIVERY OF OX2R AGONIST COUNTERS TO THE REDUCTION OF SEIZURE LIKE ACTIVITY WITHOUT SIGNIFICANT INCREASE OF WAKEFULNESS

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Introduction: We have reported that a rat model of depression had both higher orexins levels and more seizure-like activities and found that A/J mice also had higher orexin levels and more seizures. Now we report the effect of two weeks treatment with modified orexin B (OBAD), which activates OX2R only, on sleep and spontaneous seizure like activity in rats.

Methods: Adult Long Evans Hooded rats were surgically implanted with electrodes for PSG recording and with guide cannula for intra-cerebroventricular injection. The cannula was functionally tested by injecting 125 ng angiotensin II. After 10 days recovery, either OBAD (Cat# 2142, Tocris Bioscience, 4 nMol/day) or vehicle was delivered by osmotic pump for two weeks. PSGs of baseline day and the last treatment day were scored as REM sleep, NREM sleep and wake. Seizures like activities were defined as continuous (CTS, duration >=3.5 sec) and petite-continuous (P-CTS, duration <3.5 sec) seizures. Actual time of each event and the number was calculated by sleep analyzing program. Statistics were done by two ways ANOVA.

Results: Surprisingly, two weeks treatment with OBAD did not significantly increase wake time either in the light phase or in the dark phase. No differences were seen between groups of vehicle and OBAD in either NREM sleep or in REM sleep in both light phase and dark phase. However, compared to the control group, the number of P-CTS and the total seizures in the OBAD group of last treatment day were 40.65% (p=0.023) and 35.92% (p=0.038) higher, respectively, in the light phase. In the dark phase, these differences were a little bit smaller and the p value was close to but not less than 0.05.

Conclusion: OBAD counters to the reduction of seizure like activity (which was observed in the control group) without significant increase of wakefulness.

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0099

PROLONGED SLEEP DISRUPTION AND MUSCULOSKELETAL SENSITIZATION ALTER SLEEP AND CYTOKINES

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Introduction: Chronic musculoskeletal sensitivity and sleep disruption are characteristics of fibromyalgia (FM), a rheumatic disease afflicting 5% of the US population. Although the etiology of FM is still unknown, effort using animal models has been focused on understanding the pain associated with this condition. Pain can disturb sleep, and sleep disturbance can exacerbate pain in patients suffering chronic pain and in healthy controls. However, we do not understand the mechanisms by which these processes influence each other.

Methods: Sleep of male C57B/L6 mice was disrupted for 96 hours using a rotating disk method. Blood serum and brain tissue samples were collected and analyzed using a Luminex bead-based assay to quantify pro-inflammatory cytokines interleukin (IL) 1, 6, and tumor necrosis factor (TNF)-α. Musculoskeletal sensitization was induced by injecting saline into the gastrocnemius muscle.

Results: Ninety six hours of sleep disruption resulted in increased circulating levels of pro-inflammatory cytokines in serum, especially IL-6. Two unilateral injections of acidified saline 5 days apart produced robust bilateral sensitization to muscle stimulation that persists for at least 28 days. Concurrently, alterations in sleep patterns relative to baseline recordings were observed for those mice with musculoskeletal sensitization. The effect of musculoskeletal sensitization on sleep was most robust during REMS.

Conclusion: Prolonged sleep disruption up-regulates pro-inflammatory cytokines. These changes parallel the time course of the development of musculoskeletal sensitization. Sleep and pain influence each other, possibly via actions of pro-inflammatory cytokines. Future studies aim to understand the of role pro-inflammatory cytokines in the interactions between sleep disruption and musculoskeletal sensitization.

0100

STRESS-RELATED VULNERABILITY OF SLEEP AND INFORMATION PROCESSING AROUND SLEEP ONSET

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Introduction: Conditioned cortical arousal has been theorized to be a major etiological factor in chronic insomnia patients. The role of cortical arousal on sleep in non-insomniacs remained unclear. The aim of the study is to compare arousal levels around sleep onset in individuals who are highly vulnerable to stress-related sleep disturbance with those who are not.

Methods: Four healthy individuals scoring low (LF) and four healthy individuals scoring high (HF) on the Ford Insomnia Response to Stress Test (FIRST) were studied. All subjects had to sleep in the lab for three nights: a screening/adaptation night, a baseline night, and a stress night. During the stress night, subjects were informed that they would be required to give a speech immediately after waking up. An odd-ball paradigm was conducted to evoke ERPs throughout the night.

Results: Mann-Whitney U-test showed that the HF had faster N1 (Z=-2.31, p=.02) to deviate tone than the LF during the first 5 minutes of continuous stage 2 sleep. Though no other ERP differences were found to be significant between 2 conditions, Wilcoxon Rank Signed test showed the HF had a tendency of larger N1 (Z=-1.83, p=.068), smaller P2 (Z=-1.83, p=.068) to the deviate tone; the LF showed a tendency of faster N350 (Z=-1.84, p=.066) to the deviate tone during the stress condition than the baseline condition.

Conclusion: Individuals with high vulnerability showed increased information processing around sleep onset. There is a trend that when under stress, individuals with high vulnerability may have enhanced attention and reduced inhibitory process around sleep onset. The findings need to be confirmed with increased number of subjects.

0101

REGIONAL DIFFERENCES IN THE CORTICAL EEG ASYMMETRY DURING SLOW WAVE SLEEP IN THE FUR SEAL

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Introduction: Slow wave sleep (SWS) in the fur seal (Callorhinus ursinus) is frequently characterized by a highly expressed interhemispheric EEG asymmetry called the asymmetrical SWS (ASWS). The aim of this study was to examine spatial-temporal aspects of cortical EEG asymmetry during SWS in this species.

Methods: Three seals were implanted with 10 EEG electrodes, positioned bilaterally (5 in each hemisphere) over the frontal, occipital and parietal cortex. The degree of interhemispheric EEG asymmetry in the range of 1.2-4 Hz for each pair of symmetrical monopolar recordings was estimated based on the asymmetry index [$AI = (L-R)/(L+R)$, where L and R are the spectral powers in the left and right hemispheres, respectively; calculated in 20-sec epochs], and the percentage of epochs with an absolute $AI>0.3$. Each animal was recorded for 2 nights.

Results: The average AI in 5 symmetrical monopolar derivations ranged between -0.30 and -0.57 in episodes of right ASWS, between +0.25 and +0.42 in episodes of left ASWS. In contrast, AI at the same derivations for episodes of high voltage bilateral SWS were between -0.02 and +0.03. The percent of 20-sec epochs with an absolute $AI>0.3$ varied between 40 and 71% of all SWS epochs in episodes of left ASWS, between 38 and 75% in episodes of right ASWS and between 0 and 7% in episodes of bilateral SWS. In 2 out of 3 seals during ASWS both the AI and number of epochs with an absolute $AI>0.3$ in the frontal derivations were significantly smaller than the corresponding values in the parietal and occipital derivations (one-way Anova, $p<0.05$).

Conclusion: This data indicates that 1) interhemispheric EEG asymmetry during SWS in the fur seal is recorded across the entire dorsal cortex and 2) provide evidence for regional differences in the expression of slow wave asymmetry. The cause of these differences remains to be determined.

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0102

BRAIN OREXIN LEVELS CORRELATE WITH WAKEFULNESS IN A MOUSE MODEL OF TRAUMATIC BRAIN INJURY

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Introduction: The hypothalamic neuropeptide orexin (hypocretin) activates ascending arousal circuitry, and loss of orexin signaling is one cause of human narcolepsy-cataplexy. Traumatic brain injury (TBI) is associated with loss of orexin neurons and excessive daytime sleepiness. We hypothesize that 1) TBI impairs dynamics of orexin release into the brain and 2) Real-time orexin dynamics are correlated with wakefulness.

Methods: We developed a mouse model of TBI using electromagnetic controlled cortical impact (CCI), which delivered precise, graded impact to the exposed cortex at 2.5 mm depth. Microdialysis probes were implanted into the lateral hypothalamus, and brain interstitial fluid (ISF) samples collected every 3 hours for 120 hours (across 10x12-hour light:dark cycles), with CCI or sham surgery intervention following 48 hours of baseline data. ISF samples were assayed for orexin levels using ELISA. EEG/EMG data were analyzed for sleep staging using automated software.

Results: Brain ISF orexin levels were significantly suppressed in the lateral hypothalamus after CCI compared to sham surgical controls ($p<0.05$, t-test). Similarly, EEG/EMG analysis showed significantly less time spent awake during the dark phase (when mice are typically more awake) after CCI ($p<0.05$, t-test). Brain ISF orexin levels and amount of wakefulness were significantly correlated across all mice tested (r = 0.67, $p<0.05$). Immunostaining for orexin peptide revealed, surprisingly, a significant increase in the number of orexin-positive cells in the lateral hypothalamus of mice after TBI ($p<0.05$, t-test), but no significant difference in melanin-concentrating hormone (MCH)-immunoreactivity ($p>0.05$).

Conclusion: We developed a mouse model of traumatic brain injury that, despite preservation of orexin neuron numbers, causes suppression of orexin levels in the brain. Mice in the TBI group showed decreased wakefulness that correlated with lower brain ISF orexin levels. Future studies should test whether orexin-based therapeutics could improve clinical outcomes such as excessive sleepiness following TBI.

0103

DESYNCHRONIZATION OF SENSORIMOTOR AND DEFAULT-MODE NETWORKS DURING FIRST SLEEP CYCLE

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Introduction: Researches using positron emission tomography and electroencephalography (EEG) have shown dissociated patterns of brain activity during rapid eye movement (REM) sleep. Integrations between brain areas were also proven shifted during slow wave sleep (SWS) in self-consciousness-related default-mode network (DMN). Hence we tested that functional dissociations may occur in other brain networks over complete sleep cycle. In the study, the sensorimotor network and DMN were evaluated through the first sleep cycle with functional magnetic resonance imaging.

Methods: Twenty healthy male volunteers (age: 24.2±4.5 years) participated in this study. The experiments were conducted between 11 pm to 4 am. Functional data were acquired by 3T MR scanner with a 32-channel MR-compatible EEG system. During sleep scan, participants were instructed to fall into sleep until alarms of button-presses showing wake-up or desire to leave, or until the maximum interval of 125 min. Two extra 6-min resting scans were placed before and after the sleep scan on each participant. Data were polysomnographically defined uninterrupted sleep stages and underwent functional connectivity analysis with seeds located in left primary motor cortex and center of posterior cingulate cortex.

Results: Ten out of twenty participants are confirmed to have sufficient SWS and two participants show REM sleep. Connectivity maps and strengths significantly and consistently decrease with the depth of sleep

in the sensorimotor network. However, in DMN, the only significant decreased connectivity is found between PCC and medial prefrontal cortex from stage two to SWS. In contrast, REM sleep reactivates the functional connectivity in both networks as regarded as in the awake condition. Comparing the post-sleep resting scans with pre-sleep, the dissociations are observed in sensorimotor network when wake-up, but spatial reconsolidation in DMN appears to be an after-sleep effect.

Conclusion: Significant reduction of functional connectivity was found in both networks during sleep, which may be associated with the fading consciousness in sleep. The breakdown of functional connectivity may be a common feature representing the rejuvenation effect of sleep. Reconsolidation of DMN and remained dissociation of sensorimotor network might indicate the full recovery of self-consciousness but ongoing integrity of disrupted somato-sensations. Such phenomenon merit future investigations for discovering brain functions during sleep.

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0104

INTERACTIONS BETWEEN CORE AND MATRIX THALAMOCORTICAL PROJECTIONS IN HUMAN SLEEP SPINDLE SYNCHRONIZATION

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Introduction: Human sleep spindles are highly synchronous across the scalp when measured with EEG channels, but not when measured simultaneously with MEG sensors which exhibit low correlation and low coherence with each other and with EEG signals. In this study, we used a computational model to explore the hypothesis that interactions between the core and matrix thalamocortical subsystems were responsible for the complex spatiotemporal patterns of spindle synchronization observed experimentally.

Methods: To adequately investigate our hypothesis in light of the human experimental data mentioned above, we constructed a realistic four-layer model of the thalamus and the cortex, comprising two main distinct but interconnected thalamocortical pathways known from the primate literature: (i) core pathway, which has thalamic afferents in the middle layers of the cortex, mostly layers III and IV, and (ii) matrix pathway, which has thalamic afferents to superficial layers of the cortex, mostly layer I.

Results: We found that the relative synchrony of spindle oscillations between core and matrix networks depends on the pattern of intracortical connections between the networks. Increasing the fanout of thalamocortical connectivity in the matrix system while keeping it constant in the core system led to increased synchrony of the spindle activity in the matrix system. In constrast, increasing the cortico-thalamic fanout or cortico-cortical connectivity between matrix and core systems had no effect on spindle synchrony. Conversely, the latency for spindles to spread from the core to matrix subsystem was independent of thalamocortical fanout, but highly dependent on the probability of connections between the systems.

Conclusion: Our results suggests that the known anatomical differences between matrix and core subsystems in thalamocortical fanout may be necessary and sufficient to produce different levels of synchrony of spindle discharges between different cortical locations. These differ-

ences may explain the discrepancies between spindles simultaneously recorded by EEG versus MEG.

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0105

CORTICOTHALAMIC FEEDBACK CONTROLS SLEEP SPINDLE DURATION IN VIVO

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Introduction: Evidence from slice experiments and modeling studies has supported a mechanism for spindle termination mediated by upregulation of the hyperpolarization activated depolarizing current (Ih), which is dependent on intracellular Ca2+ concentration. In the present study using a combination of in vivo and modeling experiments, we provide, for the first time, compelling evidence that the cortical feedback plays an active role in terminating spindle oscillations by desynchronizing thalamocortical neurons, effectively controlling the duration of spindles.

Methods: Electrophysiological experiments were conducted in cats (n=5) under general anesthesia. Juxtacellular recordings were performed from motor and somatosensory areas of the cortex. Simultaneous dual intracellular recordings in parallel with local field potential recordings from cortical (motor cortex) and thalamic (VL nucleus) areas were carried out to assess the temporal relationships between thalamic and cortical activities during spindles. A biologically plausible neuronal network model of the thalamocortical loop was constructed to investigate the relative contribution of thalamic and cortical factors in spindle termination. Thalamocortical and thalamic reticular neurons were modeled along with the cortical pyramidal neurons and inhibitory interneurons. Each neuron consisted of a dendritic and an axosomatic compartments, and was embedded with specific ion channels all following Hodgkin-Huxley kinetics. Synaptic connections were represented by AMPA-, NMDA-, GABAa-, and GABAb-type of receptors. The spatial patterns of synaptic afferents and efferents were stochastically distributed as observed biologically.

Results: Desynchronization of firing between thalamic and cortical neurons was found to be a primary mechanism for spindle termination complimented by h-current upregulation. It leads to cortical spiking after rebound burst in the thalamus, which prevents T-channels de-inactivation and promotes spindle termination.

Conclusion: The cortical feedback actively influences the termination of sleep spindles in vivo. The cortex can control the duration of spindles, in contrast to the view that sleep spindles are purely controlled by intrinsic thalamic properties.

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0106

THE HUMAN BRAIN'S RESPONSE TO AUDITORY STIMULATION VARIES WITH THE PHASE OF SUB-1HZ OSCILLATION IN NON-REM SLEEP

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Introduction: During non-REM sleep, the brain oscillates at a frequency < 1Hz. Alternating up and down states of these slow wave oscillations correspond to depolarization and hyperpolarization of neurons and

to positive and negative fluctuations in surface electroencephalogram (EEG) amplitude, respectively. Does the human brain's *a priori* (up/down) state affect its responsiveness to auditory stimuli in sleep stage 2 (S2) and slow-wave sleep (SWS)?

Methods: We presented binaural pure tones (1 kHz) of suprathreshold intensities to 12 sleeping participants. Tones were played at an interval of 3000±200ms throughout the course of the ~2-2.5 hour recording. Normal subjects fell asleep while their brain activity and polysomnography data were recorded and scored off-line. All analysis on up versus down states used EEG data recorded from a single electrode placed at the center of the scalp (Cz). Raw single-trial data from each participant were fitted with a weighted sum of three low-frequency complex exponentials. The phase of the resultant fitted vector at stimulus onset was thresholded to yield up and down state trials (remaining trials were discarded). (A) We measured the mean amplitudes of the mid-latency P200 (P200-N100) and N300 (N300-P200) components of the AEP during up and down states separately for each participant in S2 and SWS (B) We compared the capability of the brain to detect a stimulus in the up versus down states. Single-trial (600 ms pre- → 600 ms post-stimulus) data were equally split into training and test sets for this purpose. A support vector machine pattern classifier was first trained to distinguish pre- from post-stimulus single-trial data, and then tested.

Results: (A) Mean P200 peak amplitudes were greater in the down state than in the up state in both S2 (3.3 μV vs. 2.5 μV, P = .021) and SWS (4.5 μV vs. 2.7 μV, P = .030). N300 amplitudes did not differ between states. (B) Classifier detection performance and specificity were superior in the down state in S2 (down: d' = .44, specificity = .71 ; up: d' = .36, specificity = .64) and in SWS (down: d' = .43, specificity = .68 ; up: d' = .28, specificity = .58), whereas sensitivity was slightly better in the up state in S2 (down: .55; up: .57) and in SWS (down: .56; up: .58).

Conclusion: The sleeping brain's responsiveness to auditory stimulation is modulated by the phase of the slow wave oscillation. These brain state-induced vagaries of information processing could limit the sleeping brain's ability to process information.

0107

EFFECT OF SLEEP RESTRICTION ON WHOLE BODY ENERGY EXPENDITURE IN HUMANS

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Introduction: Short sleep duration is believed to increase risk of overweight and obesity. One hypothesized mechanism underlying this association is a reduction in 24h energy expenditure (EE), contributing to a state of positive energy balance. Previous findings from our laboratory, however, indicate that one night of total sleep deprivation increased 24h EE measured in a whole room calorimeter. Therefore, we tested the hypothesis that 5 days of sleep restriction, simulating a work week, increases whole body 24h EE as compared to a 9h sleep opportunity condition.

Methods: Eight healthy (4 females), lean (BMI = 22.7 ± 1.3 kg/m2) adults (24.8 ± 9.1 yrs) completed an inpatient protocol consisting of 3 baseline days (9h sleep/night), followed by two sleep opportunity conditions (5h or 9h/night, 5 days each) performed in a cross-over design. 24 h EE was measured at baseline (day 3) and at the end of each sleep condition using a whole-room indirect calorimeter.

Results: Findings from this ongoing study support our hypothesis that sleep restriction increases energy expenditure. Specifically, 24h EE was significantly higher in the 5h than in the 9h condition (118 ± 39.9 kcal/day, $p<0.05$).

Conclusion: Contrary to current models of the impact of sleep loss on overweight and obesity, these data indicate that in healthy lean adults 24h EE is increased rather than decreased during sleep restriction. Thus, other mechanisms besides a decrease in whole body 24h EE likely contribute to risk of overweight and obesity associated with sleep restriction.

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0108

ASSOCIATIONS BETWEEN PHYSICAL ACTIVITY AND SLEEP

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Introduction: Several epidemiological studies have suggested an association between self-reported physical activity levels and subjective sleep measures. Conversely, interventional studies using acute physical training have provided inconsistent results. To our knowledge, the possible association between habitual physical activity levels and sleep-wake patterns has not been assessed with objective measures. The current study aimed to assess this association with ambulatory instruments and to identify whether polysomnographic (PSG) sleep variables correlate with physical activity levels.

Methods: Twelve young healthy adults underwent 5 to 9 days and nights of continuous actigraphy monitoring, wearing two actimeters simultaneously to measure active energy expenditure (EE) during the main wake episode and rest efficiency during nocturnal rest episode. A second sample of twelve young adults wore an EE monitor for 7 days before a PSG recording night. Activity counts recorded by the EE monitors were processed with a validated algorithm that takes into account each subject's height and weight. Two-tailed Pearson correlations were conducted between EE and ambulatory/PSG sleep variables.

Results: EE in the vigorous activity class ($r=0.64$, $p=0.03$) and the time spent in the vigorous activity class ($r=0.67$, $p=0.02$) correlated significantly with rest efficiency measured with ambulatory sleep monitoring. PSG data confirmed that EE expenditure during vigorous activity was associated with better sleep efficiency ($r=0.74$, $p=0.01$). Moreover, total EE correlated positively with %SWS ($r=0.70$, $p=0.05$).

Conclusion: These objective measures indicate that ambulatory physical activity levels during the day are associated with deeper and more consolidated sleep during the night. Compared to acute interventions, habitual physical activity patterns integrated over long periods may facilitate sleep promotion mechanisms. This provides empiric data for the therapeutic use of physical activity to improve sleep.

0109

LACTATE ACTS AS A PRIMARY ENERGY SOURCE FOR NEURONAL ACTIVITY DURING WAKING AND REM SLEEP

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Introduction: Magistretti's Astrocyte Neuron Lactate Shuttle Hypothesis (ANLSH) proposes that, in addition to glucose, neurons rely on astrocyte-derived lactate as their primary energy source. Whereas previous studies have demonstrated elevated lactate during waking, this experiment utilized biosensor technology to simultaneously record both lactate and glucose at one second intervals along with electroencephalograph (EEG) activity during a 24 h period.

Methods: Under anesthesia, C57Bl6 mice (n=6) were implanted with cortical EEG and electromyograph (EMG) recording electrodes along with bilateral guide cannulas in the prefrontal cortex region. After recovery from surgery mice were connected to a lightweight tether and placed in the recording chamber. Biosensors for glucose and lactate were inserted into separate guide cannulas. Simultaneous EEG, EMG and biosensor data was recorded for a 24 h period under LD 12:12. Sleep recordings were evaluated using a combination of cluster scoring algorithms and hand-scoring. Biosensors were post-calibrated according to standard protocols.

Results: Changes in extracellular lactate concentration increased immediately upon waking, plateauing at 123.5 ± 33.8 μM within 15 minutes ($P<0.05$). Levels remained elevated throughout the entire waking episode ($R2 = 0.998$, $P<0.001$), then declined steeply at sleep onset, resulting in a maximal change of -145.7 ± 43.8 μM ($P<0.05$) within 10 minutes. Conversely, glucose concentration upon waking initially declined by a delta of 82.1 ± 10.2 μM ($P<0.05$) within seven minutes before recovering. During sleep, glucose concentration change exhibited an initial surge, peaking at a maximum delta of 109.2 ± 19.4 μM ($P<0.05$) within 10 minutes then declined before REM onset and remained steady throughout additional slow-wave-sleep periods. REM sleep periods were similar to waking with lower concentration changes.

Conclusion: This is the first, comprehensive study of extracellular lactate and glucose over multiple sleep/wake cycles. These data strongly support the ANLSH, demonstrating lactate as a primary energy source fueling increased neuronal activity during waking and REM.

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0110

TITLE: SLEEP RESTRICTION IN RATS UPREGULATES THE EXPRESSION OF STRIATAL OPIOID PEPTIDE GENES INVOLVED IN FOOD REWARD: COMPARISON TO EFFECTS ON FEEDING-RELATED HYPOTHALAMIC PEPTIDE GENES

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Introduction: Chronic sleep restriction (SR) in rodents markedly upregulates daily food intake and produces weight loss; the neural mechanisms underlying these effects are unknown. We aimed to compare the effects of SR on the expression of striatal opioid peptide genes, thought to regulate reward-driven, "non-homeostatic" feeding, to effects on the expression of the hypothalamic peptides NPY, POMC, HCRT, and MCH. These peptides are thought to be involved in "homeostatic" feeding, and, in the case of HCRT, arousal.

Methods: Male Sprague-Dawley rats were subjected to 70% SR using the Conveyer-Over-Water (COW) apparatus, in which behavioral state is inferred from motion detection and a conveyer belt triggered when the animal falls asleep. The following control groups were used: unmanipulated home cage controls, food-deprived controls, and apparatus controls kept in the COWs but receiving conveyer belt motion only when awake. After chronic SR, rats were sacrificed, trunk blood obtained for the analysis of insulin, leptin, and ghrelin, and brains harvested for in situ hybridization.

Results: Sleep restriction markedly upregulated striatal enkephalin mRNA; none of the control groups showed this effect. NPY expression in the hypothalamic arcuate nucleus was upregulated in both the sleep- and food-deprived groups. Analysis of POMC, HCRT, and MCH gene expression is ongoing. Finally, sleep restriction suppressed plasma insulin and leptin.

Conclusion: SR markedly upregulated striatal expression of enkephalin, which mediates binge-like feeding especially upon palatable foods. In contrast, hypothalamic NPY was affected by both sleep- and food-restriction. Possibly, hypothalamic changes reflect weight loss-induced alterations in circulating hormones (particularly leptin). The striatal changes, on the other hand, may result from paracrine factors directly related to sleep homeostasis. The present findings reveal a novel neural pathway through which sleep deprivation may affect changes not only in food reward, but also drug-seeking, reward learning, and other motivational functions mediated by the striatum.

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0111

CHANGES IN INSULIN SECRETION AND SENSITIVITY RELATED TO HABITUAL SLEEP CURTAILMENT IN YOUNG ADULTS WITH PARENTAL HISTORY OF TYPE-2 DIABETES

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Introduction: Short sleep is associated with increased risk of type-2 diabetes, possibly related to chronic changes in insulin secretion and action. We examined whether habitual sleep curtailment is accompanied by alterations in insulin resistance and pancreatic beta-cell function in healthy young adults with increased risk of type-2 diabetes due to positive parental history for the disease.

Methods: Thirty one (19F/12M) consecutively enrolled non-obese participants with parental history of type-2 diabetes (mean [SD] age 26 [4] y, BMI 24 [2] kg/m2) completed a 75-g oral glucose tolerance test, overnight laboratory polysomnography, and 2 weeks of home sleep and physical activity monitoring by wrist and waist actigraphy. We used analysis of covariance (SPSS 17.0) to compare OGTT-based indices of glucose tolerance, beta-cell function and insulin resistance, while controlling for differences in everyday physical activity between usual (average sleep time 377 min/day; range 358-461; N=17) and short sleepers (average sleep 305 min/day; range 231-342; N=14).

Results: Both sleep groups were matched by age, gender and BMI, and had similar quantity and quality of sleep during laboratory polysomnography. Short sleepers had less total daily body movement and time spent in moderate plus vigorous physical activity (P<0.01). When differences in daily physical activity were controlled for, short sleepers had significantly higher insulin resistance (HOMA-IR and insulin sensitivity index, ISI; P<0.05). This was accompanied by measures of increased beta-cell function (HOMA-B and insulinogenic index, IGI; P<0.02), but comparable fasting and 2-h glucose concentrations (P=NS) compared to the subjects in the usual sleep group.

Conclusion: Objectively documented sleep curtailment in healthy young adults with parental history of type-2 diabetes is accompanied by undesirable changes in behavioral and metabolic mediators of diabetes pathogenesis, including reduced physical activity and systemic insulin resistance with compensatory hyperinsulinemia, which may further increase their pre-existing risk of developing the disease.

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0112

EFFECTS OF ACUTE SLEEP RESTRICTION AND WAKE TIME ON THE AWAKENING CORTISOL RESPONSE (ACR) IN YOUNG CHILDREN

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Introduction: The ACR is presumed critically important for healthy adaptation. Abnormal ACRs in adults have been associated with a variety health variables. Little is known about the ACR in children, including its typical characteristics and correlates. This is partly due to the number of challenges surrounding accurate measurement of the ACR. For this reason, we assessed the ACR under experimental conditions. The aims of this study were to examine whether robust ACRs exist in young children, as well as to determine the effects of acute sleep restriction and wake timing on the ACR.

Methods: Data were collected from 7 children (5 female), 2 to 4 years. Polysomnographic (PSG) recordings occurred after 4 hrs (morning nap), 7 hrs (afternoon nap), 10 hrs (evening nap), 13 hrs (Baseline night), and 16 hrs (Sleep Restriction night) of wakefulness. Salivary cortisol was collected at 4 points after each sleep period: 0 (wake time), 15, 30, and 45 minutes after wake time. Accuracy of wake saliva sampling was confirmed by comparing PSG-assessed wake time with actual sampling time. Dynamic (increase) of the ACR was computed using area under the curve (AUC) with respect to the increase and % change. Overall cortisol production post wake was calculated using AUC with respect to ground.

Results: On average, cortisol rose 50% (.18 ug/dl)from wake to 15/30 minutes and declined thereafter. Overall cortisol activity (AUCg) was higher after the Baseline than the Sleep Restriction night (d=.72). Cortisol at wake time (0) was lower after Sleep Restriction than after the Baseline night (.25 vs .37 +/-.13 ug/dl). Both overall cortisol activity (AUCg) and the dynamic of the response (AUCi) differed depending on wake time (η2=.85 and .50). Overall cortisol activity was greater after nocturnal sleep than after a morning (p<.05), afternoon (p<.05), or evening nap (p<.01). The dynamic of the response (AUGi) was more robust after the morning than after the evening nap (p<.01).

Conclusion: A profound ACR was observed in this sample of children with effect sizes similar to that found in adults. After only one night of sleep restriction, evidence of a blunted ACR was apparent. These data warrant further investigation into the cognitive, emotional, and behavioral correlates of a blunted ACR. Striking ACRs following morning and afternoon naps and a flattened ACR after an evening nap indicate short sleep periods are sufficient to produce ACRs when the timing of wake does not coincide with the circadian cortisol nadir.

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0113

SLOW WAVE SLEEP, BUT NOT INSOMNIA, IS ASSOCIATED WITH DIMINISHED ANTIBODY RESPONSE TO A HEPATITIS B VACCINE

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Introduction: Despite its prevalence and associated morbidities, the pathophysiology by which insomnia confers morbidity risk is relatively unstudied. With respect to medical morbidity, diminished immunocompetence is one possible pathway. The current study was conducted to investigate whether 1) insomnia, compared to good sleep, or 2) any specific objective sleep measure was associated with a diminished immune response to a vaccine challenge.

Methods: The study enrolled 28 pre-menopausal female subjects aged 25-50 with either Psychophysiologic Insomnia (PI) or Good Sleep (GS) into a parallel two-group design; 19 subjects (8 PI and 11 GS) completed the study. Following two consecutive nights of polysomnography (PSG), subjects received a 3-part Hepatitis B (Hep B) vaccine regimen at 0, 1, and 2 months post-PSG. Blood was obtained at 0, 1, 2, and 3 months, centrifuged and stored at -80°C. Serum samples were subsequently tested by radioimmunoassay to detect titer levels of antibodies to Hepatitis B surface antigen. Protective titer levels (seroconversion) are defined as >10 mIU/mL.

Results: Seroconversion rates did not differ by group. The groups did differ, in the opposite direction than expected, on antibody titer levels. Namely, the PI group had significantly higher titer levels than the GS group across the three time points (p< .05 in a mixed model). Among PSG measures, Slow Wave Sleep (SWS) minutes were higher in subjects who seroconverted compared to those not achieving protective levels (p=.03). No other PSG measure differentiated sero-conversion status. Amount of SWS was also positively correlated with titer levels (r=.724; p=.002 for titer 2 and r=.556; p=.025 for titer 3). Notably, neither age nor depression severity (which was minimal in most cases) was related to seroconversion rates or to titer levels, making the findings with respect to SWS intriguing.

Conclusion: These findings suggest that SWS may serve a protective function with respect to immunogenicity. This is consonant with findings from a nascent literature suggesting that diminished SWS is associated with elevated levels of proinflammatory cytokines, another marker of immune function. In addition, since decrements in the SWS of subjects with insomnia compared to good sleepers have been observed in some investigations, but not others, this may 1) further explain why insomnia status may not be as good a predictor of immune response as amount of SWS, and 2) underscore the importance of SWS as a therapeutic target.

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0114

SLEEP DEPRIVATION AND INFLAMMATION IN A MURINE MODEL

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Introduction: In rodent experimental models of sleep deprivation, shortening sleep duration has resulted in elevation of pro-inflammatory cytokines, but has involved increased physical activity which may have been responsible for the pro-inflammatory effects. A recently validated method of sleep deprivation can produce gentle movement of mice by a timed orbital shaker without increased physical activity and would allow the study of the relationship between sleep deprivation and inflammation without the confounding influence of physical activity. We set out to study the effects of chronic sleep deprivation (21 days) on inflammation in a murine model of sleep deprivation without the confounding influence of increments in physical activity.

Methods: Thirty-three mice (C57Bl/6; JAX, Bar Harbor, ME) were subjected to either chronic sleep deprivation (n=16) or control condition (n=17), but blood obtained through cardiac puncture was available in only 22 animals (11 controls, and 11 sleep deprived). Sleep deprivation was achieved by placing the mice in cages on orbital shakers that were gently activated by timers during the light cycle for 19 days and followed by activation over 24 hours/day for 2 days.

Results: Interleukin-6 level was greater in the sleep deprived group (median of 15.6; IQR, 9.2, 22.8) than in control group (4.7, IQR, 4.7, 6.9; P=0.038). Similarly, IL-2 level was greater in the sleep deprived group (median 52; IR, 32, 272) than in control group (16.1; IQR, 12.1, 16.1; P=0.049). Also, IL-4 levels were greater in the sleep deprived group (median of 133.8; IQR, 113, 228) than in control group (100.0, IQR, 88.6, 100.0; P=0.046). Whereas, IL-17a level tended to be greater in the sleep deprived group (median of 0.02; IQR, 0.01, 0.1) than in control group (0.007, IQR, 0.005, 0.008; P=0.05). But, Macrophage colony stimulating factor was lower in the sleep deprived group (median of 3.0; IQR, 2.4, 3.9) than in control group (5.0, IQR, 3.8, 15.8; P=0.033). Also, Growth regulated alpha-protein level was lower in the sleep deprived group (median 0.07; IQR, 0.02, 0.09) than in control group (median 0.16; IQR, 0.07, 0.28; P=0.014). Moreover, IL-1β, IL-7, IL-10, and IL-11 levels were not different between the two groups.

Conclusion: In this exploratory study, chronic sleep deprivation -- without the confounding influence of increments in physical activity -- was associated with a pro-inflammatory state.

Support (If Any): Johrei Foundation

0115

EFFECTS OF NEUROMODULATORY SUBSTANCES ON THE ACTIVITY OF SLEEP-ACTIVE CORTICAL NEURONS

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Introduction: Recently, we described a sleep-active neuronal population in the cerebral cortex. These cells express NPY, nNOS and the NK1 receptor. Substance P (SP) promoted wakefulness when injected ICV in rats (Andersen et al. 2006) or IV in humans (Lieb at al. 2002), while microinjections in the ventrolateral preoptic area promoted sleep (Zhang et al. 2004). To test the hypothesis that SP can modulate the activity of cortical sleep-active neurons, we performed in vitro patch clamp recordings of putative sleep active neurons while delivering SP as well as other compounds to the bath.

Methods: Patch clamp recordings were performed in cortical slices of transgenic Npy-hrGFP mice. Putative sleep-active neurons were identified as large green fluorescent neurons located in cortical layers 5 and 6. The effect of SP (150 nM), ACh (0.1 mM), 5-HT (0.5 mM) and other

compounds was measured with and without TTX (1 μM). To identify the recorded neurons, 0.4% biocytin was included in the internal solution. Inmunohistochemistry was performed after fixation of the slice in 4% PFA to obtain a triple labeling of nNOS, NPY and the recorded neuron.

Results: Our preliminary results indicate that ACh depolarizes NPY-GFP neurons by 4-13 mV while 5-HT did not affect this neuronal population. A small percentage of the NPY cells responded to SP in the presence and absence of TTX. Intriguingly, the response of different cells was either a depolarization or a hyperpolarization of 5-10 mV. Triple labeling showed that most of the SP-responsive cells are type-I nNOS neurons, suggesting that SP can effectively modulate the activity of these sleep-active cells.

Conclusion: SP can modulate the activity of type-I cortical nNOS neurons. The observation of both depolarizing and hyperpolarizing responses to Substance P by cortical NPY neurons reveals that the role of SP is complex, probably involving different transduction pathways.

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0116

MICE WITH THE HUMAN INTERLEUKIN-37 TRANSGENE SLEEP LESS AFTER SLEEP DEPRIVATION

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Introduction: Interleukin-37b (IL37) functions to suppress innate immune and inflammatory responses by inhibition of many pro-inflammatory molecules such as IL1, IL6, and tumor necrosis factor. These cytokines are involved in sleep responses to sleep deprivation (SD) and pathological conditions such as infection, insomnia and sleep apnea. Normal mice do not express functional IL37. We determined how mice transgenic for human IL37 responded to sleep loss.

Methods: Electroencephalogram (EEG) and electromyogram electrodes were provided to mice that were transgenic for IL37 (IL37tg) and to C57BL/6 wild-type controls. Spontaneous sleep and sleep responses to 6 h of SD by gentle handling were assessed. Non-rapid eye movement sleep (NREMS), rapid eye movement sleep (REMS) and waking activity and EEG power spectral analyses were determined.

Results: In both strains of mice, duration of spontaneous NREMS and REMS and NREMS EEG slow wave activity (SWA) had a significant diurnal rhythm with enhanced sleep during the light period compared to the dark period. These parameters were not significantly different in IL37tg mice compared to wild-types. NREMS was significantly enhanced during the first 2 hours following SD in wild type mice (P = 0.035). REMS was enhanced during the first 6 h post-SD (P = 0.034) in wild-type mice. In contrast, IL37tg mice slept significantly less in the 12 h after SD (P = 0.031). IL37tg mice did not demonstrate any significant differences in REMS after SD compared to spontaneous levels. NREMS EEG SWA was enhanced in both IL37tg and wild-type mice after SD, however, the IL37tg mice NREMS EEG SWA response was significantly blunted compared to wild-type mice.

Conclusion: IL37 attenuates SD-induces sleep responses to sleep deprivation thereby suggesting that pro-inflammatory cytokines are responsible for the excess sleep following sleep loss.

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0117

MENIN-DEPENDENT PI3K/AKT SIGNALING REGULATES HYPOCRETINS AND INCRETINS

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Introduction: Menin is the 67kDa product of the MEN1 gene with germ-line mutations responsible for an autosomal-dominant cancer syndrome, and expressed ubiquitously. Hypocretins and incretins, expressed in the brain and gut are appetite-stimulating peptides modulated by hypoglycemia and oral food intake. This study identifies cells expressing menin specifically in the brain and gastrointestinal tract, and describes the regulation of hypocretin and incretin by menin.

Methods: We subjected C57BL/6 (wild type) and diabetic mice to a 24hr fast followed by 4hr and 7hr re-feeding. Mice were also fed a high-fat or high fat high carbohydrate diet for 3 months and tissues collected for mRNA expression analyzed by RT-PCR. Immunofluorescence was used for co-localization assays. Expression and secretion of peptides after menin siRNA and exposure to LY296004 or UO123 were determined using ELISA. Promoter activity was analyzed by dual-luciferase assay and protein expression by western blot analysis.

Results: We demonstrate that menin is expressed in K cells of the gut and specific regions of the hypothalamus, and that fasting and re-feeding or chronic high fat diet modulated menin levels, which inversely correlated with changes in hypocretin and incretin levels. Menin negatively regulated hypocretin and incretin expression and mediated PI3K/AKT regulation of these peptides. The MAP kinase inhibitor, UO123, inhibited the expression of hypocretin and incretin independent of menin.

Conclusion: Menin is an anti-incretin, anti-hypocretin factor modulated by feeding and high fat diet via PI3K/AKT signaling.

0118

SLEEP DEPRIVATION-DEPENDENT DIFFERENTIAL REGULATION OF ATP LEVELS IN RAT HYPOTHALAMUS

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Introduction: The ATP levels surge during sleep while sleep deprivation (SD) prevents this surge in wake-, but not in sleep-associated areas of rat brain. This led us to hypothesize that different functions dictate differential energy utilization. The feeling of hunger and feeding, a wake-state-dependent behavior, is regulated by specific centers within hypothalamus. While paraventricular nucleus (PVN), arcuate nucleus (ARC), and dorso- and ventro-medial hypothalamus (DMH/VMH) regulate feeding, the lateral hypothalamus (LH) is associated both with feeding and wake/REM regulation. In order to examine the effect of waking/feeding and sleep/no feeding, on regional regulation of ATP levels, we measured ATP in PVN, ARC/DMH/VMH, and LH with and without SD.

Methods: In rats the food intake and body weight was measured during the 24h light-dark cycle and during 6h of SD performed by gentle handling. Tissue samples from the PVN, ARC/DMH/VMH, and LH were collected after 6hSD and from time-matched diurnal controls. ATP was measured by luciferin-luciferase bioluminescence assay.

Results: Across the 24 h light-dark period rats consumed approximately 28.13 ± 4.48 g of food and gained 5.22 ± 1.65g with positive correlation ($n = 10$; $r = 0.879$, $P < 0.001$) between food intake and body weight. During SD, while food intake increased significantly $+ 147.31 \pm 6.13\%$ ($n=5$/group; $P < 0.008$), they lost weight significantly ($-93.29 \pm 13.64\%$; $P = 0.017$) when compared to sleeping controls. SD resulted in significant decrease in ATP levels only in LH ($-44.60 \pm 21.13\%$; $P = 0.041$) with no change in PVN, ARC/DMH/VMH region ($p=0.953$) when compared with undisturbed controls.

Conclusion: Our data confirm the previous report by Rechtschaffen and Bergmann (1995) that despite hyperphagia rats lose weight during SD. That the SD-induced decrease in ATP concentration was limited to feeding but wake active LH, suggest function dependent differential regulation of ATP in brain regions.

Support (If Any): VA Merit Award (RB), Deutsche Forschungsgemeinschaft Fellowship (MD), NIMH Grant MH 39683 (RWM)

0119

PROTEIN-ID AND CHANGED PROTEIN LEVELS BY PROTEOMICS IN HUMAN BLOOD SERUM AFTER SLEEP DEPRIVATION

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Introduction: Sleep deprivation (SD) might lead to cell stress and may lead to changes in different types of cellular stress-related proteins and cellular pathways.

Methods: Humans (n=6-8) subjected to 3 or 6 hours of SD and blood were sampled before, during and after the SD-night at the same time points (16 time points during 48 h). Seldi-Tof-MS, Maldi-Tof-MS and an Hsp70 ELISA-kit were used to detect changes in the human blood serum proteome. Protein profile changes after SD were searched for by changed information gain in the m/z spectrum in the mass spectrometry data by principal component analysis software program.

Results: A protein of 71 kDa was decreased in the blood (serum) 0h, 3h and 9h after 3h SD. Similarly Hsp-70 with molecular weight around 70 kDa was also reduced 0h, 3h and 9h after 3h SD by the Stressgen-kit measurement. The protein profile from the Seldi-Tof-MS (2.5 - 100 kDa, n=3) measurements also showed changed expression for several proteins. Proteins highly expressed after 5 h of SD seems to be reduced and still decreased the day and night after SD respectively. Similarly, proteins expressed at a lower level after 5 h of SD seems to be increased and thereafter reduced the day and night after SD respectively. The protein profile from the Maldi-Tof-MS (0.4 - 15 kDa, n=7) also showed changed expression for several proteins. Several proteins (2.5 - 100 kDa) where differentially expressed after 3 and 6 hours of SD, specifically Hsp-70 was reduced after 3 hours of SD. One of several changed proteins were identified as Inter-alpha-trypsin-inhibitor-family heavy-chain-related protein and verified by Q-Tof-MS of the synthesised protein and have been explored together with the change in Hsp-70 with the curated database MetaCore by GeneGo (www.genego.com). The decrease of many proteins as Hsp-70 in the blood during sleep restriction is in line with what has been observed in obstructive sleep apnoeas.

Conclusion: SD might lead to cell stress. This seems to be reflected in changed protein profile in human serum. So far one of these peptides are identified and the functions ranges from stabilization of extracellular matrix, inhibition of actin polymerisation, cancer biomarker to inhibition of chemotaxis and hence the phagocytosis of PMN cells and acute phase and especially IL-6. To be able to ID changed proteins and their interactions after SD might shed light on the cellular mechanisms and cellular pathways important regarding the function of sleep.

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0120

BRAIN RESIDENT MAST CELLS AFFECT SLEEP/WAKE PHYSIOLOGY AND PHARMACOLOGY

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Introduction: Brain resident mast cells may affect sleep in some physiological and pathological conditions, since mast cells contains various chemical mediators that significantly influence sleep, such as histamine, cytokines, and prostaglandin D2. Strikingly, up to 40% of histamine contents in the brain are from brain mast cells, and brain mast cells are constitutively active. Therefore, manipulations enhancing mast cell activation likely affect sleep and other behaviors. In the current study, we examined the role of brain mast cells, especially focusing on the histaminergic system, using mast cell deficient mice and various physiological and pharmacological manipulations.

Methods: Male mast cell deficient (KitW/W-v) mice (DEF) and their wild-type littermates (WT) were used in this study. Sleep, body temperature and locomotor activities were recorded in mice fed ad lib at baseline, with 6-hour sleep deprivation (SD) and fasting for 24-48 hrs starting at dark-phase onset. In order to evaluate if mast cell derived histamine is involved in sleep/wake regulation, we have evaluated the sleep after administrations of compound 48/80 (icv), a histamine releaser from mast cells and two selective H1 receptor antagonists (mepyramine, triprolidine) in DEF and WT mice.

Results: Sleep changes in DEF mice at the baseline were subtle, though DEF mice showed an increased the amount of wake and decreased slow wave sleep (SWS), associated with increased EEG delta power, compared with WT mice. Compound 48/80 significantly increased the amount of wake in WT mice, while it had no effect in DEF mice. H1 antagonist triprolidine and mepyramine significantly increased the amounts of SWS in WT mice, but these effects were attenuated in DEF mice. WT mice fasted for 24 hrs showed a significant increase in the amounts of wake and locomotor activity in the dark period. Most strikingly, these increases were completely attenuated in DEF mice. The 6 hour SD produced only minor differences between the genotypes.

Conclusion: Our results suggest that non-neuronal histamine from brain mast cells are likely wake-promoting, and the sleep inducing effects of H1 antagonists may partially be mediated with blockades of this mechanism. In addition, brain mast cells may more specifically be involved in the regulation of enhanced wakefulness and exploring activity during food deprivation. Further studies on the roles of brain mast cells on sleep/wake in health and diseases are warranted.

0121

GENDER DIFFERENCES ON SLEEP PATTERN OF RATS IN AN EXPERIMENTAL MODEL OF OSTEOARTHRITIS

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Introduction: Osteoarthritis (OA) is a major healthcare burden with increasing incidence, characterized by degeneration of articular cartilage and it is associated with chronic pain and sleep disturbance. The current study examined the long-term effect of chronic articular pain on sleep patterns in an experimental model of OA in female compared to male rats.

Methods: Rats were implanted with electrodes for electrocorticography and electromyography and assigned in control, sham or OA groups. OA was induced by the intra-articular administration of (2mg) monosodium iodoacetate into the left knee joint in male and female (at estrus and diestrus phases) rats. Sleep was monitored at days 1, 10, 15, 20 and 28 after iodoacetate injection during light and dark periods.

Results: The results showed that the sleep architecture changed in general in both genders. These alterations occurred in the light and dark period, and began on D1 and persisted until the end of study. OA rats regardless the gender showed a fragmented sleep pattern with reduced sleep efficiency, slow wave sleep, and paradoxical sleep, as well as with fewer paradoxical sleep bouts. However, the males showed lower sleep efficiency and slow wave sleep compared to females in the dark period. Additionally, OA affected the hormonal levels in the male rats, as testosterone levels were reduced compared with the control and sham groups. In female, progesterone and estradiol remained unchanged during the study.

Conclusion: Thus, our results suggest that the chronic model of OA influenced sleep pattern on both genders, however, males appear to be more affected.

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0122

COADJUVANT-INDUCED ARTHRITIS ALTERS THE SLEEP ARCHITECTURE AND IMMUNE PARAMETERS OF PARTIALLY OR TOTALLY HYPOPHYSECTOMIZED LEWIS RATS

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Introduction: Every organism requires adequate communication between the nervous, immune and endocrine systems to ensure proper functioning of the body. When such communication is disrupted, may affects the others two systems, or cause a compensatory changes to maintain the equilibrium. One disease that disrupt all three system is arthritis. Rheumatoid arthritis affects 1% of adult human population; it is a systemic autoimmune disease characterized by chronic inflammation and stiffness of several joints, enhanced pro-inflammatory cytokine levels, pain and anorexia. Clinical reports have found that many rheumathoid arthritis patients present sleep complains such as difficulty falling asleep, poor quality sleep,and sleep fragmentation, however little is known about the mechanism that induces the sleep changes observed in rheumatoid arthritis patients.

Methods: In order to better describe the changes in the sleep-wake cycle architecture and to elucidate the mechanism by which rheumatoid arthritis induces sleep disruption we used an animal model of chronic joint inflammation in the Lewis rat. Fifty male Lewis rats, 300g body weight, were implanted for electroencephalographic and electromiographic recordings. Subjects were randomly assigned to one of five groups: intact animals, anterior hypophysectomy, posterior hypophysectomy, total hypophysectomy and sham-surgery controls (ten subjects each group). Fifteen days post-hypophysectomy a 24-hour polisomnographic record was carried on. Thereafter all subjects were intradermally injected with Freund's adjuvant supplemented with Mycobacterium tuberculous at the base of the tail. Post-immunization polisomnographic recordings were carried on at days 6, 11, and 15, during the maximal immune response. At post-immunization day 16, serum, and spleen samples were obtained to characterize the immune state.

Results: Differences between groups will be presented and also the values obtained in interleukines and corticosterone levels.

Conclusion: The results are still being analyzed, show that the process of rheumatoid arthritis induction, had significant effects on sleep archi-

tecture, when the individual lacks some or all of the pituitary hormone action.

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0123

EVALUATION OF POST-MENOPAUSAL BREAST CANCER SURVIVORS WITH SLEEP DISTURBANCES AND HOT FLASHES

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WITHDRAWN

0124

THE SLEEP-REGULATORY ROLE OF INTERLEUKIN-1 RECEPTOR ACCESSORY PROTEIN B IN MICE

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Introduction: Interleukin-1beta (IL1) has several functions including regulation of sleep, cerebral blood flow and inflammation. The IL1 receptor accessory protein (IL1RAcP) is required for IL1 signaling; a brain specific, alternatively spliced, form of IL1RAcP called AcPb interferes with IL1-IL1RAcP signaling. The goal of this study was to test the hypothesis that AcPb knock-out (KO) mice will sleep more in response to sleep deprivation (SD).

Methods: Male IL1RAcPbKO and C57BL/6 controls were surgically implanted with EEG and EMG electrodes for sleep analysis. Spontaneous sleep and sleep responses following 6 h of SD were analyzed by established criteria. EEG power analyses of non-rapid eye movement sleep (NREMS) epochs were also performed.

Results: In both strains of mice, duration of spontaneous NREMS and REMS exhibited diurnal rhythms with greater amounts of sleep observed in light periods than in dark periods (P < 0.001 for each). NREMS EEG slow wave activity (0.5-4Hz) (SWA) also exhibited a diurnal rhythm during spontaneous sleep (P < 0.001). SD significantly enhanced duration of NREMS and REMS in both strains (P < 0.001 for each). However, there were no significant differences between strains in duration of NREMS or REMS following SD. SD significantly enhanced NREMS EEG SWA during the first two post-SD hours in both strains (P = 0.002). However, NREMS EEG SWA responses to SD were not different in AcPbKO mice compared to controls.

Conclusion: IL1RAcPbKO mice have similar spontaneous sleep and sleep responses to SD as C57BL/6 mice. IL1 is involved in many aspects of sleep regulation, including changes in sleep associated with pathology. Nevertheless, current results suggest that AcPb may not be involved in the IL1-IL1RAcP-sleep signaling pathway.

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0125

THETA ALTERATIONS AND EPILEPTIFORM ACTIVITY DURING REM SLEEP IN THE NEONATALLY-TREATED CLOMIPRAMINE RAT MODEL

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Introduction: Cortical and subcortical spectral power activities vary according to pathology-specific to sleep and mood disorders (Buysse et al.,

2001). The hippocampal theta rhythm is a prominent electrophysiological marker for REM sleep (Benington et al., 1994) and has been shown to affect cortical pathways in depressed humans (Pizzagalli, et al., 2003). Furthermore, variability in spectral power also indicates epileptiform activity (see Benbadis & Rielo, 2010).

Methods: Neonate Long Evans Hooded male rats were injected s.c. with CLI 20 mg/kg (n=5) or equivolume saline (n=5) twice daily for two weeks (postnatal day 8 to 21). At 5 to 6 mos. of age, rats were anesthetized and surgically implanted with recording electrodes: 5 EEG electrodes were implanted into the skull and 3 EMG electrodes were stitched into the nuchal muscle. Following recovery, animals were moved to individual sleep chambers for 3 days adaptation prior to a baseline recording (24 hours) monitored with Somnologica™ software.

Results: The data show that CLI animals had increased REM sleep fragmentation, consistent with prior reports. There was a new finding of dramatic differences in EA, with CLI rats experiencing significantly more EA than SAL rats and a switch in theta activity at the NREM-to-REM transition.

Conclusion: We conclude that EA may be playing a role in the depressive phenotype, including REM sleep fragmentation and alterations in theta rhythm. These results support a need for further examination of a comorbidity of EA, as well as sleep disturbances in patients with MDD.

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0126
POST- AND PRESYNAPTIC EXCITATION OF BASAL FOREBRAIN CHOLINERGIC NEURONS BY OREXIN

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Introduction: The orexin neurons play an essential role in driving arousal and maintaining wakefulness. Lack of orexin neurotransmission produces a chronic state of hypoarousal characterized by excessive sleepiness, frequent transitions between wakefulness and sleep, and episodes of cataplexy. The basal forebrain is an important component of the ascending arousal system and may be a key site through which the orexin neurons promote arousal. Here we study the effects of orexin on the cholinergic neurons of the substantia innominata (SI) using patch-clamp recordings in brain slices of mice.

Methods: Recordings were conducted in wild-type (WT) mice and in mice lacking the Ox1R or Ox2R orexin receptors. In these mutant mice, the orexin receptor genes are preceded by a transcriptional disruptor (TD) sequence that prevents expression of functional Ox1R and Ox2R. We identified SI cholinergic neurons using fluorescent antibodies against the p75 receptors (Cy3-p75-IgG) steretaxically injected in the later cerebroventricle. Slices were prepared one to three days after surgery. Under fluorescent microscopy, SI cholinergic neurons appeared red and were targeted for recordings. Similar to rats, Cy3-p75-IgG labeled only cholinergic neurons in the basal forebrain of mice.

Results: Orexin-A (300 nM) directly excited SI cholinergic neurons and increased the glutamatergic input to these cells. Post-synaptically, orexin-A depolarized the SI cholinergic neurons by the activation of an inward current (Vh = -60 mV). In addition orexin-A increased the frequency of spontaneous excitatory postsynaptic currents (EPSCs) and this effect was blocked by the orexin receptor antagonist SB 334867 which at 10uM appears to block both Ox1 and Ox2 receptors. The effect of orexin-A on the glutamatergic input to SI cholinergic neurons was reduced in both the Ox1R and Ox2R TD mice compared to WT mice suggesting that presynaptic terminals are activated by both OxRs.

Conclusion: These findings demonstrate that orexin directly excites SI cholinergic neurons and increases the excitatory input to these neurons by activation of both Ox1 and Ox2 receptors. Thus, while orexin acts through either Ox1R or Ox2R in most wake promoting neurons, the activation of cholinergic neurons in the basal forebrain occurs through

both orexin receptors, emphasizing the importance of both pathways in promoting arousal and improving cognitive performance.

0127
THE RELATIONSHIP BETWEEN THETA OSCILLATION AND REM SLEEP DISTURBANCE INDUCED BY STRESSORS

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Introduction: Disturbance of rapid eye movement sleep (REMS) is common in patients with anxiety disorders, and our previous results have demonstrated that REMS was suppressed by repeated combination stressors, an anxiety model in rats. In addition, we observed the appearance of high density of theta wave EEGs (4-7 Hz) when rats were exposed to stressors. Theta waves are dominant in REMS EEGs in rodents and the stress-induced enhancement of theta wave density is suppressed by anxiolytics. This study was designed to investigate whether the reduction of REMS after exposure to the stressors is subsequently due to the enhancement of theta oscillation.

Methods: The combination stressors include footshocks and elevated plus maze (EPM). Male Wistar rats randomly received fifteen times of footshock stimuli, with the current of 5 amperes and the pulse duration of 0.1 second, within 10 minutes prior to the light onset. We interfered theta generation with a train of 100 Hz, 40 µA electrical stimuli to the median raphe nucleus (MR), which desynchronizes theta oscillation, during the footshocks. Sleep recordings were acquired for 24 hours.

Results: Footschok-induced enhancement of theta wave density was suppressed by MR stimulations; footschoks increased theta power by 13.79 ± 3.9 arbitrary units and stimulation of MR during footschocks decreased theta power by 1.22 ± 0.9 arbitrary units. MR stimulation partially blocked footschock-induced decrease of exploration time during the open arms of EPM (Naïve group: 69.54 ± 24.0 sec; footshock group: 18.1 ± 6.9 sec; MR stimulation + footshock group: 36.16 ± 9.6 sec). However, disruption of theta power by MR stimulation did not alleviate the decrease of REMS induced by the combination stressors.

Conclusion: Our results suggest that the increase of theta oscillation during stressors and stressor-induced REMS decrease may be mediated by different neuronal circuits.

0128
THE EFFECT OF TIME-OF-DAY AND LIGHT ON SLEEP PRESSURE MARKERS IN MICE

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Introduction: Sleep homeostasis refers to the increase of a pressure for sleep during wakefulness and its dissipation during sleep. The dynamics of this process is studied through EEG markers measured during non-rapid eye movement sleep (delta power: 1-4Hz) and wakefulness (theta power: 6-9Hz). Data suggest that these hallmarks are modulated by circadian time and light. We thus assessed the effects of time-of-day and acute light exposure on the dynamics of sleep pressure markers in mice.

Methods: Male C57BL/6J mice, implanted with EEG/EMG electrodes, were submitted to a 6h sleep deprivation (SD) by gentle handling starting at four different times of day: ZT0, ZT6, ZT12, or ZT18 (ZT0=Zeitgeber time 0: lights on). A week later, animals were submitted to the same SD but lights were turned off at the beginning of SD until the end of recording. Simulations were used to predict expected levels of delta power.

Results: We observed that the rebound in delta power was higher after the ZT6 and ZT12 SD than after the ZT0 SD. When the SD was repeated

in the dark, the delta rebound was reduced for both the ZT6 and ZT12 SD. The increase in theta power during SD was lower for the ZT12 and ZT18 SD than for the ZT0 SD, but only the increase during ZT0 SD appears to be blunted in the dark condition. Importantly, simulations showed that the level of delta power during the first 10 min of recovery sleep could not be adequately predicted for the ZT6 SD but only when SD was performed in the light.

Conclusion: Our data suggest that sleep pressure dynamics depends both on time-of-day and environmental light. We are currently working on the precise estimation of the effect of these variables on sleep pressure markers.

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0129

CHRONIC LIGHT AS A POTENTIAL REGULATOR OF SLEEP HOMEOSTASIS

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Introduction: Mammalian sleep is under control of circadian clock and sleep homeostasis. The mechanism of circadian clock is studied intensively although the sleep homeostasis is poorly understood. One reason of less progress in sleep homeostasis research is the lack of method to perturb sleep homeostasis dominantly without interacting the central clock. In this study, we showed that chronic light can control the amount of locomotor activity of mice both in wild-type and in arrhythmic mice.
Methods: CB57BL mice (WT) and two arrhythmic strains, cry1(-/-) cry2(-/-) mice (CRY-DKO) and bmal1(-/-) mice (BMAL-KO) were used in this study. Every mice were caged individually and their locomotor activity was detected by infrared beams. In the first experiment, mice were placed in LD=12:12 condition at least 7 days and followed by 7 days of constant darkness (# of mice: WT n=34, CRY-DKO n=6, BMAL-KO n=34). In the second experiment, WT (n=34) and CRY-DKO (n=31) were divided into four groups. Two groups were caged 3 weeks in constant light or in constant dark condition as controls. The other two groups received L-D-L or D-L-D light pattern (each letter stands for light conditions of a week) for 3 weeks. In the ongoing third experiment, EEG/EMG recordings were taken with these mice for two weeks. Each strains are divided into two groups, which are constant dark group and D-L group. Both groups were caged under constant darkness for the first 7 days, and only in the D-L group, light was switched on in the latter half period.
Results: In the first experiment, we found that switching mice from LD=12:12 to constant darkness leads in stable increase of daily locomotor activity. Interestingly, this happened not only in WT but also in CRY-DKO and in BMAL-KO. In the second experiment, shifting mice from constant darkness to constant light showed stable decrease in daily locomotor activity and vice versa. The activity difference between constant dark and light was larger in CRY-DKO than in WT.
Conclusion: Our data showed that chronic light condition is capable of controlling daily amount of the locomotor activity in mice. Importantly, the chronic light induced suppression of locomotor activity seems to occur independently from the central clock. According to these facts, we hypothesized that chronic light can control sleep homeostasis. Ongoing experiments are examining the change in sleep under different chronic light conditions in these mice.

0130

WHO IS VULNERABLE TO INSOMNIA? INVESTIGATING THE ROLE OF STRESS REACTIVITY, PERONSALITY AND COPING

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Introduction: Our understanding of the psychological and physiological characteristics related to a trait like vulnerability to sleep disruption is limited. The aim of the current work is to assess physiological stress responses and psychological factors in individuals vulnerable vs. resilient to developing insomnia. This research is the first to experimentally characterise those who are presumed pre-disposed to insomnia.
Methods: A group of good sleepers (n=25) completed the Trier Social Stress Test (TSST), which is known to have robust effects on both subjective and objective measures of stress. Salivary-free cortisol was obtained throughout the task, as an indication of stress reactivity. A 'vulnerable' and 'resilient' group were created based on responses to the Ford Insomnia Responsivity to Stress Test (FIRST) and compared on psychological variables (Personality, perceived stress, coping and sleep) and physiological stress response.
Results: Preliminary results demonstrate that those above the median split on FIRST score showed significantly higher values in neuroticism and rumination (p< 0.05) and a trend toward emotion focused and maladaptive coping strategies (p=0.055; p=0.08 respectively), as expected. There were no group differences in perceived stress, sleep parameters, depression or anxiety. While not significant, those in the 'vulnerable' group, on average, showed a greater peak in salivary cortisol compared to the 'resilient' group. Data collection is still ongoing and we hypothesise the change in salivary cortisol to become significant with further data.
Conclusion: Those vulnerable to developing insomnia show differences in personality and coping style. Data gathered to-date suggests a tendency toward increased stress reactivity amongst this group, supporting the idea that a trait-like vulnerability to insomnia exists, and is manifest physiologically. This has obvious implications for our understanding of the aetiology of insomnia.
Support (If Any): This work forms part of a Ph.D. supported by the Sackler Institute fo Psychobiological Research.

0131

FIRST NIGHT EFFECT: ASSOCIATION OF REM SLEEP REDUCTION WITH THE HYPOTHALAMIC-PITUITARY-ADRENAL AXIS (HPA) ACTIVITY

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Introduction: First night effect is a well-described phenomenon of objective sleep disturbance associated with the stress of sleeping in the unfamiliar environment of the sleep laboratory. The goal of this study was to assess whether sleep variables affected by the first night are associated with baseline cortisol secretion.
Methods: One hundred forty nine, healthy, normal sleepers (83 men, 66 women), mean age ±SD, 31.0 ±12.5, range 18.0 to 59.2 years; mean BMI±SD 24.5 ± 2.7, range 18.3 to 30.0 participated in a 4 consecutive-night sleep laboratory protocol [1 adaptation night, nights 2 and 3 and the fourth night a serial 24-hour plasma blood sampling was performed]. We tested whether the change from night 1 to the average of nights 2 and 3 of 7 key sleep variables (sleep latency, percent sleep time, wake time after sleep onset, stage 1 minutes, stage 2 minutes, slow wave sleep min-

utes, REM minutes, REM latency) predict cortisol baseline levels after controlling for age, BMI and gender, using linear regression analysis.

Results: REM sleep reduction (night 1 minus average of nights 2 and 3) was associated significantly with 24-h plasma cortisol secretion. None of the other sleep variables examined was significantly associated with baseline cortisol levels.

Conclusion: The first night effect is stronger in individuals with increased cortisol secretion. It appears that REM sleep reduction when sleeping in an unfamiliar, stressful environment is a marker of increased baseline activity of the HPA axis. This, in turn may indicate increased vulnerability to objective sleep disturbance under stressful circumstances.

0132

FALL SLEEP PATTERNS ARE ASSOCIATED WITH WINTER/ SPRING ACUTE ILLNESS AND SCHOOL ABSENCES IN ADOLESCENTS

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Introduction: Sleep restriction has been linked to decreased immune function, and longitudinal data may help determine whether sleep restriction affects the incidence and duration of acute illnesses. Our team collected data using in-person interviews across 16 weeks to assess illness and school absences.

Methods: Fifty-six adolescents aged 14 to 19 years (39% male) were assigned to Long or Short sleep groups based on one week of actigraphy during the fall (Short sleepers Mean = 5 hrs 48 [SD = 32] min; Long sleepers Mean = 7 hrs 36 [27] min). Adolescents were interviewed weekly in winter/spring (modal number of interviews = 13) using a structured protocol that included 14 questions about health events. Events were coded and entered into SPSS. For 710 completed interviews participants reported 683 illness events and 90 school absences. Average illness duration and rates per week were calculated for illness bouts and school absences. Outcomes were compared between sleep and sex groups using MANOVA.

Results: Illness bout number differed across sex and sleep groups, with males and Long sleepers reporting fewer illness bouts (males = .26 [mean] +/- .05 [SE], females = .59 +/- .05, p < .01; Long = .33 +/- .05, Short = .52 +/- .05, p < .01.) Illness duration, by contrast, showed no main effect of sex or group but an interaction (p = .04) with male Long sleepers reporting shorter illness duration than males in the Short sleep group (male Long = .09 +/- .04, male Short = .20 +/- .03; female Long = .21 +/- .03, female Short = .17 +/- .04). Long sleepers reported fewer absences (Long = .07 +/- .03, Short = .18 +/- .04, p = .02.)

Conclusion: Absences and acute illnesses were more frequent in otherwise healthy adolescents with short sleep the previous semester.

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0133

TOLERANCE OF CHRONIC SLEEP RESTRICTION IN LONG SLEEPERS DOES NOT DIFFER FOR THOSE WITH EXISTING MORBIDITIES

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Introduction: Over the past half-century, approximately 50 epidemiologic studies have found a significant association of long sleep with mortality. It has been argued that the association might represent the opposite direction of putative causality, i.e., morbidity causing long sleep. Contrary to this argument are findings that the association of long sleep with mortality is just as apparent following control for morbidities, and in samples restricted to apparently healthy individuals at initial assessment. The argument can also be addressed by assessing responses to sleep restriction. The aim of this investigation was to compare tolerance to chronic moderate sleep restriction in older long sleepers with existing morbidities vs. those who were healthier at baseline.

Methods: Forty-two adults ages 50-70 yrs who reported habitual sleep durations of ≥ 8.5 hr were assessed. Following a two-week baseline, participants were randomized to one of two eight-week treatments: (1) time-in-bed (TIB) restriction of 90 min per night relative to baseline, or (2) a control. Changes were assessed in glucose tolerance and insulin sensitivity, sleepiness, depression, health-related quality of life, functional outcomes of sleepiness, and a neurobehavioral performance battery. In three sets of analyses, responses to sleep restriction were compared between participants who were dichotomized regarding the presence or absence of morbidity, with absence defined as (1) no morbidity, except hypertension, high cholesterol, moderate snoring, migraine headaches, history of hysterectomy, smoking, and allergies; (2) no morbidity, except for hypertension and high cholesterol; (3) complete absence of morbidity.

Results: As reported previously, TIB restriction elicited no negative effects on any outcome. Moreover, there were no significant differences in tolerance to TIB restriction between healthy participants and those with existing morbidities.

Conclusion: These data provide further refutation of the argument that morbidity causes long sleep, and the hypothesis that less healthy individuals would be less tolerant of sleep restriction.

Support (If Any): HL71560, VA Merit, VA (VISN-7) Career Development

0134

A STUDY ON BEDROOM ENVIRONMENT AND SLEEP QUALITY IN KOREA

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Introduction: The purpose of this study was to investigate both the sleep environment and sleep quality in bedrooms. It was also to reveal the relationship between sleep environment and sleep quality, and to study its seasonal changes in winter, spring, and summer.

Methods: The subjects for this study were 24 women who lived in apartments in Seoul and its environs. We conducted two groups of measurements. One group considered elements of the sleep environment; mean radiant temperature, air temperature, relative humidity, carbon dioxide (CO_2) concentration, illumination, and equivalent noise level. The other looked at elements of sleep quality; the apneahypopnea index, and inspiratory flow limitation (as%FL), which were measured simultaneously while subjects were asleep.

Results: Results showed first, that people were exposed to a variety of problems when asleep, related to their sleep environment such as too low or high air temperatures, or relative humidity and high CO_2 concentrations. Second, these were seasonally dependant and people slept best during spring, then winter, and then summer. Third, the effect of the sleep environment on sleep quality varied with age.

Conclusion: The sleep environment was affected by seasonal differences, CO_2 concentration, and sleep breathing pattern.

0135

INFLUENCE OF BRIGHT LIGHT AND CAFFEINE ON SKIN TEMPERATURE PHYSIOLOGY AND SLEEP

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Introduction: Multiple mechanisms may contribute to the sleep disrupting effects of bright light and caffeine. One understudied mechanism is an impact on the thermoregulatory pattern that precedes sleep and is thought to promote sleep. Bright light has been reported to impact skin temperature physiology during the time of habitual sleep onset, yet whether caffeine alone or in combination with bright light influences skin temperature physiology is unknown. We hypothesized that caffeine would act individually and in combination with bright light to attenuate the circadian fall in core body temperature (CBT), and attenuate the circadian rise in the distal-to-proximal skin gradient (DPG) and negatively impact sleep quality near habitual bedtime.
Methods: Five healthy adults (3 females) aged (24±4 years) BMI (24.0±1.0 kg/m2) participated in a randomized, cross over, and placebo-controlled study. Each subject participated in four conditions: dim light-placebo, dim light-caffeine, bright light-placebo, and bright light-caffeine. Caffeine (2.9mg/kg) was administered 6h prior to a delayed sleep opportunity and bright light (~3,000 lux) exposure occurred 3h prior to bedtime. Dim light was ~1.5 lux. DPG was calculated as the difference between distal (foot) and proximal (infraclavicular) skin site locations. CBT was measured via an ingested temperature pill. Body temperatures were averaged into 10 minute bins and analyzed with mixed model ANOVA.
Results: Caffeine significantly delayed the circadian rise in DPG and attenuated the circadian fall in CBT. The combination of bright light and caffeine reduced slow wave sleep and increased SOL as compared to either condition alone (all p<0.05).
Conclusion: These findings indicate that caffeine alone and combined with bright light influenced the thermoregulatory pattern that typically precedes sleep. Furthermore, the combination of bright light and caffeine negatively influenced sleep quality. These findings have implications for individuals who consume caffeine and are exposed to bright light prior to bedtime (e.g. shiftworkers).

0136

BEHAVIOR OF GENIOGLOSSUS SINGLE MOTOR UNITS DURING CHEYNE-STOKES BREATHING

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Introduction: Cheyne-Stokes respiration(CSR) is characterized by rhythmic waxing and waning breathing with central apneas followed by hyperpnea. The genioglossus(GG) maintains pharyngeal airflow. We have characterized the activity of inspiratory single motor units(SMUs) in GG, assessing neuronal output from human brainstem during CSR. We hypothesized that SMUs would follow a cyclic pattern similar to breathing in CSR.
Methods: GG activity was measured using intramuscular electrodes, inserted percutaneously via ultrasound. During stage2NREM(N2), two concurrently active inspiratory phasic SMUs were decomposed from raw electromyographic signals based on spike triggered threshold crossing and detailed morphology of action potentials. The onset, peak and end motor unit firing times(%inspiration,%T_l) and frequencies(Hz) were calculated using instantaneous discharge frequencies. Measurements were compared between peak cyclic tidal volumes(hyperpneas) and last two breaths before central events(hypopneas). Total numbers of SMU action potential discharges/breath occurring were calculated.
Results: The onset firing times(mean±SEM) were later from hyperpnea versus hypopneas(2.7±6.1 4.5±8.9%T_l). The peak firing time

showed earlier onset during hypopneas versus hyperpneas(45.8±9.1 51.1±4.5%T_l). The end firing times were also earlier at the onset of the apneas (93.4±5.8 73.9±12.8%T_l). Consequently the duration of motor unit firing was reduced from the hyperpneas versus hypopneas(90.7±10.5 69.3±11.2%T_l). The onset discharge frequency remained similar from the hyperpneas compared to hypopneas(8.1±1.1 7.9±1.0Hz). The peak discharge frequency decreased from hyperpnea versus hypopnea(13.3±0.6 11.4±1.0Hz). The end discharge frequency remained unchanged between the two breathing periods (7.6±0.3 6.7±1.0Hz). The number of SMU action potentials/breath was reduced from hyperpneas versus hypopneas(16.1±2.5 11.8±2.1).
Conclusion: SMU recruitment and rate-coding occurs in GG during CSR. Combined with diminished SMU firing within a breath, SMU action potentials/breath were fewer leading into events where SMUs became silent. These data suggest that GG activity closely resembles breathing pattern during CSR.

0137

THE EFFECT OF INTERMITTENT HYPOXIA (IH), INTERMITTENT HYPERCAPNIA (IHC) OR IH/IHC ON SLEEP PATTERNS IN MICE

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Introduction: The impact of IH on sleep patterns has been investigated in mice, and has been shown to adversely affect sleep integrity, particularly REM sleep; however, during sleep-disordered breathing (SDB) IH is unlikely to occur in isolation, and is more likely to be accompanied by IHC. In addition, IHC can occur alone in the context of SDB, particularly in children. Therefore, assessment of the impact of gas exchange abnormalities either alone or in combination on sleep structure is needed.
Methods: C57BL/6 mice (n=4/group; ~5 months old) were purchased from Jackson Laboratories. Mice were implanted with telemetric transponders to measure EEG, EMG, body temperature (Tb) and gross activity (Ag). After surgical recovery, the mice were acclimatized in a custom developed chambers operated by a computer and allowing for near instantaneous environmental gas changes via 3 separate mass flow controllers linked to N2, O2, and CO2 pressurized reservoirs. IH consisted of 5.7% O2 alternating with 20.9% ever 90 sec, and IHC consisted of 5% CO2 alternating with 0% CO2 every 90 sec. During combined IH/IHC both exposures were synchronized. Following baseline recordings for 24 hours (7:00 AM -7:00 AM next day), mice were subjected to 6 hours of IH, IHC, IH/IHC or RA (room air) from 7:00 am till 1:00 PM, followed by the remaining 18 hours in RA.
Results: Sleep pattern differences occur after IH, IHC, and the combination of IH/IHC. Preliminary data indicate that these sleep differences are greatest when mice were exposed to both IH/IHC.
Conclusion: Both IH and IHC impose substantial alterations in sleep patterns and architecture in mice. These paradigms may permit delineation of sleep homeostatic response to acute and long-term gas exchange perturbations.

0138

THE EPITHELIUM OF THE CHOROID PLEXUS IS INVOLVED IN THE HYPOCRETIN TRANSPORTATION FROM THE CSF TO THE CIRCULATORY SYSTEM

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Introduction: In the CNS, hypocretins (also called orexins) are synthesized exclusively by neurons that are located in the lateral hypothalamus. However, hypocretin peptides are also present in the cerebrospinal fluid (CSF) and blood and their concentration varies depending on a number of normal and pathological states and processes. Intracerebroventricular and intravenous injections of hypocretin induce not only central but also peripheral effects, indicating that hypocretins in the CSF play a role in the functions of peripheral organs. However, it is unclear how hypocretins in the CSF reach their cognizant receptors on cells of peripheral organs. In this regard, it is known that the choroid plexus plays a critical role in transporting substances from the CSF to the circulatory system. Accordingly, in the present study, we were interested in determining whether the choroid plexus serves as a functional transport system for the conveyance of the hypocretins from the CSF to peripheral organs.

Methods: Hypocretin-1 was conjugated with supraparamagnetic particles of iron oxide (MNP). Hypocretin-conjugated MNPs were then injected into the lateral ventricle of guinea pigs. After survival times ranging from 2 to 7 hours, the animals were perfused transcardially with a fixative. The brain was removed and processed in order to carry out a Prussian blue reaction to determine the location of hypocretin-MNPs. In addition, the Prussian blue reaction was combined with antibodies against hypocretin receptor type 1 or type 2 to identify cells that express hypocretin receptors.

Results: Light microscopic analysis revealed that a majority of the epithelial cells of the choroid plexus were immunostained with antibodies against hypocretin receptor type 1 or type 2. In addition, the cells that expressed receptors for hypocretin also contained large amounts of hypocretin-MNPs, which were identified by the presence of precipitates of the Prussian blue reaction within their cytoplasm.

Conclusion: The present results indicate that hypocretins in the CSF are transported, via epithelial cells of the choroid plexus, to the circulating system. Therefore, we conclude that the CSF-Circulatory System plays an important role in transporting hypocretins from the CNS to peripheral organs.

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0139

SLEEP DURATION VERSUS SLEEP INSUFFICIENCY AS PREDICTORS OF CARDIOMETABOLIC HEALTH OUTCOMES

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Introduction: Previous laboratory and epidemiological studies suggest that reduced sleep time is associated with an array of negative cardiometabolic health outcomes. What remains unclear is the role of unmet sleep need versus reduced sleep time. The present analysis aims to explore the relative contributions of unmet sleep need (sleep insufficiency) and sleep duration.

Methods: Data from the 2009 Behavioral Risk Factor Surveillance System (BRFSS) were used (N=31,055). Outcomes included BMI (continuous), obesity (BMI=30+), and history of hypertension, diabetes, hypercholesteremia, heart attack, and stroke. Self-reported habitual sleep time (STIME) was categorized as <5, 5-6, 7[reference], 8-9, and >9 hours. Sleep insufficiency (INSUF) was coded as number of days per week of self-reported insufficient rest or sleep [reference=0]. All analyses were adjusted for: age, sex, race/ethnicity, education, income, employment, marital status, Census region, minutes of exercise, any exercise in past month, alcohol intake, heavy drinking, smoking, healthy diet, household size, overall health, physical health, and mental health. All non-BMI outcomes were also adjusted for BMI. Models included: (1)STIME, (2)INSUF, and (3)STIME+INSUF.

Results: For Model 1 (STIME), increased BMI was associated with <5h and decreased BMI was associated with 8-9h. Heart attack and stroke were both associated with <5h and >9h. <5h was associated with obesity, hypertension, and hypercholesteremia, and 5-6h was also associated with hypertension and hypercholesteremia. 8-9h was associated with an increased risk of diabetes. For Model 2 (INSUF), significant positive relationships were found for BMI, obesity, hypertension, and hypercholesteremia. For Model 3 (STIME+INSUF), STIME effects remain (with no INSUF effect) for: BMI, obesity, diabetes, heart attack, and stroke. INSUF effects remain (with no STIME effect) for: hypercholesteremia. Both STIME and INSUF effects remain for hypertension.

Conclusion: These analyses show that both sleep time and insufficiency are related to cardiometabolic outcomes, and that when evaluated together, both variables demonstrate unique effects.

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0140

THE EFFECTS OF SLEEP LOSS ON VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF)

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Introduction: It has been shown that experimental sleep-deprivation in humans activates the autonomic system, resulting in increased norepinephrine and blood pressure. Recent studies have shown that vascular reactivity in the microcirculation is impaired during sleep-deprivation. Vascular endothelial growth factor (VEGF) is a potent capillary dilator known to act directly on the endothelium. We investigated VEGF levels during total sleep-deprivation with the hypothesis that levels would be reduced by sleep loss.

Methods: A sample of 23 healthy participants (22-56 years; body mass index: 18.5-32 kg/m2) stayed in the laboratory during a 7-day in-hospital protocol under controlled conditions. After adaptation and baseline, they were randomized to either the control group (7 subjects had a 9 hour sleep opportunity on each night) or the sleep-deprived group (16 subjects stayed awake continuously for 63 hours). Both groups had 2 nights of recovery sleep following the experimental phase. Blood was sampled hourly and plasma assayed for VEGF (R&D ELISA) at 4 time-points 00:15, 04:15, 16:15 and 20:15 hours during baseline, the last 24h of sleep-deprivation and recovery.

Results: VEGF levels were not significantly different when comparing groups (sleep, sleep-deprivation) across all time-points of the study. However, after 2 nights of continuous wakefulness, VEGF was significantly lower in the sleep-deprived group compared with control sleepers during that night period (F[2,40] = 5.3, p=0.01; 30.2±16.3 vs 42.3±26.4). In addition, there was a trend towards a significant within-subjects reduction of VEGF in the sleep-deprived subjects in relation to their baseline (F[1,15]=3.7, p=0.07; 36.1±14.1 vs 30.2±16.3). No significant differences between groups were observed during the daytime.

Conclusion: These findings suggest that participants undergoing prolonged wakefulness have a reduction in nocturnal plasma VEGF compared with normal control sleepers. This reduction may contribute to reduced vascular reactivity seen under sleep-deprivation conditions.

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0141

CHANGES IN THE SLEEP ARCHITECTURE OF LEWIS RATS AFTER PARTIAL OR TOTAL HYPOPHYSECTOMY

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Introduction: Sleep is a behavioral state characterized by specific patterns of electroencephalographic activity, muscular tone and eye movements. In rodents, sleep is usually divided in two functional states, rapid eye movement (REM) sleep and non-REM sleep, also called slow wave sleep (SWS). Each of those sleep stages is also accompanied by changes in the serum concentration of diverse hormones; for example, during SWS occurs the maximal release of GH by the anterior pituitary; also, sleep-related rise in serum testosterone levels is linked with the appearance of first REM sleep episode. It has been shown that the endocrine and the nervous system closely regulate each other. Some research has shown hypophysectomy did not modify sleep architecture, and few others showed that the same procedure decrease SWS and increase REM sleep

Methods: The aim of the present report was to describe the changes in the sleep-wake cycle architecture during 24 hours in Lewis rats partially or totally hypophysectomized. Fifty male Lewis rats, 300g body weight, were implanted for electroencephalographic and electromiographic recordings. A 24-hour basal polisomnographic record was made on post-surgery day 15; thereafter, subjects were randomly assigned to one of five groups: intact animals, anterior hypophysectomy, posterior hypophysectomy, total hypophysectomy and sham-surgery controls (ten subjects each group). Fifteen days post-hypophysectomy another 24-hour polisomnographic record was carried on.

Results: Anterior and totally hypophysectomized rats progressively lost weight during the next three weeks; meanwhile, posterior hypophysectomized rats, beginning during the second week post-surgery, progressively raised their body weight until basal levels. Anterior and total hypophysectomy modified the sleep latencies and the sleep pattern as compared to intact animals and sham controls. Totally hypophysectomy apparently did not modify sleep architecture.

Conclusion: The sleep architecture of totally hipophysectomised rats is similar to controls.

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0142

EFFECT OF CHRONIC-INTERMITTENT HYPOXIA (CIH) ON NORADRENERGIC ACTIVATION OF HYPOGLOSSAL (XII) MOTONEURONS

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Introduction: In obstructive sleep apnea patients, lingual muscles are hyperactive and protect against airway occlusions. Rats subjected to CIH have increased density of noradrenergic terminals and increased α1-adrenoceptor immunoreactivity in the hypoglossal (XII) nucleus. We investigated whether the anatomical indices of increased noradrenergic innervation following CIH are associated with increased sensitivity of XII motoneurons to noradrenergic inputs.

Methods: Adult, male Sprague-Dawley rats were subjected to CIH for 10 h/day for 35 days, with oxygen levels oscillating between 24% and 7% with 180 s period. They were then anesthetized with urethane, vagotomized, paralyzed and artificially ventilated. Dorsal medulla was exposed and phenylephrine (2 mM, 10 nl), and then α1-adrenergic receptor antagonist, prazosin (0.2 mM, 3x40 nl), were microinjected into the XII nucleus while recording XII nerve activity (XIIa). The area under integrated XIIa was measured over 1 min intervals before and at different times after microinjections.

Results: During the first minute after injection, phenylephrine increased XIIa in both CIH (median: 247% of the pre-injection level, min-max: 129-500%, n=8) and sham-treated (median: 246%, min-max: 172-908%, n=13; Kruskal-Wallis, p=0.61) rats, after which activation declined over the next 15 min. Prazosin injections reduced spontaneous XIIa to 21±7%(SE) of the pre-injection baseline in CIH rats (n=7) and to 40±8% in sham-treated rats (n=10; Holm-Sidak, p=0.048) when measured 45 min after injections. The decline developed gradually, always being stronger in CIH than sham-treated rats. The effects were not associated with any significant changes in central respiratory rate, arterial blood pressure or heart rate.

Conclusion: Exposure to CIH is associated with increased neuroanatomical measures of noradrenergic input to XII motoneurons. Consistent with this, when tested under anesthesia, prazosin injections reveal a stronger endogenous noradrenergic excitatory drive to XII motoneurons in CIH than sham-treated rats.

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0143

METABOLIC EFFECTS OF INTERMITTENT HYPOXIA AND SUSTAINED HYPOXIA IN MICE

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Introduction: Intermittent hypoxia (IH) is a frequent occurrence in several sleep disorders such as obstructive sleep apnea, and both human and murine studies reveal that it may be implicated in metabolic dysfunction. Although the effects of nocturnal sustained hypoxia (SH) have not been as critically examined, it would appear that IH and SH elicit distinct metabolic adaptations. The purpose of the current study was to examine the effects on metabolism associated with chronic IH and SH in mice.

Methods: C57BL6 mice (7 week-old) were randomly assigned to Control (CTL; normoxia), IH (cycles of 3 min 6.4 % O2 and 3 min 20.9% O2 during daylight), and SH (8% O2 during daylight) for 5 weeks. These profiles were selected after screening experiments to match both duration and severity of hypoxia. Body weight was monitored weekly. Mice were then subjected to a Glucose Tolerance Test (GTT). After IP injection of 2 mg glucose/1gr body weight, glucose concentration in peripheral blood was measured with a glucometer at T0, T15', T30', T60', T90' and T120'.

Results: After 14-35 days exposures, body weights were lower in both IH and SH, with IH being slightly lower than SH. Compared to CTL, IH and SH had lower basal glycemic levels, but GTT kinetics revealed marked differences between SH and IH, with SH manifesting increased insulin sensitivity when compared to either IH or CTL.

Conclusion: IH and SH elicit differential glucose homeostatic responses despite similar cumulative hypoxic profiles. Additional experiments to identify potential mechanisms accounting for the discrepant effects of hypoxic patterns on glucose and insulin metabolism are ongoing.

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0144

VAGAL INVOLVEMENT IN TUMOUR NECROSIS FACTOR-ALPHA-INDUCED SLEEP

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Introduction: Tumor necrosis factor-alpha (TNF) enhances sleep whether administered centrally or peripherally. The blood brain barrier prevents many peripheral molecules from entering the CNS. However, cytokines can enter the CNS via leaky areas or cytokine-specific transport systems. Cytokines also stimulate the CNS through vagal afferents. Peritoneal vagal stimulation by lipopolysaccharide (LPS) or low doses of interleukin-1beta enhances sleep. Our aim was to examine the effects of vagal input on TNF-mediated sleep.

Methods: Male C57BL/6 mice vagal afferents were severed and the pyloric valve was disengaged. Sham mice underwent identical pyloroplastic surgery but the vagi were left intact. Mice were intraperitoneally (IP) injected with saline, TNF (3 µg), or LPS (1 µg) at dark onset. Two hours after injections (dark onset) somatosensory cortex (Ssctx) and liver tissues were taken for TNF mRNA expression analysis by real-time PCR. Separate groups of mice underwent vagotomy and/or plyoroplasty surgeries and were implanted with EEG and EMG electrodes for sleep analyses.

Results: TNF- and LPS-enhanced NREM sleep was attenuated by vagotomy. TNF mRNA levels in the Ssctx were enhanced after IP-TNF compared to saline (P < 0.001). However, Ssctx TNF mRNA levels following IP-TNF were not different between vagotomized and sham mice. IP-LPS enhanced Ssctx TNF mRNA levels compared to saline (P < 0.001), and vagotomy attenuated this enhancement (P = 0.01). TNF and LPS administration enhanced liver TNF mRNA levels (P < 0.001); vagotomy did not alter these liver responses.

Conclusion: Vagal afferents are involved with systemic TNF-mediated sleep. However, vagal inhibition does not attenuate IP-TNF from stimulating Ssctx TNF mRNA expression suggesting additional mechanisms or CNS areas are involved in systemic inflammation-induced sleep.

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0145

ASHWAGANDHA ANTAGONIZES APNEA-INDUCED EXCITOTOXIC PROCESSES IN THE HIPPOCAMPAL CA3-CA1 PATHWAY

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Introduction: Previously, we demonstrated that apnea-induced excitotoxic enhancement of the hippocampal CA1 fEPSP results in the neurodegeneration (apoptosis) of CA1 neurons. We also demonstrated that GABAergic drugs are capable of reducing or eliminating these excitotoxic processes. Therefore, we were interested in determining whether a natural substance, such as ashwagandha, which is believed to exert its effects by promoting GABAergic mechanisms, could suppress excitotoxic processes in CA1 neurons that is produced by apnea.

Methods: Adult guinea pigs were anesthetized with α-chloralose and immobilized with Flaxedil. Cathodal stimulation (0.2 ms, 10-50 µA, repetition rate 0.5 Hz) of Schaffer collaterals in the CA3 region of the hippocampus evoked fEPSPs that were recorded extracellularly from the dendritic field of CA1. Changes in the amplitude of CA1 fEPSPs were examined before and following the intravenous administration of ashwagandha (500 mg/kg) in conjunction with the induction of apnea by ventilatory arrest, which resulted in desaturation of blood oxyhemoglobin.

Results: In control animals, single episodes of apnea resulted in potentiation of the CA1 fEPSP for a period of one to three minutes after the termination of apnea. In animals treated with ashwagandha, the preceding apnea-induced excitotoxic enhancement of the CA1 fEPSP was abolished. In addition, ashwagandha restored to control levels the apnea-induced reduction in the paired-pulse facilitation ratio that occurred following the induction of apnea.

Conclusion: The present results indicate that ashwagandha is able to prevent the development of excitotoxic responses in the hippocampal CA3-CA1 pathway. We hypothesize that this neuroprotective effect, which likely involves the activation of specific GABA receptor subtypes, acts by suppressing the apnea-induced increase in the preterminal release of glutamate onto CA1 neurons. These findings suggest that ashwagandha is capable of functioning as a potent neuroprotective agent whose actions are mediated by GABAergic mechanisms.

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0146

COMMON CARDIAC RESPONSE TO RESTRAINT STIMULI IN RAT AND MOUSE DURING EARLY POSTNATAL PERIOD

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Introduction: Using a piezoelectric-transducer (PZT) sensor that enabled us to measure heart rate (HR) of small newborn animals noninvasively, we compared the development of HR and the HR response to restraint stress during the first two postnatal weeks between rats and mice.

Methods: Basal HRs of rats and mice were measured by the PZT sensor at postnatal day (P) 0-P14 by simply put them on the sensor for 5 min. Then, HR response to restraint stress was measured for 5 min by restraining them with ECG electrodes which were fixed on the PZT sensor. Additionally, the same protocol was performed after autonomic blockade with atropine, metoprolol or both to evaluate the relevance between the HR response and autonomic nervous system regulation.

Results: Basal HR measured by PZT sensor (PZT-HR) in rats(mice) was 220(323) b/m at P0, which steeply increased to 330(598) b/m at P2(P5) and almost linearly increased thereafter until P14 to 470(692) b/m. In contrast to stable PZT-HR, the stress by attaching ECG electrodes significantly decreased HR of rats(mice) during 5 min at P0 [181(319) to 171(302) b/m, P<0.05] through P10(P3) [427(468) to 364(436) b/m, P<0.05] after an initial HR drop at 0 min, while it induced transient bradycardia at P11(P9) -P14. The transient bradycardia was abolished by parasympathetic blockade with atropine.

Conclusion: Basal HR in both newborn rats and mice increased almost linearly with changing its slope in the first postnatal week but not in S-shape curve as described in the earlier studies. The development of parasympathetic nervous system may be also similar between them because the both exhibited transient bradycardia in response to restraint stress during the second postnatal week. These similar developments of HR and autonomic nervous system seem to be a heritable trait common in rodents at least in rats and mice.

0147

EPILEPSY ALTERS SLEEP HOMEOSTASIS

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Introduction: Sleep is regulated by homeostatic factor and circadian process. Observations argue that disturbances of sleep homeostasis are common in epilepsy patients. Much attention has been focused on the

influence of sleep on seizure occurrence, whereas disturbances in the sleep-wake continuum in epilepsy patients are common but often overlooked. Therefore, we employed kindling stimuli delivered at different zeitgeber time (ZT) points to elucidate the effect of epilepsy on the alterations of sleep homeostasis.

Methods: Rapid amygdala kindling protocol was delivered at different ZT points (ZT0 [light onset], ZT6 [middle of light period] and ZT12 [dark onset]) to induced temporal lobe epilepsy (TLE) in rats. EEGs and sleep activities were recorded after reaching full-blown epilepsy. ELISA, ribonuclease protection assay and immunocytochemistry were employed to measure corticosterone, interleukin (IL)-1 and Per1 protein expression, respectively.

Results: SWS and REM sleep decreased during the first 12-hour light period when rats were kindled at ZT0. When ZT12 kindling was given, SWS increased but REM sleep was not altered during the first 12-hour dark period. However, the 12:12h sleep-wake circadian rhythm was not altered. Corticosterone concentrations were increased after ZT0 kindling and the expression of IL-1 was enhanced after ZT12 kindling. Furthermore, corticotrophin-releasing hormone (CRH) receptor antagonist and IL-1 receptor antagonist (IL-1ra) respectively blocked ZT0- and ZT12-induced sleep alterations. In addition, the expression of Per1 protein in the suprachiasmatic nucleus (SCN) was shifted 6 hours in advance and sleep circadian was advanced 2 hours when kindling stimuli was given at ZT6. Microinjection of hypocretin receptor antagonist, SB 334867, directly into the SCN significantly blocked ZT6-kindling induced advance shifting of Per1 expression in SCN and the alteration of sleep circadian.

Conclusion: Amygdala-kindling stimuli delivered at different ZT points may alter the circadian and/or homeostatic factors, indicating the underlying mechanisms for the sleep disturbances in epilepsy patients.

0148

ASHWAGANDHA PROVIDES NEUROPROTECTION AGAINST APNEA-INDUCED NEURONAL DEGENERATION IN THE HIPPOCAMPUS OF ADULT GUINEA PIGS

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Introduction: Chronic recurrent apnea induces marked increases in neurodegeneration (apoptosis) in the hippocampus. This effect occurs as a result of an excitotoxic influx of Ca2+ ions, which is due to an abnormal increase in glutamatergic neurotransmission induced by apnea. It has been shown that apnea-induced excitotoxicity and the accompanying neurodegenerative processes are ameliorated by the activation of inhibitory inputs from GABAergic neurons. Consequently, we hypothesized that ashwagandha, which has been suggested to act as a GABA-mimetic, might prevent and/or reduce apnea-induced neurodegeneration in the hippocampus.

Methods: Adult guinea pigs were anesthetized with α-chloralose and immobilized with Flaxedil. Apnea was induced by ventilatory arrest in order to desaturate the oxyhemoglobin to 75% SpO2; ventilation was then resumed; following recovery to >95% SpO2, a succeeding apneic episode was initiated. This sequence of apnea, followed by ventilation with recovery of SpO2, was repeated for a period of 2 hours. Ashwagandha was injected, unilaterally, into the CA1 region of the hippocampus (400 mg, 0.20 μl) at a site where the largest amplitude of the field EPSP in CA1 neurons was recorded following stimulation of CA3. Injections were performed 15 minutes prior to the onset of the first episode of apnea and thereafter once every 30 minutes. Subsequently, the animals were perfused; brain sections were obtained and immunostained with a mouse monoclonal antibody raised against single-stranded DNA (ssDNA) (which is a biomarker for apoptosis).

Results: Under light microscopy, numerous neurons were labeled with the antibody against ssDNA on the side of the hippocampus that was not injected with ashwagandha. There was mass precipitation of DAB reaction products in the nuclei and the cytoplasm of these neurons. In contrast, on the side of the hippocampus in which ashwagandha was injected, there were few ssDNA positive neurons. In addition, the intensity of immunostaining within these cells was remarkably less compared with that present in cells on the contralateral side.

Conclusion: These data indicate that ashwagandha is able to prevent or reduce apnea-induced neuronal apoptosis in the hippocampus.

0149

INTERACTIONS BETWEEN TIME-ON-TASK, SLEEP HOMEOSTATIC AND CIRCADIAN PROCESSES ON VISUAL VIGILANCE

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Introduction: Vigilance performance is well known to be modulated by time awake, circadian phase and time-on-task, but whether and how these three factors interact is not known. Therefore, we examined how time-on-task decrements in visual vigilance performance interact with time awake and circadian phase using a 20-min Psychomotor Vigilance Task (PVT-20) assessed during a forced desynchrony protocol (FD).

Methods: Six healthy subjects [5 males (26.8±5.2yr;mean±SD)] were studied in a 28-h FD for 12 days. PVT-20 performance was completed near scheduled wake time and every 2h thereafter until 18h of scheduled wakefulness. Time-on-task decrements in the reciprocal mean reaction time were calculated for 2-min bins across the 20-min task. Data were averaged into 60° circadian bins, with temperature minimum assigned 0°, and into 2-h time awake bins. The primary analysis compared time-on-task decrements at 2h and 18h awake across circadian phase using repeated measure ANOVA.

Results: Significant interaction effects between time awake and circadian phase, between time-on-task and hours awake and between time-on-task and circadian phase were observed (all p < 0.05). In general, time-on-task decrements in performance were greater at 18h awake compared to 2h awake. In addition, time-on-task decrements in performance at 2h awake were similar for all circadian phases examined, whereas time-on-task decrements in performance at 18h awake were larger between 0-180 circadian degrees compared to 240-300 circadian degrees after 4 min time-on-task.

Conclusion: Time-on-task, time awake and circadian phase each modulate visual vigilance with greater impairments due to time-on-task when sleep homeostatic and circadian drives for sleep were high. Impairments in visual vigilance are greater after 4min time-on-task at 18h awake and misalignment of circadian phase. These findings have important implications for shift workers required to maintain sustained attention during round-the-clock operations.

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0150

CIRCADIAN REGULATION BEWARE, THERE'S HOMEOSTATIC PRESSURE FOR SLEEP IN THE AIR

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Introduction: In the absence of sleep restriction (equivalent to 8h/24h), REM sleep and sleep efficiency demonstrate circadian modulation. There is some evidence suggesting that under conditions of severe sleep restriction (equivalent to 4h/24h) the homeostatic drive for sleep overrides the circadian drive for REM sleep and sleep efficiency. However, it is unknown how the circadian and homeostatic processes influence sleep under conditions of moderate sleep restriction (equivalent to 6h/24h). The current study investigated the relative contributions of the circadian and homeostatic processes on REM and sleep efficiency using a forced desynchrony (FD) protocol with moderate sleep restriction.

Methods: Fourteen males (23.6±4.0yr) lived in a sleep laboratory free from time cues for 12 days. Participants were scheduled to 3x24h baseline days (8h sleep, 16h wake) followed by 7x28h FD days (7h sleep, 21h wake). Sleep was measured using standard polysomnography. Core body temperature (CBT) was recorded continuously using a rectal thermistor. Each epoch of sleep was assigned a circadian phase based on the CBT data (6x60 degree bins) and an elapsed time into sleep episode (4x105min intervals).

Results: Linear mixed model analyses showed a significant main effect of circadian phase on the percentage of REM sleep and sleep efficiency. Both REM sleep and sleep efficiency were highest around the circadian nadir and lowest around the acrophase. There was a significant main effect of elapsed time on the percentage of REM sleep and sleep efficiency. Sleep efficiency decreased across the sleep episode whilst the percentage of REM sleep increased.

Conclusion: Previous research has demonstrated the circadian modulation of sleep in the absence of sleep restriction. Results from the current study demonstrate that despite a moderate increase in homeostatic pressure, the circadian modulation of REM sleep and sleep efficiency persists. This highlights the complex interactions between the circadian and homeostatic process on sleep regulation.

Support (If Any): This study was financially supported by the Australian Research Council.

0151

TRAIT- AND STATE-DEPENDENT CHARACTERISTICS OF SLOW-WAVE OSCILLATIONS DURING NREM SLEEP IN MORNING AND EVENING CHRONOTYPES

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Introduction: Slow-wave oscillations (SWO, <4Hz, >75µV) during non-rapid eye movement (NREM) sleep are characterized by a negative phase, during which cortical neurons are mostly silent, and a positive phase, during which cortical neurons fire intensively. Longer duration of wakefulness (i.e., higher sleep pressure) associates with higher SWO density, amplitude and steeper slope between the negative and positive peaks. Spectral analysis data suggest that Morning-types show faster build-up and decay rates of sleep pressure compared to Evening-types. We thus hypothesized that SWO characteristics will show larger changes in Morning-types than in Evening-types in response to increased sleep pressure.

Methods: Morning-types (n=12, 6 men) were compared to Evening-types (n=12, 6 men) for a baseline sleep episode (BL) and for recovery sleep (REC) after two nights of sleep fragmentation. Artefact-free epochs recorded from the Fz derivation in NREM sleep were submitted to SWO detection according to published criteria. SWO density (number of SWO per minute of NREM sleep) and SWO characteristics (amplitude, duration of negative and positive phases, slope between the negative and positive peaks) were averaged for all-night NREM sleep and per NREM period.

Results: SWO slope was steeper in Morning-types than Evening-types, particularly in the first two NREM periods and during REC. Morning-types showed higher SWO amplitude than Evening-types, which difference was significant only during REC. SWO positive and negative phase durations were shorter in Morning-types than Evening-types but these differences were constant across NREM periods and between the two nights. SWO density did not differ between the groups.

Conclusion: Our data suggest that specific properties of cortical synchronization during sleep differ between Morning-types and Evening-types, although both chronotypes show similar SWO density. These

differences may involve both stable trait characteristics and specific responses to increased sleep pressure.

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0152

SLOW WAVE SLEEP IS CONSERVED DURING A SIMULATED SHIFTWORK SCHEDULE

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Introduction: Under sustained moderate sleep curtailment, slow wave sleep (SWS) has been found to be selectively conserved. We investigated whether SWS is also conserved under circadian manipulation of sleep timing.

Methods: N=27 healthy young adults (ages 22-38; 14 females) participated in a 14-day in-laboratory study. 13 subjects were randomized to a simulated shiftwork condition. After a baseline day with 10h nighttime sleep (TIB 22:00-08:00), subjects had a 5h nap (TIB 15:00-20:00), and entered a five-day nightwork period intervened by four 10h daytime sleep opportunities (TIB 10:00-20:00). Subsequently, they had a 5h nap (TIB 10:00-15:00) before rotating back to a baseline day with 10h nighttime sleep (TIB 22:00-08:00). Beginning with the first nap, the pattern then repeated itself. 14 subjects were randomized to a control condition with 10h nighttime sleep (TIB 22:00-08:00) daily. There were 13 sleep opportunities in the control condition, and 15 in the shiftwork condition, but cumulative TIB was the same. In the control condition, two out of every three 10h nighttime sleeps were PSG-recorded. In the shiftwork condition, the 10h baseline nights, 5h nap opportunities, and middle pair of each four 10h daytime sleeps were PSG-recorded.

Results: Mixed-effects ANOVA comparing SWS between sleep opportunities and conditions yielded a significant interaction (F[8,199]=9.80, P<0.001): SWS in the 5h pre-nightshift naps was relatively reduced. However, across all 15 sleep opportunities in the shiftwork condition, cumulative SWS was not significantly different than across the 13 sleep opportunities in the control condition with the same total TIB (one-way ANOVA: F[1,25]=0.098, P=0.76).

Conclusion: Our simulated shiftwork protocol resulted in sleep restriction relative to the control condition (see companion abstract by Bender et al.). Nonetheless, there was no significant difference in cumulative SWS. This finding suggests that SWS is conserved across days of sleep restriction even if TIB is distributed over circadian phase-shifted sleep opportunities and naps.

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0153

MILLISECOND LIGHT FLASHES PHASE SHIFT HUMAN CIRCADIAN RHYTHMS

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Introduction: By using light stimuli of several minutes or hours in length, previous studies have established that ocular light exposure can phase shift the human circadian clock in an intensity- and time-dependent manner. In rodents, millisecond light exposure can elicit circadian phase shifts. We therefore tested millisecond light exposure on human circadian rhythms.

Methods: Our study had seven subjects participate in a randomized crossover study (Visit A: stimulus=60 minutes dark; visit B: stimulus=one 2 msec flash of 473 lux/minute for 60 minutes on a background of dark, total of 120 msec of light). At least two weeks sepa-

rated visits. Subjects had customized, regular sleep/wake times for two weeks prior to each visit. Subjects came to the lab at habitual wake time +7 hrs and an hour later started a constant semirecumbent posture (CP) protocol lasting eight hours. Two hours after bed time, subjects were wakened and administered one of the stimuli, after which they were allowed to sleep five additional hours. Subjects were ambulatory in dim light until eight hours after waking then started a second CP lasting 10 hours. Saliva samples were collected every 30 minutes during CPs, and immediately before and after the experimental stimuli. Saliva samples were later assayed for melatonin concentrations.

Results: In the flash condition, subjects experienced a -45.0±12.9 min phase change whereas in the dark condition, subjects experienced a -3.50±7.28 min phase change (p<0.01, paired t-test). There was no difference in melatonin suppression following the flash and dark conditions (reductions of 33.8±16.4% and 8.70±17.7 %, respectively, p=0.54, paired t-test), despite robust suppression of melatonin in ~500 lux of continuous light.

Conclusion: We can generate 29% of the phase change with only 0.00051% of the light, compared to a 6.5hr light exposure. These data indicate the ability of the human circadian timing system to respond to brief light pulses.

Support (If Any): Air Force Office of Scientific Research (F2-4506); VA Sierra Pacific Mental Illness Research, Education and Clinical Center.

0154

THE EFFECT OF A SINGLE CONTINUOUS TWO MINUTE BRIGHT LIGHT PULSE ON THE HUMAN CIRCADIAN PACEMAKER

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Introduction: Animal studies have shown that the phase resetting response of the rodent circadian system is sensitive to light durations as short as 3 seconds (Nelson and Takahashi 1991). In this study, we investigated the magnitude of phase resetting response to a 2-minute bright light pulse in humans.

Methods: Twelve subjects were studied in a 9 day inpatient protocol. Subjects maintained a regular sleep-wake schedule at home for at least 2 weeks prior to inpatient admission. The 9 day protocol consisted of (in sequence): 3 baseline days (8-hr sleep,16-hr wake) scheduled at the subject's habitual times, an 8-hr sleep episode, a 50-hr constant routine (CR) procedure in which subjects remained awake in a constant posture under dim light and received hourly meals, an 8-hr post-CR sleep episode, a 16-hr wake period with light exposure (LE), a post-LE 8-hr sleep episode, a 30-hr CR and a final 8-hr sleep episode before subjects were discharged to home. During LE subjects sat in a constant posture for 4.5 hours and the bright 2-minute LE was administered at a time centered approximately 6 hours prior to habitual wake. Light levels during wake were 90 lux on baseline, and <1 lux from midway through baseline day 3 through the end of the study (including the 4.5-hr LE constant posture) except during the 2-minute LE when light levels were ~9500 lux. Light levels during sleep were ~0 lux. Circadian phase was assessed by computing the DLMO25% from plasma melatonin collected Q30. Phase shifts are reported as the difference between the final phase estimate immediately prior to LE and the first phase estimate during CR2.

Results: One subject was excluded from further analysis due to improper timing of the LE. Another subject was excluded from the final analysis due to a phase shift (of 4 minutes), which was ~3 standard deviations below the mean (mean computed without inclusion of this subject). For

the remaining 10 subjects, the average phase shift was 40 +/- 15 minutes (median 35 minutes; range 23 -67 minutes).

Conclusion: The human circadian system is more sensitive to short duration LE that would be predicted by previous studies of the human circadian phase-shifting response. This study is the first to demonstrate a significant phase shift in humans to continuous LE durations of less than 10 minutes.

0155

THE ROLE OF THE SUPRACHIASMATIC NUCLEUS IN MEDIATING THE NON-CIRCADIAN DIRECT EFFECTS OF LIGHT ON SLEEP AND ALERTNESS

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Introduction: Light can influence sleep and vigilance indirectly, through a well-defined circadian pathway involving the suprachiasmatic nucleus (SCN), or directly through non-visual, non-circadian effects. This will determine the timing and quality of sleep and alertness through an interaction with the circadian and homeostatic drives. Melanopsin (Opn4), a retinal photopigment crucial for conveying non-visual light information to brain areas, is a key mediator of this function. Recently, our group confirmed that induction of c-Fos by light in the SCN was lower in mice lacking melanopsin, linked to the reduced ability to phase-shift the circadian rhythm. However, this does not rule out the possibility of the SCN acting as a relay for these direct effects.

Methods: Wild-type and KO melanopsin mice were recorded for EEG under 3 SCN conditions: intact, sham and "arrhythmic", and the following light-dark regimens: LD12h:12h, 1h L- or D-pulses during the 12h D- or L-period, and a 24-hour period of LD1h:1h cycles. An anatomical study of the SCN and retinohypothalamic tract was performed (triple immunohistochemistry staining of the main SCN neurotransmitters, AVP, VIP, and CTB- for tracing.)

Results: Mice with lesioned SCNs have a flattened sleep/wake rhythm consistent with the removal of the circadian drive. Furthermore, after removal of the SCN, the sleep-promoting effect of light and alerting effect of darkness, evidenced under the 1h:1h LD ultradian cycle, are partly abolished in both genotypes, similar to the intact Opn4-/- mice. Anatomical analysis shows a complete lesion of the SCN sparing surrounding brain structures. Staining of the retinohypothalamic fibers to the VLPO and other areas, were conserved in lesioned animals.

Conclusion: Comprehensive analysis is ongoing to confirm these findings which suggest that the SCN is one of several possible relays mediating the direct effects of light on sleep and alertness and playing a role beyond its function as circadian master clock.

0156

COMBINATION OF BRIGHT LIGHT AND EXOGENOUS MELATONIN FOR PHASE ADVANCING THE HUMAN CIRCADIAN CLOCK

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Introduction: Photic and non-photic time cues have both been used to phase shift the human circadian clock. The combination of light and melatonin may be more efficient at phase shifting the circadian clock than either treatment alone. Therefore, we examined the influence of

a single pulse of bright light exposure and a single administration of exogenous melatonin alone and in combination in a protocol designed to induce a phase advance shift of the human circadian clock.

Methods: 32 young healthy subjects [18 males (22.3±3.9yr;mean±SD)] were studied in a 3.7 day in-laboratory phase shifting protocol. The effects of four conditions (dim light-placebo, dim light-melatonin, bright light-placebo, bright light-melatonin) on circadian phase measured by salivary dim light melatonin onset (DLMO) were assessed prior to and following treatment under constant routine conditions. Melatonin (5mg) or placebo was administered 6h prior to habitual bedtime and 3h of bright light (~3000 lux) exposure started 1h prior to habitual waketime. Subjects were otherwise maintained in dim room light (<1.8 lux) and darkness during scheduled sleep.

Results: A significant main effect for bright light (p<0.05) and a non-significant main effect for melatonin (p=0.057) were observed for circadian phase shifts. The greatest phase advances were found for the bright light-melatonin condition, with intermediate phase advances for the bright light-placebo and dim light-melatonin conditions as compared to the delay in circadian phase observed for the dim light-placebo condition.

Conclusion: Photic and non-photic time cues can be combined to induce a greater advance in circadian phase in humans than either bright light or exogenous melatonin alone. These findings have implications for the treatment of circadian sleep disorders.

0157

HOW MUCH MORNING LIGHT IS NECESSARY TO PHASE ADVANCE CIRCADIAN RHYTHMS IN HUMANS?

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Introduction: We previously tested a gradually advancing sleep/dark schedule with morning intermittent bright light (four 30-minute pulses) plus afternoon melatonin (0.5mg) (Revell et al., JCEM 2006) to advance circadian rhythms. We currently examine whether reducing the number or reducing the duration of light pulses decreases the phase advance.

Methods: Twenty-three young healthy adults (12 male) have completed this ongoing study. Following 6 nights of "stabilization" (fixed 8-hour sleep) we sample saliva every 30 minutes to determine the baseline dim light melatonin onset (DLMO). After another 3 days of stabilization, we advance sleep/dark by 1 h/night for 3 consecutive nights. Participants ingest 0.5mg melatonin 5 hours before their stabilization bedtime on the first laboratory night and 1 hour earlier each day. Participants are exposed to one of two bright light (~5000 lux) patterns beginning approximately 5 minutes after waking each morning. One group (N=11) receives a single 30-minute light pulse. Another group receives four 15-minute light pulses (N=12) with 45 minutes of room light (<120 lux) between each pulse. Saliva sampling to determine the final DLMO follows. We compare each group to our previous group (N=16), who received four 30-minute morning light pulses with 30 minutes of room light between each pulse.

Results: Larger phase advances emerged after four 30-minute light pulses (mean=2.4, SD=0.8 hours) compared to a single 30-minute pulse (mean=1.7, SD=0.9 hours) [t(26)=2.25, p=.03] and four 15-minute pulses (mean=1.8, SD=0.7 hours) [t(25)=2.13, p=.04].

Conclusion: Thus far, reducing the number or duration of light pulses produces smaller advances compared to four 30-minute light pulses; however, these abbreviated light treatments (with an advancing sleep/dark schedule and afternoon melatonin) still produce more than 70% of the mean phase advance produced by the longer treatment. Furthermore, the average phase advance after four 15-minutes pulses (total duration=60 minutes) was similar to that produced by a single 30-minute pulse.

0158

DAILY TOTAL SLEEP TIME IS REDUCED ENDOGENOUSLY DURING A SIMULATED NIGHT WORK SCHEDULE

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Introduction: Night work schedules are typically associated with sleep loss due to difficulty obtaining sleep during the day. In real-world settings, daytime sleeping is hampered by a combination of circadian, environmental, social and domestic factors. Here we focused on the circadian factor, and examined the difference in total sleep time (TST) between laboratory-controlled, simulated day and night shift schedules.

Methods: N=27 healthy young adults (ages 22-38; 14f) participated in a 14-day in-laboratory study with fixed levels of light (<50lux during scheduled wake, <1lux during sleep). They were randomized to a night shift condition (n=14) or a day shift condition (n=13). After a baseline day with 10h nighttime sleep (TIB 22:00-08:00), subjects in the night shift condition had a 5h nap (TIB 15:00-20:00), and entered a five-day night work period with four 10h daytime sleep opportunities (TIB 10:00-20:00). Subsequently, they were given a 34h "off-duty" period consisting of a 5h nap (TIB 10:00-15:00), a 10h nighttime sleep (TIB 22:00-08:00) and another 5h nap (TIB 15:00-20:00). They then entered another five-day night work period with four 10h daytime sleep opportunities (TIB 10:00-20:00). The day shift (control) condition had nighttime sleep (TIB 22:00-08:00) throughout the study. Sleep was recorded polysomnographically on two out of every three laboratory days.

Results: Using mixed-effects ANOVA, total sleep time (TST) was compared for the middle pair of each set of daytime sleep opportunities in the night shift condition versus the corresponding nighttime sleep opportunities in the day shift condition. There was a significant difference between conditions (F[1,81]=14.71, P<0.001): subjects in the night shift condition slept less (mean±s.e.: 7.5h±0.2h/day) than subjects in the day shift condition (8.3h±0.2h/day). Across all PSG-recorded nights, TST was also significantly reduced in the night shift condition compared to the day shift condition (t[23]=3.88, P=0.001), despite equal amounts of cumulative TIB.

Conclusion: Our simulated night shift protocol resulted in nearly 1h of sleep loss per day on average relative to the day shift protocol. Given ample time in bed and strict control over light exposure and other zeitgebers in the laboratory, this 1h difference would appear to estimate the magnitude of the endogenous circadian effect on sleep time in night versus day shift schedules.

0159

HEALTHY HUMANS ARE SENSITIVE TO SMALL DEGREES OF CIRCADIAN MISALIGNMENT

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Introduction: Humans report changes in sleepiness after small changes in the alignment between circadian phase and sleep of as little as 1 hour (e.g. daylight savings, weekend phase delays, travel across 1 time zone), but few studies have quantified these effects. We examined for the first time if subtle shifts away from an "ideal" phase angle (dim light melatonin onset (DLMO) to sleep midpoint interval of 6 hours) increase subjective sleepiness and worsen objective performance.

Methods: Twenty-two healthy young subjects (18-45 years, 12 men, 10 women) participated in a within-subjects repeated measures design. Each subject completed the same protocol twice, separated by at least 2 weeks. The protocol consisted of 6 days of fixed 8 hour sleep (verified with wrist actigraphy, matched to each subject's average sleep times from the week before the study), followed by a circadian phase assess-

ment during which half hourly saliva samples were collected in dim light (<5 lux) to determine the DLMO. Subjects rated their sleepiness and completed a Psychomotor Vigilance Task (PVT) several times per day. So far we have analyzed ratings completed before bedtime.

Results: The DLMO varied between the two phase assessments by an absolute median of 33 minutes. When people were further away from an "ideal" phase angle (defined above), they reported a significant increase in subjective sleepiness (Stanford Sleepiness Scale, p=0.06), physical fatigue (p=0.046), mental fatigue (p=0.03) and were more variable in their reaction time on the PVT (interquartile range, p=0.047) than when closer to an "ideal" phase angle.

Conclusion: These results (1) demonstrate that subjective sleepiness and performance consistency are sensitive to a small change in circadian phase angle and (2) support the notion of an ideal circadian phase angle in humans. Thus even healthy humans may be more sensitive to small changes in circadian phase than previously thought.

0160

ALTERED SCALE-INVARIANT CARDIAC DYNAMICS IN HUMANS ACROSS A FORCED DESYNCHRONY PROTOCOL

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Introduction: Heartbeat fluctuations in humans display a scale-invariant structure that changes with cardiovascular pathology. The endogenous circadian rhythm controlled by the circadian pacemaker is normally synchronized with daily behavioral cycles, and disturbances of such synchronization have adverse consequences on cardiovascular control. We hypothesized that the scale-invariant cardiac dynamic is altered when the endogenous circadian oscillation is desynchronized from the sleep-wake cycles.

Methods: To test this hypothesis, 5 healthy subjects (20-33 years old, 4 males) were studied throughout a 'forced desynchrony' protocol. Following two baseline days, subjects' sleep-wake cycles were adjusted to 28 hours for 7 cycles (FD cycles). Core body temperature and time since scheduled waking were used to estimate circadian phases and behavioral phases, respectively. Detrended fluctuation analysis was used for assessment of scale-invariant patterns in heartbeat fluctuations. Mixed model ANOVA with subject as a random factor was performed to determine differences in scale-invariant structures of heartbeat fluctuations among different FD cycles. To account for influences of circadian and sleep-wake cycles, circadian phase bin and behavioral phase bin (divided into six 60° bins) were also included in the model.

Results: Independent of the circadian and sleep-wake influences, the scale-invariant structure of heartbeat fluctuations showed significant changes throughout the FD cycles (p<0.0001). Specifically, the scaling exponent characterizing scale-invariant correlations of heartbeat fluctuations was identical in FD cycle 1 (Mean±SE: 1.020±0.021) as compared to baseline. The exponent increased gradually from FD cycle 1 to FD cycle 4 (1.077±0.020; ~5% increase; p=0.0003) and remained elevated above baseline (or FD cycle 1) throughout FD cycles 5-7 (p<0.02).

Conclusion: Since cardiac dynamics under pathologic conditions such as congestive heart failure also are associated with an increased cardiac scaling exponent (~1.3), the gradual increase in the exponent during the FD protocol provides evidence that disturbances of normally synchronized circadian and behavioral cycles might have adverse influences on cardiac control.

0161

DAYTIME SLEEPINESS IS ASSOCIATED WITH ALTERED BRAIN ACTIVATION DURING VISUAL PERCEPTION OF HIGH-CALORIE FOODS: AN fMRI STUDY

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Introduction: With the average sleep duration in our population declining and the obesity epidemic on the rise, it is of particular importance to understand the relationship between sleep-related factors, brain responses to food, and eating behavior. Prior evidence suggests that healthy adults activate inhibitory regions of the prefrontal cortex in response to high-calorie food images. However, insufficient sleep is often associated with reduced metabolic activity within these same prefrontal regions. We hypothesized that greater daytime sleepiness would correlate with reduced prefrontal responses during passive viewing of appetizing high-calorie food images.

Methods: Twelve healthy adults (6 men) aged 19 to 45 underwent functional magnetic resonance imaging (fMRI) while viewing pictures of high-calorie foods, low-calorie foods, and control images of plants and rocks. Subjects completed the Epworth Sleepiness Scale (ESS) for daytime sleepiness regarding their likeliness to doze during various activities (i.e reading, watching television, resting, etc). In SPM5, contrast images comparing brain activation derived from the high- versus low-calorie conditions were correlated voxel-wise with scores from the ESS sleepiness in a second-level regression model (p<.005, k=10).

Results: As hypothesized, greater ESS scores correlated with reduced activation in the dorsolateral prefrontal cortex during perception of high- versus low-calorie food images. Greater daytime sleepiness was also associated with increased activation in the right parietal and inferior temporal cortex.

Conclusion: During visual presentations of enticing high-calorie food images, greater sleepiness was associated with decreased activation in the prefrontal cortex, a region normally implicated in attention and inhibitory processing. Findings raise the speculative possibility that sleepiness may affect inhibitory control when confronted with highly appetizing high calorie foods. The extent to which the correlation between sleepiness and increased posterior cortex activation may reflect compensatory recruitment and whether these patterns may relate to actual food consumption remain unknown, but may be critical topics for further research.

0162

SEX DIFFERENCE IN SELF-REPORTED SLEEP DURATION, DAYTIME SLEEPINESS, AND CAFFEINE USE IN MORNING AND EVENING TYPES

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Introduction: It has been reported that individuals with evening diurnal preference more often report poor sleep quality than those with morning preference. This may be due to differences in the circadian timing of their sleep, and/or to their inability to obtain sufficient sleep if they are required to get up earlier than desired in the morning to meet social demands. Because of reported sex differences in morningness-eveningness, and reported sex differences in sleep duration, we conducted a questionnaire study to examine morningness-eveningness and self-reported sleep duration in men and women.

Methods: Nine hundred eleven subjects (Age: 38.4±10.9 years, range: 18-88; F:M=565:346) were recruited from visitors to the National Museum in Chunchon city, South Korea. The Korean Sleep-Wake Questionnaire (SWQ-K), which includes the Horne-Östberg Morningness-Eveningness Questionnaire (MEQ), Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and questions about sleep-wake timing and caffeine use, was administered. Standard scores on the MEQ were used to categorize subjects as morning type (MT), evening type (ET), or neither type (NT).

Results: ET individuals had higher PSQI scores (p<0.0001), higher ESS scores (p=0.055), shorter sleep duration (p=0.001), and greater caffeine use (p=0.029) than MT individuals. Among the women (n=168), the mean PSQI and ESS scores of the ET women were significantly higher than the MT women (p<0.01). The ET women also had shorter sleep durations (p<0.001) and greater reported caffeine use (p<0.05) compared to the MT women. Among the men (n=128), there was no significant difference between ET and MT in ESS score, sleep duration, or caffeine use, but the mean PSQI score of ET men was higher than MT men (p<0.01).

Conclusion: Our questionnaire results indicate that ET women report shorter sleep durations than MT women, which likely contributed to their greater self-reported daytime sleepiness and caffeine use. No such differences were reported in the men. These findings suggest an interaction between chronotype and sex that has a greater negative impact on the sleep and waking performance of evening-type women.

0163

THE EFFECTIVENESS OF A RESTART BREAK CONTAINING TWO BIOLOGICAL NIGHTS FOR MAINTAINING SIMULATED DRIVING PERFORMANCE ACROSS CONSECUTIVE WEEKS OF NIGHT WORK

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Introduction: Current hours of service regulations stipulate that U.S. commercial motor vehicle drivers must have a 34h "restart" period for recovery after accumulating 70h on duty before commencing another work period. We recently showed that in night shift workers, where the 34h restart period contains only one biological night, recovery is incomplete. The current study aimed to determine whether extending the restart period to 58h, so as to include two biological nights, would help sustain performance in night shift workers.

Methods: N=16 healthy men (ages 27.5±5.6y) participated in a 16-day in-laboratory experiment. After two baseline days with 10h nocturnal sleep (TIB 22:00-08:00), subjects were given a 5h nap, and underwent 5 days of night work and daytime sleep (TIB 10:00-20:00). This was followed by a 58h restart period, which included a 5h nap, two days with 10h nocturnal sleep (TIB 22:00-08:00), and another 5h nap. Subjects then underwent another 5 days of night work and daytime sleep. On night work days, subjects performed four 30min drives on a high-fidelity driving simulator. Mixed-effects ANOVAs were performed to examine the effect of the restart period on simulated driving performance.

Results: There was a significant effect of work week for speed variability (F[1,618]=18.1; P<0.001) and lane deviation (F[1,618]=21.3; P<0.001), with improved performance following the 58h restart period. When comparing to results from our earlier study with a 34h restart period (N=13), there was a significant interaction for speed variability, with better performance following the 58h restart period (F[1,1123]=8.1; P=0.045). However, there was no significant interaction for lane deviation (F[1,1123]=0.02; P=0.89).

Conclusion: An extension of the current 34h restart provision for U.S. commercial motor vehicle drivers in night work operations, to include an extra biological night, appears to be an efficacious, albeit perhaps not cost-effective, approach for sustaining some aspects of simulated driving performance.

0164

EFFECTS OF CONSECUTIVE NIGHT SHIFT WORK ON POLICE OFFICER PERFORMANCE

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Introduction: Motor vehicle crashes are highly prevalent among police officers. They often work long and irregular, fatiguing shifts, which may underlie the increased motor vehicle crash rate in this population. To examine this issue, we compared police officer driving performance at the end of a period of night shifts with driving performance at the same time of day following a normal night's sleep.

Methods: N=13 police patrol officers (27-46y; 1f) participated in two randomized experimental conditions in the laboratory. One condition (post-shift) involved performance testing in the morning immediately after the last work day of five consecutive days of 10.7h night shifts; the other condition (control) was conducted at the same time in the morning, but after a normal night of sleep following three consecutive nights off duty. In each condition, officers performed two 30-minute high-fidelity driving simulator test drive sessions, a shooting simulation task, and four 10-minute psychomotor vigilance test (PVT) sessions (sequence: PVT, shoot, PVT, drive, PVT, drive, PVT). Mixed-effects ANOVAs were used to examine the effects of condition and test session on PVT lapses (RT>500ms) and on lane deviation during simulated driving. One subject's driving data was excluded due to a collision that prematurely ended a simulated drive in the post-shift condition.

Results: Performance was significantly poorer in the post-shift condition for both driving simulator lane deviation (F[1,465]=9.21, P=0.003) and PVT lapses (F[1,56]=9.13, P=0.004). Post-drive PVT lapses covaried significantly with lane deviation (F[1,308]=4.40, P=0.037).

Conclusion: The present, laboratory-controlled results indicate that officers experience impaired vigilance and degraded (simulated) driving performance in the morning following a week of night shifts compared to the morning following a normal night of sleep after three nights off duty. This suggests that the high prevalence of motor vehicle crashes among police officers could be mitigated through improved fatigue management.

0165

PSYCHOMOTOR VIGILANCE PERFORMANCE AT TOP OF DESCENT DURING ULTRA-LONG RANGE FLIGHTS AS COMPARED TO LONG RANGE FLIGHTS

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Introduction: Ultra-long range (ULR) commercial flights are generally longer (>16h flight time >10% of the time) than long range (LR) flights (8h-16h flight time). Both ULR and LR flights are flown with augmented (3 or 4 pilot) crews to allow for in-flight rest. Nevertheless, because of the longer duty times involved in ULR flights, they could be more fatiguing than LR flights. We compared performance on a psychomotor vigilance test (PVT) at top of descent (TOD), a critical end-of-flight period when all pilots are to be in the cockpit either flying or monitoring, in ULR versus LR flights.

Methods: As part of a larger study, N=51 Boeing 777 pilots (age 52.3±6.7y; 1f) were studied during adjacent ULR and LR flight pairings. A 5-minute PVT ported to a PDA was taken within 1 hour prior to TOD on each leg of each pairing. Mean PVT reaction times were compared between ULR and LR within pilots, using mixed-effects ANOVA.

Results: There was no significant difference in mean PVT reaction times at TOD between ULR and LR flights (F[1,140]=2.77, P=0.10). PVT reaction times were 294ms±20ms (mean±SE) during ULR flights and 332ms±20ms during LR flights.

Conclusion: PVT performance at TOD was not significantly different between ULR and LR flights. While further data collection is ongoing, this preliminary finding suggests that ULR flights are not inherently more fatiguing than LR flights despite the longer duty times in ULR operations.

0166

SUBJECTIVE SLEEPINESS AND FATIGUE AT TOP OF DESCENT DURING ULTRA-LONG RANGE FLIGHTS RELATIVE TO LONG RANGE FLIGHTS

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Introduction: Ultra-long range (ULR) commercial flights (>16h flight time >10% of the time) involve longer duty times than long range (LR) commercial flights (8h-16h flight time). Both flight types are performed with augmented (3-4 pilot) crews to allow for in-flight rest. We compared subjective sleepiness and fatigue during ULR and LR flights at top of descent (TOD), a critical end-of-flight period when all pilots are in the cockpit either flying or monitoring.

Methods: As part of an ongoing study, N=52 Boeing 777 pilots (age 52.4±6.7y; 1 female) were studied during both ULR and LR flight pairings. Subjective sleepiness (Karolinska Sleepiness Scale; range 1-9, "extremely alert" to "extremely sleepy, fighting sleep") and subjective fatigue (Samn-Perelli Fatigue Scale; range 1-7, "fully alert, wide awake" to "completely exhausted, unable to function") were measured within 1h prior to TOD on each leg of each pairing. Sleepiness and fatigue scores were compared within pilots by flight type using mixed-effects ANOVA.

Results: Subjective sleepiness scores were 3.5±0.2 (mean±SE) during both ULR and LR flights. Subjective fatigue scores were 3.0±0.1 during ULR flights and 2.9±0.1 during LR flights. There was no significant effect of flight type on subjective sleepiness (F[1,154]=0.04, P=0.84) or on subjective fatigue (F[1,154]=0.11, P=0.74) at TOD.

Conclusion: Despite the longer duty time associated with ULR flights, subjective sleepiness and fatigue were not significantly different at TOD in ULR flights relative to LR flights. Further data collection is ongoing to increase the statistical power of the study.

0167

IN-FLIGHT AND LAYOVER SLEEP DURATION IN COMMERCIAL AIRLINE PILOTS FLYING LONG RANGE (LR) VS. ULTRA-LONG RANGE (ULR) FLIGHTS

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Introduction: Recent advances in commercial aviation have made it possible to increase flight duration beyond long range (LR; 8h-16h flight time) to ultra-long range (ULR; >16h flight time >10% of the time). A priori, the longer duty hours of ULR could result in greater risk of fatigue. A key issue is whether or not ULR flights are associated with reduced amounts of sleep. To investigate this, we compared sleep during flights and during layovers for LR vs. ULR flights, in the same pilots.

Methods: As part of an ongoing study, the sleep of N=52 Boeing 777 pilots (ages 52.5±6.7y; 1 female), studied over both LR and ULR flight pairings, was monitored by actigraphy (Phillips Respironics Actiwatch Spectrum) from three days before their first flight pairing until three days after their second flight pairing. All flights were augmented (3 or 4 pilot crews), allowing for in-flight sleep (as only 2 pilots are needed on

the flight deck during cruise). Total sleep time (TST) for both in-flight and layover sleep was compared between the LR and ULR flights using mixed-effects ANOVA.

Results: Average total in-flight sleep time for ULR flights was 233.0±11.4min (mean±s.e.), whereas for LR flights it was 136.6±10.9min (average difference 96.4min, F[1,218]=57.6, P<0.001). Average total layover sleep time for ULR flights was 256.0±17.0min, whereas for LR flights it was 256.8±18.1min (no significant difference, F[1,208]<0.01, P=0.97).

Conclusion: Compared to LR flights, ULR flights were associated with similar amounts of layover sleep and more in-flight sleep as assessed with actigraphy. Pending further data collection, we tentatively conclude that from a sleep/wake perspective, ULR flights should involve no greater fatigue risk than augmented LR flights.

Support (If Any): Continental Airlines

0168

FUNCTIONAL MRI CORRELATES OF MORNINGNESS-EVENINGNESS DURING VISUAL PRESENTATION OF HIGH CALORIE FOODS

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Introduction: Obesity rates are increasing while average hours of sleep are decreasing. It is unclear whether the link between short sleep duration and obesity might be related to sleep chronotype (i.e., Morningness-Eveningness). Evening types are more likely to have reduced sleep duration and quality than Morning types, who often show higher levels of conscientiousness and impulse control. The relationship between morningness-eveningness and functional brain responses to food has not been previously studied. Therefore, we examined this relationship using functional magnetic resonance imaging (fMRI). We hypothesized that Morningness would correlate with greater activity in the prefrontal attentional and behavioral control regions during a cognitively engaging task involving appetizing food images.

Methods: Twelve healthy adults (6 male) ranging from 19 to 45 years of age completed the Morningness-Eveningness Questionnaire (MEQ) and then underwent functional magnetic resonance imaging (fMRI) while viewing images of high and low calorie foods. Scores on the MEQ were correlated voxel-wise with brain activation during the task (high calorie foods > low calorie foods contrast) using linear regression in SPM5 (p<.005, k≥10). All scans were performed in the afternoon between 1200 and 1600.

Results: Morningness (higher MEQ scores) was associated with increased activation within the lateral prefrontal cortex. In contrast, Eveningness (lower MEQ scores) was associated with increased default mode network activation, including posterior cingulate and medial prefrontal cortex.

Conclusion: This study suggests that chronotype is associated with patterns of brain activation that may have implications for appetitive behavior and which may be relevant to the current obesity epidemic. Overall, greater morning preferences were associated with increased activation within prefrontal inhibitory networks when confronted with appetizing food images, while evening preferences were associated with a pattern commonly associated with behavioral disinhibition, self-referential thinking, and environmental disengagement. The extent to which these patterns relate to actual food consumption remain to be studied.

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0169

RELATIONSHIP BETWEEN CHRONOTYPE, GPA AND TOTAL SLEEP TIME IN A MILITARY COLLEGE POPULATION

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Introduction: Adolescents have melatonin rhythms that are phase delayed compared to adults and are naturally inclined to become sleepy later at night (Wolfson & Carskadon, 1998). Further, chronotype studies have demonstrated that eveningness-type has been associated with later bed times in adolescent populations (Giannotti, Cortesi, Sebastiani, & Ottaviani, 2002). United States Air Force Academy (USAFA) cadets are faced with a structured schedule with little free time. However, despite "taps" occurring at 1045, cadets can stay up later to study, etc. The current study investigated whether cadets' time to bed, total sleep time, and GPA is predicted by their chronotype.

Methods: Participants were 99 undergraduate USAFA cadets, approximately half male (51.5%), representing all class years, and were between 17 and 25 years of age. All participants filled out the Circadian Rhythm Scale (CRS) plus wore an actigraph for one week. Cadet GPA was obtained at semester's end.

Results: Preference for sleep time significantly predicted total sleep hours over the course of a week (R = .29, F(1,95) = 8.72 p < .01), average amount of weekday nightly sleep (R = .22, F(1,95) = 4.94, p = .03), average amount of weekend nightly sleep (R = .23, F(1,91) = 4.84, p = .03), average time to bed (R = .39, F(1,95) = 16.68, p < .01), and current semester GPA (R = .20, F(1,92) = 3.90, p = .05).

Conclusion: As participants' preference time for going to bed became later, they tended to sleep for fewer total hours, go to bed later, and have a lower GPA. In a controlled military setting, individuals who prefer to go to bed later do not receive as much sleep as individuals with earlier sleep preferences. Adolescents with evening-favored circadian rhythm cycles may be at risk to receive less sleep and lower GPA than individuals who prefer earlier bedtime.

Support (If Any): DARPA

0170

SUNLIGHT EXPOSURE AND CHRONOTYPE: COMPARISON OF TWO DIFFERENT GEOGRAPHICAL LOCATIONS

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Introduction: Sunlight is a potent zeitgeber for circadian rhythms. As such, it has been argued that circadian entrainment depends on geographical location, in particular longitude within time zone and population density (thought to be a correlate of sunlight exposure). Circadian phase is a determinant of chronotype (morningness/eveningness), and location may therefore affect chronotype distribution. We tested this hypothesis by comparing chronotype distributions between two U.S. cities (Philadelphia, PA and Spokane, WA) differing in geographical location (Philadelphia: 40°00′N, 75°09′W; Spokane: 47°40′N, 117°25′W; both on the eastern edge of their respective time zone) and population density (Philadelphia: 4,405/km², total ~1.5 million; Spokane: 1,308/km², total ~200,000). In summer, Spokane averages 58min of sunlight/day more, with the sun rising 40min earlier; in winter, Spokane averages 55min of sunlight/day less, with the sun rising 16min later than in Philadelphia.

Methods: N=543 telephone-screened, healthy, non-smoking subjects with regular sleep schedules (ages 18-40y, 62.7% males), 150 in Philadelphia and 393 in Spokane, completed the Composite Scale of Morningness (CSM) to assess chronotype. Means and variances of CSM

scores were compared between locations using independent t-test and Levene's test for equality of variance.

Results: CSM scores in Philadelphia (M=39.9, SD=5.5) were not significantly different from those in Spokane (M=38.9, SD=6.1), although there was a trend for slightly more eveningness in Spokane (t[541]=1.67, P=0.096). The variance in CSM scores did not differ significantly between the two locations (F[1,541]=2.2, P=0.14).

Conclusion: No significant differences in chronotype distribution were found between Spokane and Philadelphia despite differences in sunlight exposure and population. The purported effects of geographical location and population density, through sunlight exposure, on circadian entrainment may have been moderated in our samples by exposure to artificial light and/or social zeitgebers. If our finding generalizes to other locations, it will lessen concerns about systematic circadian confounds when combining samples in multi-site investigations.

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0171

EPIDEMIOLOGY OF BEDTIME, ARISING TIME AND TIME IN BED: ANALYSIS OF AGE, GENDER AND ETHNICITY

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Introduction: Less data exist on behavioral circadian variables than their physiological correlates. Furthermore, there is a paucity of normative behavioral sleep data in the literature. The present study attempts to address this gap by analyzing behavioral variables reported in sleep diaries from our epidemiological survey.

Methods: 772 participants from a metropolitan community were enrolled using random-digit dialing, yielding a diverse sample. Demographic data and 14 days of sleep diary data were analyzed for 756 participants. Data was first plotted to determine linearity. Hierarchical regression was performed to analyze the effects of age, ethnicity, and gender on bedtime, arising time, and time in bed (TIB).

Results: There is a negative, linear relationship between age and bedtime: as individuals age they tend to go to bed earlier. Furthermore, age has a curvilinear relationship with both arising time and TIB. Individuals initially tend to get out of bed earlier as they age until they reach mid-life, at which time they get out of bed progressively later. The relationship between bedtime and arising time produces a curvilinear relationship, wherein there is a slight decrease in TIB until mid-life, at which point TIB steeply increases. Age was moderately correlated with average bedtime (r = -.33, p<.001). All other variables were either weakly correlated or were non-significant. Age contributed 10.9% of the variance of bedtime. Ethnicity and gender added only 1.4% of explained variance. Age contributed 7.0% of the explained variance of arising time. Age also contributed 13.3% of the explained variance of TIB. Gender and ethnicity were excluded from the arising time and TIB regression models due to non-significance.

Conclusion: There are distinct behavioral sleep patterns based on age but not gender or ethnicity. These results may have significant clinical implications, particularly for older adults.

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0172

MEN AND WOMEN SLEEP AT A SIMILAR CIRCADIAN PHASE

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Introduction: Some studies have reported that women sleep at a slightly earlier clock time than men. Other studies have reported that women also have circadian clocks set to a slightly earlier time, as seen in the earlier onset of the endogenous melatonin rhythm collected in dim light (DLMO). However reports on whether women sleep at a different circadian phase to men are mixed: some report that the DLMO is earlier relative to sleep in women versus men (thus women sleep at a later circadian time), while others report no sex difference. Here we reexamined a large data set to look for sex differences in circadian phase angle.

Methods: Forty four healthy subjects (19-43 years) maintained a fixed 8 hour baseline sleep schedule (verified with wrist actigraphy) for at least 3 days, determined by their average self-reported bed and wake times from the previous week. This was immediately followed by a circadian phase assessment during which half hourly saliva samples were collected in dim light (<10 lux) for determination of the DLMO. Each man was matched to a woman (free of hormonal contraception) according to age (± 5 years) and wake time (± 30 minutes) as per Cain et al. 2010.

Results: Women slept on average 12 minutes later relative to their circadian clock than men (DLMO to bedtime interval 3.0 versus 2.8 hours respectively, p=0.55). These results are in the same direction as reported by others, but show no significant sex difference in circadian phase angle.

Conclusion: These results suggest that men and women sleep at a similar circadian phase. We are currently adding an additional 20 men-women matched pairs to this data set and so will soon have the largest data set available (n=42 matched pairs) to comprehensively examine sex differences in circadian phase angle.

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0173

ETIOLOGICAL MODERATION OF DIURNAL PREFERENCE BY AGE IN A POPULATION BASED SAMPLE OF ADULT TWINS

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Introduction: Quantitative and molecular genetic studies have shown that the self-report analogue of circadian rhythm phase - diurnal preference - is heritable. Diurnal preference is a measure of one's tendency towards morningness or eveningness. With increasing age individuals show a greater tendency towards morningness, yet why and how this age shift occurs is poorly understood. It is possible that the contribution of genetic and environmental influences on diurnal preference varies as a function of age. Accordingly, the present study focuses on age as a continuous moderator of the genetic and environmental influences on diurnal preference in a sample of twins from young to late adulthood.

Methods: Data from 768 monozygotic and 674 dizygotic twin pairs participating in the University of Washington Twin Registry was used in the current study (age range 19.12-92.75 years; mean=36.23, SD=15.54). Diurnal preference was assessed by the reduced morningness-eveningness questionnaire.

Results: Increasing age was associated with a greater tendency towards morningness (r=.42 [95% confidence interval .38, .45]). Structural equation modelling demonstrated that additive genetic influences accounted for 52% (95% CI 46-57%), and non-shared environmental influences 48% (95% CI 43-54%) of the total variance in diurnal preference. In the moderation analyses there was some evidence for moderation of the non-shared environment by age (-.04[95% CI -.07, .01]), indicating that as age increased the non-shared environmental influences on diurnal preference decreased.

Conclusion: Our results suggest that aging reduces the influence of the non-shared environment on diurnal preference. This gene by environment interaction may be driven by the decline in social, work and family responsibilities as one ages, allowing the endogenous circadian rhythm to re-emerge. Alternatively, the influence of genetics on diurnal preference may increase across the lifespan. These findings add to our understanding of the sleep-wake cycle and may have implications for molecular genetic studies aimed at identifying polymorphisms associated with diurnal preference.

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0174
VARIANCES IN DIURNAL PATTERNS OF FATIGUE AND MOOD AMONG POSTPARTUM MOTHERS

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Introduction: Circadian rhythm disruptions have been identified as present among several mood disorders. In addition, postpartum women experience temporary circadian rhythm disruption. Our goal was to describe associations between maternal diurnal rhythm dysregulation and mood among healthy women across the first 3 postpartum months.

Methods: Fifty-six primiparous mothers (26.6 years, 91.1% white, 16.0 years of education) used a personal digital assistant to report 100-point Visual Analog Scale of fatigue ratings during every diurnal infant feedings (M=2.9 times/day). The Profile of Mood States (POMS) was completed reflecting postpartum weeks 2 and 11. During these two weeks, each mother's fatigue scores were plotted against diurnal hours (06:00-24:00) and analyzed for significant trends indicating presence, grouped as "Yes" (week2 n=31,week11 n=39), or absence, grouped as "No" (week2 n=25,week11 n=17), of rhythmicity. Mothers were then further categorized into four groups: those with a significant rhythm at both weeks (Yes-Yes, n=24), no significant rhythm at either week (No-No, n=10), rhythm absent at week 2 but present at week 11 (No-Yes, n=15), and rhythm present at week 2 but absent at week 11 (Yes-No, n=7).

Results: Between groups, although there was no statistically significant difference between women with (Yes) and without (No) a diurnal rhythm at week 2, by week 11 women with a diurnal rhythm had significantly better POMS scores (p=0.013, d=.79). Using within-subjects comparison, only mothers who had a diurnal rhythm at both weeks (Yes-Yes) had a significant improvement on POMS from week 2 to 11 (p<.001).

Conclusion: Our data suggest maternal benefits from establishing and maintaining a diurnal rhythm. These findings may have implications for postpartum interventions among vulnerable women. Techniques such as scheduling and zeitgeiber exposure early after the birth of an infant may be beneficial.

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0175
A PROSPECTIVE STUDY OF WEIGHT GAIN ASSOCIATED WITH CHRONOTYPE IN COLLEGE FRESHMAN

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Introduction: During the first year of college, adolescents are susceptible to both weight gain and poor sleep habits. Sleep duration has been previously associated with weight regulation, though other aspects of the sleep-weight relationship, such as the role of circadian preference, still need to be explored. We hypothesized that eveningness would be associated with greater weight gain during the Freshman-year, perhaps due changes in sleep duration and erratic scheduling, which could lessen the chances of having consistent meal and exercise times.

Methods: A series of self-report measures involving a demographic questionnaire and the abbreviated Morningness-Eveningness Questionnaire (rMEQ) were was completed during the second week of participants' (n=137) freshman term, and follow-up measures were completed 8 weeks later. Of the initial 137 participants n=54 completed follow-up data, and thereby served as the sample of interest. Weight and height were collected to calculate BMI and assess weight gain. The rMEQ was used to assess participants' circadian preference.

Results: The rMEQ identified 1 morning, 27 intermediate (no preference) and 26 evening types; therefore, all comparisons were between intermediate and evening groups. Average BMI at baseline was found to be 22.56 for the intermediate group and 22.65 for the evening group. Over the course of the study, respondents in the intermediate group gained an average of .04 pounds, while respondents in the evening group gained an average of 2.65 pounds. T-tests found these changes to be statistically significant (t(51)= 2.15, p<.05), with evening types gaining significantly more weight compared to intermediate types.

Conclusion: These findings indicate that circadian preferences are associated with weight gain during the freshman year. Future studies should explore potential mechanisms for this relationship. For example, eveningness may increase the chances of gaining weight through changes in both sleep and daily schedules.

0176
EFFECT OF SKIN TEMPERATURE SITE LOCATION ON THE DISTAL-TO-PROXIMAL GRADIENT SKIN TEMPERATURE GRADIENT

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Introduction: Peripheral heat loss from distal skin sites has been reported to predict sleep onset latency (SOL). The distal-to-proximal skin temperature gradient (DPG) is used to express heat loss. Skin temperature regulation however, differs depending on measurement site (i.e. glabrous versus non-glabrous skin). It remains unclear if circadian variation in DPG is site dependent. We sought to compare circadian variation in skin temperature site independently and when used to calculate the DPG. Additionally, we examined the relationship between skin temperature, performance and subjective sleepiness with the DPG.

Methods: Eight healthy adults (2 females), BMI (22.4±1.8 kg/m2) aged (21.5±2.9 yrs) participated. After an 8h in lab sleep opportunity, participants were studied under constant routine conditions. Skin temperatures were recorded every minute (iButton, Maxim, Sunnyvale CA) from 8 skin sites [distal(glabrous and non-glabrous portions of the hand and foot) and proximal (upper-arm, head, and stomach)] beginning 5h after habitual wake-time until 4h after habitual sleep-time. A Psychomotor Vigilance Task (PVT) and Karolinska Sleepiness Scale (KSS) were given every 2h following habitual wake-time. Data were analyzed as deviation from the mean with repeated measure ANOVA.

Results: No significant difference in DPG was observed when comparing glabrous versus non-glabrous sites (P>0.05). We observed a significant interaction comparing hand-stomach DPG to the hand-upper arm DPG (P<0.05) and a significant interaction when comparing hand-upper arm DPG to hand-head DPG (P<0.05). PVT lapses and subjective sleepiness scores increased in conjunction with the observed rise in DPG prior to the habitual bed-time.

Conclusion: DPG increases were associated with night time performance impairment and increases in subjective sleepiness. Circadian variation of distal skin sites (glabrous and non-glabrous) did not differ when used to calculate DPG, indicating location did not differ with circadian phase. Subtle differences in DPG were observed depending on proximal location.

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0177

BMAL1 IN THE SCN CONTROLS THE CIRCADIAN TIMING BUT NOT THE AMOUNT OF SLEEP AND WAKE IN MICE

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Introduction: Several previous studies have suggested that the suprachiasmatic nuclei (SCN) might actively promote wakefulness in addition to regulating the timing of sleep-wake cycle. For example, SCN lesions in mice and primates produced an increase in sleep although contradictory evidence exists. In addition, mice harboring a null allele for BMAL1 (a key transcription factor for circadian rhythm generation) showed a loss of the circadian rhythm in sleep-wake and an increase in total sleep time. However, these studies could not determine whether the loss of the sleep-wake rhythm and increase in sleep time was a direct consequence of an absence of BMAL1 within the SCN. We therefore evaluated sleep-wake in mice lacking BMAL1 only in the SCN.

Methods: Bmal1 conditional mice (Bmal1flox/flox) were injected with an adeno-associated viral (AAV) vector containing either Cre recombinase (Cre; for BMAL1 deletion) or green fluorescent protein (GFP; vector injection controls) into the SCN and implanted with a telemetry transmitter for recording the EEG, EMG, body temperature (Tb) and locomotor activity (LMA). Two weeks after the surgery, EEG, EMG, LMA and Tb were continuously recorded from these mice for 72 hrs. The mice were then released into constant dark (DD) for 3 weeks and another 72-hr recording was performed during the last 3 days of DD exposure. The mice were then perfused with formalin and the brains were processed for GFP/Cre and BMAL1 immunohistochemistry.

Results: Histological analysis revealed that BMAL1 protein levels were undetectable in the SCN of two mice with complete bilateral SCN Cre staining. These mice displayed a loss of the sleep-wake rhythm in both LD and DD. However, there were no significant differences in the total time of sleep or wake in these mice when compared to the AAV-GFP controls.

Conclusion: BMAL1 in the SCN specifically controls the timing but not the total amount of sleep-wakefulness.

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0178

EVALUATION OF CIRCADIAN GENE AND ERβ EXPRESSION CHANGES IN WHITE BLOOD CELLS AS BIOMARKERS OF CIRCADIAN DISRUPTION IN SHIFT WORKERS: POTENTIAL APPLICATION TO STUDIES OF BREAST AND PROSTATE CANCER CHEMOPREVENTION

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Introduction: Epidemiological studies indicate that disruption of circadian rhythm by shift work is associated with increased risks of breast and prostate cancer. Rat studies demonstrated that carcinogens also disrupt the expression of circadian and circadian controlled genes (CCG). More importantly, chemopreventive methylselenocysteine (MSC) resets the expression levels and phase of CCG, including estrogen receptor β (ERβ) (Fang, Zhang & Zarbl (2010) Cancer Prevention Research 3: 640-652). Unpublished findings indicate that MSC resets circadian gene expression by restoring rhythmic fluctuations in histone acetylation on the Period 2 gene promoter, providing a mechanism for MSC-mediated restoration of circadian rhythm. The goal of this study was to determine if changes in circadian gene and CCG expression in white blood cells can serve as biomarkers of circadian disruption in shift workers.

Methods: Fifteen consented volunteers recruited from hospital interns and residents (age 21-34) were asked to keep a sleep log during this cross-over study. Blood samples were drawn at 8 AM and 8 PM, before and after completing one week of service on the night shift and at 8 AM, noon and 8 PM before, during and after completing one week of day shift. Serum melatonin was measured by ELISA and expression of core circadian genes (Period2, NR1D1) and ERβ in lymphocytes was measured by quantitative real-time PCR. Descriptive statistics and mixed linear models evaluated changes in gene expression and plasma melatonin associated with shift changes.

Results: Results found significant changes in Per2 (p=0.034) and large, although not statistically significant, changes in Melatonin (p=0.16) for evening versus day shifts based on evening samples. Substantial changes were not found for NR1D1 or ERβ, which were very low the at these time points.

Conclusion: Changes in the Per2 gene expression can serve as a biomarker of disrupted circadian rhythm in human lymphocytes, and should be useful in longitudinal studies of MSC chemoprevention of cancer in shift workers.

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0179

DISRUPTIVE EFFECTS OF COCAINE AND PER2 KNOCKDOWN ON MURINE NONPHOTIC AND PHOTIC PHASE-RESETTING RESPONSES

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Introduction: The central mechanisms by which cocaine abuse impairs circadian physiology and behavior are unclear. Here, we explore the effects of acute i.p. cocaine administration on circadian non-photic and

photic responses in Per2-deficient (Per2 KO) and albino wild-type (WT) mice.

Methods: General locomotor activity was measured using infrared sensors interfaced with a ClockLab data acquisition system. Phase-shifts were measured using an Aschoff Type II procedure. In Experiment 1, WT and Per2 KO mice received a cocaine (20 mg/kg) or saline injection at midday. In Experiment 2, WT and Per2 KO mice received the cocaine or saline injection 15 min before the presentation of phase-delaying light pulse in the early night. In Experiment 3, WT mice were outfitted with a microdialysis probe targeting the SCN. Cocaine dissolved in ACSF or ACSF alone was perfused for 80 min starting at midday.

Results: In Experiment 1, cocaine advanced rhythms relative to saline in both genotypes ($p<0.05$). Cocaine-induced advances were greater in Per2 KO vs WT mice ($2.1+0.4$ hr vs. $0.7+0.1$ hr, respectively; $p<0.05$). In Experiment 2, cocaine attenuated photic phase-delays in WT mice (cocaine: $0.6+0.2$ hr; saline: $1.5+0.1$ hr; $p<0.05$), and blocked photic phase-delays in Per2 KO mice (cocaine: $0.01+0.4$ hr; saline: $2.5+0.4$ hr; $p<0.05$). In Experiment 3, direct perfusion of the SCN with cocaine induced large phase-advances vs ACSF controls ($3.7+1.2$ hr vs $0.3+0.2$ hr, respectively; $p<0.05$).

Conclusion: These results confirm that the SCN is a direct target for the non-photic and photic actions of cocaine. Collectively, these data suggest multiple disruptive effects of cocaine on circadian timing regulation registered directly in the SCN, that are strongly influenced by the mPer2 circadian clock gene.

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0180

CIRCADIAN MODULATION OF SLEEP HOMEOSTASIS DURING AND AFTER CHRONIC SLEEP RESTRICTION IN RATS

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Introduction: Chronic sleep restriction (CSR) is a common experience for people in modern society. To study sleep patterns and circadian modulation during and after CSR, we developed a rat model of CSR that takes into account the rat's polyphasic sleep-wake patterns. In this "3/1 model", cycles of 3 h of sleep deprivation (SD; using slowly rotating wheels) and 1 h of sleep opportunity (SO) are imposed for 4 days, followed by 2 days of recovery.

Methods: EEG and EMG were recorded in adult male Wistar rats (n=5) before, during, and after 4 days of continuous 3/1 SD/SO cycles beginning at the onset of the light phase of a 12/12 h light/dark cycle.

Results: Non-rapid eye movement sleep (NREMS) rebound during SO occurred at similar levels on each day of CSR. Daily rhythms in NREMS amount during SO (assessed by peak-to-trough amplitude) were maintained at baseline levels (BSL) across the 4 days of CSR. REMS rebound during SO was delayed until the dark phase on the first day but was sustained thereafter. Daily rhythms in REMS amount during SO were also maintained at BSL over the 4 days. NREMS delta power during SO increased above BSL on the first day, then gradually declined but remained above BSL; the amplitude of its daily rhythms was reduced similarly across the 4 days. During recovery after CSR, NREMS amount increased above BSL only during the dark phase on the first and, to a lesser extent, second day. In contrast, REMS amount increased above BSL mostly during the light phase of the first recovery day, and returned to BSL on the second day. NREMS delta power was below BSL selectively during the light phase on both recovery days, but its daily rhythms were back to BSL on both days. Cumulative analyses showed that the amounts of NREMS, REMS, and EEG delta energy lost during CSR had not been recovered at the end of the second recovery day.

Conclusion: Rebound increases of both NREMS and REMS during SO were sustained during the 4-day 3/1 CSR schedule, while NREMS delta power rebound during SO gradually declined over the days. Despite significant cumulative sleep loss, daily rhythms in NREMS and REMS amounts were unaffected, whereas those in NREMS delta power were reduced in amplitude. The compensatory responses during the recovery phase were modest and gated differentially by the light/dark phase. These results suggest that the 3/1 CSR protocol may initiate both homeostatic and other regulatory processes that are modulated by circadian factors.

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0181

CIRCADIAN RHYTHMS ARE NOT ALTERED BY EXPOSURE TO VOLATILE ANESTHETICS IN A DROSOPHILA MODEL SYSTEM

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Introduction: Recent studies in mammals have shown that administration of general anesthetics such as propofol can modulate endogenous circadian rhythms, although the mechanisms by which this occurs are not well understood. We chose to see if administration of an halogenated anesthetic agent such as isoflurane would have an effect over the locomotor behavior of *Drosophila* which is a well known robust circadian phenotype. This organism would be ideal to further study the mechanisms be which anesthetics interact with the circadian clock.

Methods: Female w^{1118} flies were used for all experiments. Fly locomotor behavior was recorded using the Drosophila Activity Monitor System (Trikinetics, Waltham, MA). Flies were entrained for a minimum of three days on a 12-h light/12-h dark schedule and then placed in constant darkness. Isoflurane mixed in air was administered during the first day of constant darkness for two hours at a concentration of 1.2% during at different circadian time (CT) points. We have previously shown that at this dose of isoflurane, all flies cease their normal locomotor during their evening locomotor activity peak.

Results: Locomotor activity in constant darkness following exposure to isoflurane at four different time points (CT 0-2, CT 6-8, CT 10-12, CT 16-18) is indistinguishable from that in control flies not exposed to anesthesia with no significant differences in period or phase advances or delays suggesting preserved central clock function. Locomotor activity was also appropriately phase-advanced or delayed with timed light pulses during the subjective night, even in the presence of a dose of isoflurane known to force cessation of locomotor behavior in flies during an their active evening activity peak. This latest experiment would seem to suggest that the output of the central clock is preserved in the presence of isoflurane anestheisa as well.

Conclusion: These results suggest a persistence of circadian rhythms following exposure to isoflurane anesthesia. The lack of a direct effect of anesthesia on circadian rhythms, suggest that the previously described effects of propofol on circadian time structure may not apply to the halogenated anesthetics, at least in our *Drosophila* system. In addition, these results seem to suggest that isoflurane administration does not disrupt central clock function or it's output.

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0182

EVALUATION OF INDIVIDUAL'S CIRCADIAN CLOCK PROPERTIES AT PHYSIOLOGICAL AND MOLECULAR LEVELS

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Introduction: Behavioral and physiological processes such as sleep-wakefulness, thermoregulation and hormone secretion exhibit circadian rhythms in most organisms including humans. These rhythms are driven by a system of self-sustained clocks and are entrained by external cues such as cycles of light and dark and food intake. The mammalian central oscillator, the suprachiasmatic nuclei (SCN) incorporates environmental information and orchestrates slave oscillators in peripheral cells. The circadian clock system is composed of a hierarchy of oscillators that involve transcription and translation feedback loops of multiple clock genes. Disorganization of the circadian system is known to be closely related to many diseases including sleep, mood and metabolic disorders. Advanced sleep phase type, delayed sleep phase type and non-entrained type of circadian rhythm sleep disorders (CRSD) are thought to result from malfunction/maladaptation of the circadian system. Dissection of human circadian clock system is indispensable to understand the pathophysiology of CRSD. However, it is difficult and expensive to assess individual's circadian rhythms precisely. Therefore, more convenient measurements of circadian properties are demanded to reduce patients' burden, since they are usually required to stay in a laboratory environment free from external cues and masking effects for over a couple of weeks.

Methods: In this study, we evaluated rhythmic characteristics of physiological functions (core body temperature, plasma melatonin and plasma cortisol levels) from 14 healthy male subjects under a 28-h forced desynchrony protocol. Furthermore, we assessed clock gene expression in primary fibroblast cells established from individual's skin biopsies using a luminescence reporter assay system.

Results: We compared the period of bioluminescence rhythms with the period of physiological rhythms in the same subjects and found that there was a highly significant correlation between the period length of fibroblast rhythms and physiological rhythms.

Conclusion: Our results suggest that surrogate measurements using fibroblast cells would be a powerful tool for assessing individual's circadian properties.

0183

AN ENDOGENOUS CIRCADIAN RHYTHM IN BAROREFLEX SENSITIVITY THAT PEAKS DURING THE BIOLOGICAL NIGHT

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Introduction: Blood pressure (BP) is regulated acutely by negative feedback involving arterial baroreceptors that provoke autonomic nervous system changes resulting in altered heart rate, cardiac contractility, and vasoconstriction to maintain BP. The change in heart beat interval per change in BP is used as an index of baroreceptor sensitivity (BRS). We tested whether BRS exhibits an endogenous circadian pattern. If BRS is lower during the biological night, this could explain the endogenous circadian rhythm in vulnerability to presyncope that peaks during circadian phases corresponding to the biological night (Hu et al. 2008 Sleep 31, Suppl. A25).

Methods: Twelve healthy subjects (6 females, 20-42 years old) underwent a 13-day in-laboratory protocol, in which each subject's "day" length was adjusted to 20 hours so that behaviors distribute evenly across the circadian cycle. A 15-minute title-table test (60° head-up) was performed ~4.5 hours after scheduled awakening in each 20-hour cycle. ECG and beat-to-beat BP were recorded to estimate BRS. Core body temperature was used as a circadian phase marker.

Results: From a mean baseline BRS of 15.4 ± 1.7 (SE) ms/mmHg, BRS declined by $57.2\pm4.7\%$ within one minute of tilting up (p<0.0001), and rebounded to 22.8 ± 2.6 ms/mmHg within one minute of tilting down. BRS had an endogenous circadian rhythm (peak-to-trough amplitude ~4 ms/mmHg; P=0.003) with higher values across the biological night - when BP and heart rate were lower and incidence of presyncope was higher (81% of all presyncope events). There was no difference in the mean BRS between trials with and without presyncope.

Conclusion: The circadian system has a significant impact on BRS. Since BRS was highest during the biological night when presyncope was more frequent, the circadian rhythm of presyncope cannot be caused by the circadian variation in BRS. On the other hand, the circadian-modulated increase in BRS during the biological night could explain the increased BRS previously reported during sleep at night.

0184

SLEEP HOMEOSTASIS IN CASEIN KINASE 1 EPSILON (CK1ε) TAU MUTANT AND NULL MICE

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Introduction: Casein kinase 1 is well-known for its role in circadian organization in rodents: mice and hamsters with the tau mutation in casein kinase 1ε (CK1ε) have a significantly reduced circadian period. However, CK1ε null animals have only a very subtle circadian phenotype. In humans, mutations in CK1δ, the human homolog of CK1ε, are known to cause familial advanced sleep phase syndrome (ASPS), which alters the circadian organization of the sleep-wake cycle. Although studies in humans have demonstrated that CK1δ mutations affect the timing of sleep, there is no evidence that sleep homeostasis is affected as well. Here we report baseline sleep characteristics and responses to 6-hour sleep deprivation in tau mutant and CK1ε-null mice.

Methods: Male CK1ε-null and tau mutant mice, maintained on 12:12 light:dark (LD) cycles, had electroencephalogram (EEG) and electromyogram (EMG) recording electrodes surgically implanted. After recovery and acclimation to sleep chambers, baseline sleep was recorded over 48 hours. Sleep deprivation was performed with gentle handling during either the first 6 hours (ZT 0-6) or the last 6 hours (ZT 7-12) of the light phase, after which the animals were undisturbed for 18 hours. EEG/EMG were visually scored in ten-second epochs as belonging to one of the following vigilance states: wake, rapid eye movement (REM) or non-REM (NREM) sleep.

Results: CK1ε null mutant mice exhibited characteristics similar to wild-type animals during baseline and recovery sleep. As expected, CK1ε tau mutant mice had altered circadian timing of sleep. Interestingly, unexpected recovery sleep patterns were also observed in the tau mutants. Furthermore, the timing of sleep deprivation affected the recovery sleep patterns in these animals.

Conclusion: The tau mutation in mice leads to altered homeostatic responses to sleep deprivation. The timing of sleep deprivation influences the subsequent recovery sleep responses as well. Taken together, these results highlight the role of CK1ε in sleep homeostasis in the mouse and emphasize the interconnection between the circadian and homeostatic regulation of sleep.

0185

OVERNIGHT THERAPY? SLEEP DE-POTENTIATES EMOTIONAL BRAIN REACTIVITY

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Introduction: While the benefit of sleep on various neurocognitive processes has been established, a role for sleep in emotional brain regulation remains largely uncharacterized. This is surprising considering that nearly all clinical mood disorders express co-occurring abnormalities of sleep, most commonly in the amount and timing of rapid eye movement (REM) sleep. Using fMRI in combination with EEG sleep physiology, here we test the hypothesis that sleep, and specific aspects of REM sleep, de-potentiates the behavioral and neural reactivity associated with prior affective experiences.

Methods: Thirty-three healthy young adults were randomly assigned to either the Sleep or Wake group. Both groups performed two fMRI sessions, separated by a 12hr period containing either a full night of physiologically recorded sleep (Sleep-group), or a normal waking day (Wake-group). At each session, participants rated affective picture-stimuli on a 1-5 scale (corresponding to increasing emotional intensity).

Results: In contrast to equivalent time awake, sleep resulted in a selective and significant palliative overnight reduction in extreme emotion intensity ratings ($P \leq 0.04$). This behavioral de-potentiation was further associated with an interaction effect in the amygdala, showing overnight decreases in reactivity in the Sleep-group ($P=0.004$), while no such decrease was observed in the Wake-group. Additionally, this sleep-dependent reduction in amygdala reactivity was associated with enhanced ventromedial prefrontal cortex (vmPFC) functional connectivity ($P=0.005$). Moreover, the overnight increase in amygdala-vmPFC connectivity correlated significantly with the speed of entry into REM sleep ($R=0.53$, $P=0.025$). Importantly, no between-group differences in neural or behavioral reactivity were observed in a circadian-control task, which entailed rating a novel set of affective pictures, providing a time-of-day baseline reference.

Conclusion: Taken together, these findings support a homeostatic role for sleep, and especially REM sleep, in the optimal regulation of limbic brain networks, de-potentiating next-day emotional reactivity and re-establishing vmPFC top-down control. Such experimental findings may hold translational implications for a collection of clinical mood disorders associated with maladaptive affective reactivity, especially major depression and PTSD, both of which express concomitant REM sleep abnormalities and dysfunctional amygdala-PFC emotional activity.

0186

α-1 ADRENOCEPTOR ANTAGONIST PRAZOSIN REDUCES REM SLEEP (REMS) FRAGMENTATION AND NON-REM SLEEP (NREMS) LATENCY IN FEAR-CONDITIONED WISTAR-KYOTO RATS (WKY)

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Introduction: The α-1 adrenoceptor antagonist prazosin reduces nightmares in posttraumatic stress disorder (PTSD), which has been associated with REMS fragmentation. Defining REMS fragmentation in rats as a shift in the distribution of sequential REMS (seq-REMS, inter-REMS episode interval ≤3 min) and single REMS (si-REMS, inter-REMS episode interval >3 min) towards seq-REMS, we demonstrated greater REMS fragmentation following fear conditioning (FC) in WKY compared to Wistar rats. We hypothesized that prazosin would reduce FC-elicited REMS fragmentation and other sleep disturbances in WKY.

Methods: Male WKY were habituated and received a prazosin (0.01 mg/kg, i.p.; n=4) or vehicle (n=4) injection followed 15 min later by a 4-h baseline sleep recording. Two days later they were presented with 10 tones (800 Hz, 90 dB, 5 s; 30 s interval), each co-terminating with a foot shock (1.0 mA, 0.5 s). The following day (Day 1), and again 6 days (Day 7), and 13 days (Day 14) later, prazosin or vehicle was administered, 3 tones were presented without foot shock, and sleep was recorded for 4 h. Waking, NREMS, and REMS were manually scored. Seq-REMS and si-REMS episodes were distinguished.

Results: WKY given prazosin had a shorter sleep latency (min ±SEM) on Day 1 (Prazosin: 9.9 ±2.1; Vehicle: 29.0 ±9.1; p=0.01) and a decreased percentage of seq-REMS relative to total REMS time on Day 14 (Prazosin: 36.3% ±4.5; Vehicle: 67.1% ±6.1; p=0.02).

Conclusion: Prazosin-treated WKY had reduced time to sleep onset compared to vehicle-treated WKY on Day 1 after FC and, by Day 14, had reduced REMS fragmentation. Prazosin may facilitate REMS consolidation in fear-conditioned WKY. These findings strengthen the rationale for using WKY in the modeling of sleep in PTSD and may lead to insights into the mechanisms of prazosin action in the disorder.

0187

EXPERIMENTAL SLEEP RESTRICTION IN ADOLESCENTS: CHANGES IN BEHAVIORAL AND PHYSIOLOGICAL MEASURES OF EMOTIONAL REACTIVITY

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Introduction: The myriad biological and social changes that occur during adolescence contribute to later and erratic sleep times and insufficient sleep. Reduced sleep may impact behavioral, emotional, and social functioning at this key period of development. We examined how sleep restriction and sleep extension influenced behavioral and physiological measures of affective function in adolescents.

Methods: Sixteen healthy adolescents (ages 12-15) were studied in groups of 2-4 friends during a within-subject sleep restriction manipulation over two 48-hour laboratory visits, using crossover design. Sleep restriction consisted of six hours in bed on night 1 and two hours in bed on night 2. Sleep extension consisted of 10 hours in bed for both nights. Physiological and behavioral testing occurred on day 2 of each condition. Responses to positive, negative, and neutral auditory stimuli were examined with pupil dilation—a physiological measure of emotional reactivity. Pairs of friends completed a 5-minute videotaped discussion about resolving a conflict in their relationship. Interactions were coded for negative and positive affect using the International Dimensions Coding System-revised (IDCS-R).

Results: Compared to the sleep extension condition, adolescents showed larger pupil dilation responses to negative sounds relative to neutral sounds after sleep restriction (M±SD=0.137±.21 mm, and 0.306±.225 mm, respectively; F(1,14)=6.49, p=0.02). Adolescents displayed more negative affect during peer interactions following sleep restriction (M±SD=7.3 ±1.8) compared to the well-rested condition (M=6.4±1.2), F(1,14.9)=5.45, p=0.03. Further, after sleep restriction but not sleep extension, negative affect during peer interactions was correlated (r2=0.42, p<0.02) with pupillary reactivity to negative emotional sounds.

Conclusion: Sleep restriction in healthy adolescents influenced behavioral and physiological indicators of emotional reactivity to negative stimuli. These increased negative emotional responses raise compelling questions about the role of sleep loss on emotion regulation during a vulnerable developmental period, and their contribution to developing or exacerbating behavioral and/or emotional problems.

0188

FOOD RESTRICTION DIFFERENTIATES THE AMPHETAMINE INDUCED CONDITIONED PLACE PREFERENCE BETWEEN WILD TYPE AND HYPOCRETIN DEFICIENT NARCOLEPTIC MICE

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Introduction: The amphetamine and amphetamine-like stimulants have been prescribed to treat excessive daytime sleepiness associated with narcolepsy for more than 60 years. Interestingly, stimulant abuse is extremely rare in these patients, suggesting that the hypocretin system may be involved in the development of stimulants abuse. We have shown in past meetings that hypocretin deficient narcoleptic (DEF) mice exhibited attenuated amphetamine-induced locomotor sensitization. We then evaluated the amphetamine induced place preference test (A-CPP) in these animals to more directly evaluate the amphetamine abuse susceptibility. However, we observed only minor differences between the genotypes. Since stress responses are involved in drug addiction and since altered stress responses are seen in hypocretin deficient narcolepsy, we have evaluated the A-CPP in WT and DEF after foot shocks and during food restriction.

Methods: We performed A-CPP in three conditions, food-satisfied, food-deprived conditions and food satisfied with foot shock in WT and DEF mice. Each CPP experiment included three phases: a single pre-conditioning exposure session followed by three every other day amphetamine-conditioning sessions with 1 or 2m/kg administrations interspersed with three non-conditioning sessions. The final place preference test sessions were performed on the 8th day. Control group received saline in all sessions. In the food-deprived mice, their weights were kept in 80% of their free-feeding weights. Each day of the conditioning phase, the mice received electrical stimulations after being confined for the foot shock experiments.

Results: Foot shock enhanced A-CPP by 26.9% at 1mg/kg and 21.9% at 2mg/kg compared to the respective baseline sessions in WT mice. Enhancements of A-CPP in DEF mice after foot shock were attenuated -4.1% and -1.7% in DEF mice, but the difference did not reach the statistical significance. Food restriction enhances A-CPP robustly in WT mice and 63.9% and 55.3% increases were seen in these mice. Interestingly, these increases in A-CPP were completely attenuated in DEF mice and 13.7% and -12.8% changes were observed.

Conclusion: A-CPP was not altered in DEF mice at the baseline. Food restriction, but not foot shock differentiated A-CPP between WT and DEF mice. These results suggest that the loss of hypocretin signaling may not directly affect the behavioral conditioning by amphetamine, but altered stress responses in DEF mice likely contribute to the development of stimulant abuse.

0189

SLEEP QUALITY AND CIRCADIAN PREFERENCE PREDICT UNIVERSITY STUDENTS' DRINKING MOTIVES

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Introduction: University students drink for a variety of reasons including social, enhancement, conformity, and coping motives. Each motive is associated with different patterns of alcohol consumption. The coping motive is the most problematic with drinking to intoxication, drinking alone, and persistence of drinking problems after graduation. Our study investigated whether students' sleep quality and circadian preference predicted their endorsement of different drinking motives. Is poor sleep quality or an eveningness preference associated with drinking to cope?

Methods: Participants were 209 (157 females) introductory psychology students at a small Canadian university. Mean age was 21.80 (SD = 6.80). Participants completed questionnaires online. All questionnaires have been published with evidence of validity. They include the Sleep Quality Scale, Composite Scale of Morningness, Drinking Motives, Paulhaus Deception Bias (measure to control for socially desirable responding), and demographic questions (e.g., age and gender). The study was approved by the University's Research Ethics Board.

Results: Multiple regression analyses examined predictors of each drinking motive. Poor sleep quality was the only significant predictor of drinking to cope (p < .001). An eveningness circadian preference (p < .05) and male gender (p < .05) predicted stronger conformity motives. Male gender (p < .001) and younger age (p < .01) predicted more social drinking. Younger age (p < .001) and male gender (p < .01) predicted stronger enhancement motives.

Conclusion: Poor sleep predicted drinking to cope whereas age, gender, and circadian preference did not. Age, gender, and circadian preference predicted other drinking motives associated with less problematic alcohol consumption. Our correlational design does not permit conclusions about causality.

0190

COLLEGE STUDENTS' MUSIC BACKGROUND, SLEEP QUALITY AND PROPENSITY TO USE MUSIC AS A SLEEP AID

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Introduction: People vary in commitment to music, music aptitude, and affective reactions to music that might influence if and how music is used as a sleep aid. Soporific effects of music are usually assumed to be from relaxation, but music may serve other purposes such as distraction from thoughts or noise, which has implications for types of music selected to help sleep.

Methods: Participants were 420 (314 females) introductory psychology students at a Canadian university. Mean age was 21.01 (SD = 5.20). Participants completed online the Music Experience Questionnaire, Sleep Quality Scale, and questions about use of music as a sleep aid. The study was approved by the University's Research Ethics Board.

Results: 58% used music as a sleep aid at least once a week: 20% for relaxation, 12% for distraction, 65% for both, and 3% for neither. Poor sleepers used music more often than did good sleepers (p < .01). More music background predicted greater use of music for relaxation (p < .01), but was unrelated to its use for distraction, which was more common in poor sleepers than in good ones (p < .05). Music without lyrics was rated most effective for relaxation (p < .001), whereas music with lyrics was rated most effective for distraction (p < .01).

Conclusion: Music was used as a sleep aid to promote relaxation or distraction. Good and poor sleepers were more likely to use music for relaxation if they had more music background. Music background was not related to use of music for distraction, which was more common in poor sleepers than in good ones. Music was rated most relaxing when it was without lyrics and most distracting when it was with them.

0191

"FIRST IMPRESSIONS OF INSTRUCTORS": DOES SLEEPINESS MATTER?

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Introduction: First impressions have a lasting effect on how people are perceived. For example, impressions formed during a first class have been shown to have semester-long effects on student ratings of instructors. Rater mood has been shown to have an effect on the formation of first impressions. Whether the rater's sleepiness affects first impressions has not been explored. Sleepiness might lead to more negative first impressions based on studies showing the effects of sleepiness on negative mood or based on recent studies showing the sleepiness reduces encoding of positive more than negative information. The present study explored the possibility that first impressions of an instructor would be more negative when made by sleepy students.

Methods: Subjects were 85 college students in 3 classes on a university campus. Students' first impression of a guest instructor's personality, attractiveness, professional image, appearance, and presentation quality was assessed using visual analogue scales. Student sleepiness was measure by the Stanford Sleepiness Scale (SSS) completed at the time of a guest lecture. Mood was measured using a 9-point scale.

Results: Multiple regression analyses revealed that high sleepiness was related to negative impressions of (1) instructor's overall personality ($\beta= -.421$, $p<.01$), and 4 of the Big 5 personality factors: extraversion/introversion ($\beta= -.317$, $p<.01$), agreeableness ($\beta= -.382$, $p<.01$), neuroticism ($\beta=-.207$, $p=.058$), conscientiousness ($\beta= -.359$, $p<.01$). (2) instructor's professional image: enthusiasm ($\beta= -.261$, $p<.05$) and knowledge ($\beta= -.258$, $p<.05$). (3) instructor's appearance ($\beta= -.255$, $p<.05$) (4) presentation quality: clarity ($\beta= -.272$, $p<.05$) and information ($\beta= -.291$, $p<.01$). No main or interaction effects were found for mood or for class.

Conclusion: The findings of this exploratory study indicated that sleepier college students formed more negative first impression of instructor's personality, appearance, professional image and presentation quality. The role of sleepiness in first impression formation should be further investigated.

0192

EFFECTS OF PRE-SLEEP SIMULATED ON-CALL INSTRUCTIONS ON SUBSEQUENT SLEEP

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Introduction: Professionals who are on-call during the night but who are allowed to sleep, report poor qualitative and quantitative sleep. This has detrimental effects on mood and performance the following day. They feel sleepier, are less alert and likely to make errors. This study investigates whether a pre-sleep vigilance inducing instruction impairs the macro- and micro-structure of sleep in healthy volunteers and whether it negatively influences sleep quality, sleepiness and mood the following day.

Methods: Following an adaptation night 18 subjects (23,89 years +/- 0,78) slept two nights in the sleep laboratory: a reference night and an 'on-call' night in counterbalanced order. In the experimental condition subjects were told five seconds white noise would be presented at unpredictable intervals during the night. Subjects were instructed to press a button at hand as soon as they would hear this noise. In reality no noise was administered during the night. Sleep was recorded polysomnographicaly and evening and morning questionnaires inquired about subjects' sleepiness and mood.

Results: In comparison to the reference condition subjects felt significantly less fatigue ($p < 0,05$) and significantly more aroused ($p < 0,05$) after the 'on-call' instruction was given. During the first 120 minutes of time in bed in the 'on-call' condition subjects were significantly more awake ($p < 0,05$) and significantly less delta activity ($p < 0,05$) was found in the first slow wave sleep period. The mean length of wake episodes reported was significantly longer ($p < 0,05$) in the 'on-call' condition. Reported sleep quality was significantly lower ($p < 0,05$) after the 'on-call' night compared to the reference night.

Conclusion: A pre-sleep simulated on-call instruction has negative effect on quantitative and qualitative aspects of sleep. The procedure might be further elaborated to investigate if it is a valid model for predisposing or mediating factors in insomnia.

0193

THE RELATIONSHIP BETWEEN SOCIAL COGNITION AND SLEEPINESS AMONG COLLEGE STUDENTS

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Introduction: Sleepiness negatively impacts performance, mood, attention, and cognitive functioning; and impairs integration of emotion and cognitions when making moral judgments. Recently, research has revealed that sleep deprived participants performed worse on a complex cognitive task, but reported higher levels of estimated performance and self-rated concentration with no change in levels of off-task cognitions. Although this previous research provides us with some understanding of moral judgments and self-referential cognitions of the sleepy individual, to date no research has investigated social cognitions such as counterfactual thinking and displaced aggression.

Methods: Data were gathered from 108 college students (27 male, 81 female; age: M=24.39, SD=8.84). Participants completed self-report questionnaires for psychology course extra credit. Measures included the Epworth Sleepiness Scale, the Counterfactual Thinking for Negative Events Scale, the Displaced Aggression Questionnaire, and sociodemographic data.

Results: Displaced Aggression: Sleepiness was positively correlated with all three subscales of displaced aggression: angry rumination ($r(106)=.252$; $p<.05$), behavioral displaced aggression($r(106)=.273$; $p<.05$), and revenge planning ($r(105)=.194$; $p<.05$). Counterfactual Thinking: Sleepiness was positively correlated with counterfactual thinking overall ($r(105)=.198$; $p<.05$). Sleepier people were more likely to imagine how outcomes could have been better than reality ($r(105)=.206$; $p<.05$). Sleepier people reported more other-focused upward counterfactuals (i.e. how behavior of others could have produced better outcomes; $r(106)=.240$; $p<.05$), and more non-referent upward counterfactuals (i.e. although no behavior is altered, how outcomes could have been better; $r(105)=.217$; $p<.05$), but were not more likely to report self-focused counterfactuals (i.e. how one's own behavior could have produced better outcomes). Sleepiness was not significantly correlated with downward counterfactual thinking.

Conclusion: Sleepiness was related to the social cognitions of counterfactual thinking and displaced aggression. It may be that these changes in social cognition are the product of impairments in emotional intelligence. These results may improve understanding of social decision making and suggest techniques for improved coping.

0194

NAPPING, GPA AND MORNINGNESS-EVENINGNESS IN UNDERGRADUATE STUDENTS

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Introduction: College students are notorious for irregular sleep habits, including more evening chronotypes, disturbed sleep, and poor quantity. Sleep quantity and academic performance are significantly related, with less sleep associated with lower grade point average (GPA). Napping has been shown to improve performance; however, its prevalence among undergraduates and relation to GPA and chronotype is not well-established. The study aimed to compare GPA, chronotype, and napping habits among undergraduates during the Winter and Spring quarters (January-May 2010).
Methods: Participants included 78 undergraduates (ages 18-30) at Drexel University who were part of a larger study examining the impact of sleep education on sleep knowledge, habits and other variables. Based on mean nap length, participants were divided into 2 groups, where "good" nappers napped for an average of ≤30 minutes and "poor" napped for > 30. There were 24 good nappers (N= 11 males) and 54 poor nappers (N= 14 males). The Morningness-Eveningness Questionnaire (MEQ) assessed chronotype; nap frequency & duration were calculated from a daily sleep diary over an average of 2 weeks. GPA was extracted from transcripts. Group differences were assessed using independent t-tests.
Results: Nearly 81% of the sample took at least one nap, with 69.2% napping for an average of >30 minutes (M=57.58 ± 50.00). No significant differences existed between good & poor nappers on GPA; however, one emerged on MEQ scores for poor nappers (M=43.15 ± 7.26) versus good nappers (M=45.83 ± 10.70); t(76)= -1.296, p=0.02. Poor nappers had lower MEQ scores, indicating greater propensity towards eveningness. Interestingly, no relationship was found between GPA and napping.
Conclusion: Most of the sample reported both taking naps and napping for longer than typically recommended to experience health benefits (>30 minutes). Those whose naps averaged >30 minutes reported a tendency toward eveningness, perhaps supporting a circadian phase delay. One hypothesis is that students with evening preference who need to wake up early may compensate by extending nap duration. This may permeate a vicious cycle between napping & delaying bedtimes as homeostatic pressure is attenuated at a typical bedtime due to extended naps. While we did not find an association between napping, DSPS, & GPA, future studies may more closely examine student sleep patterns, napping habits, and chronotype with academic performance and daytime functioning.

0195

SLEEP HABITS AND INSOMNIA SYMPTOMS IN COLLEGE STUDENTS

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Introduction: Sleep problems are prevalent in college students, and can interfere with functioning. Few studies have examined sleep habits, and insomnia symptoms in college students. The purpose of this study was to ascertain typical sleep habits and the prevalence of insomnia symptoms in university students.
Methods: A survey was administered to 245 undergraduate students (71 males and 173 females) at a small university. 86.10% of participants were Caucasian, 6.10% were African American, and 7.80% were other.

Results: On weekdays, participants slept an average of 6.60 hours (SD=1.28), and on weekends 7.90 hours (SD=1.50). The average weekday bedtime was 12:39 A.M and the average wake time was 8:10 A.M. On weekends, the average bedtime was 2:31 A.M and the average wake time was 10:56 A.M. Alcohol consumption was associated with bedtimes, wake times, night wakings, sleep latency on weekends, being late or missing class, and GPA (r=.14 to .47, p<.05). GPA was also significantly correlated with bedtimes, wake times, being late or missing class, and all nighters (r=.15 to .27 p<.05). Insomnia symptoms were common with 93% of students feeling physically tired, 69.8% having trouble falling asleep, 58.5% falling asleep easily during the day, 52.6% waking frequently during the night, and 39.2% waking up in the night and finding hard to get back to sleep.
Conclusion: Students were sleep deprived by 1.40 hours on weekdays (compared to the recommended 8 hours). Additionally, sleep patterns and sleep hygiene were linked to GPA and alcohol consumption. College students also have high rates of insomnia symptoms. Given the relationship between sleep, daytime functioning, and health, sleep interventions that target college students should be developed.

0196

TIMING, EXTENT, AND INCIDENCE OF SLEEPINESS DURING COLLEGE LECTURES

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Introduction: College students are reported to have excessive daytime sleepiness (EDS) attributable to suboptimal duration, timing, or quality sleep. EDS is associated with poor academic performance and understanding of the underlying causal pathways is needed. The present study investigates fluctuations in level of sleepiness among college students during lectures. Attending a lecture is a ubiquitous college student experience that often involves sitting quietly in a comfortable setting with the lecture as the predominant source of stimulation. This circumstance likely unmasks sleepiness. The aim of this report is to describe the timing of sleepiness changes across lectures as well as the extent and incidence of increased sleepiness.
Methods: Data were collected from students during lectures presented in 5 different classes taught by different instructors. Starting at the beginning of a > 50 min lecture, students were signaled at 10-min intervals to rate their level of sleepiness (using clickers) with the Stanford Sleepiness Scale (SSS). The Epworth Sleepiness Scale was used to create low, medium, and high Epworth-Sleepiness groups.
Results: Data from two classes were dropped because of lecture interruptions (exam reviews, etc). ANOVA of data for 104 students revealed that SSS sleepiness was lowest at the beginning of the lecture and highest 30 minutes into the lecture (p < .001). This same quadratic function was observed for all 3 classes and all 3 Epworth-Sleepiness groups (all ps < .05). At the 30-min time point, 40%, 33%, and 23% of the high, moderate, and low Epworth-Sleepiness groups were very sleepy (SSS scores > 5).
Conclusion: Sleepiness may substantially impair ability to benefit from a lecture. This exploratory study suggests that sleepiness among college students is unmasked by lectures and consistently reaches a peak about 30 min into a lecture.

0197

IMPROVING ACCURACY OF SLEEP SELF-REPORTS USING A BEHAVIOR ANALYTIC APPROACH

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Introduction: Behavior analysts' relative lack of attention to sleep may be due, in part, to inaccuracy of self-report. Improving self-report accuracy would allow researchers and clinicians to assess field-based

interventions. Our goal was to evaluate the effects of correspondence training on self-report accuracy of, and corresponding changes to, wake after sleep onset.

Methods: Two males and 2 females (18-22 years) with <60% accuracy on a brief sleep knowledge quiz and no history or symptoms of sleep disorders participated. Each morning participants self-reported their minutes spent asleep and awake after sleep onset. Self-report was compared to actigraphy at daily meetings (Monday-Friday). Experimental control was established using a concurrent multiple-baseline-across-participants design. Feedback began once: (a) the participant had completed at least 4 days of baseline, (b) accuracy stabilized or consistently trended downward, and (c) wake after sleep onset stabilized or trended downward. During feedback, participants were given daily graphical and verbal feedback on their self-report accuracy, but no advice on improving sleep. Participants earned up to $5 daily for self-report accuracy.

Results: Mean self-report accuracy was 49% (range, 12%-97%) during baseline and increased to 78% (range, 45%-100%) during feedback. Although accuracy improved, total time spent awake was 34 min (range, 20-58 min) during baseline and 42 min (range, 14-110 min) during feedback. Further, sleep-efficiency ranged from 88.7%-94.5% during baseline and 86.8%-94.3% during feedback.

Conclusion: Although feedback and compensation improved self-report accuracy, it had no effect on wake after sleep onset or sleep efficiency. Thus, the change in verbal behavior was insufficient to evoke any change in nonverbal behavior. Yet sleep efficiency was already high and changing sleep time was not the study purpose. Making compensation dependent on minutes slept instead of self-report accuracy may have a more substantial influence on sleep behavior, and should be evaluated among a sleep deprived population.

0198

APPLYING THE SCIENCE OF SLEEP AND FATIGUE TO MAXIMUM DUTY PERIODS IN PROPOSED RULEMAKING FOR COMMERCIAL AVIATION

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Introduction: In 2009, the Federal Aviation Administration (FAA) chartered the Flight and Duty Time Limitations and Rest Requirements Aviation Rulemaking Committee (ARC). The ARC delivered its recommendations for new regulatory guidelines for flight crew member flight and duty times in commercial aviation to the FAA, and in 2010 after considering the ARC's recommendations, the FAA published its Flightcrew Member Flight and Rest Requirements Notice of Proposed Rulemaking (NPRM) for public comment. This NPRM contains FAA-proposed maximum flight duty period (MFDP) limits, stratified by time of day for duty start and by number of flight segments per duty period. The FAA-proposed limits deviate in several cases from the ARC's original recommendations. We used mathematical modeling of fatigue to assess whether these deviations could be overly restrictive.

Methods: We extended a published mathematical model of fatigue (McCauley et al., 2009) to account for workload from multiple take-offs and landings, so as to make it suitable for predicting fatigue across the FAA's proposed MFDPs stratified by time of day and number of flights. Representative flight schedules matching the FAA's proposed MFDPs were constructed, and where divergent, the same was done with the ARC's original recommended MFDPs. In these divergent cases, the mathematical model was applied to the two schedules, and maximum fatigue associated with them was compared.

Results: Out of 42 total cases where the FAA's proposal deviated from the ARC's recommendations, in 13 cases predicted maximum fatigue was lower in the ARC's proposed MFDPs than in the FAA's more restrictive proposed MFDPs. These 13 cases involved morning duty start times (05:00-10:00), which meant that duty end times approached the early

evening wake maintenance zone when circadian pressure for wakefulness would naturally mitigate fatigue (by up to 20.3% as predicted).

Conclusion: Using the science of sleep and fatigue, we provided plausible, quantitative evidence that some FAA-proposed limitations on MFDPs in multi-segment flight operations may be overly restrictive with respect to predicted fatigue. This information was helpful as part of commercial aviation's official commenting on the FAA's NPRM. The mathematical model on which our assessments were based will undergo validation in a high-fidelity flight simulator study to further support the findings.

Support (If Any): Regional Airline Association

0199

THE EFFECT OF CHRONOTYPE AND SEASONS ON NAP SLEEP ARCHITECTURE

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Introduction: Seasonality has been shown to affect nocturnal sleep quality, with increased rapid eye movement (REM) in winter and spring, compared with summer and fall. No studies have investigated daytime sleep across seasons. The following study analyzed sleep architecture of naps collected in Southern California across warm and cold months. We also examined sleep architecture across morningness and eveningness.

Methods: 185 healthy subjects were given a polysomnographically-recorded nap between 1-3PM. Months were divided into warm (June-Oct, Low 62°F/High 75°F,N=91/62F) and cold months (Nov-May, Low 59°F/High 69°F,N=84/56F). Using a one-way ANOVA, we analyzed minutes and percent of sleep stages, total sleep time, and sleep efficiency across chronotype (morning N=13/8F, intermediate N=127/87F, and evening N=35/23F types) as measured by the Horne-Ostberg Morningness-Eveningness Questionnaire (HO). We compared HO and sleep variables across cold and warm months using ANOVAs and correlations.

Results: In daytime naps, we found significantly higher Stage 1 (p=.01) in warm months, compared with cold months. No differences were found in other sleep stages, sleep efficiency, WASO or sleep latency. Significant differences in chronotype were found for Stage 2 (p=.003) and slow wave sleep (SWS) (p=.03). Morningness was correlated with decreased Stage 2 (p=.007) and REM (p=.01) and increased SWS (p=.03). No differences were found within morning and evening-types across seasons, however within intermediate-type, we found increased Stage 1 (p=.03) and Stage 2 (p=.02), and decreased REM (p=.05) in warm months.

Conclusion: Prior studies have reported fluctuations in nocturnal sleep architecture due to seasonal temperature changes and chronotype. We examined this question in a relatively temperate climate where cold and warm seasons differ by 10-15 degrees. Our data show sleep in individuals with a biological drive towards morningness or eveningness is less affected by seasonal cues, whereas sleep in intermediate-types is more affected by their environment (e.g. seasonal fluctuations in temperature and sunlight).

0200

SLEEPING LESS THAN USUAL AND ITS EFFECT ON EFFORT

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Introduction: Objective effort is reduced by one night of sleep deprivation. It was expected that sleeping less than usual would similarly reduce objective effort expended when compared with sleeping more than usual.

Methods: After completing a 14-day sleep diary 99 students (47 Female, age: M=23.17, SD=5.33; 52 Male, age M= 21.79, SD=4.97) from

a large urban university performed the Math Effort Task (MET), in which participants selected math addition problems at five levels of difficulty and reported on the effort they felt they expended.

Results: Average sleep time for each participant was calculated from a 14-day sleep diary. Participants who slept less on the night before the assessment than their 14-day average (N =23, M=28.24 minutes less, SD=21.14) were compared with those who slept more on the night before the assessment than their 14-day average (N=76, M=91.72 minutes more, SD=74.32). When given the option to select levels of difficulty on which to work, those who slept less than average selected more difficult problems on the MET (M = 3.67) when compared with those who slept more than average [M=3.06, t(96)= 2.028, p=0.045]. However, when asked "how much more effort" participants could have put into the task, those who slept less than their average reported they could have exerted less additional effort (M= 16.74) than those who slept more than their average [M=31.83, t(96)=-2.226, p=0.028]. There were no differences in performance accuracy when the groups were compared.

Conclusion: In contrast to expectations, those who slept less than their usual selected problems of greater difficulty but subjectively judged their effort to be near depletion. These results suggest that those who sleep less than their usual increase arousal by selecting challenging tasks or ineffectively regulate energy exertion. However, they seem aware of the depletion and report an inability to expend additional effort.

0201

DAY TO DAY FUNCTIONING IS RELATED TO PRIOR NIGHT SLEEP IN INSOMNIACS BUT NOT GOOD SLEEPERS

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Introduction: Primary insomnia is associated with impaired daytime functioning. However, little research has assessed whether the variation of sleep from night to night is related to subsequent daytime functioning. Insomniacs strongly hold the belief that a bad night's sleep is associated with impairment the following day. The validity of this belief has never been empirically tested. The aim of this study was to investigate the relation between night time sleep and subsequent daytime functioning in primary insomnia as well as good sleepers.

Methods: Seventeen older (mean = 67.8 years) primary insomnia and 17 age and gender matched good sleeper participants initially reported their beliefs about sleep and daytime functioning on the Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS-16). Then over a 14 day period participants kept concurrent sleep diaries and daytime functioning scales. For each participant night sleep measures (e.g. total sleep time, wake time after sleep onset, and sleep efficiency) were correlated with subsequent daytime functioning measures across the 2 week period.

Results: As expected, the mean DBAS-16 was significantly higher (p<0.001) and daytime functioning scores significantly lower (p<0.001) in the insomnia group than the good sleepers. The co-variation between nightly sleep measures and daytime functioning was significant in the insomnia group but not for the good sleepers. Furthermore, those insomniacs who held more strongly the beliefs about the relationship between sleep and daytime functioning, were those who showed this day-to-day relationship the most strongly across the 2 weeks.

Conclusion: These findings demonstrate that the beliefs held by insomniacs about the relationship between sleep and subsequent daytime functioning are consistent with their experience. In this light, consideration should be given as to whether the attempt in cognitive therapy to dissuade insomniacs from these strongly held and valid beliefs may be fruitless and potentially counterproductive for client/therapist rapport.

0202

EFFECTS OF SLEEP DEPRIVATION ON TASK ENGAGEMENT

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Introduction: Although research suggests that sleep deprivation may affect performance through internal attentional processes, little research has examined how sleep-deprived persons assess their personal engagement when performing. The purpose of the current study was to examine the effects of partial and total sleep deprivation on self-assessed engagement in tasks.

Methods: Participants included 32 students (17 males, 15 females) in a partial sleep deprivation study (slept about 4.5 hours between 1 and 5:30am) and 23 students (15 males, 8 females) in a total sleep deprivation study. All participants completed a variety of tasks four times during each study (partial: 7-9:30am, 9:45-12:15pm, 1:15-3:45pm, 4-6pm; total: 6:30-10:30pm, 11-3am, 3:30-7:30am, 8-12pm). At the conclusion of each testing period, participants completed three VAS questions on absorption, attention, and non-task related thoughts while completing the preceding tasks.

Results: A 2x3x4 ANOVA (partial/total by VAS by time) found a significant difference between the three VAS (p=.025) and across the four testing sessions (p<.0001). A follow-up 2x4 ANOVA (partial/total by time) was completed for each VAS measure. Absorption showed a significant decrease across time (p<.0001) and a significant interaction (p=.024). Attention resulted in a significant decrease across time (p=.001). There were no significant changes in non-task related thoughts. There were also no significant differences between sleep conditions for any of the VAS measures.

Conclusion: These findings suggest that sleep-deprived persons are less absorbed and less attentive to their tasks across multiple testing sessions under partial and total sleep deprivation conditions while non-task related thoughts did not change. This suggests that the degree of sleep deprivation makes little difference in the ability of the person to maintain overall engagement in the task. Thus, employees who are partially or totally sleep deprived should be expected to be less focused on their tasks which can lead to lower quality production.

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0203

DOES SUBJECTIVE ALERTNESS PROVIDE ACCURATE KNOWLEDGE OF PERFORMANCE IMPAIRMENT?

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Introduction: Subjective feelings of alertness may provide some insight into performance capacity, yet the accuracy of this insight when individuals are fatigued remains unclear. The aim of the present study was to investigate if subjective alertness could reflect the full extent of neurobehavioural impairment during the biological night when sleep was restricted.

Methods: Twenty-seven healthy young males were scheduled to a 7x28h sleep/wake cycle in a temporal-isolation laboratory. Thirteen participants were in a high sleep dose condition (9.3h in bed/28h), and 14 participants were in a low sleep dose condition (4.7h in bed/28h). Subjective alertness was assessed using a visual analogue scale (VAS) ('how alert do you feel now?'). Neurobehavioural performance was assessed using a 10min psychomotor vigilance task (PVT). Circadian phase was estimated from core body temperature and was divided into two broad

ranges that coincided with the biological night (270 - 90 deg) and the biological day (90 - 270 deg), respectively. All participants completed a VAS and a PVT every 2.5h during each wake period. PVT response time (RRT) and VAS ratings were standardized within individuals against their respective baseline average and standard deviation.

Results: The standardized data were analysed using a mixed-effects ANOVA with 'Condition' (high, low sleep dose), 'Prior Wake' (7 levels), 'Circadian Phase' (biological night, day) and 'Measure' (RRT, VAS) as fixed terms, and 'Participant' as a random term. There was a significant Measure x Condition x Circadian Phase. Compared to VAS ratings, RRT degraded to a greater extent after sleep restriction, especially during the biological night.

Conclusion: Subjective alertness did not reflect the full extent of reduced performance capacity during the biological night when sleep was restricted. Given that subjective alertness is often the only available information upon which performance capacity is assessed, our results suggest that fatigued individuals are likely to under-estimate their neurobehavioural impairment.

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0204
RELATION BETWEEN NONMEDICAL PSYCHOSTIMULANT USE AND SLEEP DURATION

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Introduction: Self-reported rates of nonmedical psychostimulant use among emerging adults are high (up to 43%). However, the relation between nonmedical psychostimulant use and objectively measured sleep has not been evaluated. The purpose of this study was to compare actigraphically-measured sleep among emerging adult users of nonmedical psychostimulants compared to non-users.

Methods: Sleep was assessed for one week with continuous wrist actigraphy. Nonmedical psychostimulant use was confirmed with urinalysis at daily meetings with the researcher. Participants were 14 nonmedical psychostimulant using, and 14 non-using emerging adults. The sample was 71% female and was 19.32±1.59 years in age, and an attempt was made to match groups on age, gender, grade point average, regularity of bedtime, and living arrangement.

Results: Over the 1-week period, there was not a statistically significant difference in sleep measures between users and non-users. In an examination of only nonmedical psychostimulant users, total sleep times were significantly lower on nights preceding use (M = 310.71, SD = 116.89 minutes) compared to nights not preceding use (M = 419.63, SD = 87.69 minutes) [F (1, 79) = 15.06; p < 0.001]. No differences were found between nights following and not following use.

Conclusion: This study suggests that among emerging adults using psychostimulants nonmedically, these drugs may be used to compensate for shortened total sleep time on the previous night which is not compensated for on subsequent nights. Future research should examine the possible link among nonmedical psychostimulant users' cycle of sleep loss and self-medication, as it may have serious implications for grades, mood disturbance, and reaction times.

Support (If Any): West Virginia University Doctoral Student Research support; West Virginia University Alumni Fund; and West Virginia University Behavioral and Biomedical Sciences Training Scholarship Research Award

0205
GOT SLEEP? THE IMPACT OF TRAINING SCHEDULES ON THE SLEEP OF ELITE ATHLETES

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Introduction: In any sport, successful performance requires a planned approach to training. While good-quality sleep is recognised as an essential component of this approach, the impact of training schedules on the amount of sleep routinely obtained by elite athletes has not been systematically evaluated. The aim of this study was to examine the impact of training start times on the amount of sleep obtained by elite athletes.

Methods: Data were collected from a group of 70 nationally ranked athletes from seven different sports. Participants wore wrist activity monitors and completed self-report sleep/training diaries for at least five days. Measures extracted from the diaries and activity data included: training start time, pre-training fatigue level, and total sleep time (TST).

Results: Separate linear mixed model regression analyses were used to determine (1) the effect of training start time on TST, and (2) the effect of TST on pre-training fatigue levels. There was a significant effect of training start time on TST. Specifically, TST decreased as training start time advanced, from under 5h/night for sessions that began between 05:00-06:00h, to over 7h/night for sessions that began between 10:00-12:00h. There was also a significant effect of TST on pre-training fatigue level. Pre-training fatigue level decreased as TST increased.

Conclusion: These results indicate that early morning training sessions systematically reduce the amount of sleep obtained by elite athletes and increase pre-training fatigue levels. This practice has two important implications for training performance. First, insufficient sleep and high fatigue levels immediately prior to a training day could impair an athlete's motivation and thus, their ability to train effectively. Second, people who obtain insufficient sleep over several consecutive days have impaired immune function, which in the case of elite athletes, places them at greater risk of developing respiratory tract infections and other health problems.

Support (If Any): This study was financially supported by the Australian Research Council.

0206
INHIBITION OF SELF-GROOMING IN SLEEP-RESTRICTED DAM RATS

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Introduction: It is well known that sleep curtailment leads to neurobehavioral comorbities during pregnancy such as perinatal depression and maternal fatigue. However, the effects of sleep restriction over mother-infant relationship still warranted further investigation. This study assessed the effects of sleep restriction during pregnancy over maternal behavior and maternal aggression.

Methods: Eighteen pregnant rats were distributed in 2 groups: 1) Control (n=9): not subjected to any manipulation during the gestation, and 2) Sleep restriction (n=9): submitted to sleep restriction during pregnancy through modified multiple platform method during 18h per day (from 04:00 PM to 10:00 AM). At post-partum day 5, female rats were submitted to behavioral tests to evaluation of maternal behavior. The tests were: 1) resident-intruder paradigm (introduction of a naive male rat in the home-cage of the female rat and its respective litter to behavioral observation), and 2) latency test (time to retrieve the first and eighth pup after 5 minutes of maternal separation).

Results: At the resident-intruder paradigm, sleep-deprived dams displayed grooming in lower frequency and duration, and with higher latency when compared with control animals. Parameters related to maternal aggression and maternal behavior were equivalent between groups.

Conclusion: Considering the maintenance of maternal behavioral, the inhibition of grooming seems to exert an adaptive mechanism, enabling sleep-restricted rats to display a proper parental behavior. These results corroborate previous theoretical framework by evidencing behavioral changes during lactation due to sleep disruption during pregnancy.

Support (If Any): AFIP, FAPESP/CEPID and CNPq

0207

EFFECTS OF SOCIAL INTERACTIONS ON SLEEP IN MICE

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Introduction: Although it is generally believed that increased social activities contribute to the overall reduction of sleep time in modern societies, little is known the precise influences of social environment on sleep due to the lack of animal studies. The aim of present study was to determine the effects of social interactions on sleep in mice.

Methods: Adult male C57BL/6 mice (n=7) implanted with chronic EEG and EMG electrodes were connected to the recording system and individually kept in a large plastic cage [40cm (L) x 22cm (W) x 25cm (H)] for 3 days after recovery from surgery. During this and subsequent experimental periods, a compartment (12cm x 12cm x 12cm) made of metal grids (with 0.8cm separation between vertical grids) was placed in each cage (4cm from one end of the cage) with food on the inside floor and water supply on the top. EEG and EMG were then recorded for 2 days, starting from light onset. The first day served as the baseline. On the second (social) day, a male C57BL/6 mouse was place inside of the compartment at light onset. Therefore, no other novel stimuli were present during the social day except the stranger mouse. The experimental mouse could move freely around the compartment and get visual, auditory, tactile and olfactory information from the stranger. Sleep was scored visually according to standard method based on EEG and EMG signals.

Results: Sleep time was decreased by a bout 100 min during the social interaction day. Baseline vs. social: wakefulness [683.33±41.90 min vs. 784.74±21.94 min, F(3,18)=8.647, p<0.001]; non-rapid eye movement sleep [679.62±41.82 min vs. 607.69±25.75 min, F(3,18)=8.300, p<0.001]; and rapid eye movement sleep [59.05±1.71 min vs. 47.57±5.33 min, F(3,18)=2.323, ns].

Conclusion: Our results indicate that the presence of opportunities for social interactions have significant influence on daily sleep.

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0208

GENDER-BASED DIFFERENCES IN SLEEP DISTURBANCES AND MOOD CHANGES IN A RODENT MODEL OF INSOMNIA INDUCED BY CHRONIC STRESS

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Introduction: Women show higher vulnerability to develop stress-induced disorders such as insomnia and depression. Differences in stress responsiveness may contribute to this higher susceptibility. We examined gender-based differences in the predisposition to develop insomnia and mood disorders using a rodent model of chronic mild intermittent stress (CMS). In addition, we examined whether social interactions attenuate the deleterious effects of stress on sleep and mood in female rats.

Methods: Male, female and paired-housed female rats were subjected to 4 weeks of CMS, consisting of exposure to unpredictable environmental changes. At baseline and at each week, sleep recordings (24 hours) were obtained by telemetry, and anhedonia (a key symptom of depression) was assessed using the sucrose preference test (SPT). At the end of CMS, all rats were subjected to the open field test (OFT) to measure anxiety, and to the forced swimming test (FST) to assess depressive mood.

Results: After 4 weeks of CMS, males showed increased nREM sleep and fragmentation in the light phase, whereas single-housed females displayed decreased nREM in the light phase and increased REM in the dark phase, with augmented fragmentation in both phases. Paired-housed females only showed a moderate increase in fragmentation in both phases. All groups displayed reduced sucrose preference (anhedonia) at week 3, which was more pronounced in single-housed females. Paired-housed females displayed more active behavior in the FST and OFT, suggesting that they were less depressed and anxious.

Conclusion: These results support this animal model as an approach to further study the neurobiological mechanisms underlying gender-based differences in the predisposition to develop stress-induced disorders such as insomnia. Furthermore, this model is also useful for studying how social interactions (known to increase stress coping in female rats but not in males) strongly attenuate the deleterious effects of stress on sleep and mood in female rats.

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0209

α-1 ADRENOCEPTOR ANTAGONIST PRAZOSIN REDUCES NON-REM SLEEP (NREMS) AROUSALS IN FEAR-CONDITIONED WISTAR-KYOTO RATS (WKY)

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Introduction: The α-1 adrenoceptor antagonist prazosin reduces non-nightmare distressed awakenings (NNDAs), as well as nightmares, in individuals with posttraumatic stress disorder (PTSD). Prazosin is not known to alter NREMS macroarchitecture in PTSD, but arousals during NREMS have not been assessed. Defining arousals as changes in the EEG, with corresponding EMG activation, lasting ≤3 s (except those occurring within 20 s of NREMS onset or termination), we hypothesized that prazosin would reduce the number of arousals during NREMS in fear-conditioned, stress-sensitive WKY.

Methods: Male WKY were habituated and received a prazosin (0.01 mg/kg, i.p.; n=4) or vehicle (n=4) injection followed 15 min later by a 4-h baseline sleep recording. Two days later, they were presented with 10 tones (800 Hz, 90 dB, 5 s; 30 s interval) each co-terminating with a foot shock (1.0 mA, 0.5 s). The following day (Day 1), 6 days (Day 7), and 13 days (Day 14) later, prazosin or vehicle was administered, 3 tones were presented without foot shock, and sleep was recorded for 4 h. Arousal number was extracted and normalized by total NREMS time.

Results: WKY given prazosin had fewer NREMS arousals across all recording days (p<0.001), with a significant day-by-treatment interaction (p=0.04). Post-hoc tests revealed a significant reduction in arousals in the vehicle group on Day 1 (0.165 ±0.02 [arousals/min ±SEM]) when compared to either baseline (0.250 ±0.02; p=0.004) or Day 7 (0.257 ±0.03; p=0.002). Day 14 results were similar to Day 7 (0.223 ±0.02). In contrast, in the prazosin group, arousals were 0.105 ±0.02 at baseline and did not vary from baseline on any other day. No significant changes were found in NREMS time.

Conclusion: The neurobiological mechanisms of prazosin efficacy in reducing the sleep disturbances in PTSD are unknown. NREMS, as

well as REMS, microarchitecture must be assessed. NNDAs, particularly, might emerge from NREMS. The finding that prazosin reduced NREMS arousals suggests that it may help ameliorate PTSD symptoms by consolidating NREMS.

0210

IMPACT OF PRENATAL MATERNAL BELIEFS ON INFANTS' NIGHTTIME SLEEP ARRANGEMENTS IN THE FIRST 3 MONTHS OF LIFE

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Introduction: As part of an ongoing, multi-center longitudinal study we report here, initial findings on the correlation of prenatal beliefs about infant sleep with postnatal nighttime sleep practices, during the first 3 months after birth.

Methods: From 10 Maternal and Child Hygiene hospitals in nine cities in China, 347 eligible women were enrolled in the study at approximately 34 weeks of pregnancy; after delivery 260 healthy, full-term infants met inclusion criteria and were enrolled as study subjects. Prior to delivery, all expectant mothers completed a questionnaire on attitudes towards four aspects of infant sleep: sleep location, sleep position, state of infant's consciousness at the time of being put to sleep, and dealing with nocturnal wakes. Following delivery, sleep diaries were administered over 3 consecutive nights starting at 10 and 28 days and 2 and 3 months postnatally. The correlation of prenatal beliefs to postnatal infants' sleep practices was analyzed by Kappa consistency check.

Results: On prenatal survey, 79% of women expressed a preference for the child to sleep in a separate crib in the same room with an adult and 11% anticipated co-sleeping with the child. On post-natal survey, only 38% reported their child slept in an independent crib, whereas 57% reported co-sleeping (prenatal to post-natal kappa = 0.06). Regarding sleeping position, 55% preferred the supine position on prenatal survey and 36% preferred putting the infant on the side; postnatally, the respective proportions were 71% and 29% (kappa = 0.16). On when to put the child to sleep, 63% indicated this should happen when the child was drowsy but not yet asleep, whereas 31% indicated the infant should be fully asleep; postnatally, 31% were putting the child to sleep when drowsy, whereas 64% were waiting until he/she was fully asleep (kappa = 0.02). Regarding night awakenings, 65% of the prenatal sample stated they should wait a few minutes before taking action while 33% anticipated taking immediate action; postnatally, the proportions reversed with 76% taking immediate action and only 18 % waiting a few minutes before taking action (kappa = 0.00).

Conclusion: With the one favorable exception of sleep position practices, we conclude that prenatal beliefs are poor predictors of postnatal sleep related practices and that opportunities exist for educational interventions to improve postnatal sleep practices among primiparous Chinese women.

0211

LOWER SUBJECTIVE SOCIOECONOMIC POSITION IS ASSOCIATED WITH POORER SLEEP QUALITY AND GREATER DAYTIME SLEEPINESS IN CHILDREN AND ADOLESCENTS

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Introduction: In adults, low socioeconomic position is associated with short sleep duration, poor sleep quality, more sleep complaints, and considerably more accumulated sleep debt. While researchers have started to examine whether a socioeconomic gradient exists for sleep problems in adults, relatively little is known about this relationship in children and adolescents. The aim of the present study was to identify whether a subjective socioeconomic gradient exists for sleep duration, sleep quality and daytime sleepiness, while controlling for parental objective indicators of socioeconomic position.

Methods: Participants were part of the larger Healthy Heart Project and included 244 families (parents aged 30 to 65 years: M=45.03, SD=6.13; 81.4% female; youth aged 8 to 18 years: M=12.66, SD=2.03; 46.3% female). Total household income and parental education were used as indicators of objective socioeconomic position. The MacArthur Scale (adolescent version; Goodman et al., 2001) was used to measure youth subjective socioeconomic position. Sleep duration was the difference between self-reported bed- and wake-times. Perceived sleep quality was rated on a 10-point Likert scale (1=poor to 10=excellent). Daytime sleepiness was assessed with the self-report Pediatric Daytime Sleepiness Scale (Drake et al., 2003).

Results: After adjusting for age, sex, and body mass index (BMI), lower objective socioeconomic position was significantly associated with shorter sleep duration (t=3.23, p<.01, η^2=4%), but not with perceived sleep quality or daytime sleepiness. However, lower subjective socioeconomic position was significantly associated with poorer perceived sleep quality (t=3.52, p<.01, η^2=5%) and greater daytime sleepiness (t=-2.81, p<.01, η^2=3%), after controlling for objective socioeconomic position, age, sex, and BMI.

Conclusion: These results suggest that sleep may be one pathway underlying the socioeconomic gradient in health. Future researchers should aim to elucidate how specific sleep parameters (e.g., sleep architecture) may explain how socioeconomic status influences health.

0212

SLEEP'S (COMPLICATED AND UNEXPECTED) INFLUENCES ON VERBAL MEMORY

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Introduction: Sleep protects verbal memories by boosting resistance from subsequent (prospective) associative interference. We asked: (1) Is sleep indispensable to verbal memory? (2) Does sleep protect verbal memory from retroactive and non-associative forms of interference? (3) Does sleep enhance verbal memory or help retain it better? The goal was to delineate the influences and limits of sleep's role in affecting recently acquired verbal memories.

Methods: Each volunteer (n=160 total) participated in only one of our experiments. Participants memorized unrelated pairs of words A_i-B_i. Following an intervening period of 12-24 hours that did or did not include sleep, participants memorized a second pair of interfering words A_i-C_i/C-D just before being tested on their memory of both.

Results: (1) Reducing required rehearsal during training increased the benefits of sleep on test recall 12 hours later. Increasing required rehearsal during training entirely compensated for the benefit of sleep (sleep-85%, wake-90%). (2) When observers acquired non-associative C-D pairs 12 hours following A-B pairs, sleep provided a statistically indistinguishable benefit in test recall of A-B word pairs (13%) compared with when observers acquired A-C pairs (19%). In another experiment, participants learnt 60 A-B word pairs. Twelve hours later, they acquired A-C word pairs. There was a significant (14%) sleep-dependent benefit on test recall of A-C word pairs. (3) A-B recall 12 hours versus right after training did not differ.

Conclusion: Sleep is one way, but not an exclusive one, of sheltering verbal memory from associative prospective interference. Sleep can also protect verbal memories from non-associative and retroactive interference. Sleep does not help enhance verbal memory but shelters it from fading. Additional analysis demonstrates that sleep prior to memory encoding provides no benefit. Combined, our results are more consistent with the idea that sleep benefits verbal memory by preventing its subsequent re-exposure rather than by replaying it.

0213

NOVEL OBJECT LEARNING DEPENDS ON RAPID EYE MOVEMENT SLEEP

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Introduction: A fundamental function of biological vision is to detect and recognize potential food items and predators from naturally cluttered backgrounds when form and coloration of target objects are similar to the background. Brady and Kersten (2003) previously showed that subjects can do this via bootstrapped learning. Sleep, specifically rapid eye movement (REM), has been shown to enhance perceptual learning. Here, we examined the role of REM sleep in object learning in ambiguous backgrounds.

Methods: At 9AM and 5PM, 82 subjects were tested on an object learning task. At 1PM, subjects fitted with EEG electrodes and randomized to a quiet rest condition (QR) or nap condition with or without REM. Stimuli were artificial morphogenic objects that appear to be organic forms but do not resemble a familiar class of organism and are camouflaged by similar shapes. During AM training, subjects were shown three objects in cluttered backgrounds and asked to trace each object in the foreground (Trace condition). Next, subjects passively view these camouflaged objects appearing with a characteristic sound. At PM test, subjects were asked to recognize objects in the Test condition and retrace objects in the Trace condition.

Results: REM group was significantly better than NREM and QR in recognition (Test), both QR and NREM performed just above chance. Both nap groups were significantly better than QR in the Trace condition.

Conclusion: We found an essential role for REM sleep in learning to detect and recognize novel objects from camouflage. REM occupies a large proportion of sleep during early development, and has been hypothesized to be related to cortical plasticity. The following results suggest that learning to recognize and segment objects that share the same form and coloration as their background requires REM sleep in adulthood and has implications for infant object learning.

0214

SPATIAL MEMORY PERFORMANCE SHIFTS ITS ASSOCIATION FROM SLOW WAVE SLEEP TO REM SLEEP WHEN AN EMOTIONAL COMPONENT IS ADDED

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Introduction: While many studies link slow wave sleep (SWS) to the processing of declarative memory, a small but growing literature demonstrates a role for rapid eye movement (REM) sleep when such memory is emotionally charged. Here we examined if a SWS-associated task shifts its dependence to REM sleep when this task is made emotional.

Methods: We had 16 participants undergo two matched spatial navigation tasks that differed in emotional tone and observed how performance in each task was affected by one night of selective REM deprivation. Participants slept one night in a sleep laboratory and were randomly assigned to either a REM sleep deprived (REMD; awakened after 5 minutes of REM sleep) or a control (CTL; awakened after 25 minutes of REM sleep). Ten to 12 days post-task participants were given surface maps of the two versions of the spatial task (fig. S1) and instructed to mark the houses they had visited.

Results: The REMD group was successfully REM sleep deprived, showing lower %REM sleep (M=9.51, SD=1.08) than the CTL group (M=16.71, SD=5.57; t12=3.36, p=.005). The REMD group had more missed targets than the CTL group on the emotional version of the task (REMD: M=2.86, SD=.38; CTL: M=2.00, SD=.58; t12=-3.29, p=.01) but fewer wrong targets on the neutral version (CTL: M=2.67, SD=.79; REMD: M=1.43, SD=.78: t12=2.76, p=.02). Missed targets on the emotional version of the task were negatively correlated with min in REM sleep (r16=-0.71, p=.005), and %REM sleep (r16=-0.71, p=.004). Wrong targets on the neutral version of the task were negatively correlated with min in Stage 4 sleep (r16=-0.62, p=.01) and %Stage 4 sleep (r16=-0.65, p=.006) and positively correlated with %REM sleep (r16=0.55, p=.03).

Conclusion: Together, these findings suggest that imbuing a spatial memory task with dysphoric emotions switches its association from SWS to REM sleep.

0215

SLOW WAVE SLEEP PLAYS A ROLE IN THE TRANSFER OF STATISTICAL INFORMATION FROM THE MEDIAL TEMPORAL LOBE TO THE STRIATUM DURING CONSOLIDATION

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Introduction: Memory consolidation during sleep has been increasingly documented in the last decade. Perceptual learning, and in particular the important field of exposure learning, is currently under-represented in this research. Here we studied the impact of sleep upon abstraction of statistical patterns from exposure learning with behavioural, sleep and functional imaging measures.

Methods: 36 participants divided equally between Sleep and Wake groups took part in a statistical learning task which involved exposure to a structured auditory stream followed by an immediate-recall session, and after a consolidation gap a delayed-recall session, in both of which they were required to identify short sequences with a structure similar to the exposure stream. The Sleep group were trained and immediately tested at 3pm on Day 1. Their overnight sleep was then monitored with polysomnography, and they were retested in the fMRI scanner at 3pm on Day 2. Participants in the Wake Group were trained and immediately tested at 3pm and then placed immediately in an fMRI scanner for the second test session, with no consolidation delay.

Results: Behaviourally, identification of structured sequences improved more in the Sleep than the Wake group, and this improvement correlated with the amount of slow wave sleep obtained. Functionally, we found a decreased dependence on the medial temporal lobe and increased activation of the striatum after sleep during correct identification of structured sequences. Importantly, this functional shift correlated with the amount of slow wave sleep obtained.

Conclusion: Our findings broadly support the standard model of consolidation and highlight the importance of slow wave sleep in this process. They also suggest the existence of a new form of trade-off between the medial temporal lobe and the striatum similar to a classical training effect, but which here is dependent on sleep.

0216

THE INFLUENCE OF SLEEP INERTIA ON ATTENTION SWITCHING

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Introduction: Sleep inertia (SI), the grogginess felt upon awakening, is associated with cognitive performance impairments. The greatest impairments occur immediately upon awakening and dissipate over the next few hours. We sought to extend the understanding of SI on cognitive performance by assessing the impact on attention switching between spatial orientation and mathematical tasks.

Methods: Performance of ten healthy subjects [4 females (21.5±3.5yr;mean±SD)] on the Switching Task was assessed within 1min of scheduled awakening and every 10min thereafter until 1h awake. The Switching Task, known to be sensitive to sleep deprivation, cued subjects to switch attention between two simultaneously presented tasks. Subjects either mentally rotated a mannequin and indicated the hand holding a specified stimulus or completed a simple mathematical task and indicated if the sum was greater or less than five. Transitions between tasks were analyzed using 1/mean correct reaction time while accuracy and speed were analyzed with throughput for each task. Data were analyzed as deviation from the mean with repeated measure ANOVA.

Results: Significant main effects of time for the mannequin throughput and transitions to the mannequin task across SI tests were observed (p<.05). Performance was worse immediately upon awakening and improved with time awake. The mannequin throughput and the transitions to the mannequin task showed a greater magnitude of improvement from the first SI test to the last SI test than the math throughput or transitions to the math task.

Conclusion: SI influences cognitive processes involved in shifting spatial attention. Transitioning to a spatial orientation task appears to be influenced to a greater extent by SI than shifting to simple mathematical calculations. These findings suggest that impairment due to SI may have negative cognitive consequences on individuals who are required to switch attention to relatively complex tasks immediately upon awakening from sleep (e.g., surgeons, fighter pilots).

0217

SLEEP-DEPENDENT IMPROVEMENT OF SPATIAL MEMORY ACCURACY, INDEPENDENT OF NAVIGATION SPEED

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Introduction: Converging evidence indicates a mnemonic benefit of sleep across a wide variety of learning domains, including the recall of implicit, explicit, emotional, and spatial information. In previous studies, we demonstrated that a brief daytime nap following training enhances retention of spatial memory in a virtual maze paradigm. Here, we extend this finding to an overnight protocol, using a modified maze with additional performance measures, separately examining change in spatial memory accuracy from navigation speed.

Methods: Participants (n=30) completed a 3D first-person perspective virtual maze task. The task involved a 5min exploration period followed by 3 test trials, in which participants navigated to a specified goal point as quickly as possible. Following training at 10am or 10pm, subjects either spent the night in the lab with EEG monitoring, or else went about their normal activities during a day of wakefulness. Retesting on the maze task occurred 12hrs later. Performance measures included improvement in distance traveled, speed, and completion time.

Results: Following sleep, maze completion times were significantly decreased, relative to those subjects who remained awake (p=.03). Furthermore, while there was no difference in speed improvement between groups, sleep participants improved more than wake subjects in minimizing the distance traveled to the goal (p=.004). Analysis of sleep architecture revealed no significant correlations between sleep stages and performance measures.

Conclusion: This data provides evidence that overnight sleep benefits spatial memory for a complex virtual environment, extending our previous findings using naps. That sleep was beneficial for improvement in distance traveled to the goal, coupled with an absence of a sleep effect on speed, indicates that the observed effect is based on improvement of spatial route memory, rather than improved ability to generally move about the maze.

0218

MEN NEED A NAP TO SHOW PERCEPTUAL LEARNING, BUT WOMEN DO NOT

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Introduction: Sex differences in performance have not been found under sleep deprivation conditions, although well-rested men generally exhibit better spatial orientation and reaction times compared to women. Perceptual learning of texture discrimination is sleep-dependent and specific to the trained condition. Daytime naps improve task performance within the same day. We employed a nap paradigm to compare the benefits of sleep for perceptual learning of motion discrimination in men and women.
Methods: 95 healthy subjects (age=20.2±2.15yrs) completed a motion direction discrimination task. At 9AM, thresholds were obtained for trained and untrained directions of motion, followed by 40min of training. Subjects were classified into one of two groups: naps (N=51,36F) (75min; polysomnography-recorded) and no-nap (N=44,22F). At 4PM, thresholds were re-tested. Learning was computed for two conditions (trained/untrained directions) for each group (nap/no-nap). We hypothesized nappers would show more learning than non-nappers and men would outperform women.
Results: GroupxCondition ANOVA showed a main effect of group on learning (p=.03). Men and women displayed equivalent task performance. However, sex-specific ANOVAs revealed men who napped exhibited increased learning in the trained direction of motion relative to men who did not nap (p=.03). There was no effect of napping in women. Post-hoc t-tests showed women learned both with (p<.001), and without napping (p=.01), whereas men only learned following a nap (p=.003). Neither men nor women exhibited effects of napping in the untrained direction of motion.
Conclusion: Sleep plays an important role in the consolidation motion perception learning, but this effect may be specific to men. Contrary to our hypothesis, men required sleep to show learning on this task, whereas women performed equally well after either wake or sleep. Further research will investigate whether these sex effects are due to attentional or bottom-up processing differences. These data have implications for assigning individuals to duties requiring sustained visual performance based on sex.
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0219

REWARD VALUATION IN SLEEP-DEPRIVED INDIVIDUALS

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Introduction: Sleep deprivation (SD) has broad and substantial effects on cognitive processing, typically reducing performance across a range of cognitive tasks. Yet, relatively little is known about how it may alter individuals' preferences among different outcomes; i.e., does SD only impair cognitive abilities, or does it change the very values we ascribe to different rewards? We investigated these questions in experiments that examined anticipation, receipt, and exchanges between monetary and social rewards.
Methods: Twenty-two male participants were scanned using functional magnetic resonance imaging (fMRI) after a normal night of sleep (rested wakefulness state, RW) and after 22 hours of SD while performing a modified monetary incentive delay (MID) task. Participants made speeded responses to cues that signal potential monetary or social rewards. Successful responses to reward cues resulted in winnings of $1,

$5 or $10 or in the display of a female face rated from 1 to 5 stars. Post-scan, participants performed an economic exchange task, in which they could trade some of their accumulated earnings for opportunities to view more attractive faces. Participants then rated the attractiveness of all viewed faces.
Results: SD elicited variable but robust individual differences in economic preferences - with some participants exhibiting increased social value and others reduced social value - that correlated strongly across participants with their state-related change in attractiveness rating. Hence, a participant who showed a greater tendency to exchange money for attractive faces when SD was more likely to rate faces as more attractive under the same condition. This suggests state-driven changes in the valuation of social or monetary rewards or both. These SD-related changes in exchange rate were associated with SD-related changes in individuals' fMRI activation to the social stimuli within the ventromedial prefrontal cortex and amygdala, regions previously shown to respond to experienced value of social rewards. Notably, SD did not affect activation in the nucleus accumbens or ventral tegmental area, nor did it affect activation associated with the experienced value of monetary rewards.
Conclusion: Thus, SD has distinct effects on the decision value and experienced value of social rewards, those effects can be observed even in the absence of any effects associated with monetary rewards, and those effects do not require SD-related changes in expected value signals.
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0220

GENETIC DETERMINANT AND COGNITIVE CONSEQUENCES OF SLEEP DISTURBANCES IN MICE MODELS OF DOWN SYNDROME

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Introduction: Down syndrome (DS) results from the triplication of part of the chromosome 21, including App, precursor of beta-amyloid peptides. DS is associated with learning disabilities and sleep disturbances. In mice, sleep features are under strong genetic control and long term memory requires the integrity of sleep. The aim of the present study was to 1-characterize sleep and EEG in different genetic models of DS for identifying key genomic area for this phenotype. 2- Modulate sleep quality in DS models to improve long term memory.
Methods: Mice models used were: Ts65Dn with a triplication of part of the mouse chromosome 16 (synthenic to the human chromosome 21) including App, Ts65/App++- bear the same triplication but for App which is present in normal dosage (backcross with App-KO), TS mice are compared to their normal diploids littermates (2N). Sleep and EEG spectral analysis were studied after chronic recordings at the age of 3 months. Long term memory was measured by the novel object recognition test. Sleep deprivation was used to modulate sleep quality.
Results: In baseline conditions, Ts65Dn are characterized by a delayed sleep onset in the dark period, decreased sleep amounts, increased REM-sleep amounts, reduced NREM sleep delta power and the presence of abnormally high theta activity in NREM and REM sleep. Normalization of App in Ts65/App++- rescues most of the abnormal sleep architecture seen in Ts65Dn, and partially the spectral aspects. Increasing NREM sleep SWA after the novel object recognition training recued the long term memory deficits.
Conclusion: App plays a prominent role in generating sleep and EEG abnormalities in DS mice models as early as 3 months of age. Interestingly, improving the poor sleep quality in Ts65Dn mice could rescue their long term memory impairment. Those results illustrate the possible involvement of App in the normal regulation of sleep, and the interplays between sleep and memory.
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0221

ROLE OF SLEEP IN VISUOMOTOR ADAPTATION MEMORY CONSOLIDATION ASSESSED BY fMRI

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Introduction: The aim of this study was to determine the influence of sleep on the cerebral correlates of visuomotor adaptation consolidation using fMRI.

Methods: Thirty-one subjects were scanned during 2 separate sessions referred to as the training and retest sessions while they performed a motor adaptation task that required to reach for visual targets using a mouse with the hand while adapting to systematic rotation imposed on the perceived dot trajectory. After training, subjects were randomly assigned to one of two groups according to whether they would be allowed to sleep or be totally sleep deprived during the first post-training night. The retest session took place 72h after training for subjects of both groups allowing two recovery nights for sleep deprived subjects.

Results: Several parameters were used to measure performance (different measures of speed and accuracy). For the training session, an ANOVA conducted on these parameters showed that performance improved with practice in both groups similarly. The ANOVA on between-session effects revealed a significant main effect of session and a group by session interaction. Planned comparisons showed a stabilization of performance in the sleep group but a significant deterioration of performance in sleep deprived subjects between sessions. The main effect of practice of the learned deviation during training and retest sessions recruited a large cerebello-cortical network. Responses increased linearly with performance improvement over the training session bilaterally in the putamen, motor cortex, intraparietal sulcus, in the right cerebellum and left medial prefrontal cortex. No changes in brain responses were observed between training and retest sessions in sleepers as compared to sleep-deprived subjects, suggesting a stability of the cerebral network used during training to perform the task during retest. In contrast, in sleep-deprived subjects as compared to sleepers, responses increased at retest as compared to training in a cerebello-cortical network.

Conclusion: In sum, visuomotor adaptation consolidation is sensitive to the sleep status: sleep led to a stabilization of performance whereas performance deteriorated after sleep deprivation. The maintenance in performance levels observed in sleepers was accompanied by a stabilization of cerebral responses. In contrast, the deterioration of performance in sleep-deprived subjects was illustrated by increased responses in a cerebello-cortical network.

0222

EFFECTS OF SLEEP EXTENSION AND ACUTE SLEEP DEPRIVATION ON COGNITIVE PERFORMANCE IN HABITUAL SHORT SLEEPERS AND LONG SLEEPERS

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Introduction: Previous studies found that short sleepers live under and tolerate higher homeostatic sleep pressure than long sleepers. However, it is not known whether this is reflected in trait-like differences in objective performance. Here we investigated whether short and long sleepers differ in sustained attention when exposed to high levels and low levels of homeostatic sleep pressure.

Methods: Young (18-30 y) healthy short sleepers (n=7, habitual bedrest <6.5 h) and long sleepers (n=11, >9 h) completed a 28-day inpatient protocol consisting of 4 days of habitual sleep (HS), 20 days of extended (12 h) sleep (ES) opportunities, a 36h sleep deprivation (SD) interval and 2 days of recovery sleep. The psychomotor vigilance task (PVT) was administered several times throughout the wake episodes. Sleep was recorded with polysomnography. Total sleep time (TST) and PVT lapses (reaction times, RT > 500 ms), median speed (1/RT) and the interpercentile range (IPRange, difference between the 90th and 10th percentile, 1/RT) were analyzed with a mixed model ANOVA with Group (short, long) and Condition (HS Days 3-4, ES Days 21-23) as fixed effects. For the SD interval, factors Group and Time awake were used.

Results: In the HS condition, TST was less for the short sleepers (Mean±SE: 342±10 min) than for the long sleepers (535±8 min). During the ES condition, TST increased in the short sleepers (533±18 min, $p < 0.001$) but was unaffected in the long sleepers (530±16 min). In the HS condition, there were no differences in PVT performance between short and long sleepers. When given extended sleep opportunities, PVT performance improved in the short sleepers (ES vs. HS: lapses 1.0±0.5 vs. 2.4±0.5; median speed 4.09±0.23 x 10-3 vs. 3.95±0.17 x 10-3 ms-1; IPRange 1.46±0.12 x 10-3 vs. 1.86±0.12 x 10-3 ms-1, $p < 0.001$) but not in the long sleepers. ANOVA on PVT performance during SD revealed that the short sleepers showed fewer lapses (Group x Time awake, $p < 0.001$) and a more stable response pattern (IPRange: Group, $p < 0.04$) than the long sleepers, particularly in the latter part of the SD.

Conclusion: Differences between short and long sleepers in sleep duration may reflect a trait-like difference in the tolerance to homeostatic sleep pressure rather than in the capacity to sleep. Short sleepers seem to possess a 'cognitive reserve' that becomes apparent under very low and very high levels of homeostatic sleep pressure.

0223

SLEEP DEPRIVATION IMPAIRS EFFECTIVE CONNECTIVITY DURING RESTING STATE

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Introduction: Slow waves are a landmark of deep sleep and are thought to play a key role in preparing our brain to process new information. Slow waves are thought to travel over the cortex mostly in an anterior-to-posterior direction and a recent study has identified the cingulate cortex as one of their favorite routes. During wakefulness, cingulate cortices are also major hubs of information exchange in the brain. Therefore, we hypothesize that, without the beneficial effect of slow wave activity (SWA), the transfer of information along the cingulate cortex during the following day is reduced and, because of the directionality in SWA, the reduction is more pronounced in one direction than the other.

Methods: As a measure of effective connectivity, we used Granger Causality (GC) on high-density EEG between preselected sources during wakefulness, after normal sleep and sleep deprivation. The information flow of the brain was manipulated by asking 8 participants to keep their eyes open or closed for two minutes, while EEG signal was recorded from 64 electrodes. GC was assessed between three regions along the cingulate cortex for both directions: anterior-to-posterior and posterior-to-anterior.

Results: After normal sleep, GC from the posterior to the anterior cingulate cortex was higher during eyes-open than during eyes-closed, in

agreement with enhanced flow of sensory information from the visual cortex to more frontal cortical areas. This increased posterior-to-anterior connectivity during eyes-open no longer occurred after sleep deprivation. In the opposite direction, anterior-to-posterior, GC was not different between eyes-open and eyes-closed during waking after normal sleep or sleep deprivation.

Conclusion: Sleep deprivation impairs the increased posterior-to-anterior information flow that is normally present during eyes-open wakefulness. This effect was limited to the posterior-to-anterior direction, which is involved in the transfer of sensory information to the frontal cortex. These findings suggest that SWA has a preferential directionality in its restorative action, which is necessary to maintain the next day's efficient transmission of sensory information to higher order cortical areas.

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0224

SLEEP IS MORE THAN REST

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Introduction: Sleep has been shown to facilitate neural and behavioral plasticity compared to active wakefulness. However, conflicting hypotheses propose that sleep-specific brain activity after training fosters neural reorganization (sleep hypothesis), or alternatively, that sleep provides a window of reduced stimulus interference passively protecting novel memories (rest hypothesis).

Methods: One hundret thirteen healthy subjects (aged 16 to 30 yrs.) were tested on a basic texture discrimination task in the morning and retested in the afternoon, after a 1 hour period of daytime sleep, passive waking with maximally reduced interference, or active waking. Changes in texture discrimination performance have been shown to depend on local synaptic plasticity in the primary visual cortex.

Results: Active and passive wakefulness were associated with deterioration in performance, presumably due to synaptic over-potentiation across within-day sessions. In contrast, sleep not only restored performance in comparison to active waking, as has been shown previously, but also in direct comparison to passive waking. Control experiments excluded that the detrimental effects of wakefulness were due to stress or fatigue. The restoration of performance across periods of sleep correlated with electroencephalographic slow wave activity, potentially related to synaptic downscaling

Conclusion: We conclude that sleep is more than a resting state of reduced stimulus interference, but actively restores performance, presumably by refining underlying synaptic plasticity.

0225

SLEEP PROMOTES CONSOLIDATION AND GENERALIZATION OF EXTINCTION LEARNING IN SIMULATED EXPOSURE THERAPY FOR SPIDER FEAR

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Introduction: We examined sleep's effects in a model of exposure therapy (therapeutic extinction) for simple phobia. Given that extinction of experimental fear conditioning generalizes over sleep, we hypothesized that sleep would also allow extinction learning to generalize from an extinguished phobic object to a novel one.

Methods: 32 females (age=20.1, SD=1.9) within spider-fearing ranges on Fear of Spiders (FSQ, 101.9, SD=14.6) and Spider Phobia (SPQ, 23.9, SD=4.0) questionnaires, were pseudorandomly assigned to a Sleep (N=14) or Wake (N=18) group. Groups did not differ in age, FSQ, SPQ, Pittsburgh Sleep Quality or sleepiness scales. During Session 1 ("Sess1": evening Sleep, morning Wake), participants viewed 14, 60-sec videos of the same spider and wrote ratings (-10 to +10) for Disgust,

Fear and Unpleasantness. Session 2 ("Sess2") occurred 12 hours later with 6 videos of the "Old" (Sess1) spider and 6 of a "Novel" spider. A 10-msec, 83dB white noise stimulus was delivered during ~75% of videos. Skin conductance responses (SCR) were continuously monitored. Four 6-video "Phases" included "Exposure_1" (Sess1, videos 1-6), "Exposure_2" (Sess1, 7-12), "Sess2_Old" (videos 1-6) and "Sess2_Novel" (7-12). Each Phase included 4 "SCR-to-noise" stimuli.

Results: There was a significant Phase x Group interaction ($p<.05$) with Sess2_Novel eliciting more Fear than Sess2_Old significantly in Wake ($p<.001$), but as only a trend in Sleep ($p<.1$) indicating less extinction generalization following wake. For Unpleasantness, Phase interacted with Group ($p<.05$) with significantly increased Unpleasantness (loss of extinction) from Exposure_2 to Sess2_Old in Wake ($p<.01$) but not Sleep. For SCR-to-noise, Phase interacted with Group ($p<.01$) with Exposure_2 significantly higher than Sess2_Novel ($p<.05$) for Sleep indicating decreased reactivity from Sess1 to Sess2. However, no Phase differences in Wake indicated maintained reactivity between sessions.

Conclusion: Following simulated exposure therapy, subsequent sleep allowed for greater extinction retention (Unpleasantness, SCR-to-noise) and generalization (Fear) relative to an equivalent interval spent awake.

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0226

MODIFYING THE SUSCEPTIBILITY OF MEMORIES

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Introduction: Sleep has long been thought to play an integral role in the acquisition of healthy memories. Using a paradigm developed by Hupbach et al. (2007) to study memory reconsolidation, we investigated the role of sleep deprivation in the formation and updating of memories. During the process of reconsolidation, a reminder returns an initial memory to a labile state, making it susceptible to new information that can become incorporated into the original memory. This research asks, what is the susceptibility of memories that have been consolidated during sleep deprivation?

Methods: Twenty-nine participants learned a set of objects (Set 1) in Session 1. They were then deprived of sleep for 24-hours, after which they either received a reminder of the previous task reactivating the original memory, or not. The morning after they were sleep deprived, all participants learned a second set of objects (Set 2). They returned to the lab twenty-four hours later for recall and recognition tests.

Results: Preliminary evidence suggests that sleep deprivation modified the extent to which memories could be updated. Those in the sleep-deprived group showed lower intrusion rates as compared to the fully-rested control group (MDeprivation = 9.3%, N=8; MControl =21.4%, N=21; p=.03). Participants did not have diminished recall performance compared with controls (p=.13), suggesting this is not an issue of inadequate reactivation due to poor consolidation of the Set 1 memory, but rather subjects deprived of sleep are less able to update their memories. Data collection is ongoing with a target N of 16 in each group.

Conclusion: Our study suggests that sleep enables flexibility in recently formed memories. Without sleep, memory traces remain insulated and isolated, unable to be modified. This generation of flexibility may be crucial for the process of reconsolidation. Thus sleep is likely crucial for healthy consolidation and subsequent reconsolidation.

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0227

SLEEP HYGIENE, CHRONOTYPE AND ACADEMIC PERFORMANCE DURING THE TRANSITION FROM HIGH SCHOOL THROUGH FOUR YEARS OF COLLEGE

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Introduction: Sleep hygiene (behaviors that may facilitate or interfere with sleep) and chronotype (the circadian pattern at which one feels most comfortable) are both environmentally influenced. We examined these variables longitudinally, from senior year in high school to college graduation, to describe changes in these variables and their relationship to academic performance across time.

Methods: During pre-freshman summer, participants (N=89, 17-20 yrs) gave access to their high school and college academic records and completed questionnaires regarding their high school sleep (Epworth Sleepiness Scale, Horne and Ostberg Morningness-Eveningness Questionnaire, Sleep Timing Questionnaire, and The Sleep Hygiene Index). Participants completed these same questionnaires at the end of their freshman (N=34) and senior year (N=43) of college. Chronotype was identified using Horne-Ostberg criteria.

Results: In high school, poor sleep hygiene was associated with lower GPA (r(80)=-.277; p<.05). Sleep hygiene worsened upon entering college (t(33)=-4.44; p<.05) and poor sleep hygiene tended to persist through the senior year. Students whose sleep hygiene worsened during college, also showed a greater decline in their GPA during college (r(36)=.286; p<.05). Evening types showed greater GPA declines transitioning from high school to college (t(76)=1.85; p<.05) and had lower freshman GPA compared to morning and intermediate types combined (t(76)=1.67; p<.05); however, by their senior year in college, there were no significant GPA differences between these groups. Evening types shifted significantly more toward morning chronotypes by the end of college (t(10)=-3.38; p<.05).

Conclusion: Declines in sleep hygiene across the college years were associated with declines in grades. Evening chronotype was associated with a decline in academic performance from high school to college. A shift from evening towards morning type through college was associated with grade improvement. Understanding both sleep hygiene and chronotype may help students improve academic performance in the transition from high school to college and across the college years.

0228

A DIFFERENTIAL BENEFIT TO MOTOR SEQUENCE LEARNING FOLLOWING A DAYTIME NAP IN YOUNG AND ELDERLY ADULTS

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Introduction: Newly acquired memories are initially labile, subject to loss or modification until they are transformed into a more stable form (i.e., "consolidated"); a process that sleep has been reported to contribute. However, considering that with age, sleep becomes fragmented; can age-related changes in sleep explain memory deficits observed with normal aging? It was hypothesized that age would be associated with a deficit in performance gains following motor sequence learning (MSL).

Methods: We investigated through behavioural studies in healthy young (20-35yr, n=30) and elderly individuals (55-75yr, n=30), the effects of sleep on MSL consolidation (5-item sequence, 12 sequences/block, 14 blocks/session) before and after a retention period with a 90-min daytime nap or period of wake.

Results: A 2 (young, old) x 2 (sleep, wake) x 14 (blocks 1-14) x 2 (training, re-test) mixed-design ANOVA was used to investigate sleep-related changes in MSL performance in young vs. elderly subjects following a retention interval filled with either sleep or wake across 14-blocks of MSL from training to re-test. A significant 4-way interaction was observed (F(13,689)=1.86, p=0.032). Four separate 2 (sleep, wake) x 14 (blocks 1-14) mixed-design ANOVAs were performed to investigate the simple effects. A significant interaction between sleep/wake condition and block was observed at re-test for young subjects only (F(13,338)=1.92, p=0.027). Bonferroni-corrected t-tests were used to determine when performance differed in groups that took a nap, or remained awake during the retention interval. Only the young nap group improved performance in blocks 3-14 at re-test (p<0.0036).

Conclusion: The benefit of sleep on MSL has been previously studied in young subjects. This study suggests that the beneficial contribution of sleep to memory consolidation diminishes with age. Further investigation of the sleep characteristics and their neural correlates may provide insight into whether age-related changes in sleep observed with age are related to age-related changes in cognitive decline.

0229

AGE-RELATED FAILURE OF HUMAN MEMORY CONSOLIDATION CAUSED BY A LOSS OF PREFRONTAL NREM SLOW WAVE OSCILLATIONS

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Introduction: NREM slow-wave quantity and quality is disrupted in older adults. In parallel, aging is associated with an impaired ability to form and retain episodic memories. However, the role of age-related sleep disruption in cognitive memory decline remains largely uncharacterized. Here we examine whether age-related SWS disruption leads to a failure of sleep-dependent episodic memory consolidation.

Methods: Twenty-four participants, equally divided between healthy older adults (70.5±1.6 years) and healthy young adults (20.3±0.5 years) were trained to criterion on an episodic word-pair task in the evening, and performed an immediate memory test pre-sleep, followed by a delayed memory test during fMRI scanning after sleep. Intervening sleep was measured using full-head (19-channel EEG) polysomnography.

Results: While both groups showed equivalent immediate memory retention pre-sleep, a highly significant difference in delayed offline retention was observed after sleep, with older adults demonstrating impaired overnight consolidation, relative to young adults (p=0.009). Co-occurring with this impaired memory consolidation in older adults were decreases in SWS amount (p=0.004) and slow-wave activity (SWA) (p<0.001), most prominent over prefrontal cortex (PFC). Within the young group, the strength of overnight memory consolidation was directly proportional to SWA, especially over PFC derivations (r>0.87, p<0.006). In contrast, this relationship between SWA and memory consolidation was entirely absent in older adults (r<0.02). Furthermore, older adults expressed impaired post-sleep retrieval activation in the hippocampus, precuneus, and medial PFC, relative to young adults. Most striking, SWA not only predicted overnight consolidation in young but not older adults, it similarly and differentially mediated activity in these three retrieval-related memory regions.

Conclusion: Here we demonstrate that the overnight consolidation of episodic memory normally present in the healthy young brain is impaired in older adults. Moreover, this age-related impairment appears to be mediated by a failure of slow-wave sleep consolidation mechanisms that facilitate systems-level reorganization in hippocampal-neocortical networks.

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0230

IMPAIRED HIPPOCAMPAL-DEPENDENT LEARNING IN OLDER ADULTS MEDIATED BY DEFICIENT SLEEP-SPINDLE GENERATION

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Introduction: Recent evidence in young adults suggests that NREM sleep-spindles restore hippocampal-dependent memory encoding ability, promoting efficient post-sleep learning. Aging is associated both with impaired hippocampal-dependent learning and disrupted NREM sleep, yet the causal interaction between these factors remains unknown. Combining EEG and fMRI, here we examine whether age-related deficits in sleep-spindle generation lead to a compromised next-day ability to form hippocampal-dependent episodic memories.

Methods: Twenty-three participants, divided between healthy older adults (n=12, 70.5±1.6 years) and healthy young adults (n=11, 20.2±0.6 years) obtained a full night of polysomnographically recorded sleep (whole-head, 19-channel-EEG), followed the next day by a hippocampal-dependent episodic learning task performed during event-related fMRI.

Results: Following sleep, older adults exhibited a 49% deficit in next-day episodic learning ability relative to young adults (p=0.013), further paralleled by significant deficits in hippocampal-encoding activation. Co-occurring with these neural and behavioral impairments was a 30% reduction in sleep-spindle density in older adults (p=0.045), most prominent over frontal cortex. In young adults, the density of frontal sleep-spindles accurately predicted next-day hippocampal-encoding activation (r=0.68, p=0.022), and learning ability (r=0.63, p=0.038). In contrast, this mediating spindle relationship with next-day hippocampal activation and concomitant learning ability was lost in old adults (all r<0.3, p>0.35). Indeed, the strength of predictive association between frontal sleep-spindles and next-day hippocampal-encoding activity differed significantly between the young and old groups (p=0.018).

Conclusion: Here we demonstrate that the restitutive benefit of sleep on next-day hippocampal-dependent encoding ability in the healthy young brain is impaired in older adults. Moreover, such age-related memory impairment appears to be mediated by a failure in the generation of sleep-spindles, specifically over frontal cortex, leading to a compromised ability to form new episodic memories. Such findings suggest that sleep disruption in the elderly is an overlooked but potentially significant mediating factor contributing to cognitive decline in later life.

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0231

DIFFERENCES IN SOCIAL INTERACTION BETWEEN OEXIN/ATAXIN-3 AND WILDTYPE MICE

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Introduction: Hypocretins/orexin (Hcrt) regulates general behaviors e.g., wake/sleep, locomotion, feeding, and reward. The Hcrt system has been also implicated in exploring behavior, stress response, learning and memory. To test the hypothesis that Hcrt plays a role in social interaction, we used a validated protocol that two enclosures with either a strange or littermate mouse are placed in a normal home cage to investigate social interaction of the test subject of either wildtype (WT) or orexin/ataxin-3 (AT) mice, in which the Hcrt neurons almost completely degenerated after 4 postnatal weeks.

Methods: General behavior and social interaction were automatically quantified using AfaSci's home cage monitoring system-SmartCage. The social interaction test was conducted in light phase and consisted of three consecutive 10-min sessions: 1) Habituation, the test mouse explored two empty enclosures; 2) Sociability: one stranger (from different cage) or littermate mouse was randomly placed in one enclosure; 3) Preference for social novelty: a new unfamiliar mouse (stranger 2) was placed into the other enclosure. The CageScoreTM software calculated occupancy time of the test mouse in two different zones corresponding to the enclosures. Active counts, active time, traveling distance and velocity, and rearing counts of the test mouse were also automatically analyzed.

Results: When using stranger 1 for sociability test and stranger 2 for social novelty test, there were no significant differences in both interactions between the genotypes. When using littermate for sociability test, the WT test subject did not show any sociability. In contrast, the AT subject exhibited a similar degree of sociability as seen with the stranger 1. In the consequent social novelty test using a stranger there were no significant differences between the two genotypes (n=8 per genotype). The AT mice significantly decreased in active counts, active time, travel distance (but not velocity), and rearing counts compared to the WT littermates during the dark period in a 24-h recording.

Conclusion: The AT mice have normal social interaction ability as the WT mice. However, the AT mice treat their littermates as strangers and show great interest in exploring during the sociability test, suggesting that the AT mice may have social memory deficits compared to WT littermates. The AT mice displayed a decrease in wake activity, locomotion and rearing during the dark phase compare to their WT littermates.

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0232

ELECTROPHYSIOLOGICAL EVIDENCE OF IMPACT ON AUDITORY PRE-ATTENTIVE BRAIN MECHANISM IN HABITUAL SHORT SLEEPERS: STUDY I

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Introduction: Reduced TIB relative to biological sleep-need is common. The impact of habitual short sleep on automatic (pre-attentive) auditory processing has not been studied to date. An established electrophysiological index of pre-attentive auditory processing is the fronto-centrally distributed event-related potential (ERP) called mismatch negativity (MMN). The current study investigates the effects of chronic - 6h/night of sleep on frontal brain areas involved in auditory attention.

Methods: 10 self-defined short sleepers (2-wk diary TST≤6h) (age: 35±10yrs, 5F) and 9 subjects with TST=7-8h, (age: 30±6yrs, 6F) participated. ERPs were recorded via a 64-EEG channel system. Two test conditions: "ignore" and "attend" were implemented in a standard odd-

ball auditory task utilizing 160 novel sounds (20%) intermixed with tone (75%) and 5% target-sounds. In the ignore task, subjects were asked to ignore the sounds and watch a silent movie. Whereas in the attended task they were instructed to pay attention to the sounds and count target sounds for 7.5 minutes on 2 trials. MMN was analyzed and compared between groups on the two task conditions and frontal/central/parietal electrodes by 3-factor ANOVA. Sleep diary data was compared between groups by t-test.

Results: TST was significantly shorter in the short sleepers compared to normal sleeping subjects (7.8h vs. 5.8h, P<0.001). A 3-way interaction (Groups×Task×Frontality) indicated that the MMN was significantly larger (F(8,136)=2.40; P<0.02) in amplitude for the control group vs. short sleepers. Subsequent post-hoc analysis revealed that this difference was due to greater frontal reduction of the MMN amplitude in the attended condition in short sleepers vs. controls (-0.004µV vs. -1.4µV, P<0.01, respectively).

Conclusion: The MMN is associated with memory processes controlling the access of auditory sensory input to conscious (attentional) perception and higher forms of memory. Thus, the current results suggest that habitual short sleep is associated with deficits in this pre- attentive process of auditory modality.

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0233

CLASS START TIMES, SLEEP SCHEDULE AND CIRCADIAN PREFERENCE: PRELIMINARY PATH ANALYSIS PREDICTING ACADEMIC PERFORMANCE IN COLLEGE STUDENTS

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Introduction: School start times affect many important domains of achievement and health in high school students; this variable has been investigated in both correlational studies and quasi-experiments for over a decade. Later school start times in high school decrease truancy, improve mood, and are thought to indirectly affect learning through these and other pathways. We examined the possibility that class start times may play a parallel role for college students. We sought to describe a preliminary path analysis of the direct and indirect effects of class start time, chronotype, alcohol use, and sleep schedule on GPA.

Methods: 193 college students (56% female) participated. 18% were first year students, 37% sophomores, 23% juniors, 22% seniors. Students completed cognitive tasks, questionnaires about sleep, class schedules, substance use, and mood, and a one-week retrospective sleep diary. All data were collected on a weekday one month before the end of the semester. GPA was recorded from University records and self-report.

Results: Weighted mean total sleep time for weekdays and weekends was 7.9 hours (SD=1.5). Students reported later bed and rise times and longer sleep on weekends. A path analysis examined the relationship between class start times, sleep and circadian preference, and academic performance. Later class start times were associated with delayed sleep midpoint (standardized path coefficient = .28), which led to more missed classes (.14) and lower GPA (-.14). Owls were particularly likely to have a delayed sleep period (-.34). Furthermore, those students with later class start times consumed more alcohol and reported more binge drinking (.25). Owl status was also predictive of higher alcohol consumption and was negatively associated with academic performance.

Conclusion: Preliminary results from path analysis modeling lend support to the hypothesis that class start times have an indirect and significant effect on academic performance in college students.

0234

SLEEP AND TESTING PROMOTE CONCEPTUAL LEARNING OF CLASSROOM MATERIALS

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Introduction: Most memory studies employ word or syllable materials to assess an individual's ability to learn and retain information. Though sometimes useful, such methods may not be applicable to real-world classroom learning. In the present work, we developed and administered an introductory microeconomics lecture. We later assessed performance on trained concepts and novel (but related) concepts. Our interest was in the effect of quality of delay (sleep or wake), length of delay, and initial testing, on later test performance.

Methods: Participants were university undergraduates who had never taken an economics course. They completed a virtual lecture in the morning or evening that trained them on supply and demand microeconomics concepts and problems. A test was administered either immediately, after 12 hours (sleep- or wake-filled), or after 1 week. The test included simple supply and simple demand problems that were previously trained (basic problems) as well as untrained problems that required integration of supply and demand knowledge (integration problems).

Results: Performance on the microeconomics task declined with longer delays. Interestingly, performance was preserved following sleep delays, especially for the cognitively-taxing integration problems. Furthermore, when the study phase was followed by an immediate test phase, performance was preserved even after a one-week delay.

Conclusion: The finding that sleep and testing benefited learning of microeconomics concepts is consistent with theories that reactivation of learned information helps to consolidate, or stabilize, memories. Testing promotes such explicit reactivation, and recent sleep research has demonstrated that learned information is often replayed during slow-wave sleep. The present research uniquely extends prior work to an ecologically-valid task that students would encounter in a university classroom. Thus, this research has strong implications for educational practice, which too often ignores the utility of sleep (and testing) to promoting learning of higher order concepts.

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0235

STUDENT CLASS YEAR, AGE, SLEEPING BEHAVIOR AND PERFORMANCE: A FIVE YEAR TIME SERIES STUDY

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Introduction: Several studies have documented that sleep tends to decrease for adolescents between the ages of 13 and 18 even though the physiological need for sleep increases during this period (Carskadon, 1990; Wolfson & Carskadon, 2008). The United States Air Force Academy (USAFA) is a unique environment; it places unusual demands on cadets and each class year tends to have similar daily scheduling. The current study investigated whether age or class year tended to have a stronger association with sleep behaviors and school outcomes.

Methods: From 2004 to 2009, 1,273 cadets at USAFA across all class years completed the Brown University Collegiate Sleep Habits Survey, containing questions related to sleep, mood, behavior, health, and academics. Age range was 17-26 (M = 19.9) and 79.1% male.

Results: Class year significantly differed in self-reported amount of weekday sleep (p < .01), how long it takes to fall asleep (p = .02), the number of times they fall asleep in class (p < .01), and in GPA (p < .01). Lower age was associated with increasing times they fell asleep in class (p < .01) and in decreases in GPA (p < .01). A curvilinear relationship

was present between age and amount of sleep in that sleep peaked at age 22 and dropped off through age 26.

Conclusion: As cadets rise in class year they tend to report receiving more sleep during the week, taking less time to fall asleep, falling asleep in class less often, and receiving higher grades. Age is related to GPA and the number of times cadets fall asleep in class, suggesting some of the differential relationship may be due to structural scheduling attributes of class year. However, the curvilinear relationship that exists between age and sleep suggests underlying physiological differences are also influencing sleep.

0236

SLEEP QUALITY, DAYTIME SLEEPINESS AND ATTENTIONAL AND EXECUTIVE PERFORMANCES AMONG HEALTHY YOUNG PUBERTAL FRENCH ADOLESCENTS

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Introduction: Only 20% of adolescents typically obtain the 9h of recommended sleep and less than 45% obtain 8h of sleep. This study explored relationships between subjective sleep quality and quantity, and executive functioning in healthy pubertal adolescents.

Methods: Hundred and ninety-three healthy adolescents, age range 13-15 (99 girls: 14.0y ± 0.6y; 94 boys: 14.0y ± 0.6y), participated to this study. They completed sleep questionnaires Pittsburgh Sleep Inventory Questionnaire (PISQ), Epworth Sleepiness Scale (ESS). Neuropsychological assessment included subtests (6) from the WISC-IV to control for normal IQ and the CANTAB battery (Cambridge guessing task (CGT), Visuospatial working memory (VWM), Pattern Recognition Memory (PRM)). To assess gender differences, we performed t tests or Mann-Whitney U tests on sleep and cognitive variables. Factorial analyses were used to verify gender differences according to sleep quantity (+/- 9h, 8h, and 6.5h) on cognitive performance.

Results: Compared to boys, girls had better global score in the CGT, and also a higher quality decision-making and they showed a more conservative betting behavior in this task. For both genders, higher score in PSIQ was associated with poorer VWM and immediate PRM recall. Lower subjective sleep quality was also associated with more conservative decision-making in the CGT and poorer PRM recall. Higher score in ESS was associated with lower delay in making a decision in the CGT and less impulse control, i-e greater impulsivity when adolescents experience daytime sleepiness. Moreover, girls sleeping longer during weekend compared to weekday tend to show less impulse control than those who have stable sleep schedule during a week. There was no significant gender difference on cognitive performance according to sleep duration sub-groups.

Conclusion: Subjective appreciation of quality and quantity of sleep is associated with specific executive functions related to visuospatial working memory, visual memory and also to risk-taking and impulsivity in reward-related decision-making. Moreover, weekend oversleep in girls was associated with better impulse control during risky decision-making. Further studies are recommended to better understand those relationships.

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0237

DOES VARIABILITY IN MOOD AND SLEEP PREDICT COGNITION IN OLDER ADULTS?

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Introduction: Increased variability of total sleep time (TST) has been shown to negatively affect cognition in the college student population. While it is likely that variability of TST continues to negatively affect cognition in later life, this has yet to be empirically demonstrated As a result of age-related changes in sleep architecture and age-related increases in medical comorbidities, older adults are vulnerable to sleep disruption. Depression, which is both predicted by and predictive of sleep disruption in later life, has been shown to negatively affect cognition. The present study explored the relationship between TST variability, depression, and cognition in older adults, while controlling for age and health. We hypothesized that increased TST variability and depression would significantly predict decreased cognition.

Methods: 103 community-dwelling older adults (Mage=72.81, SD=7.12) completed daily sleep diaries for 14 days, a Demographics and Health Survey, BDI-II, and the Cognistat. Hierarchical multiple regression analyses were used to examine whether TST variability (defined as standard deviation) and BDI-II scores predicted Cognistat scores in older adults.

Results: Both TST variability and depression were found to have a significantly, negative predictive relationship with reasoning similarities (R=.43) and calculations (R=.28) of the Cognistat. Overall, TST variability and depression accounted for 17% of the variance in reasoning similarities, and TST variability accounted for 6% of the variance in calculations. Depression was not correlated with calculations, so TST variability appeared to carry the weight of that model.

Conclusion: Increased depression and variability of TST may lead to decreased cognition in older adults, specifically executive functioning and semantic memory. Future research can investigate potential mechanisms by which TST variability could impair cognition (e.g., daytime sleepiness, inadequate REM sleep, insomnia), and the potential contribution of depression (covariant, mediator, moderator) to TST variability's relationship with cognition.

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0238

SLEEP SPINDLES ARE ASSOCIATED TO VERBAL LEARNING IN OLDER SUBJECTS

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Introduction: Sleep spindles are involved in declarative sleep-dependant memory consolidation. Trait-like association between spindles and other cognitive functions is also often reported in the literature. This study aimed to evaluate the association between sleep spindles and cognitive performances in older healthy subjects.

Methods: Twenty-seven healthy volunteers (22 M; 60y ±9) without sleep disorder participated in a baseline nocturnal sleep in laboratory and a neuropsychological assessment, including a verbal memory test: The Rey Auditory Verbal Learning Test (RAVLT). Sleep was recorded with standard polysomnography (PSG). Spindles detection was performed on artefact free NREM sleep for F3, F4, C3, C4, P3, P4, O1 and O2 (linked-ears), with an automatic algorithm. All night spindle mean density (nb/min), duration (s), amplitude (µV) and frequency (Hz) were analysed.

Regression analyses were performed between spindles characteristics and raw scores on RAVLT.

Results: No significant correlation was found between age and spindle characteristics or between age and RAVTL scores. Spindles density in frontal (F3 and F4) derivations were positively correlated ($p < .05$) with RAVLT learning scores (trials 1 to 5) ($R > .43$,) and delayed recall performance ($R > .42$). In addition, spindles amplitude in F4 derivation was positively correlated with RAVLT learning performance ($R = .40$,) and delayed recall performance ($R = .42$).

Conclusion: Higher number and amplitude of spindles in frontal areas are linked to better verbal learning and delayed recall performance in older subjects. These results suggest that neuronal mechanisms underlying the spindles generation play a role in learning and verbal long term memory capacities in aging.

0239

SHORT NAP IMPROVES COGNITIVE PERFORMANCE FOR SEARCHING A TARGET FROM DISTRACTIVE STIMULI

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Introduction: To investigate the effects of a short nap and light exposure on cognitive function, visual search performance was examined.
Methods: Eleven participants (31.9 ± 7.19, range 23-43 years old, 5 males) carried out a visual search task twice a day (1200-1330h, 1430-1600h) before and after an afternoon short nap (20 min) or rest. Subjective sleepiness (Karolinska sleepiness scale, KSS) was scored before and after the task.During the second task (1430-1600h), bright light treatment (2000 lux) was applied in the two conditions. The participants took part in a total of four experimental conditions (control, short nap, bright light, and short nap and bright light conditions). Except during the light treatment, participants stayed in the dim lighted environment (< 100 lux).In the visual search task, participants searched a 90° rotated character "T" (target) among randomly rotated and deployed characters "L" (distracter) on the computer display. In the task, participants were required to indicate the direction of "T" (either right or left) by pressing a button of a gamepad with right or left forefingers as quickly as possible. One session of the task consists of 288 trials, which takes about 20 min to be completed. The task was carried out in sequence with other types of cognitive performance tasks (not shown here).
Results: The search time (correct reaction time) was significantly shorter in the nap and the nap and light conditions than in the control condition ($p < .05$). There was no significant difference between the bright light and the control conditions. Subjective sleepiness (KSS) was also significantly lower in both the nap condition and the nap and light condition compared to the control condition ($p < .05$).
Conclusion: Short nap improves cognitive performance to search a target from distractive stimuli.

0240

EFFECT OF NIGHT SHIFT SCHEDULE ON VISUAL ENCODING IN A STIMULUS ONSET ASYNCHRONY TASK

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Introduction: Distinct cognitive processes need to be disentangled to better understand the effect of sleep and sleep loss on cognitive performance. We distinguished semantic encoding and decision times by varying stimulus onset asynchronies (SOAs) in a category matching task. The task involved 200 trials in which two words were presented either simultaneously (0ms SOA) or with delays between the first and second word (200ms, 400ms, 600ms, or 800ms SOAs). Subjects had to decide whether the two words belonged to the same semantic category.

Response time (RT) was measured from the onset of the second word. The longer the SOA, the more time the person has to encode the first word before measurement of RT began. The SOA at which there was no further advantage to RT represented the time used to encode the first word, uncontaminated by decision and response processes.
Methods: N=16 healthy men (ages 27.5 ± 5.6y) participated in a 16-day in-laboratory study with two 5-day periods of simulated night work. The SOA task was administered at baseline (14:30) and on day 5 of each night work period (02:30). RT stabilized consistently at a presentation interval of 400ms; accordingly, encoding time was calculated as the difference between RT at 0ms and at 400ms.
Results: Mixed-model ANOVA was used to examine whether there were differences between sessions in grand mean RT and in encoding time for correctly answered trials, distinguishing "Yes" and "No" decisions. Grand mean RT of correct answers significantly improved across sessions ("Yes": F[2,30]=9.6, P<0.001; "No": F[2,30]=14.4, P<0.001). However, encoding time showed no significant difference across sessions ("Yes": F[2,30]=0.4, P=0.67; "No": F[2,30]=0.8, P=0.47).
Conclusion: There was a differential effect of repeated SOA task administration on overall reaction time, which showed a learning curve, versus encoding time of the first word, which remained stable over test sessions. The SOA task may be useful for specifically investigating visual encoding in sleep research.

0241

PROSPECTIVE MEMORY: A SIMULATED NIGHT SHIFT STUDY

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Introduction: The effects of fatigue on prospective memory (PM) - remembering to carry out a deferred task - have not been systematically examined. Using a variant of a published PM task, we investigated whether PM was impaired due to fatigue in a simulated night shift study.
Methods: N=39 healthy subjects (ages 27.7 ± 5.6y; 13f) underwent two 5-day periods of night shifts (n=28) or day shifts (n=11) with an intervening restart period of 34h or 58h. A PM test bout was administered on day 5 of each shift work period. At the beginning of the test bout, instructions were shown for a word rating task, in which subjects were asked to rate how pleasant each of 300 words was to them on a 5-point scale. They were also asked to remember to press the slash key every time an animal word (e.g. "snake") appeared (12 times in total). After showing the instructions but before starting the word rating task, a 10-minute psychomotor vigilance test (PVT) was administered. Immediately afterwards, subjects were given the word rating task, without seeing the instructions again. Errors of omissions (number of times not pressing the slash key prior to an animal word) were analyzed as a measure of PM impairment; lapses (reaction times >500ms) on the PVT were analyzed as an objective measure of fatigue.
Results: For PM errors of omission, mixed-effects ANOVA of shift condition by shift work period yielded no significant effects of condition (F[1,37]=0.67, P=0.42), session (F[1,37]=0.30, P=0.59), or interaction (F[1,37]=1.18, P=0.29). For PVT lapses, there were trends for effects of condition (F[1,37]=3.82, P=0.058) and session (F[1,37]=3.57, P=0.067), but no significant interaction (F[1,37]=0.95, P=0.34).
Conclusion: The simulated night shift schedule caused moderate fatigue as suggested by the PVT results, but had no significant effect on PM. More research is needed to determine whether the PM assay was relatively insensitive, or whether PM was robust to moderate fatigue.

0242

RESPONSE INHIBITION IN THE GO/NO-GO TASK: COMPARING SIMULATED DAYSHIFT AND NIGHTSHIFT SCHEDULES

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Introduction: We examined whether a classic assay of response inhibition, the Go/No-Go (GNG) task, could be repeated reliably in the same subjects under different simulated shiftwork conditions.

Methods: N=45 healthy subjects (ages 27.3±5.3y, 13f) underwent a 16-day in-laboratory study. 17 subjects were randomized to a dayshift group and 28 subjects were assigned to a nightshift group. Subjects completed 3 GNG sessions: session 1 at baseline (11:00); session 2 after a week of dayshifts or nightshifts (11:00 for dayshift, 23:00 for nightshift); and session 3 after a brief rest period followed by another week of dayshifts or nightshifts (same times of day). Subjects learned which random digits were "go" items (requiring a response) and which were "no-go" items (requiring withholding of a response). Inhibitory control was measured by reversing "go" and "no-go" items at unpredictable intervals after learning the number sets. Correct responses to "go" items (hits) and incorrect responses to "no-go" items (false alarms, FAs) were recorded.

Results: Mixed-effects ANOVAs revealed a significant increase in hits (F[2,86]=7.52, P=0.001) and decrease in FAs (F[2,86]=4.17, P=0.019) across sessions regardless of group. There were no significant group effects or interactions. Hits increased from session 1 to 2 for the nightshift group, but not for the dayshift group. There was no change in hits from session 2 to 3 in either group. FAs decreased from session 1 to 2 in the nightshift group, and tended to decrease in the dayshift group. Further, FAs tended to increase from session 2 to 3 in the nightshift group, with no change in the dayshift group.

Conclusion: The GNG task displayed a learning curve spanning just two test sessions, whether subjects were on a dayshift or nightshift schedule. This is in line with findings from previous studies in well-rested subjects. The absence of a significant difference between shiftwork schedules indicates that the task may not be very sensitive to fatigue.

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0243

EFFECTS OF PARTIAL SLEEP DEPRIVATION ON COGNITIVE PERFORMANCE IN MAJOR DEPRESSIVE DISORDER

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Introduction: Very few studies have evaluated the effects of repeated partial sleep deprivation (PSD) on cognitive performance in individuals with major depressive disorder (MDD). We compared cognitive performance in participants assigned to a modest repeated PSD versus no sleep deprivation while initiating an antidepressant trial.

Methods: Twenty-two subjects who met DSM-IV criteria for MDD participated (Age 25.2 ± 6.7 years, 9 women). Subjects received 8 weeks of fluoxetine 20-40 mg and were randomized to two weeks of no sleep deprivation (NSD, 8 hours time in bed [TIB], n=7), or two weeks of PSD (6 hours TIB, n = 15). Following an 8-hour TIB at-home schedule, participants underwent neuropsychological testing at baseline (B), and the morning after the first (T1) and last experimental nights (T2). Tests included the Facial Emotion Perception Task, Buschke Selective Reminding Test (SRT), and the go/no-go task.

Results: No group differences were found on baseline neuropsychological test variables. A significant group by time interaction was found for SRT d prime (F = 4.91, p = .012), indicating that performance declined in the NSD group (B = 4.7, T1 = 3.6, T2 = 3.5), but improved for the PSD group (B = 3.6, T1 = 3.8, T2 = 4.2). A trend for a group by time interaction emerged on the Facial Emotion Perception Task (F = 2.86, p = .07). Accuracy declined slightly for the NSD group (B = 89%, T1 = 88%, T2 = 85%), but increased between T1(87%) and T2 (90%) for the PSD group. No group differences in performance were evident on the go/no-go task.

Conclusion: Repeated partial sleep deprivation in conjunction with fluoxetine improved verbal memory and identification for facial emotions more than no sleep deprivation with fluoxetine. We are continuing to enroll participants in the protocol to investigate these relationships further.

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0244

REDUCED VISUAL PROCESSING CAPACITY IN SLEEP DEPRIVED PERSONS

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Introduction: A night of total sleep deprivation (SD) can impair cognitive performance by causing deficits in attention. Attention capacity is limited. According to Lavie's load theory of selective attention, the ability to process task-irrelevant distractors depends on whether sufficient resources remain after the processing of a task-relevant stimulus. In this study, we examined repetition-suppression to task-irrelevant, background scenes as participants attended to central faces that differed in perceptual clarity. We predicted that the magnitude of repetition suppression to task-irrelevant scenes would show a state and perceptual load interaction that would demonstrate reduced perceptual processing capacity in sleep-deprived persons.

Methods: 18 young adults screened for sleep history underwent fMRI after a normal night of sleep (RW) and after about 24h of sleep deprivation in a counterbalanced fashion. They were instructed to detect repeated faces in a series of centrally presented faces framed by scene pictures. Half the blocks contained non-repeating scenes, while the remaining blocks contained alternately repeating scenes. Faces were degraded in half the blocks to increase perceptual load. A localizer was used to identify the parahippocampal place area (PPA) in each subject. Repetition suppression effects to task-irrelevant scenes were measured within these PPA.

Results: SD was associated with lower hit rates. Participants also detected the face repetition better in the low-load condition relative to the high-load condition in both states. We found a significant state by load interaction for repetition suppression effects in the PPA, whereby significant repetition suppression to distractor scenes was present in RW, at both levels of perceptual load, and in SD during the low-load condition. This finding follows the prediction of reduced perceptual capacity in SD. Additionally, SD-related reduction of repetition suppression correlated with the corresponding state change of Fusiform Face Area (FFA) activation (r = 0.50, p < 0.05). Reduction in response to faces in the FFA serves as an indirect marker of reduced capacity during SD suggested by its correlation with reduced performance accuracy across state (r = 0.44, p < 0.05).

Conclusion: Sleep deprivation can impair cognitive performance by reducing visual processing capacity. This was indexed by the attenuation of repetition suppression to unattended stimuli as well as the change in task-related activation to attended stimuli across state.

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0245

EFFECT OF SLEEP DEPRIVATION ON ITEM AND SOURCE MEMORY

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Introduction: In this pilot study, we investigated the effect of sleep deprivation on source memory as contracted with item memory. Source memory, which involves remembering the source (as opposed to the content) of an item of information, has been shown to involve frontal brain areas, whereas item memory utilizes predominantly temporal and parietal brain areas. We employed a source memory task, during which a list of 96 words was read to the subjects, twice, through headphones using male and female voices. A series of words from the list mixed with new words was then visually presented to the subjects, and they were asked whether or not they had heard the word (item memory); and whether the source was a male or female voice (source memory).

Methods: Out of a total of N=19 subjects (ages 20-55y, 9f), the first ten subjects completed an overnight laboratory sleep deprivation experiment, during which the source memory test was administered at 21:30, 00:45 and 04:00. The other nine subjects were studied afterwards in a control experiment for which they entered the laboratory to perform the source memory test at 09:30, 12:45 and 16:00 (12 hours out of phase with the first group). The number of items recognized correctly (hits) and incorrectly (false alarms), and the number of items of which the source was identified correctly were compared between sleep-deprived subjects and controls using mixed-effects ANOVA.

Results: Sleep deprivation resulted in significantly more false alarms for item memory (F[1,34]=4.59, P=0.040), but there was no difference with controls for item hits (F[1,34]=2.30, P=0.14). No significant difference was found between groups for source memory (F[1,34]=0.07, P=0.79). There were no significant effects of test session for item and source memory outcomes (F[2,34]≤1.53, P≥0.23), and no significant interactions (F[2,34]≤0.86, P≥0.43).

Conclusion: This pilot study suggested that although one night of sleep deprivation increased the number of false alarms for item memory, this duration of sleep deprivation may not impair source memory.

0246

ENHANCEMENT EFFECT OF SLEEP ON NOVEL WORD ASSOCIATION: AN EVENT-RELATED POTENTIAL STUDY

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Introduction: The effect of sleep on declarative memory remains contradictory. Prior studies showed that learning of related word pairs benefited from sleep consistently, learning of unrelated word pairs however showed mixed results. It is possible that the behavioral measures used in previous studies are not sensitive enough to reveal subtle effects of sleep on new association. N400, an event-related potential (ERP) component reflecting relatedness among words in semantic memory, was used in the present study to investigate effect of sleep on the physiological process underlying new association of unrelated word pairs.

Methods: Eleven subjects (4 males, mean age=22.9) participated in the study. They were randomly assigned to either Sleep group or Wakefulness group. In the learning phase, participants were asked to memorize 80 visually presented unrelated word-pairs, and followed by a pre-test phase with a recognition task. The participants then underwent either nocturnal sleep (Sleep group) or sleep deprivation (Wakefulness group), and a post-test was conducted after subjects had one night of recovery sleep. During both pre-test and post-test sessions, primes and target words were presented successively for the subjects to judge whether they are among the original pairs or new pairs. ERPs were recorded during both test phases.

Results: The behavioral data showed that improvement of recognition from pre-test to post-test were not different between Sleep and Wakefulness groups (t=1.61, p=0.14). Decrease in reaction time however was greater following sleep compared to wakefulness (t=2.80, p<.05). N400 peak amplitude also attenuated significantly after sleep (F=71.86; p<0.1) but not after wakefulness (F=5.25; p=0.08).

Conclusion: The results showed that the sleep has an enhancing effect on the formation of new association of unrelated word pairs. The effect may not be significant enough to be shown in recognition task, but can be reflected in measures of neurophysiological activities.

0247

SLEEP FITNESS INVERSELY MODULATES CONSCIOUS AND NONCONSCIOUS CONTROL

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Introduction: Control is achieved by awareness of conflict and strategic change in behavior and/or nonconscious adaptation to environmental contingencies that modify behavior. Participants are slower to respond to an arrow if a previously presented arrow points in the opposite direction. When the arrows frequently disagree, participants can exert conscious control and overcome the interference caused by the 1st arrow. Remarkably, this reduction of interference is also found when the participants are unaware that the 1st arrow was shown. Without awareness of the 1st arrow and its frequency, participants still exert nonconscious control. Many factors alter successful conscious control from psychopathology to drug abuse to sleep deprivation. Dramatic deficits in conscious control are found under sleep deprivation, but it is unknown if sleep fitness alters nonconscious control in the same way.

Methods: 10 participants were tested on conscious and nonconscious control tasks on two occasions: after 8 nights of good sleep; or after 7 nights of good sleep plus 1 night of sleep deprivation (counterbalanced across subjects). Sleep was measured by actigraphy and sleep logs. The amount of interference was compared within subject across sleep fitness (rested vs. sleep deprived) and type of control (conscious vs. nonconscious).

Results: The conflicting arrows produced significant interference that was modulated by proportion of conflict in both control conditions. In short, we found significant conscious and nonconscious control. Sleep fitness had a significant inverse effect on the two types of control. Conscious control decreased while nonconscious control increased when going from well rested to sleep deprived.

Conclusion: While conscious control is impeded by sleep deprivation, nonconscious control is facilitated. Conscious control may play a significant role in overriding nonconscious control, and in some constrained situations; nonconscious control is more efficient in the absence of this conscious constraint. Sleep deprivation shifts control toward more nonconscious processes.

0248

POSITIVE AIRWAY PRESSURE EFFECTS ON PERCEPTUAL SKILL LEARNING IN PATIENTS WITH SLEEP APNEA

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Introduction: The purpose of this study was to learn whether PAP therapy improves perceptual learning in patients with sleep apnea. Sleep may facilitate brain plasticity and result in memory consolidation, a phenomenon that has been called sleep dependent learning. Most sleep dependent learning research has been done in young normal subjects, and little is known about how sleep dependent learning might be affected by sleep disorders, including sleep apnea.

Methods: 18 subjects undergoing clinical polysomnogram tests (age range 21-53) were given a visual texture discrimination task (VDT) (Karni & Sagi, 1991) before and after sleep. In this task subjects are shown peripheral targets made of contiguous diagonal bars that differ in orientation from a background of jittered horizontal bars. Subjects view the display for 17 ms which is then replaced with a mask containing randomly oriented patterns. The subject's ability to perceive the orientation of the peripheral target is measured at different stimulus and mask intervals to obtain a threshold of perception for each testing session.

Results: Subjects included 13 patients undergoing diagnostic polysomnograms and 5 patients who underwent PAP titration. Eight of the 13 subjects undergoing diagnostic polysomnograms had apnea and the remainder were being tested for other sleep complaints. Subjects who underwent PAP titration had improved perceptual detection of the targets after sleep, compared to subjects who were not treated with PAP therapy (p = .019). When the apnea patients given PAP therapy were compared to just the 8 apnea patients without therapy, those on PAP therapy improved after sleep, whereas those without PAP did not (p=.037). Total sleep time and sleep efficiency were similar for patients with apnea with and without therapy, and those who did not have apnea.

Conclusion: These results suggest that treatment of sleep apnea may result in improved perceptual skill learning in patients with sleep apnea.

0249

POLYSOMNOGRAPHIC EFFECTS OF COGNITIVE WORKLOAD ON SLEEP

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Introduction: Sleep physiology reflects the interaction of homeostatic and circadian processes, but aspects of sleep may also reflect plastic processes (e.g., learning and memory) occurring during wakefulness. We sought to determine the effects of high (HW) versus low (LW) cognitive workload on PSG measures following sleep restriction (SR) and no sleep restriction (NSR).

Methods: In a laboratory experiment underway, N=49 healthy adults (33.4±8.7y;22f) had 3 baseline nights (8h TIB) followed by 5 SR (4h TIB) or 5 NSR (8h TIB) nights. Subjects were randomized to 1 of 4 conditions: HW+SR (N=20); HW+NSR (N=13); LW+SR (N=8); LW+NSR (N=8). The HW vs. LW conditions differed in the duration of cognitive testing throughout each day (LW=½HW). PSG was recorded on baseline night 3 (B3) and experimental night 5 (SR5, NSR5). Sleep was scored blind to condition. One-way and mixed-model (night×condition) ANOVAs compared differences among conditions; paired t-tests compared B3 to SR5/NSR5 within each group.

Results: B3 sleep outcomes did not differ across conditions. The HW+NSR group, but not the LW+NSR group, showed an increase in SOL (p=0.005) from B3 to NSR5. Across days, the HW+NSR group showed less S2 %TST (p=0.026) than the LW+NSR group. Stage 2 latency decreased with SR (p=0.006), especially in the LW+SR group (p=0.02). The HW+SR and LW+SR groups showed significant, but not differential, increases in SE and SWS%TST, and decreases in TST, SOL, WASO, Stage 1 and 2%TST, and REM duration from B3 to SR5 (all p<0.002).

Conclusion: The final sample size will provide more power to test the interaction of workload and sleep restriction. In addition, NREM slow-wave energy (SWE) is being analyzed to evaluate the effects of workload on sleep homeostasis. Sleep restriction had the expected robust effects on sleep physiology, but differences in cognitive workload did not manifest in sleep responses evaluated thus far.

0250

SLEEP AND ENVIRONMENTAL CONTEXT: INTERACTIVE EFFECTS FOR MEMORY

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Introduction: Numerous studies have demonstrated a beneficial effect of post-learning sleep for declarative memory, indicating a sleep dependent consolidation process. Reinstating an environmental context which was present at learning during subsequent retrieval also leads to superior declarative memory performance. Here, we examined the interaction between these effects by testing the impact of sleep upon the context-dependent facilitation of memory.

Methods: We used a 2x2 repeated measures ANOVA design with retrieval context (same/different to encoding) and retention type (sleep/wakefulness) as factors. Thirty-two participants encoded word lists in each of two rooms (A and B) which differed in terms of size, odour, and background music. Immediately after learning and following a twelve hour retention phase containing either a night of sleep or a day of wakefulness, memory for all previously studied words was tested using a category cued recall task in room A or B alone. Accordingly, a comparison could be made between words retrieved in a context which was the same or different to that of the learning phase.

Results: Memory performance was assessed by the number of words forgotten between encoding and retrieval (immediate-delayed retrieval). The data revealed an interaction between retrieval context and retention type (ANOVA: F(1, 31) = 7.18, p = 0.012). This was driven by greater forgetting after wake than after sleep (T-test: t(1,31) = 2.73, p = 0.01) when context differed from train to test.

Conclusion: Our findings are suggestive of a sleep-related reduction in the extent to which context impacts upon retrieval. As such, our data provide initial support for the suggestion that sleep dependent consolidation processes may promote a decontextualisation of recently formed declarative representations.

0251

EVIDENCE FOR THE RE-ENACTMENT OF A RECENTLY LEARNED BEHAVIOR DURING SLEEPWALKING

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Introduction: Animal studies have shown that sequenced patterns of neuronal activity may be replayed during sleep. However, the existence

of such replay in humans has not yet been directly demonstrated. Here we studied patients who exhibit overt behaviors during sleep to test whether sequences of movements trained during the day may be spontaneously reenacted by the patients during sleep.

Methods: We recruited 19 sleepwalkers (who displayed complex and purposeful behaviors emerging from non REM sleep), 20 patients with REM sleep behavior disorder (who enacted their dreams in REM sleep) and 18 healthy controls. Continuous video sleep recordings were performed during sleep following intensive training on a sequence of large movements (learned during a variant of the serial reaction time task).

Results: Both patient groups showed learning of the intensively trained motor sequence after sleep. We report the re-enactment of a fragment of the recently trained motor behavior during one sleepwalking episode.

Conclusion: This study provides, to our knowledge, the first evidence of a temporally-structured replay of a learned behavior during sleep in humans. Our observation also suggests that the study of such sleep disorders may provide unique and critical information about cognitive functions operating during sleep.

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0252

SLEEP AND MEMORY CONSOLIDATION: META-ANALYSIS OF THE LITERATURE

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Introduction: In the investigation of sleep and memory processing, scientific disagreement persists. To identify origins of disagreement, meta-analysis of the literature was undertaken.

Methods: 1. Each of 30 representative studies was categorized according to sleep state (Stage 2, slow wave sleep, or REM) most closely associated with consolidation of an experimental learning task. To correctly categorize certain studies, spindle density was accorded category status. Human studies and rat studies were examined separately. 2. Under each stage rubric (e.g., SWS: Human), studies were summarized according to independent variable (e.g., "Retention interval: early sleep or wake vs. late sleep or wake"); dependent variable (e.g., "visual texture discrimination"); result (e.g., "Early sleep and in particular early plus late sleep facilitate learning"); and author-designated memory category (e.g., "visual procedural").

Results: Only sleep state categories and the relations of these to author-designated memory categories are reported here. *Human Studies*: Stage 2 and/or spindle density facilitates or is increased by motor procedural learning; is decreased by declarative learning (word pairs with retroactive interference). Spindle density increases during the first 270 minutes of sleep after intensive verbal declarative (word pair) training. SWS (early sleep) facilitates verbal declarative, nonverbal declarative, and visual implicit/visual procedural learning; transfers implicit to explicit learning ("insight"). Stage REM (late sleep) facilitates procedural, visual implicit, verbal nondeclarative, nonverbal nondeclarative, declarative, and episodic learning. *Rat Studies*: Spindle density increases during the first hour of sleep after declarative (odor + reward) learning. SWS replays spatial learning. Stage REM facilitates spatial learning and complex operant learning; replays spatial learning; interacts with fear conditioning.

Conclusion: Disagreement in the sleep and memory literature originates in factors ranging from historical inconsistencies in nomenclature to unitary mapping of memory category onto sleep state. Consistencies within

and across human and animal data, and recent emphases on the neural state architecture of sleep, may augur paradigm convergence.

0253

EFFECTS OF SLEEP ON KNOWLEDGE INTEGRATION AND AUTOMATICITY OF PROCESSING

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Introduction: Recent research indicates that sleep benefits consolidation of novel words. We investigated effects of sleep on knowledge integration and automaticity of processing using Size Congruity Effects (SCEs) and Semantic Distance Effects (SDEs) in second-language learning. SCEs occur when participants compare semantic size or physical font size of written-word pairs: correct responses are faster when both dimensions are congruent. SDEs involve swifter semantic size judgements for distant items (e.g., BEE-COW) compared with closer items (e.g., DOG-COW). These effects reflect automaticity in activating meanings; well-integrated novel words may exhibit greater SCE and SDE effects than unintegrated items. We predicted that participants who slept between learning and testing would show stronger SCE/SDEs for Mandarin characters learnt during training than participants who remained awake for a comparable duration.

Methods: Participants learned six Mandarin characters referring to different-sized animals in the evening (N=12) or morning (N=12), and tested after 12-hours of sleep or wake. During testing, participants saw item-pairs differing in physical (font) size and semantic (referent) size. In half the trials, relative physical and semantic sizes were congruent and in half they were incongruent. In separate tasks, participants selected the physically or semantically larger item. Both tasks were conducted using newly learned Mandarin characters; equivalent tasks using English stimuli provided baseline performance and controlled for circadian effects.

Results: Repeated-measures ANOVAs revealed significant interactions between sleep and congruity, and between sleep and semantic distance for semantic comparisons of Mandarin characters, whereby participants who slept exhibited stronger SCEs and SDEs than those who remained awake. There were no equivalent interactions between sleep and congruity or semantic distance for English stimuli.

Conclusion: Participants who slept between training and testing showed stronger SCEs and SDEs for Mandarin semantic comparisons. This suggests that sleep is associated with enhanced automaticity in second-language learning, supporting an integrative role for sleep in declarative memory consolidation.

0254

GENDER EFFECTS ON FALSE MEMORY FORMATION

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Introduction: Sleep deprivation (SD) at retrieval enhances false memories (FM), while sleep satiety at retrieval reduces FM. Existing literature about FM formation does not examine effects of type of SD or interaction of gender and SD on FM formation. Here, we describe the effects of gender and type of SD on recognition and FM formation rates in an object memory task.

Methods: Thirty-nine subjects were assigned to either 30h total sleep deprivation (TSD, n=21, 12F, age=24.6±4.8) or partial sleep deprivation (PSD, 4h TIB/night for 5 nights; n=18, 11F, age=25.1±5.8) and administered the Deese-Roediger-McDermott Shapes task while well-rested (WR; 9h TIB/night for 6 nights) and during SD (counterbalanced order). During testing, four types of shapes were presented: true shapes (shapes previously shown), lures (probes for FM), different color foils (DC: dif-

ferent color, different shape from true shapes), and same color foils (SC: same color, different shape). Mixed-model ANOVAs focused on recognition of true shapes and false positive rates.

Results: There was no effect of night, type of SD, or gender on true shape recognition (d-prime). Lure rates were unaffected by night and type of SD, but women identified more lures than men regardless of night or type of SD (p=.05). Total foil rates (DC+SC) were significantly greater after SD (p=0.031), but were not affected by type of SD or gender. Specifically, SC foil rates were higher during SD than WR (p=.024). There was no difference for DC foil rates.

Conclusion: Contrary to the word version of this task, these data show object memory is not impaired, and FM for objects is not enhanced, with SD. Gender did not influence the effects of SD, although women did report more FM than men. The fact SC, but not DC, foils were endorsed more after SD suggests SD impairs finer discriminations between targets and distractors.

0255

AVOIDANCE LEARNING-INDUCED SLEEP ALTERATION IN RATS

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Introduction: The benefit of sleep to consolidation of declarative memory and non-declarative memory has been supported by both human and animal studies. Understanding the alterations of sleep architecture after learning is important to unveil the role of sleep in memory processing. Present study was designed to identify changes in the post-training sleep architecture induced by avoidance learning in rats, and how the alterations in sleep parameters correlate with behavioral performance. In addition, previous studies focused on the effect of sleep on certain types of memory, while the sleep alterations induced by one type of memory may influence the learning for another type of memory. We are currently investigating whether the consolidation of conditioning memory facilitates other types of associative memory.

Methods: Male Sprague-Dawley rats were randomly assigned to the control and learning groups. Rats in the learning groups were trained with shuttle avoidance task for two sessions with a five-day interval. EEGs were recorded and analyzed to assess the changes in sleep architecture after learning.

Results: The behavioral results have shown that the avoidance performance improved at the third day of training. After a 5-day retention period, the performance remained the same as that in the first training day. EEG analysis of six 4-hour time blocks has revealed the rapid eye movement (REM) sleep windows, the period of increased REM sleep, were during 13-16 hours of the first post-training day and 6-10 hours of the second post-training day.

Conclusion: Our results suggest that REM sleep may play a role in memory consolidation of avoidance learning.

0256

A NOVEL MURINE FEAR CONDITIONING MODEL USING MILD HYPERCAPNIA AS A CONDITIONED STIMULUS TO STUDY SLEEP DISTURBANCES IN PTSD

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Introduction: Sleep disturbances are a common outcome of PTSD, and animal fear conditioning (FC) models are increasingly used to explore the mechanistic relationships between PTSD and sleep. This study compared the physiologic and sleep responses of classic tone-footshock (T+FS) with a novel model using mild transient hypercapnia (HC) paired with footshock (HC+FS).

Methods: Experiments were conducted in adult male FVB/nJ mice chronically instrumented with arterial catheters and polysomnographic electrodes. After recovery from surgery and acclimation to the experimental chamber, two separate groups of animals were exposed to repeated episodes of either T+FS (30 second duration; n = 16) or HC+FS (60 second duration; 2.5% increase in CO_2; n = 16). We assessed blood pressure, heart rate, and EMG (activity) during training and sleep before and after training.

Results: In the T+FS paradigm, blood pressure and heart rate were unaffected by tone, but EMG activity was significantly increased by tone (107±12 to 147±21 EMG activity % quiet wake; $p<0.05$) preceding FS. In contrast, in the HC+FS paradigm heart rate decreased (712±14 to 671±21; $p<0.001$) and EMG activity decreased (113±8 to 98±7 EMG activity % quiet wake; $p<0.05$) in response to HC preceding FS. In the five hours immediately following FC training, the HC+FS mice exhibited an increase in NREM sleep associated with a smaller number of NREM bouts of longer duration, a strong trend for decreased REM sleep, as well as an increase in REM latency and propensity to fall asleep after an arousal. An comparable pattern of sleep disturbances was seen in the T+FS paradigm.

Conclusion: We conclude that sleep disturbances are similar between FC paradigms regardless of whether tone or HC is used as the conditioned stimulus. However, unlike tone, mild HC elicits bradycardia and reduced activity that is potentially accounted for by the recently described hypercapnic FC sensor in the amygdala.

0257

EVALUATION OF COGNITIVE IMPAIRMENT IN SLEEP APNEA: A NOVEL ANIMAL MODEL APPROACH

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Introduction: Sleep apnea syndrome (SAS) is associated with various cognitive impairments - especially in the areas of learning, memory and mental flexibility. However, the mechanisms underlying this cognitive dysfunction remain poorly understood. We previously characterized strain-dependent spontaneous sleep-related apneas in rats, showing that Brown-Norway (BN) rats exhibit a high apnea propensity during sleep, corresponding to moderate SAS in humans, whereas Zucker Lean (ZL) rats express low levels of apnea. The aim of the current research was to define the domain-specific cognitive impairment exhibited by animals with a high apnea frequency (BN) with respect to control (ZL) rats.

Methods: We studied adult male BN (n=6) and ZL (n=4) rats using a novel object recognition test to assess working memory. After exposure to an object for 5 minutes, each rat was presented with the familiar object paired with a novel object. We examined delays of 1min and 24h between the two presentations. The recognition index (time spent in contact with the novel object divided by total time spent in contact with either object) was measured. Behavioral testing was followed by 6h polysomnography (cortical EEG, nuchal EMG and respiration). Apneas were detected as cessation of respiration for at least 2s.

Results: The apnea index (apneas/hour of sleep) in BN rats was more than double the index in ZL animals (20.5±2.5 vs 9.02±2, $p<0.05$). Novel object recognition was impaired in BN versus ZL rats after a 1-minute delay (78.2±4.1% vs 87.7±2.9%, $p<0.05$) and a 24h delay. Consistent

with the expectation that increased delay leads to decreased performance, the recognition index for both strains decreased after a 24h delay (64.4±4.2%) compared to a 1-minute delay (84.1±2.4%).

Conclusion: This study represents a novel approach to study cognitive impairments in sleep apnea and demonstrates that BN rats, which express more frequent sleep apneas, also exhibit short-term memory impairment.

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0258

COMPARISON OF BEHAVIORAL METHODS FOR ASSESSMENT OF WORKING MEMORY IN BROWN NORWAY AND ZUCKER LEAN RATS

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Introduction: We compared alternative methods for assessment of learning and memory in Brown Norway (BN) rats which exhibit a high apnea propensity during sleep, and Zucker Lean (ZL) rats which have low levels of apnea.

Methods: Experiments were conducted in adult male BN (n=6) and ZL (n=4) rats. In one testing paradigm, spatial cues were used to probe cognition. Animals were initially allowed to freely explore a Y-shaped maze for 12min. Spontaneous alternations between arms provided a measure of working memory. Subsequently, we tested each rat's ability to learn and remember which arm of a 4-arm radial contained a food reward. For the second paradigm, we used a novel object recognition test, in which a rat was exposed to an object for 5 minutes. After a delay of either 1min or 24h, the familiar object was paired with one new object and presented again. The time spent in contact with novel object divided by total time spent in contact with either object was calculated.

Results: The spontaneous alternation test showed impairment in BN rats (45.9±2.7% alternation vs 71.8±3.7% in ZL, p<0.05). In the 4-choice spatial discrimination test we found that BN rats exhibited hypoactivity and spent a significantly longer time in the maze versus ZL animals, because spatial discrimination required significant navigation. Novel object recognition was impaired in BN versus ZL rats both after a 1-minute delay (78.2±4.1% vs 87.7±2.9%, p<0.05) and after a 24h delay.

Conclusion: Exploration of different behavioral methods to assess short-term memory in BN and ZL strains demonstrated more adequacy of the spontaneous alternation and the novel object recognition tests over the 4-choice spatial discrimination test due to hypoactivity of BN rats characterized by high apnea propensity.

Support (If Any): Supported by a Grant through the University of Illinois at Chicago Chancellor's Discovery Fund.

0259

ANTAGONISM OF OREXIN 1 RECEPTORS ELIMINATES MOTOR HYPERACTIVITY AND IMPROVES HOMING RESPONSE ACQUISITION IN JUVENILE RATS EXPOSED TO ALCOHOL DURING PERINATAL PERIOD

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Introduction: Consequences of prenatal alcohol exposure (AE) include motor hyperactivity, disrupted sleep and cognitive deficits. Hypothalamic orexin (ORX)-synthesizing neurons are important for the maintenance of wakefulness and facilitate motor activity but may also contribute to anxiety disorders. We tested whether ORX plays a role in behavioral consequences of prenatal AE in a rat model.

Methods: Male Sprague-Dawley rat pups received 2.625g/kg of alcohol intragastrically twice daily on postnatal days (PD)4-9, a developmental period equivalent to the third trimester of human pregnancy (AE group). Control pups were sham-intubated (S group). On PD12-14, rats received daily injection of either the ORX-1 receptor antagonist, SB-334867 (SB; 20mg/kg, i.p.) or vehicle (V). On PD16, they were subjected to the homing response (HR) test, an established measure of early learning. Nest-seeking trials were repeated up to 10 times until HR acquisition was achieved (4 successful nest findings within 60s in 5 consecutive trials). On PD17, motor activity was monitored for 10min in a novel environment using infrared light beams. All SB/V injections and tests were conducted during the lights-off phase (8-12 PM).

Results: The percentage of tests in which HR acquisition was not achieved, the shortest HR latency, and the number of trials needed to reach the shortest latency were all higher, whereas the percentage of successful trials was lower, in AE-V than in S-V rats (p=0.0009-0.03; N=12 and 13/group). In contrast, these measures were not significantly different between AE-SB and S-SB rats (N=13/group). Motor activity in AE-V rats (1003±97(SE) beam crossings) was higher than in S-V (578±85; p=0.003), S-SB (563±110; p=0.007) or AE-SB (654±105; p=0.02) rats (S-SB and AE-SB groups not different).

Conclusion: Our findings suggest that motor hyperactivity and cognitive deficits following perinatal AE are secondary to increased ORX activity and that these symptoms may be alleviated by systemic antagonism of ORX-1 receptors.

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0260

SLEEP DEPRIVATION-INDUCED LEARNING AND MEMORY IMPAIRMENT IN EARLY DEVELOPMENT

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Introduction: Sleep plays an integral role in consolidation and subsequent retrieval of memories. Studies have extensively shown effects reduced sleep has on task-oriented activity in adults, but relatively few have focused on its ramifications in the developing brain. The aim of the current study is to measure the effect chronic sleep disturbance has on memory formation as measured by Morris water maze performance.

Methods: C57bl/6J mice (P=25-28) underwent two weeks of a sleep disturbance protocol modeling either sleep deprivation (4hrs/day, n=7) or sleep fragmentation (12hrs/day, n=6). Actigraphy monitored sleep patterns during sleep deprivation. Working memory performance was evaluated by measuring time and distance needed to locate a submerged platform in a Morris water maze. The platform was removed for a final probe test to establish memory retention trends.

Results: Learning curves in cohorts of both sleep deprivation (SD) and sleep fragmentation (SF) showed no significant difference from control groups. Probe tests conducted at the end of the 5 day testing period showed that SF significantly attenuated memories formed during the preceding 30 trials (5 days; 6 trials/day); showing a 68% reduction in NE:SW quadrant distance ratio when compared to controls (P<0.05). Actigraphy showed that, although activity counts were increased across the board in both SD and SF cohorts, only subjects undergoing SF showed significant irregularities in sleep periodicity.

Conclusion: Results indicated that neither sleep deprivation nor sleep fragmentation had significant effects on learning curves when compared to controls. However, complete sleep disruption, as seen in the SF model, drastically hindered memory retention as shown in probe tests. The disconnect from expected learning curves could be attributed to the lack of cognitive and physical requisites during normal active periods, leaving possibility for a simple shift in sleeping patterns.

0261

PARAPLEGICS WALK IN THEIR DREAMS

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Introduction: Mental activity during sleep can replay and consolidate recently-acquired skills, or activate innate programs. To fuel the discussion of this field, we studied the occurrence of walking within dreams of subjects with congenital and acquired paraplegia.

Methods: The dreams of 15 subjects with paraplegia (10 with spinal cord injury and 5 with congenital paraplegia) and 15 healthy, able-bodied volunteers were prospectively collected at home via dream diaries over a 6-week period. Sets of dream reports were manually searched for the terms that referenced the experience of walking or moving voluntarily the legs (walking dreams), with a double blind scoring. In addition, dream contents were classified using Hall and Van de Castle categories. The subjects completed questionnaires of sleep quality, depression, anxiety, and post-traumatic stress disorder. They underwent verbal memory tests.

Results: We collected 207 dreams from paraplegics and 208 from controls (29,369 words). In 9/10 subjects with spinal cord injury and 5/5 subjects with congenital paraplegia, there were walking dreams, composed of feelings of walking (40%), running or fleeing (7.5%), dancing (7%), standing up (5%), bicycling (5%), and practicing sports (skiing, playing basketball, swimming or climbing). Paraplegics experienced walking dreams (38.2%) just as often as controls (28.7%), but they reported twice as many clauses about walking than controls. There was no correlation between the frequency of walking dreams and the duration of paraplegia.

Conclusion: Subjects who had never walked or stopped walking 4 to 64 years prior to this study still experience walking in their dreams, suggesting that a cerebral walking program, either genetic or developed via mirror neurons (neurons activated when observing others performing an action) is activated to replay walking during sleep.

0262

ETIOLOGY OF NIGHTMARES: ENVIRONMENTAL AND GENETIC CORRELATES

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Introduction: Previous studies have suggested several environmental factors that affect nightmares, and the variance in tendency to experience nightmares has been shown to have a heritable component of 40-50%. However, systematic analysis of environmental factors is scarce and to our knowledge, the genetic correlates of nightmares have not been studied. In the present study, we investigated various environmental and genetic factors affecting self-reported nightmare frequency in adult population.

Methods: Data from three nationwide Finnish cross-sectional surveys (Finrisk) from years 1997, 2002, and 2007 will be used (N= 25 436, ages 25-74). For investigation of environmental correlates for nightmares, the data includes information on a variety of topics related to health and life style, such as sociodemographic background, physical and psychological health, and environmental stress. For identification of genetic risk factors for nightmares, data from 550 000 genome-wide distributed single nucleotide polymorphisms (SNPs) from 2000 subjects will be correlated with the self-reported frequency of nightmares. Results will be replicated in an independent population-based sample of twins.

Results: Preliminary analysis on environmental correlates revealed several statistically highly significant associations between nightmares and items related to factors such as anxiety, depression, life dissatisfaction, work related stress, as well as other sleep disturbances (p for all < 0.0001). Preliminary genetic analysis identified associations with nightmare frequency and SNPs at vicinity of genes expressed in central nervous system (p < 10E-6).

Conclusion: A number of health-related, environmental and genetic factors were shown to associate significantly to frequency of nightmares in a population-based sample of 25 436 adults. This data will be used as a template for additional analysis on modelling the effect of environmental, health related and genetic factors on frequency of nightmares.

0263

CHRONIC SLEEP FRAGMENTATION INCREASES MITOCHONDRIAL REACTIVE OXYGEN SPECIES PRODUCTION AND OXIDATIVE STRESS IN CORTEX

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Introduction: Sleep fragmentation (SF) is an important component of many sleep disorders, including obstructive sleep apnea and is believed to contribute to end-organ morbidity. However, the mechanisms underlying SF-associated functional alterations remain elusive.

Methods: C57BL/6 mice (n=7) were chronically implanted with telemetric transponders to measure EEG, EMG, body temperature (Tb) and gross activity (Ag) at 8 months. After surgical recovery, the mice were acclimatized in a custom developed SF chamber. Following that, the mice were subjected to 15 days of chronic SF for 12 hours/day from 7am to 7pm (every 2 min). Sleeping mice served as control. After the SF procedure the mice were sacrificed, and the brain was harvested and dissected. The cortex was assayed for the oxidative markers malondialdehyde (MDA) and 8-hydroxy-2'-deoxyguanosine (8-OHdG). In addition, mitochondrial isolation was conducted in cortices from SF and control and ROS production was determined using flow cytometric approaches.

Results: Following 15 days of SF, there were significant increases in both MDA and 8-OHdG in the cortex. In live isolated mitochondria, a marked increase in ROS production was apparent.

Conclusion: SF induces oxidative stress in cortex via mechanisms that involve excessive production of ROS in mitochondria.

0264

SLEEP DEPRIVATION UNDER SUSTAINED HYPOXIA PROTECTS AGAINST OXIDATIVE STRESS

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Introduction: We previously showed that sleep deprivation alters antioxidant responses in several rat brain regions. We also reported that chronic hypoxia modifies antioxidant responses and increases oxidative stress in rat cerebellum and pons, relative to normoxic conditions. In the current study, we exposed rats to (6h) sleep deprivation under sustained hypoxia (SDSH), and compared changes in antioxidant responses and oxidative stress, in the neocortex, hippocampus, brainstem and cerebellum, to those occurring in control animals subjected to the same level of sustained hypoxia but left undisturbed (UCSH).

Methods: We measured changes in total nitrite levels, as an indicator of nitric oxide production, superoxide dismutase (SOD) activity and total glutathione (GSHt) levels as markers of antioxidant responses, and levels of thiobarbituric acid reactive substances (TBARS) and protein carbonyls, as signs of lipid and protein oxidation products, respectively. We also measured changes in the activity of hexokinase (HK), the rate limiting enzyme in glucose metabolism.

Results: We found that SDSH increased nitric oxide levels and decreased the levels of TBARS in the rat hippocampus relative to control hypoxic conditions. On the other hand, SDSH decreased nitric oxide levels and increased GSHt levels in the rat cerebellum relative to UCSH. Furthermore, SDSH increased GSHt levels, without affecting the levels of either nitric oxide, TBARS or carbonyl proteins in the rat neocortex and brainstem, compared to UCSH. SOD activity was not affected in any of the brain regions studied here. Additionally, we observed an increase in HK activity in the neocortex of SDSH rats compared to UCSH rats, suggesting that elevated glucose metabolism may be a potential source of increased free radical production in this brain region.

Conclusion: We conclude that acute (6h) SDSH differentially affects various rat brain regions, but overall it protects against oxidative stress.

Short term insomnia may therefore serve as an adaptive response to prevent sustained hypoxia-induced cellular injury.

0265

SLEEPLESS NIGHTS AND STRESSFUL DAYS: SLEEP DEPRIVATION AND MENTAL STRESS AMPLIFY SURGES IN BLOOD PRESSURE

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Introduction: Sleep disturbances and psychological stress are highly prevalent, and both are implicated in the etiology of cardiovascular diseases. Given their tendency to co-occur, they may act synergistically in cardiovascular pathogenesis. To test for additive effects of sleep deprivation and psychological stress on blood pressure, we examined acute stress reactivity following rested and sleep-deprived experimental conditions in healthy young adults.

Methods: Participants included 20 young adults 20-25 years old free from current or past sleep, psychiatric, or major medical disorders. Using a within-subjects crossover design, we examined acute stress reactivity under two experimental conditions: following a night of normal sleep in the laboratory and following a night of total sleep deprivation. Two standardized psychological stress tasks were administered, a Stroop color-word naming interference task and a speech task, which were preceded by a pre-stress baseline and followed by a post-stress recovery period. Each period was 10 minutes in duration, and blood pressure recordings were collected every 2.5 minutes throughout each period. Mean blood pressure responses during the stress and recovery periods were examined with a mixed effects analysis of covariance, controlling for baseline blood pressure.

Results: There was a significant interaction between sleep deprivation and stress on systolic blood pressure, F(2,83.4)=4.35, p=0.016. Systolic blood pressure was higher in the sleep deprivation condition compared with the normal sleep condition during the speech task, t(18)=2.93, p=0.009), whereas blood pressure did not differ between the sleep conditions during the Stroop task or the post-stress recovery period.

Conclusion: Sleep deprivation amplified systolic blood pressure increases to psychological stress. Sleep loss may increase cardiovascular risk by dysregulating stress physiology. Based on these data, stress may be particularly important to address in individuals with sleep problems and vice versa in reducing cardiac vulnerability. Educational or behavioral interventions to prevent sleep loss could buffer the adverse health outcomes associated with stress.

0266

INCREASES IN NOREPINEPHRINE ARE ASSOCIATED WITH FEWER MICROSLEEPS DURING SUSTAINED WAKEFULNESS

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Introduction: Sleep loss is a significant and unique stressor, as sleep itself is a biological resource necessary to regulate multiple physiological systems. It was hypothesized that levels of norepinephrine, a marker of autonomic activation, would increase in response to sleep loss while levels of self-reported stress would not.

Methods: A tightly-controlled experimental design was utilized to examine the effects of 64 hours of sustained wakefulness in healthy adults. Dependent measures were daytime and nocturnal urinary norepinephrine levels, self-reported stress levels, and microsleeps assessed with polysomnography. After two nights of baseline (9-hour) sleep, 16 participants (5 women, 11 men) completed the vigil, followed by two nights of 9-hour recovery sleep. Seven control participants (4 women, 3 men) had a 9-hour sleep opportunity on all study nights. Participants remained in the laboratory for the duration of the study, under low lights and postural control during nighttime periods.

Results: Nocturnal norepinephrine increased significantly in the sleep-deprived group from baseline through the sleep deprivation period (t=-3.92, p=.002) and returned to baseline with recovery sleep; there were no significant changes in the control group. Change in daytime norepinephrine levels relative to baseline was negatively correlated with 1) the increase in microsleeps over the entire wakefulness vigil (rho=-.80, p=.002) and 2) the number of microsleeps during the last day of sustained wakefulness (rho=-.79, p=.001). Subjective stress levels also increased with sleep loss relative to baseline in the sleep-deprived group (p<.005), but were not significantly associated with microsleeps or norepinephrine levels.

Conclusion: Sleep loss resulted in a significant increase in nocturnal norepinephrine levels and self-reported stress levels. Increases in daytime norepinephrine levels were also associated with fewer microsleeps during sleep loss. These findings suggest that the subjective and physiological stress responses to sleep loss may differ, and that norepinephrine may serve an adaptive function in maintaining short-term sustained wakefulness.

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0267
SLEEP PATTERNS IN AN EXPERIMENTAL MODEL OF SLEEP FRAGMENTATION IN MICE

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Introduction: Sleep fragmentation (SF) is an important component of many sleep disorders, including obstructive sleep apnea. However, sleep homeostatic responses during acute and prolonged SF have not been explored.

Methods: C57BL/6 mice (n=6; 12 week-old) were chronically implanted with telemetric transponders to measure EEG, EMG, body temperature (Tb) and gross activity (Ag). After surgical recovery, the mice were acclimatized in a custom developed SF chamber. Following baseline recordings of 24 hours (7am -7am next day), mice were subjected to acute (12h) and chronic 7 days and 15 days of SF for 12 hours/day from 7am to 7pm (every 2 min). Continuous sleep recordings were carried out on day 1 and at days 7 and 15 of SF.

Results: During day 1, animals showed increased Wake, decreased SWS and REM for the first 4h, after which Wake and SWS gradually returned to baseline. REM sleep however remained lower throughout the SF procedure and showed a rebound during the dark period (when SF was ceased). Delta power during SWS was markedly higher and SWS latency lower when compared to BL. Following 7 days of daily SF, animals exhibited no differences in Wake, SWS or REM sleep, even though the total number of arousal and waking events during the SF period remained identical to day 1 SF. Furthermore, EEG delta power was markedly higher throughout the SF-day 8 procedure, and SWS latency was lower when compared to both day 1 SF and BL. Similarly, after 15 days of SF, all parameters returned back to baseline levels, except the SWS latency, which remained markedly reduced indicating the presence of increased sleep propensity despite no evidence for sleep curtailment.

Conclusion: These findings support the hypothesis that SF elicits initial discrepant SWS and REM homeostatic responses, and leads to excessive sleepiness, even though the total sleep duration, the global distribution of sleep states across the 24 hour cycle and the delta power are not

significantly different from control conditions. Thus, sleepiness may be elicited by sleep manipulations that do not entail sleep curtailment.

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0268
CHRONIC SLEEP RESTRICTION RESULTS IN ALTERED BONE METABOLISM

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Introduction: Previous studies of sleep-deprived rats revealed a progressive decline in serum osteocalcin, a marker for bone formation processes, and a progressive increase in serum alkaline phosphatase, which suggests altered bone metabolism. The purpose of the present study was to investigate the effects of chronically inadequate sleep on bone metabolism.

Methods: Multiple cycles of 10-day sleep restriction and 2-day sleep *ad libitum* periods were employed during 72 days in rats (SR; N=7) by application of 6-sec ambulation requirements according to validated schedules. Controls (AC; N=10) were produced by consolidating the ambulation requirements to allow for periods of uninterrupted sleep. Harvested tibia were decalcified, sectioned, stained and evaluated by qualitative histology and quantitative histomorphometry. Data were analyzed by t-tests.

Results: Bone metabolism was abnormal in sleep-restricted rats, as indicated by a low percentage of new bone (AC: 21.4 ± 15%; SR: 0.5 ± 0.8%, P=0.002) and slight osteoid thickness (AC: 4.0 ± 1.6 μm; SR: 0.6 ± 1.1 μm, P=0.0002), in association with osteoblasts that were both small in number and volume (per field, SR: 0.4 ± 0.8 cells; AC: 28.3 ± 18.4 cells, P=0.001; SR: 12 ± 23 μm³; AC: 77 ± 46 μm³, P=0.004), without a reduction in osteoclasts (AC: 6%; SR: 10% surface area,). In sleep restricted rats, megakaryocyte number was doubled (P<0.002) and the proportion of fat in marrow was only 37% of that of the AC group (P=0.004).

Conclusion: The low number and activity of osteoblasts responsible for forming new bone, without a decrease in osteoclasts, is diagnostic of osteopenia, a risk factor for osteoporosis. Increased numbers of platelet-producing megakaryocytes indicates increased hematopoiesis under conditions of sleep restriction. Decreased fat implies diminished energy storage in the marrow. These results are relevant to elucidating the effects of adverse sleep conditions on bone metabolism during growth and development.

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0269
HIGH-FAT DIET PROTECTS AGAINST WEIGHT LOSS ASSOCIATED WITH CHRONIC PARTIAL SLEEP RESTRICTION IN RATS

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Introduction: Substantial epidemiological evidence links short sleep to increased obesity risk in humans. However, rodents exposed to chronic partial sleep restriction (CPSR) have been consistently observed to lose weight. Here we report that high-fat diet protects rats against weight loss associated with CPSR.

Methods: Rats were provided with a high-fat diet (60% kcal from fat) after electroencephalogram (EEG) and electromyogram (EMG) recording electrode implantation surgery and recovery. After acclimation to diet and recording chambers, the animals underwent a protocol consisting of 5 days baseline, 10 days CPSR and 5 days undisturbed recovery (n=6), during which body weight and food intake were measured daily. CPSR was achieved using a system that monitors EEG/EMG and uses

an auto-scoring program to start a slowly rotating bar in the animal's cage upon detection of sleep onset (Pinnacle Technology, Inc.). During CPSR, the program was on for 16 hours (Zeitgeber Time (ZT) 8-24) and off for 8 hours (ZT 0-8). A standard 12:12 light:dark (LD) cycle (lights on at ZT 0) was used throughout.

Results: The CPSR protocol results in a consistent 25% reduction in total daily sleep amount. Throughout CPSR, rats fed a high-fat diet maintain baseline body weight, whereas rats on regular chow exhibit weight loss (HF: + 0.333 ± 3.37 grams, RC: -27.667 ± 3.07 grams; p < 0.05, Student's t-test). Rats on a high-fat diet also consume significantly more calories during CPSR (average daily caloric intake: baseline = 0.200 ± 0.005 kcal/g BW, CPSR = 0.245 ± 0.003 kcal/g BW; p < 0.001, Student's t-test), which was not observed in animals fed regular chow.

Conclusion: A high-fat diet leads to increased caloric intake and prevents weight loss associated with CPSR in rats, providing an animal model of CPSR that may more closely reflect the effects of short sleep in humans.

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0270
MODIFYING SLEEP DURATION REVERSES RELATIONSHIP BETWEEN BODY WEIGHT AND SLEEP DURATION

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Introduction: In a rodent model of experimental sleep deprivation, shortening sleep duration has resulted in weight loss, but involved increased physical activity which may have caused the weight loss. A recently validated method of sleep interruption can produce gentle movement of mice by a timed orbital shaker without increased physical activity. Such a technique facilitates the study of the relationship between sleep and obesity without the confounding influence of physical activity. We set out to study the effects of chronic sleep deprivation (21 days) on weight changes in a murine model of sleep deprivation without the confounding influence of increments in physical activity. A secondary objective was to study the cross-sectional association between body weight and sleep duration in a murine model.

Methods: Thirty-three mice (C57Bl/6; JAX, Bar Harbor, ME) were subjected to either chronic sleep deprivation (n=16) or control condition (n=17). Sleep deprivation was achieved by placing the mice in cages on orbital shakers that were gently activated by timers during the light cycle for 19 days and followed by activation over 24 hours/day for 2 days.

Results: At baseline, before sleep deprivation, EEG-derived sleep efficiency of mice in the top 50th percentile of weight (median 55.7%; IQR, 47.1, 58.4) tended to be lower than that of mice in the bottom 50th percentile (median 63.6%; IQR, 56.8, 68.8; P=0.06). Animals subjected to chronic sleep deprivation without increments in physical activity exhibited significant weight reduction (-6.4 ± 5.3%) when compared to animals in the control condition (2.1 ± 4.6%; P<0.0001). Sleep deprived mice lost weight despite consuming 53% more food than control mice (P=0.003).

Conclusion: In our murine model, the cross-sectional association between short sleep duration and greater body weight was reversed by an intervention-based reduction in sleep duration. Intervention-based modification of sleep duration may change the directionality of the observational relationship between body weight and sleep duration.

Support (If Any): Johrei Foundation

0271
INDIVIDUAL DIFFERENCES IN RESPONSES AND RECOVERY TO SLEEP DEPRIVATION AND SLEEP RESTRICTION ARE TRAIT-LIKE

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Introduction: Results from prior studies established that inter-individual vulnerability to total sleep deprivation is trait-like. In the present study, we determined whether this trait-like responsivity was found under both acute, total sleep deprivation and chronic sleep restriction conditions.

Methods: Subjects (11 males and 8 females, mean age [SD] = 28.1 [4.7]) participated in both total sleep deprivation (TSD - 63 hours awake) and chronic sleep restriction (CSR - 7 nights, 3 hours time in bed [TIB] per night) conditions. Both conditions were preceded by 7 nights Sleep Extension (10 hours nightly TIB) and followed by 3 nights Recovery (8 hours nightly TIB). The 10-min Psychomotor Vigilance Task (PVT) was analyzed for speed (1/reaction time*1000) and lapses (reaction times >500 msec). For each subject, speed and lapses were averaged over the last 12 hours of TSD (08:00 - 20:00) and last 12 hours of CSR (CSR7; 08:00 - 20:00). A variance components analysis was performed and intraclass correlation coefficients (ICC) were computed. The same was calculated for the first 12 hours of the first Recovery Day (R1; 08:00 - 20:00) from both TSD and CSR.

Results: Volunteers responded similarly to TSD and CSR (ICC lapses = 0.86, p = 0.007; ICC speed = 0.79, p = 0.010) and showed similar recovery from TSD and CSR (ICC lapses = 0.75, p = 0.013; ICC speed = 0.89, p = 0.006).

Conclusion: We found strong evidence for trait-like inter-individual variability in response to TSD and CSR as measured by PVT speed and lapses: subjects who displayed greater vulnerability to TSD also displayed greater vulnerability to CSR. These results expand upon previous findings showing trait-like vulnerability under TSD and show that such vulnerability extends to other forms of sleep loss including CSR. The results further suggest that TSD may serve as an assay to predict individual responsivity to CSR. Analyses are currently underway to determine the extent to which genetic polymorphisms contribute to this trait-like vulnerability and to which other measures (e.g., objective and subjective sleepiness) reveal trait-like inter-individual variability.

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0272
CIRCADIAN CLOCK T3111C POLYMORPHISM ASSOCIATED WITH INDIVIDUAL DIFFERENCES IN EXECUTIVE FUNCTIONING, SLEEPINESS AND MOOD DURING SLEEP RESTRICTION

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Introduction: The CLOCK T3111C polymorphism has been reported to be associated with aspects of sleep, sleepiness, and morningness-eveningness in healthy adults, and with insomnia in bipolar disorder and major depressive disorder. We evaluated the CLOCK T3111C polymorphism's role in cognitive, sleepiness, sleep homeostatic and mood responses during baseline and chronic partial sleep deprivation (PSD).

Methods: 6 C/C, 45 C/T and 78 T/T healthy adults (29.9±6.9y;63females) completed 2 baseline (10h TIB) nights, followed by 5 consecutive PSD nights (4h TIB) in a laboratory experiment assessing neurobehavioral measures (cognitive and executive function tests, subjective sleepiness, mood and fatigue, MWT) and physiological sleep responses. The C/C and C/T groups did not differ in outcomes and were combined; comparisons were conducted between C allele carriers (C/C+C/T;N=51) and the T/T genotype (N=78). T/T genotypic and T allelic frequencies were higher in African Americans than Caucasians; reported results were significant after controlling for ethnicity.

Results: During PSD, C allele carriers showed poorer executive functioning performance on the Tower of London (p's<0.05), which assesses planning and problem solving abilities. This group also showed greater total mood disturbance (TMD) and greater subjective sleepiness and fatigue during PSD (p's<0.05). At baseline, C allele carriers had greater TMD and confusion (p's<0.05), but did not differ in circadian phase typology, physiological sleep characteristics, physiological or subjective sleepiness, or cognitive performance. Both groups demonstrated similar cognitive performance (PVT, Digit Span) decreases, and increases in SWE and subjective and physiological sleepiness (KSS, MWT) in response to PSD.

Conclusion: This is the first report of the CLOCK T3111C polymorphism predicting performance on one measure of executive functioning, as well as sleepiness and mood during sleep restriction. The CLOCK T3111C polymorphism may be a genetic marker for a cognitive-mood diathesis more so than a sleep-circadian diathesis, since it did not predict sleep homeostatic or circadian measures relative to PSD.

0273

PREPROHYPOCRETIN/PREPRO-OREXIN (HCRT) -909C/T POLYMORPHISM PREDICTS INDIVIDUAL DIFFERENCES IN MWT LATENCY, SLEEP PHYSIOLOGY AND HOMEOSTASIS DURING BASELINE AND SLEEP RESTRICTION

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Introduction: The orexin-hypocretin system is involved in normal regulation of sleep and wakefulness and is disturbed in narcolepsy. The -909 C/T polymorphism of the prepro-hypocretin/prepro-orexin (HCRT) gene is associated with an increased risk of sudden onset of sleep (SOS)/sleep attacks in Parkinson's patients, though it is not associated with narcolepsy. We evaluated the role of this polymorphism in mediating sleep and wake responses during baseline and chronic partial sleep deprivation (PSD).

Methods: 16 C/C, 59 C/T and 54 T/T healthy adults (29.9±6.9y;63 females) completed 2 baseline (10h TIB) nights, followed by 5 consecutive PSD nights (4h TIB) in a laboratory experiment assessing physiological sleep responses (including NREM slow-wave energy [SWE]) and neurobehavioral outcomes (i.e., cognitive tests, subjective sleepiness and fatigue, and sleep propensity as measured by MWT). Comparisons were made across the 3 genotypes. T/T genotypic and T allelic frequencies were higher in Caucasians than African Americans; reported results were significant after controlling for ethnicity.

Results: At baseline, the C/C group showed decreased sleep homeostatic pressure (SWE) during the night (p<0.05), but comparable SWE elevation to PSD. Relative to T allele carriers, C/C subjects also had more stage 2 sleep and less SWS during baseline (p's<0.05) and during PSD (p's<0.05) and greater REM latency reductions (p<0.05) during PSD. C/C subjects showed longer MWT latencies during PSD (p<0.05) but not at baseline. No differences were found for circadian phase typology, habitual sleep, demographics, subjective sleepiness, or cognitive performance. All genotypes demonstrated similar cognitive performance (PVT, Digit Span) decreases, and increases in subjective sleepiness (KSS) in response to PSD.

Conclusion: The HCRT -909 C/T polymorphism is associated with differences in sleep homeostasis during fully-rested conditions, as well as in physiological sleepiness and sleep structure during PSD. The C/C genotype appears particularly buffered from the physiological, but not the cognitive performance effects of sleep restriction.

0274

EFFECTS OF RECOVERY SLEEP FOLLOWING MODEST SLEEP RESTRICTION FOR ONE WORK WEEK ON DAYTIME SLEEPINESS AND PERFORMANCE: GENDER DIFFERENCES

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Introduction: One work week of modest sleep restriction adversely impacts sleepiness, performance and inflammatory cytokines. Many individuals try to overcome these adverse effects by extending their sleep during the weekend. The aim of this study was to assess this common practice on sleepiness and performance and to test for possible gender differences.

Methods: Thirty four normal sleepers (16 men, 18 women), mean age ± SE, 24.5±0.6, were studied for 13 consecutive nights in the sleep laboratory: 4 baseline nights (8 h/night), followed by 6 restriction nights (6h/night); followed by 3 recovery nights (10h /night). Objective and subjective sleepiness (Multiple Sleep Latency Test and Stanford Sleepiness Scale), respectively, and performance (Psychomotor Vigilance Task) were measured on days 4 (baseline), 10 (after one week of sleep restriction) and 13(after 2 nights of recovery sleep).

Results: Subjective and objective sleepiness increased significantly after restriction and improved after recovery; performance decreased significantly after restriction but did not improve after recovery, in both genders. Increased baseline SWS was associated with lesser deterioration in median reaction time (RT) after restriction (r=-0.52, p=0.035) and greater improvement after recovery (r=0.57, p=0.01) in women. Increased baseline SWS was associated with lesser degree of subjective sleepiness after restriction (r= - .58, p=0.01) and greater improvement after recovery (r=.54, p=0.02) in women. No association between baseline SWS and change in objective sleepiness was found after restriction and recovery, respectively.

Conclusion: Extended "recovery" sleep over the weekend reverses the impact of one work-week of mild sleep restriction on sleepiness but does not improve performance suggesting that complete performance recovery may require more that just two days. In addition, it appears that increased SWS in women compared to men protects them from the effect of sleep loss on sleepiness and performance impairment, whereas it enhances recovery from these effects of modest sleep loss.

0275

EFFECTS OF SLEEP DEPRIVATION ON NEURAL CORRELATES OF RISK-TAKING

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Introduction: Sleep deprivation (SD) can induce significant deficits in vigilant attention, working memory, and executive function. However, the effects of SD on risk-taking behavior are unclear, with some studies reporting greater risk-taking behavior while others reporting no changes following sleep loss. The present study used functional MRI with a modified balloon analog risk task (BART) paradigm and examined the effects of 24h of total sleep deprivation (TSD) on the neural correlates of risk-taking.

Methods: A total of 27 healthy adults (13 male) were scanned on a Siemens 3T Trio scanner while performing a modified BART task at rested baseline (BL) and after 24h of TSD, using a standard EPI sequence. During the BART, subjects were required to sequentially inflate a virtual balloon that could either grow larger or explode. Imaging data were analyzed by SPM5.

Results: Behavioral data showed no changes of risk-taking propensity from BL to SD (6.5 vs. 6.6, p>.7). Imaging data showed robust activation in the mesolimbic, frontal, and visual pathway areas during the BART both at BL and during SD, which replicated our previous studies. Direct comparisons between these brain activation patterns indicated no differences from BL to SD. However, direct comparisons between the neural responses to the loss events (balloon explosion) showed reduced activation in the left insula. Furthermore, at BL, both SPM whole brain analysis and independent ROI analysis showing that insular and striatum activation level negatively correlated with risk-taking propensity, which also replicated our previous finding. However, such negative correlations were not found after SD.

Conclusion: Consistent with literature, our data showed that 24h of TSD did not change risk-taking behavior. However, significantly reduced activation in the insula was observed during loss events following TSD, which may reflect diminished negative emotional response to loss outcomes during risk-taking. Moreover, the loss of negative correlations between risk-taking behavior and activation level in insular and striatum following TSD, suggesting that one night sleep loss can alter neural mechanisms mediating inter-individual differences in risk-taking propensity without actual behavioral changes. Overall, our data suggest that sleep loss alters neural responses associated with risk-taking and support the hypothesis that neuroimaging findings may be a precursor to the behavioral changes following long-term sleep deprivation.

0276

DIFFERENTIAL EFFECTS OF TOTAL SLEEP DEPRIVATION ON REGIONAL CORTICAL ACTIVITY AT REST AND DURING PSYCHOMOTOR VIGILANCE TEST PERFORMANCE

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Introduction: Sleep deprivation (SD) degrades multiple aspects of neurocognitive performance. With few exceptions, recent neuroimaging studies have reported hypo-activation in fronto-parietal regions during various tasks following sleep loss. However, most of these studies focused on the effects of SD on task-induced neural activation, while the effects of SD on resting brain function without task requirements remain unexplored. The present study used arterial spin labeling (ASL) perfusion fMRI and examined the effects of 24h of total SD on brain function at rest and during a psychomotor vigilance test (PVT).

Methods: A total of 31 healthy adults (16 male) were scanned on a Siemens 3T Trio scanner at non-task resting states and during the PVT after normal sleep and after 24h of TSD, using a a pseudo-continuous ASL sequence. Data were analyzed by SPM5. One mean resting CBF image was generated for each condition from each subject before and after TSD. Whole brain general linear modeling analysis was conducted.

Results: TSD significantly disrupted PVT performance (p<.001). TSD also reduced the task-related activation in the fronto-parietal attentional network and sensorimotor cortex, but not in the thalamus and basal ganglia. However, when separately examining CBF changes at rest and during the PVT, differential effects were observed. Robust regional CBF increases were observed in multiple cortical regions, including bilateral sensorimotor and premotor cortex, occipital and temporal visual areas, cingulate cortex, precuneus, and frontal cortex at pre-task resting state. In contrast, much less regional CBF changes were found during the PVT, including decreased CBF in the thalamus and fronto-parietal areas and increasing CBF in the insula.

Conclusion: The fronto-parietal hypo-activation found with ASL is consistent with previous literature and supports the decremental effects of TSD on task-related brain activation. However, TSD induced more robust CBF increases at the resting state prior to the task, suggesting the importance of measuring non-task resting neural activity changes for interpretation of task-related regional brain function alterations following SD. Regional CBF increases in sensory, motor, and frontal cortices at rest may reflect compensatory neural activity during SD to maintain a state of wakefulness and prevent involuntary lapsing into microsleeps. Increased CBF after TSD also support the synaptic homeostasis hypothesis which suggests that neuronal potentiation increases with time awake.

0277

AN fMRI STUDY OF SLEEP DEPRIVATION AND REWARD IN HEALTHY YOUNG ADULTS

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Introduction: Sleep loss produces abnormal increases in reward-seeking behavior, though the neurobiological mechanisms underlying this phenomenon are poorly understood. We examined the impact of sleep deprivation upon reward neural circuitry in healthy young adults using functional Magnetic Resonance Imaging (fMRI) and a well-validated monetary reward card-guessing paradigm. We also examined associations between recent sleep history and reward responding when participants were tested under sleep-deprived and rested conditions.

Methods: Using a within-subjects crossover design, 22 young adults (age 18-25 years) were tested following a night of total sleep deprivation and a night of normal sleep. We compared blood oxygen-level-dependent (BOLD) responses to the winning of monetary reward in a computer task during sleep-deprived and rested conditions. We used a region of interest approach focused on the ventral striatum (VS) and medial prefrontal cortex, areas critical to reward processing. We used regression analyses to examine relationships between reward response and total sleep time (TST) derived from actigraphy in the five days preceding each fMRI scan.

Results: VS activity was significantly greater during reward trials under sleep-deprived versus rested conditions. TST during the preceding five days was positively associated with activity in the anterior cingulate cortex (ACC) during reward trials, both under rested and sleep-deprived conditions. Thus, lower TST prior to either testing session was associated with less ACC activation to reward.

Conclusion: Our findings support the hypothesis that sleep loss produces aberrant functioning in reward neural circuitry, resulting in over-valuation of positively-reinforcing stimuli. Naturalistic variation in sleep duration was linked to frontal hypoactivation during the processing of reward. Such processes could lead to impaired decision-making and abnormally increased pursuit of reinforcers, which could plausibly lead to negative health and behavioral consequences.

0278

SLEEP DEPRIVATION INCREASES AMYGDALA REACTIVITY DURING EFFORTFUL ATTEMPTS AT EMOTION REGULATION VIA COGNITIVE REAPPRAISAL

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Introduction: Although sleep loss is known to affect overt emotion, little is known about how sleep deprivation impairs emotion regulatory processes and their underlying neural circuitry. We therefore examined an explicit emotion regulation task using functional MRI (fMRI) following sleep deprived and rested conditions. We hypothesized that impaired emotion regulation following sleep deprivation would be associated with heightened amygdala activity—an area critically involved in the processing and generation of emotion—when attempting to down-regulate emotional responses via cognitive reappraisal.

Methods: Using a within-subjects crossover design, 26 healthy participants (18-25 years old) underwent fMRI scanning in the morning following a night of normal sleep and following a night of sleep deprivation. Prior to the first fMRI scan, participants were trained in specific reappraisal strategies (i.e., instructions to decrease one's emotional response by reinterpreting pictures; e.g., when viewing a person who appears hurt, thinking that help is on the way or that the person is not in as much pain as it seems). Participants viewed International Affective Picture System stimuli with either neutral or negative content for 7-seconds. For negative pictures, participants were instructed to either simply view or down-regulate (e.g., via reappraisal) their emotional responses.

Results: A significant trial type by sleep condition interaction was detected in the right amygdala, $F=2.02$, voxelwise $p=0.018$, 7 voxels contiguity, small volume corrected $p<0.05$. Post-hoc testing revealed greater activation during reappraisal trials when participants were under sleep deprived compared to rested conditions, $F(1,25)=13.32$, $p<0.001$. Consistent with prior reports, amygdala activity decreased relative to baseline during reappraisal trials when participants were rested, but increased relative to baseline when these same participants were sleep deprived.

Conclusion: Sleep deprivation induced a hyperactive response in the amygdala during explicit attempts to decrease emotional responses, suggesting a failure to regulate emotional responses on a neural level or that emotion regulation requires more intense neural activity after sleep deprivation.

0279

EFFECTS OF SLEEP EXTENSION ON EEG POWER SPECTRA IN SUBJECTS WITH HABITUAL SELF-SELECTED SHORT SLEEP SCHEDULES

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Introduction: Slow wave activity (SWA) is commonly used as a physiological marker of homeostatic sleep drive that increases following acute total sleep deprivation and chronic sleep loss of <4h/night. We examined whether SWA and other EEG bands were influenced by two weeks sleep extension in individuals with habitual self-selected short sleep schedules.

Methods: Twenty-six subjects (12 women) aged $22.4+4.0$ (mean+SD) with habitual self-selected short sleep durations of ~6h/night participated in a month long protocol. Two weeks of wrist actigraphy verified subjects' habitual sleep schedules. Subjects were then randomized to maintain their habitual sleep schedule (control group) or extend time in bed by ~2h/night during the second two weeks. At the end of each two-week segment, in-laboratory PSG was performed. EEG data were sampled at 256 samples per second with a 12-bit A-D board and artifacts were manually removed from the EEG records prior to analysis. Power spectra at brain site C3 x A2 were calculated for SWA (0.25-4.75Hz), alpha (8.0-12.0Hz), and beta (15-35Hz) EEG activity. Data were analyzed using repeated measures ANOVA for the rise time of SWA and the decline in alpha and beta during the first NREM cycle.

Results: During the first NREM cycle, the rise in SWA was not influenced by sleep extension, nor was the decline in alpha activity. Beta activity, however, was found to be significantly higher after 2 weeks of sleep extension (minutes 2-12 after sleep onset; $p<0.05$). No significant changes in SWA, alpha, or beta EEG activity were observed for the control group.

Conclusion: Contrary to expectations, the rise in SWA was not influenced by sleep extension, nor was the decline in alpha activity; rather beta EEG activity increased following sleep extension. These findings suggest that beta EEG activity may represent a physiological marker responsive to changes in prior sleep history in humans.

0280

ELECTROPHYSIOLOGICAL EVIDENCE OF IMPROVEMENT OF THE BRAIN MECHANISM OF AUDITORY PRE-ATTENTIVE PROCESSING IN HABITUAL SHORT SLEEPERS AFTER SLEEP EXTENSION: STUDY II

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Introduction: It has been shown that chronic short sleep is associated with an impairment in neurophysiological processes underlying pre-attentive auditory processing. The aim of this study was to evaluate whether one week of extended time in bed (TIB) in short sleepers improves this brain function. An electrophysiological index of pre-attentive auditory processing is the fronto-central event-related potential (ERP), called mismatch negativity (MMN), which was used to test this hypothesis.

Methods: 10 short sleepers (sleep-diary TST≤6h) (age: 35±10yrs, 5F) participated. TIB conditions (6 or 9 hour TIB) were counterbalanced. Sleep was recorded by the Zeo sleep-monitoring system for a week in both habitual and extended sleep conditions at home. At the end of each week the ERPs were recorded via 64-EEG channel system. Two test conditions: "ignore" and "attend" were implemented in a standard oddball auditory task. ERP brain response mismatch negativity (MMN) was compared across sleep conditions by 3-way ANOVAs (factors: task type, frontality, TIB length).

Results: TST was significantly longer in the extended vs. habitual sleep condition for sleep diary (7.8h vs. 5.8h, P<0.001) and Zeo (7.2h vs. 5.8h, P<0.001) measures. A 3-way interaction (TIB length×Task×Frontality; F(5,45)=4.43; P<0.002) indicated that the MMN was significantly increased in amplitude after extended sleep at frontal electrode sites. The subsequent post-hoc tests revealed that this was due to MMN amplitude enhancement in the attended task following sleep extension (-1.7μV vs. -0.004μV-habitual TIB P<0.001), on frontal electrode sites as compared to rest of the brain.

Conclusion: One week of extended TIB up to 9-hrs attenuates the impairment seen in frontal brain regions involved in sensory memory processing controlling the access of attentional input and higher forms of memory in "short sleepers".

Support (If Any): Zeo Inc.

0281

SLEEP DEPRIVATION EFFECTS ON CEREBRAL RESPONSE AND PERFORMANCE IN OLDER AND YOUNGER ADULTS DURING INHIBITION

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Introduction: Few studies have examined the effects of total sleep deprivation (TSD) in older adults (>60 years) on cognitive performance, and fewer have utilized functional MRI (fMRI) to examine cerebral activation after TSD in this population. Here, we examined BOLD activation in older adults (OA) and younger adults (YA) during the response inhibition portion of a Go-NoGo task following 12hrs and 36hrs of wakefulness. We hypothesized OA would demonstrate increased cerebral activation in areas associated with inhibitory processes while maintaining intact performance after 36hrs TSD.

Methods: Participants (28 OA: 6M, age=67.6+/-1; 28 YA: 9M, age=28.4+/-0.9) performed a Go-NoGo task during fMRI after 12 and 36 hours of wakefulness. Performance data were available for 22 OA and 26 YA. Group-by-night ANOVAs were performed for behavioral and fMRI data, focusing on inhibition ("nogo") trials.

Results: No significant performance differences were observed between the groups. Imaging results, however, revealed a significant group-by-night interaction. Specifically, OA showed a pattern of increased activation from 12-36 hrs wakefulness in widespread areas of the brain, which included regions typically associated with inhibitory processes (e.g., bilateral inferior and medial prefrontal areas, bilateral anterior cingulate, and bilateral precuneus). Most of these regions showed no change with TSD in YA, although a few showed either increased or decreased activation after TSD.

Conclusion: OA performed at an equivalent level to YA after 36rs wakefulness on a task of inhibition, which involves response conflict, motor inhibition, and cortical attention. In contrast, OA appeared to require greater cerebral resources to maintain performance. These findings suggest age combines with prolonged wakefulness to produce neurophysiological stress requiring cerebral compensatory processes. This compensation, in turn, helps maintain performance on the task.

0282

EFFECTS OF TOTAL AND PARTIAL SLEEP DEPRIVATION ON RISK PREFERENCE

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Introduction: Sleep deprivation affects risk preference differentially when risk is framed as either 'winning' or 'losing' money. Prior studies have all examined Total Sleep Deprivation (TSD) effects on risk preference and have not varied risk levels systematically. Here we examine the effects of Total and Partial Sleep Deprivation (PSD) on Risk Preference while varying risk level (med/high) and real monetary Payout (gain/lose).

Methods: 37 subjects (TSD: n=20, 11F, age=25±5.2; PSD: n=17, 8F, age=24.2±5.7) were administered a Lottery Choice Task twice: 1) Well-Rested (WR), after 9hrs TIB for 6 nights; and 2) after either 24hrs TSD or 5 nights of PSD (4hrs TIB/night).

Results: A 2x2x2 repeated measures ANOVA yielded a 3-way interaction of Night by Payout by Risk following PSD (p=.018). PSD subjects were risk avoiding for medium risk loss choices and risk seeking for medium risk gains choices during WR testing. Following PSD, risk preference was moderated, resulting in less risk avoidance for losses and risk neutrality for gains. A similar interaction was seen in TSD subjects, although it was not significant (p=.164).

Conclusion: The aim of this study was to determine if individuals preferred different levels of risk following TSD and PSD, when those choices were framed as gains or losses. Our findings suggest that whether a question is framed in terms of gains or losses can have significant effects on decision making following PSD. Factors that could have influenced our results are inherent in the unique design of this study. We incorporated: PSD, which could produce distinctly different behavioral responses than TSD; a strictly monitored Well-Rested condition, compared to other studies' "habitual" sleep/wake condition (which may not be a sufficient amount of sleep); and parametrically varied Risk levels.

0283

DOES VULNERABILITY TO SLEEP DEPRIVATION INFLUENCE THE EFFECTIVENESS OF STIMULANTS ON PSYCHOMOTOR VIGILANCE?

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Introduction: There are trait-like individual differences in the ability to resist the adverse effects of sleep loss on performance. However, it remains unknown whether these traits influence the effectiveness of various stimulant medications during prolonged sleep deprivation. Here, we broadly classified individuals as either "resistant" or "vulnerable" based on a median split of their performance on a psychomotor vigilance test (PVT) during two nights of sleep deprivation and examined whether this trait-like resistance affected responses to several common stimulant medications the following morning.

Methods: From a sample of 53 healthy subjects, a median split was used to classify 27 (17 men; mean age = 24.0 years, SD = 4.4) as "resistant" and 26 (12 men; mean age = 23.0 years, SD = 3.7) as "vulnerable" to sleep deprivation based on PVT performance during the first 41 hours of sleep deprivation. At 44 hours awake (3:00 am), participants were administered either 600 mg caffeine, 400 mg modafinil, 20 mg d-amphetamine, or placebo. Performance on the Palm PVT was assessed at 47 hours of wakefulness (6:20 am).

Results: A significant vulnerability group by drug interaction was found (p=.005). For those receiving placebo, the resistant group far outperformed the vulnerable group (p=.0003). For those receiving stimulants, there were no differences among vulnerability groups. For vulnerable subjects, all three stimulants outperformed placebo (p<.001), and d-amphetamine was significantly better than modafinil for these subjects (p=.05). In contrast, among resistant subjects, stimulants were not significantly more effective than placebo.

Conclusion: Compared to resistant subjects, those classified as vulnerable to sleep loss were more adversely affected by sleep deprivation and showed greater improvements from all 3 stimulants. Resistant subjects showed less decrement from sleep loss and showed little improvement from stimulants. During acute sleep deprivation, stimulants normalize performance of vulnerable individuals but have only modest benefit for those who are resistant.

0284

EFFECTS OF SLEEP DEPRIVATION ON CORTICAL ACTIVATION DURING DIRECTED ATTENTION IN THE ABSENCE OF VISUAL STIMULI

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Introduction: Sleep deprivation (SD) is associated with faltering attention that is accompanied by reduced stimulus-related fronto-parietal and extrastriate visual cortex activation. Here, we studied the contribution of deficits in endogenous and bottom-up effects attention in the period before and subsequent to stimulus onset and their effects on fronto-parietal and visual cortex activation.

Methods: Twelve healthy adults with regular sleep habits underwent 2 fMRI scanning sessions: one following a night of normal sleep and one following 24 h of SD. Using a covert attention task (Kastner et al,. J Neurosci 1999) we compared the effect of attention on baseline shifts in the preparatory period and stimulus-related activity following a night of normal sleep and after a night of sleep deprivation to ascertain the effects of SD on attention in the absence and presence of visual stimulation.

Results: After a normal night of sleep, the engagement of spatial attention in the absence of visual stimulation during the pre-stimulus period elicited significant baseline shifts of BOLD signal in top-down control regions i.e. frontal eye field (rEF), supplementary eye field (SEF), and intraparietal sulcus (rIPS), and multiple retinotopically defined areas. V1, V2m V3a, hV4, and VO1. Stimulus-related activation in also showed significant effects of attention FEF, IPS and VO1 but in limited extrastriate visual areas hV4, V01. SD compared directly to RW resulted in significant reduction of attention-related baseline shifts in cognitive control areas FEF and IPS, as well as in visual area VO1. Interestingly, there was an effect of SD on the non-attended visual stimuli during the stimulus period in the same areas observed for attended stimuli.

Conclusion: Our results suggest that attenuation of endogenous attention in SD dominates prior to the appearance of an expected stimulus, whereas impaired bottom-up effects of attention makes a significant contribution to stimulus-related activation in higher visual and fronto-parietal cortices

0285

SLEEP DEPRIVATION REDUCES DEFAULT MODE NETWORK CONNECTIVITY DURING REST AND TASK PERFORMANCE

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Introduction: The Default Mode Network (DMN) is a set of brain regions that spontaneously shows highly correlated neural activity even when a subject is at rest. This study investigated whether Sleep Deprivation (SD) reduces DMN functional connectivity as compared to Rested Wakefulness (RW) and whether the effect of SD varies under different task contexts.

Methods: Twenty-six healthy dextrals (11 male, 22.5 ± 2.0 years) underwent fMRI twice, during RW and after SD. In each session, participants were scanned while resting with their eyes open and while they performed a Visual Attention Task (VAT). 7 default mode network nodes were identified. Functional connectivity was defined as the low frequency correlation for each pair of nodes, in resting state and during the VAT, during both RW and SD. One-tailed t-tests were performed on the correlation values to assess the effect of SD.

Results: In both states and both task contexts all 7 default mode network nodes were significantly connected to one another (p<.05). Nevertheless, SD was associated with significant declines in connectivity between 4 node pairs (p<.05) when participants were resting. The effect of SD was even more evident during the VAT, with 16 node pairs showing connectivity decline (p<.05). Participants also performed slower, less accurately and more variably on the VAT following SD (p<.05).

Conclusion: The results demonstrate that SD is associated with reduced DMN connectivity and that this reduction is more widespread during task performance as compared to rest. Further studies should evaluate whether reduced DMN connectivity may contribute to the commonly observed declines in behavioural performance seen after SD, perhaps through interactions with task-related brain regions.

0286

EVALUATING SPEED-ACCURACY TRADEOFF IN SLEEP-DEPRIVED PERSONS

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Introduction: Previous research indicates that the effects of sleep deprivation vary on different tasks. The purpose of the current study was to evaluate speed-accuracy tradeoff as a metric that may help distinguish the differential effects of sleep deprivation.

Methods: Participants were 58 students (38 males, 20 females). During a night of sleep deprivation, participants completed a variety of tasks across four testing sessions (6:30-10:30pm, 11-3am, 3:30-7:30am and 8-12pm). Three Automated Neurological Assessment Matrixes tasks were used: the Code Substitution Learning (CDL), Code Substitution Immediate Recall (CDI), and Code Substitution Delayed Recall (CDD). The CDL asked participants to learn a specific pairing of 9 symbols to the numbers 1 through 9. The participants next completed the CDI where they matched the symbol to the correct number. About five minutes later, after completing two other short tasks, the participants completed the CDD where they again matched the symbol and number. The task took a total of 10 minutes to complete including the 5-minute delay. Throughput (correct responses/reaction time) was used as a measure of speed-accuracy tradeoff.

Results: A 4x3 ANOVA was completed to examine throughput across the four testing sessions for each task (CDL, CDI, CDD). There was a significant main effect for testing sessions (p<.0001) indicating that throughput decreased across the night for all tasks. There was also a significant main effect for task (p<.0001), with the CDL resulting in slower throughput than CDI and CDD. The interaction effect was not significant.

Conclusion: The current results suggest that throughput decreased under sleep deprivation indicating a speed-accuracy tradeoff, where speed decreased as accuracy increased. This indicates that increases or stable performance under sleep deprivation conditions could be over-representing performance especially if the person must operate in work environments requiring quick responses.

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0287

EFFECTS OF SLEEP DEPRIVATION ON SPEECH MOTOR RETENTION

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Introduction: Sleep deprivation is reported to affect parameters of speech production, including voice, articulation, nasalization, and rate of speech, to varying degrees depending on the speech task examined. Little is known, however, about the effects of sleep deprivation on the production of newly acquired speech utterances. The present study was aimed at the investigation of reaction time and durations of repeated productions of novel nonsense words (nonwords) to document the effects of sleep deprivation on variables of speech motor preparation and execution.

Methods: A within-subjects experimental design was utilized, wherein 11 healthy young adults (M = 22.09 years; SD = 3.08 years) repeated six nonwords varying in length and complexity after auditory models, first during an initial "acquisition phase" at 3 hours awake (baseline) and then, again, during a "retention phase" at 21 hours awake (sleep deprivation). Each nonword was repeated 15 times during each phase. Speech acoustic recordings were made with a head mounted microphone and a portable audio recorder. Reaction time (onset of auditory stimulus to onset of speech response) and nonword production duration (onset of nonword production to it's offset) was measured for each nonword using the acoustic analysis software PRAAT. The effect of sleep deprivation was examined by comparing the last two productions of each nonword during the acquisition phase to the first two productions of each nonword during the retention phase.

Results: A repeated measures ANOVA revealed significant main effects of Condition (Baseline vs. Sleep deprivation) and Nonword Complexity (all p < 0.01) on reaction time, but no significant interaction. Similar re-

sults were found for nonword production duration, with significant main effects of Condition and Nonword Complexity (all p < 0.05).

Conclusion: The findings suggest that sleep deprivation results in the slowing of speech preparation processes (reaction time) and speech execution processes (nonword duration) during novel nonword repetition.

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0288

PILOT ASSESSMENT OF COMPUTERIZED NEUROPSYCHOMETRIC MEASURES IN PARTIAL SLEEP-DEPRIVATION

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Introduction: Sleep deprivation induces neurocognitive impairments in memory, attention, and executive functioning. We applied a standardized battery of computerized neuropsychological measures previously used in neurological, driving, and pharmaceutical research arenas to evaluate neurocognitive impairments following acute partial sleep deprivation, and to test the stability of these measures when repeated on successive days.

Methods: Four right handed men aged 22-45 years (mean=30) with a median of 18 years of education participated. Wrist actigraphy measured sleep duration, and a battery of computerized neuropsychological testing including CNS Vital Signs (CNSVS, Chapel Hill, North Carolina) and Useful Field of View (UFOV, Punta Gorda, Florida) were administered at baseline, following one night of acute partial sleep deprivation, and again following one night of recovery sleep. Paired group comparisons were analyzed with Wilcoxon Signed Rank tests utilizing JMP (SAS, Chicago, IL).

Results: Mean sleep durations were 9.37 hours at baseline (prior to cognitive testing), 3.53 hours during acute sleep deprivation, and 8.32 hours during recovery sleep. CNSVS scores that deteriorated following acute sleep deprivation included Composite Neurocognitive Index (baseline, deprivation condition = 58.5 vs. 47.5 percentile rank score), composite memory (98.5 vs. 92.5), visual memory (46.5 vs. 42), and verbal memory (52 vs. 50.5) (p=0.04). Each of these measures improved following recovery sleep (p=0.16). Stroop task performance, reaction time, continuous performance task, and UFOV subtask and total scores improved following both sleep deprivation and recovery sleep.

Conclusion: Computerized neuropsychological testing identified selected reversible neurocognitive impairments in memory and global neurocognitive function associated with acute partial sleep deprivation. Reaction time, executive function, and complex attention showed successive improvements in performance suggesting susceptibility to learning/practice effect with repetition. Future research is needed to extend these results to the evaluation of chronic partial sleep deprivation, and to identify potential interventions and countermeasures to improve sleep deprivation-induced cognitive impairments.

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0289

EFFECTS OF COGNITIVE WORKLOAD AND SLEEP RESTRICTION ON THE MAINTENANCE OF WAKEFULNESS TEST

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Introduction: The Maintenance of Wakefulness Test (MWT) measures the ability to resist sleep in an environment of decreased stimulation. Sleep deprivation reduces MWT sleep latency onset, but it is not known if cognitive work affects the MWT. This study investigated the effects of high cognitive workload (HW) versus low cognitive workload (LW) on MWT sleep latency following both sleep restriction (SR) and no sleep restriction (NSR).

Methods: As part of a larger experiment, N=47 healthy adults (33.1±8.9y; 21 females) completed 3 baseline nights (8h TIB), followed by 5 SR nights (4h TIB) or NSR nights (8h TIB) in a laboratory setting. Subjects were randomized to 1 of 4 experimental conditions: HW+SR (N=16); HW+NSR (N=15); LW+SR (N=10); LW+NSR (N=6). The HW vs. LW conditions differed in duration of cognitive testing each day (LW=½HW). Modified 30-min single-trial MWTs were conducted at 1445h-1600h after baseline night 3 (B3) and after SR1, SR4 and SR5 nights or equivalent NSR nights. Sleep latency was defined as time to the first microsleep (10s EEG theta) or 30 min if no sleep occurred. One-way and mixed-model (night×condition) ANOVAs compared differences among conditions; paired t-tests compared B3 to SR5/NSR5 within each group.

Results: MWT latencies for the 4 groups did not differ at B3. Latencies decreased significantly from B3 to SR5 (p=0.006) in the sleep restriction conditions. The day x condition interaction (p=0.003) indicated the HW+SR group had a greater decrease in MWT latency (p<0.0001) than the LW+SR group (p=0.106).

Conclusion: As expected, sleep restriction decreased MWT latency. Although there was no differential effect of variation in workload on MWT latency in NSR conditions, there was evidence that HW potentiated a decline in MWT latency in SR subjects. However, these results are preliminary and a larger sample size will help resolve the reliability of this finding.

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0290

COMBINED EFFECTS OF HIGH COGNITIVE WORKLOAD AND SLEEP RESTRICTION ON BEHAVIORAL ALERTNESS

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Introduction: Although sleep loss degrades cognitive functions, little attention has been devoted to determining whether waking cognitive activity potentiates the effects of sleep loss, yet time on task is often considered an important fatigue factor in addition to time awake. This project evaluated the effects of variation in cognitive workload and variation in sleep restriction on behavioral alertness as measured by the Psychomotor Vigilance Test (PVT).

Methods: N=51 healthy adults (33.7±8.8y; 22 females) of N=80 total subjects to be tested, completed a 10-day laboratory experiment with randomization to 1 or 4 conditions (low cognitive workload [LW]+ sleep restriction [SR]; high cognitive workload [HW]+ SR; LW + no sleep restriction [NSR]; HW+ NSR). SR entailed 5 nights at 4h TIB; NSR entailed 5 nights at 8h TIB. Subjects had 3 workload test sessions/day of either 180 min (HW) or 90 min (LW). One-way and mixed-model (night×condition) ANOVAs compared differences across the 4 experimental conditions; paired t-tests examined group differences from baseline to SR5/NSR5.

Results: Analyses of preliminary data indicated that high workload combined with sleep restriction potentiated deficits in alertness as measured by PVT lapses of attention (p<0.0001), as well as perceptions of sleepiness and fatigue (KSS and VAS, respectively; p's<0.0001), but the HW+SR combination did not affect performance on two executive functioning tests [COWAT (p=0.39), Hayling (p=0.07)].

Conclusion: The preliminary results from this experiment suggest that the combination of high workload+sleep restriction enhances deficits in behavioral alertness. If these findings sustain with the final sample size, they will provide the first evidence that the duration of cognitive work performed while awake during chronic sleep restriction can contribute to reduced behavioral alertness. This would suggest that the two primary sources of fatigue in many work environments (i.e., time awake and time on task) can have additive effects on alertness.

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0291

COLLEGE STUDENTS' SLEEP HABITS AND GPA

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Introduction: Despite the rampant degree of college students' sleep deprivation and poor sleep habits, there is a paucity of studies on students' sleep habits and affects on GPA. The available studies focus on freshman in Introduction to Psychology courses and may not be generalized to all college students.

Methods: Graduate and undergraduate students were surveyed prior to an educational sleep conference. The survey included: demographics, GPA(self-reported), Pittsburg Sleep Quality Index(PSQI), Epworth Sleepiness Scale(ESS), Morning-Eveningness Questionnaire(MEQ), and Sleep Hygiene Index(SHI).

Results: Surveys were distributed to 315 students; 201 participated(63% response rate): 57% graduate, 43% undergraduate; 82% felt sleepiness affected academics/GPA. The majority(82%) reported drowsy driving with 21% having accidents or near-accidents. The mean PSQI was 6.5(>5 shows poor sleep quality); the mean ESS was 7.8(>10 indicates sleepiness). The mean MEQ indicated no preference for morningness or eveningness. 89% of students pull "all-nighters" occasionally(2-3 a semester) to weekly. Associations were noted between the PSQI to 1. poorer sleep hygiene r=.46(p=<.0001), 2. shorter sleep duration r=.53(p=<.0001) and 3. eveningness preference-MEQ r=.28(p=.001). Higher ESS related with poorer sleep hygiene r=.24(p=.002) and shorter sleep duration r=.32(p=<.0001). Lower GPAs correlated to higher ESS(p=.03). Lowest GPA(2.5-2.99) students were sleepy(ESS of 10.6). The GPA was unrelated to PSQI, SHI, or shorter sleep. Eveningness preference had poorer sleep quality(p=.004) and hygiene(p=.01).

Conclusion: Graduate and undergraduate students have poor sleep quality, shorter sleep duration and poor sleep hygiene. Students with a moderate to strong eveningness preference, have poorer sleep quality and shorter sleep duration. Lower GPAs are associated with excessive daytime sleepiness. Contrary to other studies, the only sleep variable related to GPA was ESS. The majority report drowsy driving with many students having accidents or near accidents.

0292

THE EFFECT OF SLEEP RESTRICTION AND DRIVING SIMULATION WORKLOAD ON THE PSYCHOMOTOR VIGILANCE TEST

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Introduction: Few studies have investigated the effects of workload and sleep restriction on vigilant attention. The aim of the current study was to examine the impact of both 4 days of sleep restriction and cognitive workload on the Psychomotor Vigilance Test (PVT).

Methods: Participants in this preliminary study (N=10) were healthy males (age range 23-32), with an average Body Mass Index (BMI) of 23.58kg/m2. They completed a controlled laboratory based sleep restriction protocol of 2 nights of baseline (B1 & B2, 10h time in bed for sleep [TIB]; 1000h-800h) followed by 4 nights of sleep restriction (SR1-4, 4h TIB a night; 400h-800h) and 1 night for recovery (10h TIB; 1000h-800h). Participants remained in the laboratory for the entire study, food intake, lighting and activity were strictly controlled. Testing was conducted 3 times each day at 900h, 1200h, and 1500h, and included a 10 minute Psychomotor Vigilance Test (PVT) directly before and after a, 40 minute York Driving simulation. Sleep was recorded with polysomnography. A mixed model repeated measures ANOVA was conducted to examine the effect of sleep restriction and driving task workload on PVT lapses (number >500 milliseconds).

Results: Sleep restriction (F=8.03, p=0.01) increased PVT lapses before and after the driving task (F= 8.02, p=0.03). However the interaction effect was not statistically significant (F=0.59, p=0.58). Lane position (F=2.24, p=0.14), road position (F=1.24, p=0.31) and crash status (F=2.79, p=0.11) on the York driving task were not found to be significantly affected by 4 nights of sleep restriction.

Conclusion: While driving performance was not significantly impaired by 4 nights of sleep restriction, sleep restriction and workload associated with the 40 minute driving task increased PVT lapses. They did not, however, act synergistically to potentiate deficits in PVT performance.

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0293

SLEEP, SLEEPINESS AND BEHAVIOR IN FRENCH NAVY SHIFT WORKERS: EVIDENCE FOR A DIFFERENTIAL VULNERABILITY

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Introduction: Preliminary field studies in French military unit have shown that fatigue and sleepiness are complex concepts that cover two different operational situations. For some navy soldiers, fatigue and sleepiness seem mainly linked to a shift work situation whereas for the others it seems mainly due to working conditions (workload). However such studies do not allow determining neither the physiological consequences of these two situations nor the factors responsible for. Here we investigate in a controlled environment (sleep laboratory) fatigue and sleepiness due to shift work condition.

Methods: 39 shift workers underwent a polysomnography and a multiple sleep latency test (MSLT) before (S1) and just after a military deployment (S2). Chronotype, subjective sleepiness, sleep quality, fatigue, and cognitive performance (PVT, Iowa Gambling Task) were also evaluated during these two sessions. All subjects carried out actimeter during the whole experiment.

Results: Preliminary results from 16 young subjects (24.7 years old ± 4.2) confirm the shift workers status with a chronic sleep restriction (Total sleep time < 6 hour/day). After the deployment there is an increase of subjective fatigue (Pichot: 15 versus 9.5, p < 0.01) with diurnal sleepiness (MLST, S1 = 12 min; S2 = 10.2 min, p < 0.05). There is no modification of sleep quantity (S1=538, S2=530 min p > 0.80) and quality. Interestingly, we observe resistant (R) and vulnerable (V) subjects profiles for performance in PVT (Lapses # for R, S1=9.2, S2=4.7, p > 0.17 and V, S1=7.5, S2=16.6, p < 0.01) with parallel modification of sleepiness (MSLT for R, S1= 11.6, S2=10.5 p > 0.5 and for V, S1=12.3, S2=9.6, p < 0.01). After the deployment, we also have 2 profiles in the gambling task: risky and cautious behavior. They are respectively associated with long lasting sleepiness (MSLT < 10 min in S1 & S2) or no sleepiness (S1=14 and S2=11 min).

Conclusion: These preliminary results are in accordance with field studies showing cognitive deficits and risky decision behavior in navy soldiers who complaint from fatigue, sleepiness and sleep quality. We show here that in chronic sleep restriction induced by shift working some French navy soldiers are vulnerable in terms of objective sleepiness, attention processes and risky behavior and others are resistant. Determinants of this vulnerability are key question for our future studies.

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0294

LOCAL, USE-DEPENDENT CHANGES IN THE WAKING EEG AFTER PROLONGED WAKEFULNESS

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Introduction: In humans, prolonged wakefulness is commonly associated with increased sleepiness and impairment in behavioral performance. Previous work has shown that sustained wakefulness is associated with a progressive, homeostatic increase in EEG power density in the theta/alpha frequency range. In this study we investigated whether specific behavioral manipulations targeting distinct cortical areas could locally regulate these changes during prolonged wakefulness.

Methods: Sixteen subjects (right-handed, 22+/-2.7y, 7 females) participated in two prolonged wakefulness experiments (24-h). During each experiment, subjects were exposed to six 2-h bouts of either audiobook listening (AB) or driving simulator playing (DS). These tasks were chosen as previous imaging studies showed that speech listening tasks and driving simulation tasks involve different cortical areas, with the former activating the left fronto-temporal cortices and the latter activating occipito-parietal networks. Resting waking high density EEG (256 channels) with eyes open was recorded for 4 min before and after each task bout, preceded by subjective sleepiness evaluation and a 10-min psychomotor vigilance test (PVT).

Results: After 24-h prolonged wakefulness, both tasks induced a global homeostatic increase in the resting waking EEG power in the theta/alpha frequency (6-9 Hz), concurrent with increased subjective sleepiness and PVT reaction times (p<0.05, paired t-test). Analysis contrasting topographical changes between the two experiments further demonstrated a task-specific effect on the theta/alpha frequency, with a local power increase over the left fronto-temporal derivations for the AB experiment and over the parietal-occipital derivations for the DS experiment (p<0.05, SnPM cluster test).

Conclusion: Our results support the notion that prolonged engagement in a particular task leads to a local, use-dependent enhancement of sleep propensity in the task-related regions compared with other regions. The regional difference in the homeostatic sleep regulation may result from disproportionate activation of cortical neuronal circuits during prolonged wakefulness.

0295

LOCAL, USE-DEPENDENT CHANGES IN THE SLEEP EEG AFTER PROLONGED WAKEFULNESS

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Introduction: Sustained wakefulness is associated with a homeostatic rebound in NREM sleep EEG power density in slow frequencies (<12 Hz). Here we investigated whether specific behavioral manipulations targeting distinct cortical areas during prolonged wakefulness could locally affect EEG homeostatic changes during subsequent recovery sleep.
Methods: Sixteen subjects (right-handed, 22+/-2.7y, 7 females) participated in two prolonged wakefulness experiments (24-h). During each experiment, subjects were exposed to six 2-h bouts of either audiobook listening (AB) or driving simulator playing (DS). These tasks were chosen as previous imaging studies showed that speech listening task and driving simulation task involve different cortical areas, with the former activating the left fronto-temporal cortices and the latter activating occipito-parietal networks. For every participant, we recorded baseline sleep EEG several weeks before the experiments and recovery sleep EEG at the end of each experiment with a 256-channel EEG system.
Results: Both manipulations led to a global increase in slow frequency NREM EEG power (<12 Hz; p<0.05, paired t-test) in recovery compared to baseline sleep, confirming a homeostatic control over these frequencies. Individual slow waves, known to be homeostatically regulated, showed increased negative peak amplitude, slope and incidence (p<0.05, paired t-test) after prolonged wakefulness. Further analyses contrasting topographical changes in the two recovery nights showed a local increase in the slow wave activity (SWA, 1-4 Hz) and spindle power (12-14 Hz) located over left fronto-temporal derivations for the AB condition and over parietal derivations for the DS condition (p<0.05, SnPM cluster test). These changes were spatially overlapping with the EEG changes in the wake EEG induced by the two conditions after sustained wakefulness (see companion abstract).
Conclusion: Our results show a task-specific local regulation of sleep SWA and spindle after prolonged wakefulness in locations overlapping with waking EEG changes.

0296

COMPARATIVE STUDY ON THE EFFECT OF A UNIQUE INTAKE OF DOXYLAMINE, ZOPICLONE AND DIPHENYDRAMINE ON SIMULATED DRIVING PERFORMANCE IN HEALTHY VOLUNTEERS

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Introduction: Z drugs and anti-histaminic components have both been used as hypnotics but their differential effects on driving performances have rarely been studied. The present study was designed to compare the effect of a unique bedtime dose of Doxylamine 7.5mg versus an hypnotic (Zopiclone 7.5mg) and an antihistaminic (Diphenydramine 25mg.) on simulated driving performance assessed as standard deviation of the vehicle position from the center of the road (SDLP).
Methods: Thirty six healthy volunteers (aged 21-44 years) participated in this open, randomized, 3×3 crossover study. The study consisted in 4 periods of treatment, separated by 5-7 days of washout; the first period was the control session (placebo). During each period of treatment, the medication was administered at the bedtime and 40 min driving tests on a car simulator displaying normal highway traffic conditions were performed 11 and 13.2 h later.

Results: Driving abilities differed according to the substance administered. The standard deviation (SD) of the vehicle position from the center of the road was comparable for Doxylamine 7.5mg and Zopiclone 7.5mg, but lower for Diphenydramine 25mg compared to Zopiclone 7.5mg. This result was consistent for both driving sessions (11 and 13.2 h post-dose).
Conclusion: Doxylamine demonstrated an identical effect to Zopiclone on driving performances confirming the need of warning for patients using this anti-histaminic hypnotic.

0297

INFLUENCE OF SLEEP DEPRIVATION ON STATE-ANXIETY AND ARTERIAL BLOOD PRESSURE IN HUMANS

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Introduction: 24-hour total sleep deprivation (TSD) has been reported to either increase or not change resting mean arterial pressure (MAP), yet the mechanisms underlying these differences remain equivocal. Hypertensive responses to anxiety are well documented, and TSD commonly increases state-anxiety. Therefore, we hypothesized that TSD would increase state-anxiety, resting MAP, and pressor responses to acute mental stress. Furthermore, we hypothesized that increases in state-anxiety after TSD would correlate to increases in MAP.
Methods: We examined 16 subjects (13 men, 3 women) once after a normal sleep night (NS) and once after 24-hour TSD (randomized order). Sleep durations were monitored prior to each testing session by means of actigraphy. The Spielberger State-Trait Anxiety Inventory was used to determine state-anxiety after TSD and NS. Three consecutive recordings of resting supine arterial blood pressure were taken with an automated sphygmomanometer. Following a 5 min resting baseline, continuous arterial blood pressure (Finometer) and heart rate (electrocardiogram) were monitored during 5 min of acute mental stress evoked by mental arithmetic. All resting variables were compared using paired t-tests, while responses to mental stress were analyzed with repeated measures ANOVA.
Results: Raw (29±2 vs. 34±2; P<0.01), standard (43±2 vs. 48±2; P<0.01), and percentile (27±6 vs. 46±7; P<0.01) state-anxiety scores were higher after TSD compared to NS. TSD significantly increased resting MAP (74±2 to 77±2 mmHg, P<0.03), while increases in MAP during mental stress were similar between TSD and NS (Δ8±1 vs. Δ8±1 mmHg). Increases in state-anxiety with TSD were not correlated to increases in resting MAP (P≥0.65) or MAP responses to mental stress (P≥0.31).
Conclusion: TSD elicits concurrent increases in state-anxiety and resting MAP, but these responses appear to occur independently. Thus, increased state-anxiety does not appear to be a primary mechanism for TSD-mediated increases in resting arterial blood pressure.

0298

ELEVATED STRESS RESPONSES FOLLOWING SLEEP DEPRIVATION IN HEALTHY ADULTS

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Introduction: The relationship between sleep deprivation and stress is not well understood. We sought to determine the extent to which acute sleep loss altered both the anticipation of, and reaction to, low and high stressors, hypothesizing that sleep deprivation would increase subjective and physiological stress responses to a high stressor in particular.
Methods: N=26 healthy adults (12f) completed a laboratory experiment that began with a baseline sleep period (9h TIB) followed by cognitive

testing under conditions of a low stressor (easy tasks completed without time pressure) and then by a high stressor (difficult tasks completed with time pressure). Visual analog scales of stress were completed before and after each testing session. On the second night of the study, subjects were randomized to receive either total sleep deprivation (0h TIB, N=12) or sleep (9h TIB, N=14), and the next day they again completed testing under the same stressor conditions as the baseline day, but were also exposed to a novel stressor (i.e., Trier Social Stress Test). Salivary cortisol was assessed 20 min and 5 min before stressor onset (baseline measures) and 5 min, 20 min and 40 min after stressor completion (reactivity measures).

Results: Relative to no sleep deprivation, sleep deprivation was associated with greater self-reported stress before both the low stress (p<0.001) and before the high stress (p<0.001) cognitive testing. There were no differences in subjective stress following low or high stress cognitive testing. Sleep deprivation was also associated with greater cortisol reactivity to the Trier stressor (p=0.03), which remained significant even after controlling for the effect of sleep deprivation on baseline cortisol levels (p=0.002) prior to stressor onset.

Conclusion: Sleep deprivation is associated with elevated subjective stress in anticipation of performance testing and elevated physiological stress at rest and in responses to a social stressor.

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0299

MOOD AND REM SLEEP EFFECTS OF A 6-DAY 4-H SLEEP RESTRICTION PROTOCOL IN HEALTHY FEMALE SUBJECTS

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Introduction: Sleep disturbances are tightly linked to major depression and are traditionally considered as a symptom of the disease. However, insomnia often precedes the onset of a depressive episode and sleep disruption or restriction could be a causal factor of depression. Accordingly, the present study investigates whether sleep restriction in healthy subjects could induce depressive-like mood and sleep EEG alteration.

Methods: 14 healthy female subjects aged 30-40 years underwent a 6-day actigraphy-controlled 4-h sleep restriction protocol. Objective and subjective assessments of sleep as well as of mood, emotion and vigilance were obtained before (D1) and during (D2 to D8) the sleep restriction period with polysomnographic recordings, the profile of mood scale (POMS), the emotional visual analogue scale (e-VAS), the Karolinska sleepiness scale (KSS) and the psychomotor vigilance task (PVT), the three latter assessments being obtained five times daily at 3-h intervals.

Results: A cumulative detrimental effect of the sleep restriction procedure was observed on PVT performances that parallels deterioration of scores on KSS and POMS fatigue/vigor/confusion subscales. Restricted sleep comprised proportionally more slow wave sleep and less stage 2 sleep (all p <.001 for D1 to D2 and D1 to D7 comparisons). The level of REM sleep percentage was comparable at D1, D2, and D7. However, at D7, REM sleep was shifted from the last third of the night to the two other thirds and REM sleep latency was shortened (both p <.05). Significant day and time effects (both p <.001) and day x time interaction (p <.05) were observed for e-VAS showing that emotions were gradually rated as less positive from D2 to D8 and progressively worse during the morning.

Conclusion: The present results show that a 6-day 4-hour sleep restriction paradigm in healthy female subjects induces some depressive-like disturbances.

0300

NIGHT-WORK AND INFLAMMATORY MARKERS

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Introduction: Various adverse health effects associated with shift work have been documented in the medical literature . These include increased risk of cardiovascular disorders, inflammatory disorders, cerebrovascular disorders, and mortality. Sleep deprivation has been shown to be associated with an elevation in inflammatory makers such as IL-6 , TNF-α and CRP. It is hypothesized that the increased risk of many disorders associated with shift work may be due to inflammatory processes resulting from sleep deprivation. The purpose of the present study was to investigate the relationship between night work and inflammatory markers.

Methods: Fifty workers were selected according to specified inclusion and exclusion criteria and randomly assigned to one of two groups in a cross over study. The 25 workers in group one were scheduled to work the following consecutive shifts: 3 days shifts, 1 day off and 3 night shifts. The 25 workers in group two were scheduled to work the following consecutive shifts: 3 night shifts, 1 day off and 3 day shifts. Blood samples were obtained between 7 and 8 AM after the periods of day-work and night-work and tested for inflammatory markers.

Results: There was a statistically significant increase in IL-6, WBC, neutrophils and lymphocytes following night work compared to day work. TNF-α was increased but it was not statistically significant, and also the change in monocyte count was not significant.

Conclusion: This study demonstrated an increase in inflammatory markers following night work, as reported in several pervious studies on sleep deprivation. No significant changes in monocyte count can be justified by the results of a study showed the elevation in blood levels of inflammatory markers is due to increase in gene expression, not in monocyte count.

Support (If Any): Tehran University of Medical Sciences

0301

FIVE CONSECUTIVE NIGHTS OF SLEEP RESTRICTION INCREASES LEPTIN AND IMPAIRS GLUCOSE METABOLISM

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Introduction: Attention has focused increasingly on the metabolic consequence of sustained sleep restriction (SR). However, not all studies have controlled energy intake or activity, and results are varied. The current laboratory study investigated the effect of SR on interstitial glucose and on plasma glucose, insulin and leptin.

Methods: N=10 men (ages 23-32y), with an average BMI of 23.58kg/m2 completed a controlled, in-residence laboratory-based, SR protocol of 2 nights baseline (B1 & B2, 10h TIB; 10:00h-08:00h) followed by 5 nights SR (SR1-5, 4h TIB; 04:00h-08:00h) and 1 night recovery (10h TIB; 10:00h-08:00h). Meals were timed (0910h, 1300h, 1830h), food intake was calorie controlled, and physical activity was minimized. On B1 and SR5, blood was sampled via an indwelling catheter at 09:00h (fasting) and at 2h intervals from 10:00 until 20:00, and abdominal subcutaneous, interstitial glucose was measured for 24h using a continuous glucose monitor.

Results: Paired t-tests revealed that pre-prandial, interstitial glucose was higher at SR5 (6.78±1.42mmol/l) than at B1 (5.07±1.35mmol/l p<0.001). Plasma glucose was increased at SR5 (5.70±0.90ng/ml)

compared to B1 (5.14±0.54ng/ml; p=0.042). Plasma leptin was also increased at SR5 (4.65±0.76mmol/l) compared to B1 (4.34±0.81mmol/l; p=0.009). Plasma insulin was not significantly different between SR5 and B1.

Conclusion: SR induced a disturbance in glucose metabolism, with high glucose levels that were not compensated by increases in insulin. The increased leptin observed with SR suggests a positive energy balance, possibly due to participants' sedentary behavior in the laboratory. These data support the idea that SR may promote insulin and leptin resistance, which could lead to obesity and Type 2 diabetes.

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0302

INFLUENCE OF FOOD RESTRICTION ON CARDIOVASCULAR PARAMETERS IN MALE RATS SUBJECTED TO PARADOXICAL SLEEP DEPRIVATION

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Introduction: The purpose of this study was to determine the paired consequences of food restriction (FR) and paradoxical sleep deprivation (PSD) for cardiovascular parameters in male rats.

Methods: For FR rats, restriction began at weaning with 6 g/day of food and then was increased by 1 g/week until reaching 15 g/day by for 8 weeks. At adulthood, both rats subjected to FR and those fed ad libitum were either exposed to PSD for 96h or maintained in their home-cage groups.

Results: Animals subjected to FR showed a significant increase in high-density lipoprotein (HDL) levels compared to animals that had free access to food. After the PSD period, the FR animals had reduced concentrations of HDL relative to their respective controls, although the values for FR animals after PSD were still higher than those for the ad libitum group. Concentrations of low-density lipoproteins (LDL) were significantly increased in animals subjected to PSD under the ad libitum diet. The levels of triglycerides, very low-density lipoproteins (VLDL) and glucose in FR animals was decreased when compared to both ad libitum groups.

Conclusion: These results may help us to understand the mechanisms underlying increased life expectancy under long-term FR.

Support (If Any): Fapesp(#01030-5), CEPID (#98/14303-3), AFIP, CNPq

0303

SLEEP DEPRIVATION INCREASES BODY WEIGHT GAIN IN OBESITY RESISTANT RATS

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Introduction: Reduced sleep time and quality increases the risk for obesity. Earlier, we showed an association between resistance to weight gain and enhanced sleep quality in obesity-resistant (OR) rats. However, it is unknown if sleep-deprivation in OR rats promotes weight gain. OR rats express higher amounts of orexin-receptor genes in sleep regulatory areas. The orexin system is critical to energy homeostasis and sleep/wake regulation. Moreover, sleep-deprivation impairs orexin functioning. Thus, we hypothesize that partial sleep-deprivation (PSD) in OR rats might increase their body weight gain, and examined the effect of

PSD on body weight in OR and control (obesity-prone) Sprague-Dawley (SD) rats.

Methods: Obesity-resistant and SD rats (3-months) were implanted with transmitters for recording sleep/wake behavior. Following 24-h baseline recordings, rats were subjected to 8-h daily sleep-deprivation (light-phase) by exposure to environmental noise (random street noises; 500-20000Hz; 85 dB) for 9 days. Recording was scored as wakefulness (W), slow-wave-sleep (SWS) and rapid eye movement sleep (REMS) in 10-s epochs. Total number of transitions between stages, food intake and changes in body weight during 9 days of PSD were also documented.

Results: Exposure to noise decreased time spent in SWS and REMS, while increasing the time spent in W (P<0.001) in both group of rats. Sleep-deprivation significantly (P<0.001) increased the number of transitions between stages in all animals. The body weight gain was not different between OR and SD rats during control conditions or during sleep deprivation. However, sleep deprived OR and SD rats gained significantly more weight compared to non-deprived OR (P<0.01) and SD animals (P<0.05), which was associated with increased food intake during PSD in both OR (P<0.0001) and SD rats (P<0.001).

Conclusion: Sleep-deprivation and deteriorating sleep quality increases the risk of weight gain in OR and SD rats, supporting the hypothesis that sleep plays an important role in effective body weight regulation.

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0304

FATTY ACID BINDING PROTEIN 4 MEDIATES INTERMITTENT HYPOXIA-INDUCED ATHEROGENESIS IN MICE

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Introduction: Obstructive sleep apnea (OSA) which is characterized by intermittent hypoxia (IH) during sleep has emerged as an independent risk factor for cardiovascular disease, and more specifically coronary heart disease. IH is associated with disruption of lipid metabolism, activation of inflammatory pathways, and endothelial dysfunction. More recently, IH promotes atherosclerotic lesion formation in a mouse model of atherogenesis. However, the molecular mechanisms underlying IH-associated atherogenesis remain largely unknown. Adipocyte fatty acid binding protein (FABP4) plays a critical role in the process of atherosclerosis, supporting the notion FABP4 may also play a potential role in IH-induced atherogenesis.

Methods: Macrophage transformation, activation of inflammatory pathways, foam cell formation were assessed in apoE-/- transgenic mice. Mice were exposed to IH (alternating 21% and 5.7% O2 from 7AM to 7PM each day) with or without FABP4 inhibitor. The primary monocytes were isolated after the treatments. The mRNA and protein expression of FABP4 was assessed by real-time PCR and western blotting. Monocyte transformation and migration were assessed by flow cytometry and immunohistochemistry. Induction of inflammation was examined by measuring TNF-α, IL-1, and IL-6 production. Foam cell formation was examined by oil red O staining.

Results: IH induced increased mRNA and protein expression of FABP4 in isolated primary monocytes of apoE-/- mice. IH was associated with transformation of monocytes to activated macrophages, as evidenced by increased expression of CD14 and CD68. IH also increased the migration of activated macrophages, as evidenced by immunohistochemistry in apoE-/- mice. In addition, IH also induced the elevated expression pro-inflammatory cytokines, TNF-α, IL-1, and IL-6 in the serum of apoE-/- mice. IH promoted foam cell formation in primary monocytes. All IH-induced changes were attenuated by treatment FABP4 inhibitor.

Conclusion: FABP4 plays an important role in IH-induced atherogemesis and may become a viable therapeutic target aiming to prevent and potentially reverse OSA-associated atherosclerosis.

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0305

POST-STRESS SLEEP IS AN IMPORTANT DETERMINANT OF SUBSEQUENT STRESS RESPONSES

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Introduction: We have demonstrated that controllable stress (modeled by escapable shock; ES) and uncontrollable stress (modeled by inescapable shock; IS), and reminders of ES and IS, are followed by increased and decreased REM, respectively. These differences suggest that REM may play a role in adaptive responding to stress. We trained mice with ES followed by 6 h REM deprivation (RSD) to determine whether post-stress REM was important for subsequent responding to stress.

Methods: Male BALB/cJ mice (n=12) were implanted for recording sleep via telemetry. After recovery from surgery, uninterrupted baseline sleep was collected for 2 days. Then mice were trained with ES (20 shocks: 0.5 mA, 5.0 sec maximum duration, 1.0 min intervals). After training, half were allowed to sleep undisturbed and half were awakened at REM onset for 6 h. One week later, the mice were returned to the shock chamber (Con) and allowed to explore for 30 min. They were then placed back in their home cages and sleep was recorded for 6 h.

Results: Compared to time matched baseline, RSD produced a 90.4% reduction in REM and a 39% reduction in NREM. Mice allowed to sleep freely after ES showed a 14.3% increase in REM and a 2.8% increase in NREM. On subsequent exposure to Con, mice that received RSD showed reduced REM during the first 2 h (p < 0.05). NREM was also reduced during the first 2 h of Con (p < 0.05), but was increased during the second 2 h of Con (p < 0.05). Mice allowed to sleep freely after ES training did not show reductions in REM or alterations in NREM after Con.

Conclusion: Stressed mice are easily agitated which likely reduced the selectively of RSD. However, interrupting sleep after training with ES produced responses to subsequent fearful contexts similar to those produced by IS. This suggests that post-stress sleep is important for adaptive responding to stress.

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0306

CHANGES IN BLOOD AMINO ACID LEVEL ASSOCIATED WITH SLEEP DEPRIVATION IN RATS

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Introduction: Since some of critical neurotransmitters that control sleep/wake status are amino acids per se (i.e., GABA, glutamate, glycine) or synthesized from amino acids (i.e., monoamines), it is possible that an altered balance and quantity of amino acids can cause sleep disturbances. Similarly, sleep disturbances may induce changes in amino acid balances. In addition, since sleep disturbances are associated with changes in blood leptin and ghrelin levels, sleep disturbances may also cause metabolic changes in blood amino acids. However, there are no reports to directly address these questions. We therefore evaluated any changes in blood amino acid level associated with sleep changes using rodents.

Methods: Adult male Sprague-Dawley rats (n=6) were acutely sleep deprived with gentle handling from ZT 0 (light on) to ZT 6 and then recovery sleep was allowed from ZT 6. The blood samples were collected from the tail vein every 3 hours from ZT 0 to ZT 12 in these rats.

The same rats were used in a control test, and blood was also collected at each time point. Plasma amino acid concentrations were measured by an automatic amino acid analyzer.

Results: We could reliably measure more than 40 amino acids, including proteiogenic and non-proteiogenic amino acids from small amount of plasma (7 μl). Most of the amino acids measured, such as tyrosine, declined across time in both the baseline and sleep-deprived groups, suggesting that blood amino acid is regulated with circadian mechanisms. Noticeable changes between the baseline and sleep-deprived groups were for glutamic acid (Glu), but no differences were seen in a large majority of amino acid measured. Of interest however, changes in Glu may have been due to the sleep deprivation, since the increase in Glu in the sleep-deprived rats was reduced when the rats were allowed to have recovery sleep.

Conclusion: Our results showed that a large majority of blood amino acid levels is influenced by circadian mechanisms. Acute sleep deprivation for 6 hours induced small changes in blood amino acid levels. Therefore, further investigations of chronic sleep restriction or sleep and circadian disease-oriented experiments will be required to substantiate the relationship between changes in amino acids and sleep.

0307

SLEEP DEPRIVATION IMPAIRS RECOGNITION OF SPECIFIC EMOTIONS

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Introduction: Mood and emotional processes are particularly sensitive to sleep deprivation. Recent evidence suggests that sleep loss impairs the recognition of angry and happy faces, but prior studies have only included a limited number of emotion categories. In the present study, we evaluated the effects of one night of sleep deprivation and recovery sleep on the 6 basic emotion categories.

Methods: Healthy individuals (29 males; 25 females) completed the Ekman Emotion Hexagon Test (EHT), which presents a series of 120 standard facial expressions the six primary emotions that have been computer morphed with their most highly confusable expression counterparts (e.g., happiness-surprise; surprise-fear) to create continua of expressions that differ in discriminability. Each expression is a mix of two emotions (e.g., 30% fear+70% sadness). The subject was required to identify the dominant emotion in each expression. The EHT was administered following a normal night of sleep, again following 23.5 hours of sleep deprivation, and after 12 hours of recovery sleep. Data were analyzed with repeated measures analysis of variance.

Results: There was a significant session x valence interaction (p=.001). Post hoc comparisons revealed that sleep deprivation was associated with significantly reduced accuracy for identifying happiness and sadness (p<.05), which returned to normal following recovery sleep. In contrast, none of the other emotions showed significant declines as a function of sleep loss, although recovery sleep did improve accuracy for identifying anger, fear, and surprise. Disgust recognition was unchanged across sessions.

Conclusion: Sleep deprivation adversely affected the recognition of the two most common human emotional expressions, happiness and sadness, while leaving other more primitive survival-oriented recognition systems unaffected. Interestingly, these two emotions are the most important to prosocial interpersonal behaviors involving affiliation and empathy. Thus, sleep loss may have particularly adverse impacts on social communication and interpersonal interactions that require sensitivity to these emotional communications.

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0308

SLEEP DEPRIVATION BLUNTS THE PERCEPTION OF EMOTIONAL INTENSITY IN FACES

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Introduction: Sleep deprivation affects brain functioning in regions important for emotional processing. Recent research has shown that sleep loss impairs the accurate recognition of some facial expressions of emotion, particularly anger and happiness, but it remains unclear the extent to which this is due to alterations in the perceived intensity of the emotions or some other aspect of facial perception. Here, we evaluated the effect of 25 hours of sleep deprivation on the intensity of facial perception.

Methods: Fifty-four (29 men) healthy individuals rated a series of 40 faces from the University of Pennsylvania Emotional Acuity Test (PEAT) on a 7 point scale ranging from "very sad" to "neutral" to "very happy" following a normal night of sleep, again after 25 hours of sleep deprivation, and finally after 12 hours of recovery sleep. Ratings were transformed to a 4-point intensity scale ranging from 0 (neutral) to 3 (very happy/sad). Data were analyzed using a repeated measures analysis of variance.

Results: There was a main effect of valence ($p < .00001$), with happy faces rated as more intense than sad, and a main effect of session ($p < .00001$), suggesting a decline in intensity following sleep deprivation. A significant session x valence interaction ($p = .044$) revealed that both happy and sad faces were blunted by sleep deprivation, but only the happy faces showed a rebound in intensity following recovery sleep. Sad face ratings remained blunted following recovery.

Conclusion: Emotional perception of happy and sad faces was significantly blunted during a single night of sleep deprivation relative to baseline. Recovery sleep increased ratings of happy faces but had no effect on ratings of sad faces. Sleep loss appears to blunt the perception of emotional intensity and may have lingering effects on negative affect perception following recovery sleep, a finding that could have implications for interpersonal functioning.

0309

IS LACK OF SLEEP CAPABLE OF INDUCING DAMAGE IN AGED SKIN?

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Introduction: Skin naturally changes with age, becoming more fragile. Various stimuli, such as stress, can alter skin integrity. The aim of this study was to evaluate if the consequences of sleep deprivation on skin's DNA integrity augment to the deleterious effect of aging in mice.

Methods: Female hairless mice with 15 months of age were submitted to 72 hours of paradoxical sleep deprivation (PSD) or to 15 days of chronic sleep restriction (SR). Immediately after, punch biopsies of the skin were taken and processed to evaluate DNA damage by single cell gel (comet) assay.

Results: PSD or RS did not potentiate the adverse effect caused by aging on genetic damage, depicted by tail movement and tail intensity values from the comet assay.

Conclusion: Taken together, the findings are consistent with the notion that sleep loss does not override the genetic damage in elderly hairless mice as detected by single cell gel (comet) assay.

0310

BED TEMPERATURE AND HUMIDITY DURING SLEEP IN MILD THERMAL CONDITIONS

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Introduction: During sleep the human body is in continuous interaction with its microclimate. Traditionally, temperature is monitored in the environment surrounding the bed, neglecting the bedding system as part of the thermal environment. This study aims to quantify heat and water vapor transfer inside a bedding system at mild thermal conditions.

Methods: Polysomnography was performed during the nights on twelve healthy test persons (aged 20.8±2.5 y). Temperature (TE) and relative humidity (RH) were monitored at the following levels: 12 sensors 70 cm above the bed (3 TE, 9 combined TE-RH), 2x3 combined TE-RH sensors above and under the duvet, and 2x15 combined TE-RH sensors inside the bedding system on two horizontal levels. Three different thermal conditions were considered: a constant room temperature of 20°C and initial bed temperature of 19.1±1.4°C, a rise in room temperature from 20°C to 25°C 30 minutes after lights out, and a constant room temperature of 20°C and initial bed temperature of 13.2±1.7°C. Sensible and latent heat flow through both duvet and bedding system were calculated from temperature and humidity gradients.

Results: Sensible heat flow through the duvet was significantly higher in a room temperature of 20°C compared to 25°C (15.2±4.4 W/m2 vs. 8.5±1.4 W/m2, p<0.05). This difference in heat flow was not present through the bedding system. However, sensible heat flow through the bedding system increased during the night with initial bed temperature of 13.2°C (24.9±1.8 W/m2 vs. 18.2±2.4 W/m2, p<0.05). This higher heat flow was not apparent through the duvet. Calculated latent heat loss revealed no differences between conditions and throughout the night.

Conclusion: This study acknowledges the importance of the bed as part of the thermal sleep environment. Results show that sensible heat losses through the bed are mainly influenced by the initial bed temperature, rather than by differences in room temperature.

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0311

AUTOMATED SLEEP STAGING WITH ONLY TWO ELECTRODES (FP1-FP2) ON THE FOREHEAD

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Introduction: Complexity of the standard sleep montage and laboriousness of manual sleep scoring are major obstacles to more widespread use of sleep monitoring outside of dedicated facilities. We present an algorithm for automated sleep staging that requires the use of only two disposable electrodes on the forehead (Fp1 and Fp2).

Methods: EEG (standard and Fp1-Fp2), EOG and chin EMG were recorded from eleven healthy sleep-deprived subjects and eighteen normal subjects during nocturnal sleep. For each 30-second segment of the Fp1-Fp2 EEG ratios were calculated between delta and beta power (DBI), sigma and beta power (SBI), beta power and power above 30Hz (BEI), and delta power before and after removal of ocular artifacts (EMI). Arousals and spindles were detected by comparing the second-by-second fluctuations of alpha, beta and sigma power to the respective averages over 90 seconds. DBI, SBI, EMI, BEI, spindle counts, and arousal durations and counts were fed to a hierarchical decision tree that classified each epoch as Wake, NREM1, NREM2, NREM3 or REM sleep.

The records were also scored per AASM criteria and epoch-by-epoch comparisons (n=23,361) were performed between the visual and automated scoring.

Results: Overall agreement and kappa (80.9%/0.71) as well as Se/PPV for detection of Wake (84%/62%), NREM1 (31%/37%), NREM2 (81%/82%), NREM3 (88%/88%) and REM (88%/84%) equal or outperform similar efforts in the literature. However, the algorithm tended to score too much Wake during wake-sleep transitions, and consequently to slightly underestimate total sleep time and sleep efficiency (TST:-10±12min; SE:-4.2±4.4%). There were no differences in the algorithm's performance between the sleep-deprived and non-deprived subjects.

Conclusion: Sleep can be scored accurately using only two electrodes below the hairline. Future research should focus on improvements of differentiation between wakefulness and early stages of drowsiness, and on validation studies in pertinent clinical populations.

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0312

MOVEMENT TOWARD A NOVEL ACTIGRAPHY DEVICE

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Introduction: Although it is the gold-standard, disadvantages of polysomnography include its expense, time-intensiveness, and first-night-inducing effects. In contrast, actigraphy, used in the field by both researchers and clinicians to identify sleep/wake time and patterns, is relatively low-cost and time-efficient. Its major limitation is that actigraphy poorly identifies wake after sleep onset compared to polysomnography. A new very low-cost, web-based device has been marketed as a new form of ambulatory sleep monitoring. The purpose of our study was to determine, without any conflict of interest, how this device compares to both polysomnography and a commonly used brand of actigraphy.

Methods: Twenty four healthy adults (40% female, 26.1 [range=19-41] years, 92% white) with no history or symptoms of any sleep disorder wore a FitBit device adjacent to a MiniMitter AW-64 on their non-dominant wrist during a single night of standard research polysomnography.

Results: Recording time was 465.0 (SD±48.4; range=340-543) minutes. Percent of the recording period spent in sleep as identified by both FitBit (r=.43, p=.035) and AW-64 (r=.58, p=.003) were significantly correlated with polysomnography, as well as with each other (r=.92, p<.001). FitBit (p<.001) and AW-64 (p<.001) also both differed significantly from polysomnography as well as from each other (p<.001). Compared to polysomnography, FitBit overestimated sleep by 14.5% (SD±10.7%) and AW-64 overestimated sleep by 9.3% (SD±9.7%). Bland Altman plots demonstrate similar profiles for both activity monitoring devices: agreement was highest among participants with high sleep efficiency and lowest among participants with low sleep efficiency.

Conclusion: Consistent with AW-64, FitBit underestimates wake during the sleep period. Considering the costs and benefits of polysomnography and current actigraphy methods, this new, web-based device may be a low-cost alternative to current ambulatory monitoring methods. Additional research on specific patient populations and younger age groups will be needed.

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0313

VALIDATION OF A MODIFIED BRIEF VERSION OF THE PSYCHOMOTOR VIGILANCE TEST (PVT)

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Introduction: The Psychomotor Vigilance Test (PVT) objectively assesses fatigue-related changes in behavioral alertness associated with sleep loss, extended wakefulness, circadian misalignment, and time on task. However, the standard 10 min PVT is often considered impractical in applied contexts. To address this limitation, we developed a modified briefer (3 min) version of the PVT (PVT-B).

Methods: The PVT-B was validated in controlled laboratory studies with 74 healthy subjects (34 female, aged 22-45 y) that participated either in a total sleep deprivation (TSD) study involving 34 h awake (N=31) or in a chronic partial sleep deprivation (PSD) protocol involving 5 nights of 4 h time in bed (N=43). PVT and PVT-B were performed regularly during wakefulness. Mixed model ANOVAs were used to test the sensitivity of PVT-B and PVT to TSD and PSD, on each of 5 key PVT outcomes.

Results: Effect sizes were largest for sensitivity of response speed to both forms of sleep loss for both the PVT-B and the PVT. Effect sizes were also larger for TSD than PSD, and larger for PVT than for PVT-B for all outcomes. Effect sizes for the PVT-B were still substantial, and compared to the 70% decrease in test duration, the 23% average decrease (range 7%-69%) in effect size was acceptable. After reducing the lapse threshold from 500 ms to 355 ms for the 3 min PVT, there was no indication of differential sensitivity to sleep loss between PVT-B and PVT for the primary PVT outcome variables of lapses and response speed (P>0.15).

Conclusion: PVT-B tracked standard 10 min PVT performance throughout both TSD and PSD, and yielded high effect sizes. PVT-B is a useful tool for assessing behavioral alertness in settings where the duration of the 10 min PVT is considered impractical, although further validation in applied settings is needed.

0314

AN EVALUATION OF SPLIT AND MANUAL TITRATION STUDIES IN SQUH SLEEP LABORATORY ACCORDING TO AASM CRITERIA

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Introduction: PAP devices are used to treat patient with sleep related breathing disorders and their sittings are obtained by full night or split night titration studies. This study was conducted in Sultan Qaboos University Hospital as a part of auditing the service in the sleep laboratory according to AASM grading system of PAP titration which include four different grades describe the result of titration (optimal, good, adequate and unacceptable) which concentrate in reduction of RDI and the presences of supine REM sleep.

Methods: Split night and manual titration studies from 2008, 2009 and 2010 (excluding December of 2010) were reviewed. The data were collected retrospectively from Polysomnography reports and hospital medical records.

Results: From 654 PSG studies where reviewed only 96 (15%) were split and manual titration studies. The percentage of split and manual titration studies increased year by year (9%:2008, 22%:2009, 21%:2010).

Among those titration studies in 2008 29% optimal, 12% good, 24% adequate and 35% unacceptable. While in 2009 47% optimal, 24% good, 8% adequate and 21% unacceptable and the case in 2010 were 49% optimal, 12% good titration, 19.5% adequate and 19.5% unacceptable. From this statistics the reasons for this are lack of trained technologists to perform the titration correctly and the lack of a titration protocol which only seen after 2008. The second reasons for this failure was due conditions directly related to patients such as central sleep apnea, Chain-Stokes breathing and emergence of complex sleep apnea.

Conclusion: The primary reason related to technologist in which they are not providing patient with enough education about the device (acclimatization), so patients will not easily accept the device. In order to overcome this, more training is required and follow up and checking technologist titration randomly and continuously to make sure they are using the proper way of titration.

0315

UNSUPERVISED PARADOXICAL SLEEP DEPRIVATION USING POLYGRAPHIC SIGNALS IN RATS: A NEW ALTERNATIVE TO THE "FLOWER POT" TECHNIQUE

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Introduction: Selective paradoxical sleep (PS) deprivations (PSD) can be efficiently performed by using the classical "inverted flower pot" method. Once installed on one or several platforms surrounded by water animals refrain from entering PS, and present a PS hypersomnia (rebound) when placed back in their home cage. In the first hours of deprivation this method also suppresses SWS; hence it cannot be used for short selective PSD. As a non-stressful alternative, manual deprivations are possible but involve an operator who constantly scrutinizes the sleep recordings and manually wake-up the animal. Here we introduce an approach based on a real-time detection of PS coupled to a new mechanical device to awaken the animal.

Methods: Our adaptative algorithm identifies PS from EEG and EMG signals. When PS is detected, a stimulus is applied with a device placed underneath the cage that produces a sudden descent of the cage's floor followed by a slow return to its initial level. This new method was used in two paradigms, a 6-hour PSD, and a 72-h PSD.

Results: When applied to baseline recordings, our algorithm gave a high concordance with human scoring (>95%). Notably, the specificity to detect PS reached 98%. A first group of rats went through a 6-h manual PSD. Manual PSD was followed by an increase in PS amounts: 29.2±2.9% vs 12.6±2.6% in baseline (n=3, over 2h). With the unsupervised PSD, PS rebounds had a slightly less magnitude 22.1±7.6% vs 14.0±3.3%. Another group of animals went through a 72h PSD using the platform technique and, two weeks later, through a second 72h-PSD with our new device. The rats were then euthanized 180 minutes after the end of PSD, and brain sections were collected for Fos-labeling. On average, PS amount during the rebound was smaller after the unsupervised PSD (23.3±3.3% vs 41.2±5.1% over 3h; n=6), while SWS amount did not significantly differ (46.6±10.8 vs 43.7±4.5%). The smaller rebound with the unsupervised PSD might primarily result from a lower stress level and to a less extent from residual PS bouts. Analysis of Fos labeling (n=3) revealed similar activation levels after PS hypersomnia, as those described after the classical PSD.

Conclusion: Altogether our results show that our approach can efficiently overcome the limitations of manual detection when performing short PSD, and constitutes a valuable alternative to the classical technique for long PSD.

0316

COMPARISON OF MOTIONLOGGER WATCH AND ACTIWATCH ACTIGRAPHS TO POLYSOMNOGRAPHY IN HEALTHY YOUNG ADULTS

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Introduction: Although validation studies have legitimized the use of actigraphy, few studies have directly compared different commercially available actigraphs with polysomnography. We compared the reliability of the Motionlogger Watch and the Actiwatch-64 to polysomnography (PSG) for identifying sleep/wake.

Methods: Twenty-nine volunteers (20 males; mean (SD) age = 24.3 (5.4)) received 1 night of 8 hrs baseline sleep (23:00 - 07:00) and remained awake for 36 hours followed by 11 hours recovery sleep (20:00 - 07:00) in the laboratory. Analyses were performed as two sets: 1) epoch-by-epoch agreement and 2) sleep parameter concordance with repeated-measures ANOVAS employed to determine differences between metrics and nights.

Results: The Motionlogger Watch showed significantly higher sensitivity (sleep identification), specificity (wake detection), and overall agreement with PSG compared to the Actiwatch (though sensitivity and overall agreement was high and specificity was low for both measures) and overall agreement was higher overall on recovery versus baseline. The Actiwatch differed from PSG, underestimating total sleep time and sleep efficiency and overestimating number of awakenings for both nights and underestimating sleep latency on baseline. The Motionlogger Watch differed from PSG on recovery; underestimating total sleep time and sleep efficiency and overestimating sleep latency.

Conclusion: The present study builds upon previous reports by evaluating a new commercially available actigraph (Motionlogger Watch) and using two sets of analyses for a more comprehensive examination. Our data suggest that actigraphy may be a useful and reliable alternative to PSG for assessing sleep-wake in the laboratory in healthy young adults and that the Motionlogger Watch may offer some advantage compared to the Actiwatch. An important consideration, however, is that while both actigraphs showed high sensitivity to detecting sleep and overall agreement, specificity for detecting wake was much lower. While room for improvement remains, actigraphy serves as a useful and reliable tool for sleep researchers, especially in situations where PSG may not be practical.

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0317

SLEEP/WAKE CLASSIFICATION WITH HEAD ACTIGRAPHY

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Introduction: Wrist actigraphy is often used in conjunction with unattended cardio-respiratory monitoring to provide an estimate of the total sleep time. Head movements have rarely been used for the same purpose; however, head-worn recorders (e.g. Night Cap, ARES, ZEO) have been introduced with some success, and further advances in the miniaturization of sensors and circuits may lead to a more widespread use of such devices. We therefore investigated the utility of head actigraphy in differentiation between wakefulness and sleep.

Methods: The algorithm was developed on 22 subjects (RDI=27±29; range: 3-98) and cross-validated on 50 subjects (RDI=30±25; range: 2-103). Subjects underwent concurrent overnight recording with standard laboratory polysomnography (PSG) and the head-worn ARES recorder with integrated 3-axis digital accelerometer (ACT). The algorithm classified 30-second epochs as Wake or Sleep based on the intensity and duration of head movements in the current epoch and three epochs before and after it. PSG recordings were manually scored according to the AASM criteria. Epoch-by-epoch comparisons (n=36,991) were per¬formed and sensitivity (Se), specificity (Sp), agreement (Ag) and kappa calculated. PSG-ACT differences in sleep latency (SL), total sleep time (TST) and sleep efficiency (SE) were tested with paired t-test, and impact of RDI on per¬formance with Pearson correlation coefficient and ANOVA.

Results: The algorithm's performance was similar in the development (Se:67%;Sp:91%;Ag:86%;kappa=0.57) and validation group (Se:67%;Sp:88%;Ag:84%;kappa=0.54). Differences in TST (PSG - ACT: -0.7±34min; range:-84 to +86min) and SE (PSG - ACT= -1±10%; range=- 26 to 21%) were non-significant, but head actigraphy slightly underestimated SL (PSG - ACT= 2±6min; range=-15 to 30 min; p=0.003). Performance was not significantly affected by RDI in mild and moderate OSA (RDI<40 h-1), but deteriorated on average by 4% for RDI>40 h-1.

Conclusion: Accuracy of sleep/wake classification with head actigraphy is similar to that reported for wrist actigraphs.

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0318

FREE HOME SLEEP SCREENING WITH LEVEL III DEVICE TO RAISE AWARENESS OF OBSTRUCTIVE SLEEP APNEA

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Introduction: Bellin Health decided to do community education and offer free home level III sleep screenings. The intent was to provide free data to patients and providers proving the necessity for an in-lab polysomnogram. Bellin Sleep Center screened 985 persons from 2008-2010 representing communities throughout Northeast WI.

Methods: The Medical Director and Team Leader for the Bellin Sleep Center started visiting PCP and Specialty Care offices and informing doctors and staff about sleep apnea, sleep screening and testing offered at the Bellin Sleep Center. This resulted in requests to place home sleep screening devices in various community clinics in the Bellin Health System. We also went to various community events promoting the home screening to the general public.

Results: All patients with an AHI of greater than 5 were recommended for a formal split-night polysomnogram by the Medical Director, although not all chose to have further testing. In 2008, the Sleep Center sent out 27 home sleep screening devices, of these 10 people had an AHI (Apnea Hypopnea Index) of 5 or greater. 60% of those people returned to Bellin Sleep Center for an in-lab polysomnogram. In 2009, 208 sleep screening were done and 138 patients had an AHI of 5 or greater. 58% of those people returned to the sleep center for a polysomnogram. In 2010, 750 sleep screenings were done, of these 514 had an AHI of 5 or greater. 48% of those people returned to the sleep center for a polysomnogram, which so far gave us 245 sleep studies.

Conclusion: Evidence shows community education has been a huge success. Our primary care physicians have been further educated to look for signs and symptoms of obstructive sleep apnea. The opportunity allows the patient a free evaluation to make an educated decision in their healthcare. We are gaining acceptance of home sleep evaluations while earning the respect of the area physician and community.

0319

RELIABILITY OF SLEEP SPINDLE IDENTIFICATION BY EXPERTS, NON-EXPERTS AND AUTOMATED METHODS

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Introduction: A sleep spindle is a brief (0.5 to 1.5sec) burst of brain activity in the sigma range (12-15Hz) that can be measured on the electroencephalogram (EEG). Sleep spindles are a defining hallmark of stage 2 sleep and can be identified by visual inspection of the EEG. Recently, spindles have been implicated in memory consolidation and arousal thresholds. Significant alterations in spindles are observed in schizophrenia, autism, epilepsy, mental retardation and sleep disorders. Annotating and analyzing EEG data from thousands of patients will be required to further understand the role of spindles in these processes. The purpose of this study is to quantitate and compare the precision and accuracy of visual spindle identification by experts, non-experts, and automated spindle-detection algorithms.

Methods: We have designed a novel web interface to allow the identification and annotation of sleep spindles in EEG data from stage 2 sleep. We recruited two groups of annotators to identify the presence and duration of sleep spindles: i) trained experts (Registered Polysomography Technologists - RPSGT) and ii) crowds of non-expert annotators who were trained using written instructions and were recruited through Amazon Mechanical Turk. We also developed techniques to consolidate multiple human annotations into a 'most correct' annotation, as well as statistical techniques to compare the quality of human collected spindle data with the results of previously-published automated spindle-detection algorithms.

Results: We find that there is a core set of spindles that can be easily detected by all methods. However, a sizeable subset of the spindles are difficult to identify, even by experts. We also find systematic differences between automated and human annotation methods.

Conclusion: The data suggest that the identification of spindles in EEG data is a difficult task. Differences exist in the reliability of spindles identified by experts, non-experts and automated methods of spindle detection.

0320

TRANSFORMED ATTRIBUTES FACILITATES AUTOMATIC SCORING OF EMOTIONAL TONE OF DREAMS

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Introduction: The goal of this research program is to develop an automatic scoring system of the emotional tone of dreams that will replace the subjectivity and inconsistency of human judging and improve the comparability of research on dreams from different laboratories. We previously demonstrated that a machine learning model, based on word associations, emotional progression and dreamer's ratings produced a moderate machine-human agreement on both a negative and positive scale. Improvement was made by adding adverb modified word-vectors (accompanying abstract). Here we attempt to further improve the accuracy by incorporating the mathematical transforms of all attributes to correct for possible skewed data distribution.

Methods: A human judge scored 457 dream reports on 1 to 4 negative and positive affect scales. Its reliability had been established with another experience judge (80% agreement). Our computer model was trained with 66% of 457 dream reports and tested on the remaining dreams on both scales. In the attribute extraction stage of the machine learning, the data was mathematically transformed with log, square and square-root functions.

Results: Cohen's kappa coefficient for computer-human agreement was applied. We found that compared to our previous results, the machine-human agreement remained at 78.7% (kappa 0.54) on the positive scale, but improved from 67.3% (kappa 0.55) to 69.2% (kappa 0.57) on the negative scale.

Conclusion: This study shows that transformed data improves automatic scoring for negative affect but not for positive affect. This may be due to the fact that the level of agreement was already high and close to human-human agreement. It will be interesting to test additional attributes to improve the model for negative scale. It will also be interesting to remove the dreamer's ratings from set of attributes, in order to have a system that solely depends on dream-report.

0321

ADVERB MODIFIERS IMPROVE AUTOMATIC SCORING OF EMOTIONAL TONE OF DREAMS

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Introduction: The goal of this research program is to develop an automatic scoring system of the emotional tone of dreams that will replace the subjectivity and inconsistency of human judging and improve the comparability of research on dreams from different laboratories. We previously demonstrated that a Logistic Regression model in machine learning, based on word associations, emotional progression and dreamer's own ratings produced a moderate machine-human agreement on both a negative (kappa 0.47) and a positive scale (kappa 0.52). Here we attempt to improve the accuracy by utilizing adverbs for their amplification quality.

Methods: A human judge scored 457 dream reports on 1 to 4 negative and positive affect scales. Its reliability had been established with another experience judge (80% agreement). Our computer model was trained with 66% of 457 dream reports and tested on the remaining dreams on both scales. The algorithm was expanded to incorporate attributes pertaining to the modifying power of adverbs. A sentence-parser was used to identify the words that adverbs modify. The adverb scalar was estimated by first rank ordering frequently used adverbs. The ranking was done by 6 undergraduates. The highest ranking adverb was assigned a value of 3, the lowest 0. The other 42 ranked adverbs were assigned linearly extrapolated values. The word's word-vector was multiplied by the adverb's scalar. These attributes were used to build the model.

Results: On the negative affect scale, the performance of human-machine agreement improved from 62% (kappa 0.47) to 67.3% (kappa 0.55). On the positive scale, the performance improved from 77% (kappa 0.52) to 78.7% (kappa 0.54).

Conclusion: The amplification properties did improve the performance of machine learning on both scales. The positive scale agreement is approaching the human-human agreement standard of 80%. Further attempts will be made to improve the performance on the negative scale.

0322

RELIABILITY OF ASSESSING MOOD IN THE CONTEXT OF SLEEP

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Introduction: Many instruments that assess mood include items about sleep, which may present confounds when evaluating mood in the context of sleep. Therefore, sleep questions are often removed from the

mood scale scores. The current study assessed the reliability of a mood measure with and without sleep-related items.

Methods: Online surveys querying mood, workload (e.g., exams, homework), and medication use during the two weeks prior were presented once biweekly after weeks 2, 6, 8, and 10 during the first semester of college; the survey was presented on 2 consecutive days after weeks 4 and 12. Analyses included 178 Brown University first-year students (mean surveys completed=5.41). Ages were 18-21 years (mean=18.1), and 108 were females.

Results: The reliability of a 6-item depressed mood scale (Kandell & Davies, Archives of General Psychiatry, 1982) was examined as 1) full scale; 2) full scale excluding an item assessing difficulties falling and staying asleep; and 3) full scale excluding the sleep difficulty item and a "tiredness" item. Intraclass correlations (ICC) were computed for consecutive-day assessments and separately for the 6 biweekly surveys. The reliability estimates (ICC) across biweekly assessments ranged from .65-.68, .64-.68, and .63-.67 for the 3 "scales," respectively. Thus, the ICC values for repeated assessments administered over 2+ weeks were stable and not a function of the particular weeks compared. Time between repeated assessments, however, was important as indicated by the ICC values for the 3 "scales" on day-to-day administrations, which were .91, .92, and .91 for week 4 and .88, .87, and .88 for week 12.

Conclusion: This analysis indicates stability in participant responses on a mood questionnaire with or without sleep and tiredness items across consecutive-day and bi-weekly administrations.

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0323

VALIDATION OF URDU VERSION OF THE EPWORTH SLEEPINESS SCALE

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Introduction: The Epworth Sleepiness Scale (ESS) is a questionnaire widely used in English speaking countries for assessment of subjective daytime sleepiness. Our purpose was to translate and validate the ESS for use in Urdu -speaking countries.

Methods: The original ESS was translated into the Urdu version (ESS-Ur) in three phases- translation and back translation, committee based translation, and testing in bilingual individuals, before final approval of the ESS- Urdu version. Subsequently, a prospective study was performed in 89 healthy bilingual subjects to assess the validity of the ESS-Ur version compared to the original ESS in the English version.

Results: Both English and Urdu versions of the ESS were administered to eighty nine subjects (67% women and 33% men). The mean composite Epworth score was 7.53 in English language and 7.7 in the ESS-Ur (p=.76). The ESS-Ur was highly correlated with the Epworth-English Sleepiness scale (rho=.938, p<.01).

Conclusion: Our study validates the ESS-Ur scale as an effective tool for measuring ESS in Urdu-speaking populations. Future studies assessing the validity of the ESS-Ur in patients with sleep disorders needs to be undertaken.

0324

REACTION TIME AND ERRORS ON THE PSYCHOMOTOR VIGILANCE TASK: THE INFLUENCE OF INTERSTIMULUS INTERVAL

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Introduction: The standard form of the Psychomotor Vigilance Task (PVT) is a 10 minute task with interstimulus intervals (ISI) ranging from 2 to 10 seconds. There is anecdotal evidence that short ISIs are associated with longer reaction times (RT). Short ISIs may lead a stimulus is presented before a participant is ready to respond and so result in longer RTs. The current study aims to investigate firstly whether there is an effect of ISI on RT and errors within the PVT and secondly if the proposed effect changes with time of the day, hours of prior wake or time on task (TOT).

Methods: Twelve male participants (22.42+/- 2.31 years) completed 49 PVTs across a single beat period of 7x 28h days of Forced Desynchrony. Participants were tested at 2.5 hour intervals each 28h day producing seven levels of prior wake.The endogenous circadian rhythm for each participant was estimated from continuous measurements of core body temperature. For analysis, RT from each reaction trial within the PVT was assigned to a one second ISI bin, a two minute TOT bin, a prior wake level, and one of six 60° divisions of the circadian cycle. The frequency of errors (false starts and lapses) were also calculated for each ISI group.

Results: A mixed models analysis was used to analyse the effect of ISI on RT. RTs that followed short ISIs (2 to 4 seconds) were significantly slower than RTs that followed longer ISIs. This main effect of ISI on RT was independent of the effects of time of the day, hours of prior wake and TOT. There were significant associations for both false starts and lapses with ISI group. The probability of a lapse was higher for short ISIs, while the probability of a false start (FS) increased as ISI increased.

Conclusion: The findings that short ISIs were associated with longer RTs is consistent with the theory that after a response is made time is needed to be ready for the next stimulus. While short ISIs were also associated with increased lapses, the likelihood of a FS may be due to some other effect. Short ISIs were not more sensitive to effects of PW, circadian phase or TOT. Hence the variance in RT scores due to ISI is independent of the variation caused by the sleep/wake drives- the sensitivity of interest within the PVT. Removing short ISIs from the PVT could reduce some unwanted variation but this may also change the dynamics (temporal uncertainly) of the test.

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0325

COMBINING LANE DEVIATION WITH STEERING METRICS OF SIMULATED DRIVING TO DETECT DRIVER DROWSINESS

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Introduction: Lane deviation metrics have frequently been used as an index of drowsy driving in cars and trucks. Here we show that metrics derived from steering performance constitute an additional dimension of driving performance, which when combined with lane deviation may non-invasively enhance the ability to detect driver drowsiness.

Methods: N=35 healthy adults (ages 22-39y; 12f) participated in a 2-week in-residence laboratory study, which included a practice day and

two 5-day simulated shift work periods separated by a rest break of one or two days. 11 subjects were assigned to a day shift condition (daily TIB 22:00-08:00), whereas 24 subjects were assigned to a night shift condition (daily TIB 10:00-20:00). In both day and night shift conditions, each shift work day included four 30min driving sessions, at fixed intervals over time of day (AM or PM depending on condition). Subjects drove a simulated Ford Taurus in a standardized scenario of rural highways in a high-fidelity driving simulator (PatrolSim IV, MPRI, Salt Lake City, UT). Ten straight, uneventful road segments with a speed limit of 55mph (cumulative driving time ~5min) were designated to extract 87 potential driving performance metrics (72Hz sampling).

Results: The variance in the data set of 35 subjects by 40 driving sessions by 87 metrics was examined with principal component analysis. This yielded two dominant dimensions of driving performance, which were represented by metrics reflecting steering variability and lane deviation, respectively. The steering dimension explained 39% of the variance and the lane dimension explained another 9% of the variance. Mixed-effects ANOVA revealed significant interactions of condition by time of day for the steering dimension (F=4.26, P<0.001) and lane dimension (F=3.01, P=0.006).

Conclusion: Steering-related metrics may provide more information about driving performance than lane-related metrics. Real-time drowsy driver detection may substantially improve with technologies incorporating steering-based driving metrics.

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0326

UNOBTRUSIVE TRACKING OF SLOW EYELID CLOSURES AS A MEASURE OF FATIGUE FROM SLEEP LOSS

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Introduction: Sleep loss results in deficits in behavioral alertness and cognitive performance. Techniques are needed that objectively and unobtrusively identify the presence of fatigue while people are engaged in safety-sensitive work. Double-blind controlled trials by our laboratory have found that tracking slow eyelid closures (i.e., PERCLOS) is one of the most reliable ways to detect reductions in behavioral alertness as measured by lapses of attention due to sleep loss. In a collaboration to develop an unobtrusive and practical way to track PERCLOS, we used video of the human face during Psychomotor Vigilance Test (PVT) performance to determine if a computational model-based tracker of eyelid closures based on optical computer recognition (OCR) could predict PVT lapses during sleep deprivation.

Methods: N=26 (ultimate N=40) healthy adult subjects (35±8y; 12f) completed a 3-night laboratory experiment and were randomized to either acute total sleep deprivation (TSD; 0h TIB) or no sleep deprivation (NSD; 9h TIB) on the second night. Subjects completed a 20-min PVT every 2h while awake. Images of the face were recorded during each PVT test bout using a high-definition digital camera. PERCLOS was automatically scored by a special OCR algorithm developed by Metaxas et al., and compared to human-scored PERCLOS values (i.e., manually scored frame-by-frame by 4 human scorers blinded to condition).

Results: Analyses of preliminary data from N=8 subjects suggest that the OCR algorithm can successfully track and score the state of the eyelid in an on-line, real-time manner, and detect the occurrence of PVT lapses of attention.

Conclusion: Early results suggest that the potential for an automated OCR detection algorithm using video of the face during performance is

promising. Development of an unobtrusive fatigue monitoring system will improve safety and performance in situations involving sleep loss.

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0327

COMPARING ESTIMATION TECHNIQUES FOR INDIVIDUALIZED FATIGUE MODEL PARAMETERS

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Introduction: A number of mathematical models of fatigue are available to make population-average predictions of cognitive performance. To also allow for prediction of individual subjects' performance, a statistical technique called Bayesian forecasting has been applied. This method relies on Bayesian priors, which reflect the population distribution of vulnerability to sleep loss and other relevant individual characteristics. In simple models with few individualizable parameters, Bayesian priors can be estimated with readily available, maximum likelihood-based, non-linear mixed-effects regression techniques. However, for more elaborate fatigue models, the computational demand of such techniques is overwhelming. Here we investigated an alternative method based on bootstrapping.

Methods: To generate a theoretically verifiable test case, we considered a linear random-effects model with one parameter. From this model, we simulated 100 data sets with N=10 subjects and 10 data points per subject, with a true mean of 10, true between-subject variance of 1, and true within-subject variance of 0.1. We re-estimated the population mean, between-subject variance and within-subject variance, and compared results from bootstrapping to a standard theoretical method of moments estimator by examining the bias and variance for the two estimation techniques.

Results: The bootstrapping method yielded an estimated mean (±s.e.) of 9.9±0.3, an estimated between-subject variance of 1.0±0.3, and an estimated within-subject variance of 0.10±0.01. The method of moments estimator yielded an estimated mean of 10.0±0.3, an estimated between-subject variance of 1.0±0.5, and an estimated within-subject variance of 0.10±0.01.

Conclusion: The bootstrapping method and the method of moments estimator yielded highly comparable results. Thus, our simulation provided evidence that bootstrapping is viable as a method to estimate population variance parameters for use as Bayesian priors in individualized predictions of fatigue.

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0328

REPLICABILITY OF INTERSTITIAL GLUCOSE PROFILES RECORDED WITH A SUBCUTANEOUS GLUCOSE MONITOR

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Introduction: We implemented the Medtronic *i*Pro subcutaneous glucose monitor to measure 24h glucose profiles in the laboratory. These monitors were chosen for their small size and ability to calibrate to absolute levels based on concurrent, episodic plasma glucose samples. We examined the replicability of the calibrated subcutaneous glucose data collected with this device across repeated 24h recordings within subjects.

Methods: N=12 healthy males (ages 28.1±4.8y) participated in a strictly controlled in-residence laboratory experiment. After two baseline days

with 10h nighttime sleep (TIB 22:00-08:00), subjects were given a 5h nap (TIB 15:00-20:00), and underwent 5 days of night work with daytime sleep (TIB 10:00-20:00). Subjects then had a recovery period, which began with a 5h nap (TIB 10:00-15:00) and was followed by 10h nighttime sleep (TIB 22:00-08:00). On the second baseline day and after recovery, 24h glucose profiles were measured in interstitial fluid (sampled every 5 minutes), using the subcutaneous glucose monitor inserted into an area of the lower back accommodating subcutaneous placement while minimizing catheter movement due to pressure from clothing. Additionally, blood was taken at 2h intervals by intravenous catheter, spun, aliquoted, stored at −80°C, and assayed for glucose by Biovision Glucose Assay. Subjects were mobile during scheduled wakefulness; meals provided were identical for the two measurement days to control for carbohydrate intake.

Results: The intravenous glucose levels were entered into Medtronic glucose software to calibrate the interstitial glucose profiles. These profiles were analyzed using mixed-effects ANOVA to compare baseline glucose traces to post-recovery traces. Over all subjects, the baseline glucose trace explained 4.8% of the variance in the post-recovery trace. Analyzing only the two subjects with the least noisy data, the baseline trace explained 44.4% of the variance in the post-recovery trace.

Conclusion: Although in specific cases, 24h subcutaneous glucose profiles were replicable within subjects, this was not true in general. Post-recovery glucose profiles may have differed from baseline profiles due to the intervening night work schedule. Even so, the data seemed particularly noisy, potentially because subjects were ambulatory, which may have resulted in movement artifact. This could be mitigated by keeping subjects stationary and/or changing catheter placement location.

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0329

DETECTION OF HYPOVENTILATION BY CONTINUOUS MONITORING OF MAIN STREAM END-TIDAL CO2 IN OBESE PATIENTS WITH SUSPECTED SLEEP APNEA

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Introduction: Hypoventilation is considered both a serious co-morbidity and consequence of sleep apnea, which increases with prevalence in obese patients. It is substantially under-diagnosed prior to the advent of clinical respiratory failure. We evaluated the incidence of a new diagnosis of hypoventilation using the systematic monitoring of main stream end-tidal CO_2 (ETCO2) the extent of under-diagnosis.

Methods: Three hundred eighty-four community-based obese adults with a body mass index (BMI) of 30 kg/m2 or more were referred for clinically suspected sleep apnea. All patients were monitored with nocturnal polysomnography over a 17-month period. Participants were evaluated by a sleep medicine specialist, questionnaire and one night of polysomnography. Main stream ETCO2 was monitored on all patients, including during the diagnostic portion of split-night polysomnography.

Results: Patients were a mean (SD) age of 50.5 (SD 11.9) years and 71.4% were men. The mean apnea-hypopnea index was 53.0(SD 37.0) and 85.4% of patients met diagnostic criteria for at least moderate obstructive sleep apnea. Of the patients with obesity, 233 (60.7% of 384) had a BMI of 30-35.9 kg/m2, 83 (21.6% of 384) had a BMI of 36-40.9 kg/m2 and 68 (17.7% of 384) had a BMI of 41 kg/m2 or more. Overall, 23 (6.0% of 384) had at least 10% of total sleep time with an ETCO2 of 50mmHg or higher. With increasing obesity, the number with this degree of hypoventilation was 6 (2.6% of BMI 30-35.9), 5 (6.0% of BMI 36-40.9), and 12 (17.6 % of BMI 41 or more). None of these patients were known for hypoventilation prior to polysomnography.

Conclusion: We conclude that hypoventilation is frequent in patients with obesity, and that continuous monitoring of main stream ETCO2 facilitates diagnoses that were previously undiagnosed.

0330

A PILOT EVALUATION OF A NOVEL SCREENING TOOL FOR SLEEP RELATED BREATHING DISORDERS

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Introduction: Polysomnography (PSG) is the standard procedure for the diagnosis of sleep related breathing disorders (SRDB) and patients are typically referred for overnight studies when they are identified as being at risk by a clinician. Various tools are in use today to identify patients at risk for SRDB and refer them subsequently for studies. The ASA (American Society of Anesthesiologists) and other professional bodies have published guidelines calling for the recognition of patients suffering from SRDB during perioperative care. The Capnostream20p capnograph/pulse oximeter with SSDx algorithm is used in many hospital type environments whenever patient monitoring is required. The monitor provides an Apnea Index (AI), based on summation of the no-breath events per hour recognized by the capnograph, and an Oxygen Desaturation Index (ODI), using pulse oximetry. The information is presented in a simple summary report. The purpose of our evaluation was to assess the level of agreement between the indices generated by the device and overnight polysomnograph studies.

Methods: During routine overnight sleep studies 39 adult patients were monitored with the device. The sleep study was interpreted by a trained clinician who was blinded to the device. The AI and ODI values generated by the device were compared to the sleep study outcomes.

Results: A statistically significant model using the maximal AI and ODI values to predict OSA was defined. At a cut-off point of 19 - (ODI max+AI max) >19., sensitivity equals 0.87 and specificity 0.82. The PPV with actual prevalence of 0.68 (per the clinical data gathered) equals 0.91 and NPV = 0.75.

Conclusion: The results indicated that the device showed high sensitivity and specificity, and hence can be used as a tool for screening and assisting in the diagnosis of adult patients with medium and severe Obstructive Sleep Apnea in the hospital environment.

Support (If Any): Oredion Medical 1978 LTD

0331

OBSTRUCTIVE SLEEP APNEA PREDICTION BY BREATH SOUND ANALYSIS DURING WAKEFULNESS

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Introduction: Obstructive sleep apnea (OSA) is highly prevalent in the general population. While prompt initiation of treatment is particularly important for patients with severe OSA, only about 30% of the patients referred to a sleep lab are found to be in that category. Although there are clinical algorithms that can predict the likelihood of a patient having OSA, there are no easy clinical or laboratory predictors for the severity of OSA other than a sleep study. The goal of this study was to investigate the feasibility of developing a fast, simple and accurate screening tool for stratification of severity of OSA during wakefulness.

Methods: We studied 35 OSA patients with various degrees of severity and 17 age-matched control subjects, who were also tested by full-night polysomnography (PSG) for validation. The subjects were instructed to breathe, once through their nose and once through their mouth with a nose clip in place, at their normal breathing level for at least 5 breaths, and then breathe at the their maximum flow level for another 5 breaths. The breath sound signals were picked up by a Sony (ECM-77B) microphone placed over the neck and digitized at 10240 Hz rate. The recordings were repeated in two body positions: sitting upright, and supine. Data were analyzed using spectral and waveform fractal dimension techniques followed by statistical analysis to extract the most significant features for stratification of OSA severity.

Results: Several sound features were found to be statistically significant between the OSA and non-OSA groups. Using Maximum Relevancy Minimum Redundancy method, we reduced the number of features to two. Unsupervised clustering of the two most significant features showed an overall accuracy of over 84% (sensitivity=88%, specificity=80%) for separating healthy from OSA patients as well as stratification of the OSA severity among the patients group.

Conclusion: The results hold promise in sound analysis of different breathing maneuvers for OSA screening during wakefulness. It is known that OSA patients on average have smaller and more collapsible pharynx. This is compensated by the increased dilator muscle activity during wakefulness. They tend to have more negative pharyngeal pressure, which is detectable by breathing sound through the nose due to higher resistance. Given that breath sounds are directly related to the pharyngeal pressure, our proposed method is sensitive to the severity of OSA even during wakefulness.

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0332

THE RELATIONSHIP BETWEEN TRACHEAL RESPIRATORY SOUNDS AND FLOW IN OSA PATIENTS DURING SLEEP

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Introduction: One of the main applications of acoustical flow estimation is sleep apnea detection and monitoring. Although acoustical flow estimation was investigated extensively, all of the previous studies were focused on data of healthy individuals during wakefulness. The goals of this study were to investigate the flow-sound relationship in OSA patients during sleep and wakefulness and to examine the accuracy of acoustical flow estimation algorithms during sleep.

Methods: We studied tracheal sound, flow, and body positions from 13 patients referred for full night sleep study. For every individual, the relationship between tracheal sound's average power and flow were investigated during sleep and wakefulness at different body positions. Furthermore, the flow-sound model parameters were estimated based on two calibration schemes using data recorded during either wakefulness or sleep; the flow estimation accuracy with each calibration approach was compared.

Results: The results show that during sleep and wakefulness, flow-sound relationship follows a power law, but with different parameters. Therefore, if the model is calibrated using wakefulness data, the flow estimation error would be high during sleep. On the other hand, when the calibration parameters are extracted from data recordings during sleep, the flow estimation error remains less than 10%.

Conclusion: The results confirm reliability of the acoustical flow estimation for investigating flow variations in OSA patients during both sleep and wakefulness. However during sleep, the model parameters should be extracted from sleep data to have small errors. The variations of flow-sound relationship from wakefulness to sleep may be used to assess the changes in the breathing control mechanisms during sleep.

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0333

EFFECT OF ADENOTONSILLECTOMY ON CORTICAL PROCESSING OF RESPIRATORY AFFERENT STIMULI DURING SLEEP IN CHILDREN WITH THE OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Children with obstructive sleep apnea syndrome (OSAS) have impaired cortical processing of respiratory afferent stimuli manifested by blunted respiratory-related evoked potentials (RREP). However, whether the impairment in the cortical processing is restricted to respiratory stimuli, or whether it is reversible after successful treatment, is unknown. We hypothesized that 1) children with OSAS have normal cortical processing of non-respiratory (auditory) stimuli during sleep, manifested by normal auditory evoked potentials (AEP); 2) children with OSAS would show normalization of RREP responses compared to normal children during sleep after adenotonsillectomy.

Methods: Fifteen children with OSAS and 6 controls aged 5-16 years old were studied. Six children with OSAS repeated the test 2-3 months after surgery. Subjects slept wearing a mask connected to a nonrebreathing valve. Multiple 400 ms inspiratory occlusions were performed during N2, N3 and R sleep. Auditory stimuli were applied as a monotonous series of 80 dB, 1000 Hz, 50 msec tone pips, with a variable inter-stimulus interval of 15-30 sec during those sleep stages when occlusions were not applied. Surface EEG activity was averaged and RREP and AEP peak amplitudes and latencies were analyzed using mixed effects models.

Results: Group effect on RREP N350 and N550 amplitude was significant. The average amplitudes of RREP N350 or N550 for controls were significantly higher than OSAS before surgery, but no difference exist between controls and OSAS after surgery. For OSAS, the amplitudes of RREP N550 and P900 increased significantly after surgery. Group effect on AEP components was not significant.

Conclusion: Children with OSAS have specific abnormalities of respiratory afferent pathways with intact non-respiratory (auditory) pathways. These abnormalities can be at least partially reversed by successful surgical treatment, suggesting that the impairments are secondary to OSAS rather than congenital.

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0334

SELECTION OF PATIENTS FOR ORAL APPLIANCE THERAPY USING MANDIBULAR PROTRUSION DURING SLEEP

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Introduction: Mandibular protruding oral appliances provide a convenient, well-tolerated therapy for obstructive sleep apnea (OSA). However, not all apneics are successfully treated by this therapeutic modality, and inability to select suitable patients has proven to be a major roadblock to widespread adoption of this approach. We have evaluated the predictive accuracy of a mandibular protruding device (Zephyr Sleep Technologies) in a polysmnographic titration study to correctly identify patients who will and will not experience successful treatment with a custom-fitted mandibular protruder (MAS, SomnoMed).

Methods: Consecutive patients (n=18) with a range of severity of OAS underwent an overnight PSG titration study in which the mandible was progressively protruded until all evidence of obstruction was eliminated, if possible. The PSG data for each patient were classified as favorable (obstruction eliminated), unfavorable (obstruction persisted) and inconclusive. All patients were fitted with the therapeutic device by a blinded dentist and received two nights of portable monitoring with a well-validated recorder (Sagatech).

Results: The results for patients in the favorable (n=6) and unfavorable (n=8) categories were flawless, i.e., all of the former were therapeutic successes (RDI<10 hr.-1) and all the latter were therapeutic failures (RDI>10hr.-1), yielding highly significant predictive accuracy (P<.001). Patients with inconclusive PSG test results (n=4) had mixed outcomes, two successes and two failures.

Conclusion: We conclude that mandibular protrusion titration in a PSG setting can prospectively predict outcome with oral appliance therapy with substantial accuracy.

Support (If Any): Supported by a Government of Alberta grant to Zephyr Sleep Technologies.

0335

LONG TERM USE OF A NASAL EXPIRATORY POSITIVE AIRWAY PRESSURE (EPAP) DEVICE AS A TREATMENT FOR OBSTRUCTIVE SLEEP APNEA (OSA)

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Introduction: Obstructive sleep apnea (OSA) is a common disorder often resulting in adverse cardiovascular consequences, daytime sleepiness, and disturbed nocturnal sleep of the patient and bed partner. An expiratory positive airway pressure (EPAP) nasal device (PROVENT® Therapy, Ventus Medical Inc., Belmont, CA) has been developed to provide a new therapeutic option for OSA patients. Prior studies have documented safety and efficacy, including a large multi-center, randomized, double blind, sham controlled trial with three month follow-up. An extension of the three month study was conducted to evaluate the long-term durability of EPAP treatment response after 12 months of follow-up.

Methods: Patients in the EPAP arm of the randomized study who met adherence and efficacy criteria were enrolled. Polysomnography on the patients wearing the device was performed after 12 months of treatment. Subjective sleepiness was evaluated with the Epworth Sleepiness Scale and patients used a daily diary to record compliance with prescribed treatment. The 12 month results were compared against baseline results from the initial three-month randomized trial.

Results: Thirteen sites enrolled 41 patients; 7 terminated the study before 12 months, leaving 34 in the ITT analysis group. The median AHI was reduced from 15.7 to 4.7 events/hour (week 1 device-off versus month 12 device-on). The decrease in the AHI (median) was 71.3% (p<0.001). The proportion of sleep time with snoring was reduced by 74.4% (p<0.001). Over 12 months of EPAP treatment, the Epworth Sleepiness Scale decreased from 11.1 ± 4.2 to 6.0 ± 3.2 (p <0.001) and the median percentage of reported nights used (entire night) was 89.3%.

Conclusion: The nasal EPAP device significantly reduced the AHI, snoring duration and improved subjective daytime sleepiness after 12 months of treatment. Long-term adherence to EPAP treatment was excellent.

0336

UPPER AIRWAY RESPONSES TO HYPOGLOSSAL NERVE STIMULATION DURING SLEEP IN OBSTRUCTIVE SLEEP APNEA

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Introduction: Hypoglossal nerve stimulation (HGNS) can recruit the lingual musculature during sleep, reduce pharyngeal collapsibility and treat obstructive sleep apnea (OSA). Nevertheless, responses to graded increases in HGNS intensity have not been characterized. We hypothesized that increasing levels of HGNS would produce progressive relief of upper airway obstruction during sleep.

Methods: Eight patients with moderate to severe OSA were implanted with a novel HGNS system (HGNS™, Apnex Medical, Inc.). HGNS was applied during non-REM sleep over a range of current amplitudes (mA) with fixed frequency and pulse width. Inspirations were stimulated repeatedly at each current level on alternating breaths. Maximal inspiratory airflow (VImax) and the presence/absence of inspiratory airflow limitation (IFL) were assessed in stimulated and unstimulated breaths at each HGNS level. Titration responses were characterized by the (a) baseline and peak VImax response to HGNS, (b) mA at recruitment threshold and peak response, (c) increase in VImax from baseline to peak (ΔVImax) and (d) plateauing of VImax with further increases in current and the elimination of IFL.

Results: VImax increased linearly from a HGNS recruitment threshold of 0.95±0.40mA (mean±SD) to a peak response at 1.36±0.35mA. VImax rose from a baseline of 211±137mL/s to a peak of 557±55mL/s (ΔVImax = 347±147mL/s), and decreased to baseline levels immediately after stimulation. HGNS completely or nearly completely eliminated IFL at the peak VImax in 88% of patients, and VImax plateaued thereafter in 50% of patients.

Conclusion: We conclude that HGNS produced marked increases in airflow over a narrow current range without arousing patients from sleep, indicating substantial improvements in pharyngeal patency. The increases in airflow were of sufficient magnitude to eliminate upper airway obstruction (IFL) in the majority of breaths and patients, suggesting potential efficacy of HGNS across a broad range of OSA disease severity.

Support (If Any): Apnex Medical

0337

THE INFLUENCE OF NASAL ALTERATIONS IN ADHERENCE TO THE CONTINUOUS POSITIVE AIRWAY PRESSURE IN OBSTRUCTIVE SLEEP APNEA PATIENTS

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Introduction: Studies examining the influence of the alterations in the upper airway involved in continuous positive airway pressure (CPAP) adherence are controversial, and they did not use different evaluation techniques. Therefore, we attempted to assess the influence of subjective and objective nasal alterations in patient adherence to the CPAP in the treatment of obstructive sleep apnea (OSA).

Methods: This is a prospective investigation examining 34 patients with moderate to severe OSA who were recommended for CPAP treatment. The patients answered questionnaires and underwent a physical examination, flexible nasofibroscopy, nasal peak inspiratory flow, acoustic rhinometrics, and polysomnography for pressure CPAP device titration. After titration, the patients proceeded to use the CPAP with a pressure-based timer device and were observed for 6 months under supervision and education program. Those patients who stopped using the CPAP device by the sixth month and those who made use of the device for fewer than 4 hours per night were considered poor users.

Results: 11 (33.4%) patients were female and 23 (67.6%) were male. The mean age was 53.1 ± 9.1 years. 16 (47.1%) had good adherence (average of hours/night: 5.7 ± 1.5) and 18 (52.9%) had poor adherence (average of hours/night: 1.6 ± 1.3). Comparing good adherence with poor adherence groups the former had higher BMI (30.4±4.8 vs 27.0±4.0 Kg/m2; p=0.030), larger cervical circumference (39.5±3.9 vs 36.0±3,1 cm; p=0.006), higher apnea and hypopnea index per hour of sleep (53±25 vs 37.8±22.3; p=0.032) and lower minimum oxyhemoglobin saturation (75.4±11.0 vs 82.8±6.9; p= 0.041). No differences were observed between the groups in any of the subjective and objective nasal assessments.

Conclusion: The different nasal parameters evaluated were not found to be associated with CPAP adherence in this group of moderate to severe OSA patients.

Support (If Any): AFIP, FAPESP/CEPID and CNPq

0338

EXPLORING PATTERNS OF CIRCADIAN USAGE OF POSITIVE AIRWAY PRESSURE DEVICES COLLABORATIVELY WITH PATIENTS WITH OSA AIDS IN INDIVIDUALIZED TROUBLESHOOTING AND INCREASES ADHERENCE - TREASURES AT OUR FINGER TIPS

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Introduction: Positive airway pressure (PAP) therapy is commonly prescribed for obstructive sleep apnea. However patients have often difficulties adhering to therapy. Newer generations of PAP devices track usage and treatment parameters. Summary statistics and graphic displays of different parameters are available for download. In this report, typical patterns of use in graphic circadian usage displays and identification of individual barriers are described.

Methods: Case series. Exploration of variability in circadian usage displays in clinic visits.

Results: Limited adherence to PAP therapy can be related to behavioral, technical or comorbid conditions. Graphic circadian usage displays offer insight into usage patterns such as variability in usage onset, usage interruptions and usage off-set. Collaborative exploration of graphic circadian usage patterns with open-ended, non-judgmental questioning allows identification of individual patient's barriers. Behavioral barriers (e.g. delaying PAP usage by falling asleep viewing TV or ending usage early after nocturia) can be identified. Technical difficulties - such as inappropriate pressure settings, mask fit, device malfunction (e.g. "water damage") - and comorbid conditions (e.g. chronic liver disease) can lead to easily noticeable variability in usage pattern and other download parameters. Six examples of different typical circadian usage patterns demonstrate how patient-centered recognition of barriers, subsequent troubleshooting and collaborative goal setting can lead to improved adherence measurable in repeat downloads. Depending on the importance of the identified barrier and success of the chosen interventions increases in median daily usage of up to 4 hours can be observed.

Conclusion: Collaborative exploration of circadian usage patterns, identification of individual barriers to PAP therapy, collaborative goal setting and repeat download are helpful steps in increasing individual adherence to PAP therapy. Circadian usage data and other elements of downloads are valuable in identifying device malfunction. Downloads can be used as feed-back, motivational and educational tool.

0339

THE EFFECT OF 3-4 WEEKS OF CONTINUOUS POSITIVE AIRWAY PRESSURE ACCLIMATIZATION ON EARLY COMPLIANCE

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Introduction: Effectiveness of Continuous Positive Airway Pressure (CPAP) as a treatment for Obstructive Sleep Apnea (OSA) can be limited by poor compliance. Potential PAP titration candidates should receive adequate PAP education, hands-on demonstration, careful mask fitting, and acclimatization during the night of the titration study. Our research evaluates the effect of 3-4 weeks of acclimatization after PSG but before the titration night, on CPAP compliance.

Methods: Consecutive adult OSA patients were included in two groups. Group A: Patients who had an acclimatization of 3-4 weeks on CPAP pressures of 8-10 cmH2O before their titration studies, and Group B: Patients who underwent CPAP titration studies after the initial diagnostic polysomnograms without acclimatization (control). Compliance was evaluated for the first month of CPAP use after titration. Compliance measures obtained from the digital electronic compliance card included percent of days with more than 4 hours of use (CPAP-4H) and average

hours the device was used: (CPAP- H), using bivariate correlations and independent sample- t tests.

Results: 40 (20 in each group) patients were enrolled at the time of submission of this abstract. 25 males and 15 females) had compliance card information and were included in the data analysis. Mean (SD) for age =54.93 (12.69), and AHI= 32.98 (31.77). There were no significant differences of baseline characteristics (age, AHI, Lowest O2, PLMI) between the two groups. Although there were trends for higher CPAP-4H and CPAP- H in group A, when compared to group B, but they were not statistically significant. CPAP-4H (SD) = [68.27 % (23.34) vs. 62.95 % (28.42); p=0.522], CPAP-H (SD)=[5.45 (1.621) vs. 4.70 (1.89); p= 0.185].

Conclusion: We find no significant differences in compliance outcomes among OSA patients who were acclimated on 3-4 weeks of CPAP prior to their titration studies when compared to control. We find a trend of higher compliance in these patients and enrolling more patients will help increase the power of our study.

0340

THE ASSOCIATION OF POSITIVE AIRWAY PRESSURE (PAP) ADHERENCE WITH EPWORTH SLEEPINESS SCALE (ESS) AND QUALITY OF LIFE (QOL) IN SUBJECTS WITH OBSTRUCTIVE SLEEP APNEA (OSA) PARTICIPATING IN THE HOMEPAP STUDY

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Introduction: While PAP is efficacious in the treatment of OSA, resistance and intolerance to treatment limit its effectiveness. We investigated the association between PAP adherence with changes in ESS and SF-36 in the HomePAP study, a multi-center trial comparing PAP adherence in subjects with moderate to severe OSA (with an ESS >12) randomized to Lab- or Home-based evaluation and treatment.

Methods: 135 subjects completing 3-month follow-up were included. Associations between PAP adherence with percentage of subjects achieving ESS normalization (<10), and absolute/%change in ESS and SF-36 from baseline to 3-month were assessed using multivariable regression adjusting for age, sex, race, BMI, baseline AHI, baseline ESS, and optimal PAP pressure. Adherence measures included average hr nightly use, ≥4 hr of use per night, and >4 hr of use >70% of nights.

Results: Sample characteristics: age 48±12 yr, 62% Caucasian, 65% male, BMI 38.5±8.7 kg/m2, 39% ≥ college-educated, baseline ESS 14 ± 4, and AHI 43±26. ESS normalization was achieved in 65%, 78% and 92% of subjects with average nightly use of 0-4 hr, >4-6 hr, and >6 hr, respectively (p=0.003 for trend). After multivariable adjustment, subjects with PAP use ≥4 hr were 3-fold (OR: 3.0 [1.17, 7.71] more likely to have a normalized ESS score compared to subjects with poorer adherence. No association was observed between ESS and adherence defined as >4 hr of use >70% of nights. Younger subjects (p=0.023) and those with higher baseline AHI (p=0.013), and lower baseline ESS (p=0.043) were significantly more likely to achieve ESS normalization. No significant associations were seen for absolute/% ESS change or absolute/%SF-36 change.

Conclusion: Increased PAP adherence defined by >4 hr of use per night is associated with greater likelihood of ESS normalization but unassoci-

ated with changes in the SF-36. OSA severity and age also affect ESS normalization.

Support (If Any): American Sleep Medicine Foundation 38-PM-07 Grant: Portable Monitoring for the Diagnosis and Management of OSA

0341

EFFECT OF AN INTERNET INTERVENTION ON CPAP ADHERENCE

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Introduction: CPAP is the gold-standard treatment for OSA and it is generally accepted that CPAP adherence can be substantially improved. A key advantage to using CPAP is its ability to objectively measure and store both treatment adherence and efficacy data. New methods utilizing this data are needed to help increase CPAP adherence.

Methods: The Patient-Centered Collaborative Care (PC3) intervention is a multi-component intervention that is comprised of telemonitoring of objective CPAP adherence and efficacy data, an interactive website, and clinical support on an as needed basis. The PC3 patients were given access to an interactive website that provided nightly CPAP adherence, OSA and CPAP education; basic troubleshooting, and reference information about their CPAP device. Providers tracked PC3 patients' CPAP adherence via the ResTraxx Data Center website. The PC3 intervention was designed to supplement and not replace the clinical care process. The study was a randomized, controlled trial of Usual Care compared to PC3. Usual Care was comprised of a one-week phone call, a one-month visit (inclusive of data download and review), and any extra support requested by the participant.

Results: 241 patients newly diagnosed with OSA and prescribed CPAP were studied. At baseline, mean age=52.1±13.3, mean Apnea-Hypopnea Index=36.4±26, and mean body mass index= 32.4± 8.0 (mean±SD). There were no baseline differences in AHI, BMI or ESS between the groups. Nightly CPAP adherence measured at the 2-month timepoint was 3.3±2.4 and 4.1±2.3 hrs/night (p=.016) and at the 4-month time-point was 3.2±2.3 and 3.9±2.3 hrs/night (p=.035) for UC and PC3, respectively. There were no differences between the groups on follow-up measures of Patient Assessment of Chronic Illness Care, sleep apnea symptoms (e.g. Epworth Sleepiness Scale and Sleep Apnea Quality of Life Index), or depressive symptoms (e.g. Center for Epidemiologic Studies Depression Scale).

Conclusion: The PC3 intervention has the potential to help improve CPAP adherence in clinical settings.

0342

REM REBOUND AND CPAP COMPLIANCE

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Introduction: Obstructive sleep apnea causes significant disruption in sleep architecture and can lead to little to no REM sleep. Research suggests that REM rebound during initial CPAP treatment correlates with subjective improvement in sleep quality. This study examines whether REM rebound during initial CPAP treatment in a split night study also predicts better compliance with CPAP.

Methods: All split night studies performed in the Cleveland VA during 2008 and 2009 were examined. Excluded were studies that did not identify an optimal pressure setting or ended prematurely and patients did not follow up. Demographic and PSG findings including diagnostic and treatment REM percent and duration of longest REM period were examined. CPAP compliance, defined as percentage of days used more

than 4 hours, was obtained from the medical record. The cohort was divided into those with and without REM rebound in the treatment portion, defined as a single REM period ≥45 minutes or ≥30% treatment REM sleep that was ≥20% increase from baseline. Overall compliance was compared using two-sided student's t testing.

Results: 43 records were studied, 17 with REM rebound (RR) and 26 with no REM rebound (NRR). There was no difference in age, BMI or ESS between the two groups (p>0.05), There was no significant difference in diagnostic AHI between RR 42.3±26.8 and NRR 35.1±23.2, p=0.37. As defined there were significant differences in longest treatment REM period duration in RR and NRR groups, 55.1±17.4 and 18.6±12.4, respectively, p<0.01 and in treatment REM percentage in RR and NRR groups, 33.0±10.0 and 12.6±7.7, p<0,01. There were no differences in CPAP compliance (%) in RR and NRR groups, 37.8±32.4 and 41.0±38.5, respectively, p=0.774, nor in percentage days used CPAP, 62.5±33.9 and 60.6±35.0, p=0.86.

Conclusion: This study did not confirm the association of REM rebound on initial CPAP treatment and greater CPAP compliance.

0343

FINANCIAL INCENTIVE INCREASE CPAP ACCEPTANCE IN ADULTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Continuous positive airway pressure (CPAP) treatment is the most effective and cost-effective treatment for obstructive sleep apnea, yet many low-socioeconomic patients do not accept this technology. No study has explored the effect of financial incentive on CPAP acceptance in health care systems with cost sharing as an expenditure-control strategy. In the current study we explored whether financial incentive has a role in patients' decisions to accept CPAP.

Methods: Longitudinal interventional study. The group receiving financial incentive (n=137, 50.8±10.6 years, apnea hypopnea index (AHI) 38.7±19.9 events/hr) and the control group (n=121, 50.9±10.3 years, AHI 39.9±22 events/hr) underwent attendant titration and a two-week adaptation to CPAP. Patients in the control group paid a cost sharing of $230 to $660, depending on their supplementary medical insurance coverage, while patients in the financial incentive group paid a subsidized price of $55 for a CPAP device.

Results: CPAP acceptance was 43% greater (p=0.02) in the financial incentive group. Multivariable logistic regression (adjusting for age, gender, BMI) revealed that CPAP purchase among low socioeconomic people was influenced by financial incentive (OR, 95% CI) (4.98, 1.74-14.15), age (1.09, 1.03-1.14), AHI (30 vs. <30 events/hr) (5.13, 1.77-14.83), and family/friends having positive experience with CPAP (3.88, 1.01-18.89). Among average and high-income patients, CPAP purchase was determined by AHI (30 vs. <30 events/hr) (2.75, 1.18-6.47).

Conclusion: Minimizing cost sharing reduces a major barrier for acceptance of CPAP treatment among low-socioeconomic status patients. Thus, financial incentive should be applied as a policy to encourage CPAP treatment especially in this population.

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0344

THE EFFECTS OF INDIVIDUAL VERSUS GROUP EDUCATION ON CPAP ADHERENCE IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Despite its proven benefits, adherence to and acceptance of CPAP therapy remains suboptimal. Various educational strategies to

improve adherence have had inconsistent benefits. Education in group settings has been shown to improve outcomes in other disease states. The purpose of this study was to compare the impact of individual versus group educational programs on CPAP adherence.

Methods: Retrospective review of consecutive patients newly diagnosed with OSA between January 2009 and March 2010. All patients received extensive education prior to initiating CPAP therapy either individually or as part of a group educational program. We compared objective measures of CPAP use between these two groups.

Results: 1858 patients (996 group, 862 education) were included. 79.1% were men with a mean age of 47.4±10.5 years. Mean BMI and apnea-hypopnea index were 30.3±5.1 Kg/m2 and 31.9±22.2 events/hour, respectively. Mean baseline ESS was 13.1±5.2. Patients who underwent a group educational program had significantly greater use of CPAP. Specifically, percentage of nights CPAP was used (66.4% vs. 61.6%, p=0.022) and the hours used per night CPAP was utilized (4.0h vs. 3.7h, p=0.043) were greater in those undergoing group versus individual education. Discontinuation was also less common among those undergoing group education (15.6% vs. 10.0%, p<0.001). Regular use of CPAP was slightly greater in those who received group education (44.6% vs. 40.46%, p=0.09).

Conclusion: Compared to patients receiving individual CPAP education, those that participated in a group educational program were less likely to discontinue therapy and had greater adherence to CPAP. Group clinics not only reduce costs and increase access to care, they may also enhance the acceptance of and adherence to therapy. In sleep centers where individual counseling may not be available or feasible, group counseling provides a more efficient and potentially more efficacious educational strategy that can improve adherence to CPAP therapy.

0345

NEUROCOGNITIVE FUNCTIONING IN OBSTRUCTIVE SLEEP APNEA; (1) EFFECTS OF ARMODAFINIL ADMINISTERED PRIOR TO CONTINUOUS POSITIVE AIRWAY PRESSURE AND (2) EFFECTS OF CONTINUOUS POSITIVE AIRWAY PRESSURE AFTER DISCONTINUATION OF ARMODAFINIL

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Introduction: Obstructive sleep apnea (OSA) has been associated with deficits in neurocognitive function including attention, information processing speed, memory and executive function. Armodafinil has been shown to effectively reduce sleepiness and to improve vigilance and long-term memory when used in conjunction with CPAP. The current study was designed to assess the effects of armodafinil on neurocognitive function in newly diagnosed OSA patients with EDS during a 2-week "waiting period" prior to initiation of CPAP and to assess performance following 6-weeks of CPAP.

Methods: Sixty-nine newly diagnosed OSA patients, awaiting CPAP therapy, were randomized (1:1) to placebo or armodafinil (150 mg/day) treatment. Patients completed computer-based neuropsychological testing at baseline, after 2 weeks of drug treatment, and following 6-weeks of CPAP treatment.

Results: Compared to placebo, armodafinil improved vigilance (p=0.04). Similar improvement was seen on this vigilance measure following CPAP (p=0.03). Information processing speed and perceptual motor functioning was not affected by armodafinil, but improved significantly following CPAP. Treatment with armodafinil had no significant effects on measures of memory, except for a decline in performance on symbol-digit delayed recall (p=0.01). In contrast, following CPAP there was a trend for improved symbol-digit delayed recall (p=0.11) as well as a trend for improved learning on two other memory tasks. On one of the four delayed recall tests (Misplaced Objects) there was a decline with

CPAP (p=0.01). Executive function tasks showed improvements following both armodafinil and CPAP treatment.

Conclusion: Armodafinil improved alertness in untreated OSA patients prior to initiation of CPAP therapy. Improvements were also seen on measures of executive function but not on measures of memory. Performance declined on one of four measures of delayed recall. Treatment with CPAP resulted in improvements on measures of vigilance, information processing speed, perceptual motor speed, learning, and executive function, but not long-term memory.

0346

OBSTRUCTIVE SLEEP APNEA (OSA): COGNITION, QUALITY OF LIFE AND ADHERENCE TO POSITIVE AIRWAY PRESSURE (PAP) TREATMENT AFTER 18-MONTHS OBSERVATION TIME

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Introduction: Obstructive Sleep Apnea (OSA) is associated with neurocognitive and cardiovascular morbidities and reduced quality of life (QoL). Literature data on improvement after treatment are still mixed. Even if PAP treatment is the most effective treatment, adherence is often below expectations and is frequently a challenge for patients starting this psychologically impacting treatment. Aim of this study was to evaluate neurocognitive function, QoL and adherence to treatment in consecutive OSA patients compared to age-matched normal controls (BL) and to assess changes after 18-months of PAP treatment with C-flex.

Methods: 67 male untreated patients (mean age 50.3 ± 10.4, mean education level 11.1 ± 4.1) with severe OSA (mean AHI=55.1±22.8) and 15 normal controls matched on age, education and gender. Neurocognitive functioning (global cognitive functioning, attention, vigilance, short- and long-term memory, executive functions, visuo-constructional abilities), sleepiness, mood and QoL were assessed at BL in patients and controls. The same parameters as well as objective compliance to PAP in terms of hours of use per night and percentage of days of use were assessed by EncorePro software after 18-months of treatment.

Results: 10 patients were excluded from the analysis because of low compliance to PAP within the 18-months observation period. Patients showed significantly lower score than healthy subjects in all neurocognitive domains (p<.001) as well as in FOSQ (p<.001) and in the physical health dimension of SF-36. SF-36 general and psycho-emotional health resulted non significantly different than controls. All cognitive domains significantly improved after 18-months of treatment (p<.001). Sleepiness (Epworth Sleepiness Scale) as well as mood (Beck Depression Inventory) significantly improved (p<.001) over time. Also FOSQ (all subscales) and SF-36 (all dimensions) showed a significant improvement after 18-months (p<.001). During the 18-months mean adherence to PAP was 365.22±65.68 minutes and percentage of days of use was 88.46±15.1.

Conclusion: Our data showed that cognitive functions and QoL, all impaired when compared to normal controls at BL significantly improved after 18-months PAP treatment when patients, if adherent to the treatment with the device, are able to reach the scores of healthy subjects. Adherence to PAP can be considered the trigger of improvement both in cognition and QoL but it still remain a challenge for both patients and physicians.

0347

THE ASSOCIATION OF SLEEP-DISORDERED BREATHING AND COGNITIVE FUNCTION IS MODIFIED BY THE APOLIPOPROTEIN E-EPSILON4 ALLELE IN WISCONSIN SLEEP COHORT STUDY PARTICIPANTS

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Introduction: Sleep-disordered breathing is associated with decrements in cognitive function. Additionally, the Apolipoprotein E-4 (ApoE-epsilon4) allele is associated with cognitive decrements, as well as greater risk of SDB. We sought to determine if ApoE-epsilon4 status modifies the association of SDB with cognitive function in Wisconsin Sleep Cohort Study participants.

Methods: 765 adult subjects (44% female, age range 30-81 years), selected from an employed-population sample in 1988, were polysomnographically-assessed for SDB and also had cognitive evaluations at 4-year intervals (a total of 1857 studies). For this analysis, cognitive function protocols included the: Symbol-Digit Modalities Test; Auditory Verbal Learning Test; and Oral Word Fluency Test. ApoE genotype was determined using the polymerase chain reaction-restriction fragment length polymorphism method. To test whether ApoE genotype modifies the association of SDB and cognitive function, linear mixed-effects models regressed cognitive test scores on: SDB categories (apnea-hypopnea index [AHI]<5 events/hr; 5≤AHI<15; AHI≥15); ApoE-ε4 status; SDB category*ApoE interaction term; and age, gender, BMI, and education. Models accounted for the presence of multiple sleep studies per subject.

Results: 30% of subjects had at least one ApoE-ε4 allele. AHI was <5 events/hr in 62% of polysomnography studies; 22% had 5≤AHI<15; and 16% had AHI≥15. In regression analyses, the association of SDB and the Oral Word Fluency Test was modified by ApoE-epsilon4 carrier status (interaction p-value=0.03) such that ApoE-epsilon4-positive subjects (but not ApoE-epsilon4 negative subjects) in higher SDB categories had poorer fluency scores than subjects without SDB. Similarly, the word recognition score on the subscale of the Auditory Verbal Learning Test was modified by ApoE-epsilon4 carrier status (interaction p-value<0.001) such that ApoE-epsilon4-positive (but not negative) subjects in higher SDB categories had poorer word recognition scores than subjects without SDB.

Conclusion: In ApoE-epsilon4-positive subjects (but not ApoE-epsilon4-negative subjects), more severe SDB was associated with decrements in auditory-verbal learning and oral word fluency.

Support (If Any): 1UL1RR025011 R01HL62252

0348

AVERAGE OXYGEN SATURATION, VERBAL MEMORY AND EXECUTIVE FUNCTION IN A COMMUNITY-BASED HIGH RISK POPULATION IDENTIFIED BY THE BERLIN QUESTIONNAIRE

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Introduction: Cognitive functions in community-dwelling adults at high risk of obstructive sleep apnea have not been described, nor are associations between cognitive functions and obstructive sleep apnea severity fully understood. The study aimed to describe verbal memory and executive function in community-dwelling adults identified by the Berlin Questionnaire and to investigate associations between these cognitive domains and different obstructive sleep apnea severity indicators.

Methods: Among 29,258 age and gender stratified persons 30-65 years who received the Berlin Questionnaire by mail, 16,302 (55.7%) responded. The clinical sample (n = 290) was recruited from 1085 randomly drawn persons (56.1% males) at high risk of obstructive sleep apnea (mean age 48.2 years). Verbal memory was assessed by Rey Auditory Verbal Learning Test and executive function by Stroop test. Obstructive sleep apnea severity indicators were assessed by polysomnography.

Results: Mean (standard deviation) verbal learning score was 42.0 (8.9), mean interference time was 31.1 (12.7), median (25th percentile, 75th percentile) apnea-hypopnea index was 7.7 (2.4-22.2) and mean average oxygen saturation was 94.3 (2.0). Verbal learning score was independently associated with average oxygen saturation (β= 0.721, p = 0.025) and interference time was independently modified by an age-average oxygen saturation interaction (β= -0.087, p = 0.029) in multivariate linear regression models adjusted for putative confounders.

Conclusion: Verbal memory and executive function impairments were mild in community-dwelling adults at high risk of obstructive sleep apnea. Average oxygen saturation was the indicator of obstructive sleep apnea severity most strongly associated with cognitive function.

Support (If Any): The Akershus Sleep Apnea Project is supported by the South-Eastern Norway Regional Health Authority, grant number 2004219 and the University of Oslo, Norway.

0349

PREDICTORS OF NEW-ONSET SLEEP-DISORDERED BREATHING IN A BASELINE COHORT PRECISELY CHARACTERIZED AS FREE OF SDB: THE WISCONSIN SLEEP COHORT STUDY

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Introduction: Sleep-disordered breathing (SDB) is prevalent and associated with multiple clinically-relevant sequelae. We assessed risk of new-onset SDB over eight years of follow-up in Wisconsin Sleep Cohort subjects who were precisely-determined (by two baseline polysomnography studies) to be initially free of SDB.

Methods: Our baseline sample comprises 1524 subjects (30-60 years old) at initial sleep study. Subjects are restudied every 4 years. To ensure a baseline cohort free of SDB (apnea-hypopnea index [AHI]<5 events/hour) we identified subjects with two consecutive studies with an AHI<5. Poisson regression estimated relative risks of the relation¬ship between new-onset mild or worse SDB (new cases of AHI≥5 measured during 8 years of follow-up) and age, gender, overweight, and other variables. Using regression models, we also estimated risk of new-onset SDB in persons who were (and remained) normal weight to characterize the natural history of SDB in a population free of trends in increasing obesity prevalence.

Results: 519 subjects were initially free of SDB. In these subjects, the probability of developing new-onset SDB over an 8-year period in men was 0.25 (95% CI= 0.14-0.42); the risk in women was 0.15 (95% CI=0.08-0.26). Male to female relative risk was 1.7 (95% CI=1.1-2.5). Older age, smoking and alcohol use were not significantly associated with higher risk of new-onset SDB. Baseline overweight, and increasing weight, were associated with increasing risk of new-onset SDB. We estimate that, had the baseline cohort been (and remained) normal weight, the risk of new-onset SDB would have been approximately half the risk observed in the entire cohort: in men the 8-year risk would have been 0.13 (95% CI=0.07-0.26), and in women, 0.08 (95% CI=0.04-0.15).

Conclusion: Adults, especially overweight and male subjects, are at high risk for new-onset SDB. All examined ages were at comparable risk for developing new-onset SDB.

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0350

CLINICAL RECOGNITION OF OBSTRUCTIVE SLEEP APNEA IN A POPULATION-BASED SAMPLE

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Introduction: Historically most OSA has been clinically unrecognized and thus, untreated. Based on 1990s data, 6 - 15% of prevalent OSA, depending on severity, was clinically recognized in mixed gender populations. This under-recognition was attributed to limited physician awareness and limited access to sleep laboratory services, both of which have increased in the past decade.

Methods: A modified Berlin Questionnaire was completed by participants in a longitudinal population-based study in Olmsted County, Minnesota. The Berlin Questionnaire high risk classification was used as a surrogate for prevalent OSA. Those with clinically recognized OSA were identified by an electronic search using the resources of the Rochester Epidemiology Project and subsequent manual record review. Descriptive, bivariate and multivariate analyses were then used to determine rates clinical recognition, and factors associated with clinical recognition.

Results: Analysis in a mixed gender population demonstrated that OSA clinical recognition among those with prevalent OSA with a mild or greater severity was 22.7 % (95% CI 19.6 - 25.8%). Among those with prevalent OSA men are more than twice as likely to be recognized in bivariate analysis. Multivariate analysis in a mixed gender population identified length of formal education, and two measures of obesity, body mass index (BMI) and neck circumference, as significant predictors of clinical recognition. In gender specific analyses length of education and waist circumference predicted clinical recognition for men. Only BMI was predictive for women.

Conclusion: Clinical recognition of OSA has increased since reports using 1990s data. However, about 75% of prevalent OSA remains unrecognized and is thus untreated. Markers of obesity and education are predictive of clinical recognition.

0351

PREVALENCE OF SLEEP DISORDERED BREATHING IN MIDDLE-AGED GENERAL POPULATION: THE HYPNOLAUS STUDY

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Introduction: In studies from the 80's and 90's, the prevalence of sleep disordered breathing (SDB) in middle-aged general population is estimated at 9% in women and 27% in men. Considering the recent improvements in the sensitivity of recording techniques, our aim was to reevaluate the prevalence of SDB in the general population.

Methods: 505 subjects (47.1% women, 50.3±5.6 years old, BMI 25.7±4.4 kg/m2) participating in an ongoing population-based cohort study (HypnoLaus, Lausanne, Switzerland) underwent complete polysomnographic recordings at home and had an extensive clinical workup including Epworth Sleepiness score Score (ESS). Prevalence of SDB was determined according to apnea-hypopnea index (AHI) using two different scoring criteria: AASM 2007 and AASM 1999.

Results: With AASM 2007 criteria, prevalence of SDB with AHI thresholds of 5/h, 15/h and 30/h was 45.7%, 15,7%, and 6.3%, respectively in men, and 19.3%, 4.2%, and 0.8% respectively in women. Mean ESS score was 6.9±4.2 in men and 6.4±3.8 in women. 18% of the men and 12.6% of the women had an ESS >10. The prevalence of ESS>10 and OSA with the same thresholds (5/h, 15/h and 30/h) was 6.3%, 3.4%, and 0.4%, respectively in men and 2.1%, 1.3%, and 0% in women. With AASM 1999 criteria, prevalence of OSA with the same thresholds was 77.2%, 37.5%, and 14.6% in men and 51.3%, 15.1%, and 4.6% in women. Prevalence of OSA and ESS>10 was 12.0%, 6.7%, and 2.6% in men and 5.5%, 2.1%, and 0.4% in women.

Conclusion: In HypnoLaus population-based study, prevalence of SDB is much higher than previously reported, especially in middle-aged men. This appears to be due to differences in scoring criteria and to a higher sensitivity of nasal pressure sensors compared to thermocouples. These results warrant a reconsideration of the criteria for the definition of sleep disordered breathing.

0352

DEMOGRAPHIC CHARACTERISTICS IN CHINESE PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Many studies for data collected in consecutive patients mentioned that the average age in Caucasian with obstructive sleep apnea (OSA) is over fifty years old. Through individual clinic observation, Chinese patients with OSA appear to be younger and less obese, but possibly more severe, relative to Caucasian. These demographic characteristics for OSA in Chinese patients have not been emphasized in literatures.

Methods: We analyzed demographic data of age, sex, body mass index (BMI), apnea/hypopnea index (AHI) after routine polysomnographic recording in consecutive 1208 subjects (male 82%) who presented with suspicion of OSA and in consecutive 559 subjects (male 52%) with the chief complaint of insomnia.

Results: In OSA group for AHI greater than 30, the means of age, AHI, BMI and percentage were 44.7±11.6, 57.4±16.4, 28.7±11.2, and 46.9%, respectively; in OSAS with AHI less than 5, those means were 39.6±16.2, 2.3±1.3, 24.0±5.8, 16.4%. In insomnia group for AHI greater than 30, those values were 44.2±13.9, 50.7±15.0, 26.4±3.5, 8.2%, respectively, whereas the means for AHI less than 5 were 40.1±12.8, 1.9±1.5, 22.2±3.6, 63.3%.

Conclusion: The data reveal that, for severe OSA (AHI greater than 30), two groups even with different clinic features of OSA (47%) and insomnia (8%) have similar severity of OSA (AHI 57 vs. 51), age (44.7 vs. 44.2), and BMI (28.7 vs. 26.4). Relative to those values in Caucasian in some literatures, Chinese OSA patients are possibly younger, not that obese, and even more severe. Those basic demographic data suggest that it requires more extensively research for some biological high risk factors for Chinese OSA (e.g., craniofacial characteristics).

0353

SLEEP AND BREATHING:MANAGEMENT OF SLEEP APNEA PATIENTS IN THE PUBLIC HEALTH SYSTEM OF BRAZIL

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Introduction: The Obstructive Sleep Apnea (OSA) is a growing public health problem. Most patients remain undiagnosed and untreated. Polysomnography is the gold standard for diagnosis, however inaccessible and expensive for our population. The home polygraphy (HP) is a viable alternative. Objective: To describe an accessible model for diagnosis and treatment of OSA in patients from public health system of Brazil.

Methods: Patients referred to the sleep clinic of Heart Institute of University of Sao Paulo and evaluated after the Berlin questionnaire and the Epworth Sleepiness Scale (ESS), those with high probability of OSA performed to home polygraphy:Stardust II. This device assesses airflow, pulse oximetry, respiratory effort and body position. The severity of OSA was classified according to the apnea and hypopnea index (AHI) as mild (5-14), moderate (15-29) and severe (equal to or greater than 30 events/hour). Patients with severe OSA or moderate OSA more cardiovascular comorbidities were referred to CPAP. That moderate OSA without cardiovascular comorbidities were for speech therapy and mild OSA for weight loss.

Results: Caracteristics of the sample:56 patients, 70% male, mean age 53 years, mean body mass index: 32 ± 6.9 kg/m2. Comorbidities:current smoker 17. 9% (n=10), COPD 12. 5% (n=7), atrial fibrillation 12. 5% (n=7), CHF 16% (n=9), diabetes mellitus 19. 6% (n=11), CAD 19. 6% (n=11) and hypertension 60% (n=34). Average ESS: 12 (3-23); ESS $\geq$10 in 57% (n=32). Obese BMI $\geq$30 were 55% (n=31). Snoring: 82% (n=46). Married 67.9% (n=38). The mean AHI: 27 events/hour, with most of the sample was moderate to severe apnea. Those who had minimum oxygen saturation below 90% was 75% (n=42). Only 16% (n=9) had to repeat the examination and oximetry loss represented the mainly reason for the repetition in 88% (n=7). Unfortunately, due to financial constraints, few patients were using CPAP. Speech therapy was a therapeutic option for those with moderate OSA and without disease cardiovasculares. Dos seven patients referred to speech therapy, six join treatment

Conclusion: The home polygraph is an accessible model home for the management of obstructive sleep apnea patients in the public heathy system of Brazil and exercises techniques of speech therapy can help treat

0354

EFFECT OF ETHNICITY AND ACCULTURATION ON OBSTRUCTIVE SLEEP APNEA PREVALENCE AND SEVERITY IN NON-HISPANIC WHITES AND HISPANICS OF MEXICAN DESCENT IN SAN DIEGO COUNTY: PRELIMINARY FINDINGS

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Introduction: We studied the prevalence and severity of obstructive sleep apnea (OSA) in non-Hispanic whites (NHW) and Hispanics of Mexican Descent (HMD), and examined the effect of acculturation. We hypothesized that HMD would have a greater prevalence of OSA proportional to degree of acculturation.

Methods: Subjects were recruited using random digit dialing as part of the Sleep Health and Knowledge in U.S. Hispanics Study. Home polysomnography (PSG) was performed. The Short Acculturation Scale for Mexican Americans was used.

Results: We performed 363 PSGs (195 NHW and 168 HMD). Hispanics of Mexican descent were heavier (BMI 29.1±7.4 vs. 27.7±5, p=0.032) and younger (43. ±15.1 vs. 55.7±16.3 years old, p< 0.001) than NHW.

Obstructive sleep apnea (defined as AHI $\geq$ 5) was highly prevalent overall (66.9%). There was no difference in average AHI between NHW and HMD (19.8±22.5 and 20.4±24.2, p=0.79) or in the prevalence of OSA (Men 77.6% vs. 70.4%; women 58.6% vs. 55.2%. p=0.117). There was no difference in the prevalence of mild, moderate, or severe OSA (defined as AHI 5 to <15, $\geq$15 to <30, and $\geq$30, respectively) between NHW and HMD (29.7% vs. 19.6%; 19.5% vs. 16.1%; 21.5% vs. 26.8%, p=0.067, respectively). There was no significant difference in the prevalence and severity of OSA between the least and highly acculturated HMD (64.6% vs. 59.4%, mean AHI 20.8±24.8 vs. 19.8±23.5/hr, p>0.3). In logistic and linear regressions male sex, age, and BMI were independent predictors of OSA or AHI severity. Ethnicity was not a predictor after controlling for age, gender and BMI.

Conclusion: The prevalence of OSA was higher than previously reported, potentially accounted for by the obesity epidemic. There was no difference in the prevalence or severity of OSA between NHW and HMD. Acculturation did not affect the prevalence or severity of OSA.

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0355

SLEEP APNEA AND REM-LIKE SLEEP PROBLEMS: A UNIQUE HEALTH PROBLEM FOR HMONG IN WISCONSIN

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Introduction: In 1977, a high mortality rate of nocturnal unexplained death (SUNDS) was documented in Hmong immigrants. Sleep apnea and other sleep disorders were hypothesized as contributing factors to SUNDS. However,research on sleep problems of Hmong has been minimal. We compared sleep problems in a sample of 434 Hmong,age >30 years, with matched Wisconsin Sleep Cohort participants (WSC, n=1162) to determine if Hmong are at high risk for sleep disorders that could contribute to SUNDS.

Methods: Three Wisconsin population-based samples of Hmong were recruited in 1995-7 and surveyed on sleep habits and other factors. A subsample (n=37) underwent in-home polysomnography to determine apnea and hypopnea frequency (AHI).Multiple logistic regression was used to estimate odds ratios (OR) for predictors of self-reported (SR) habitual snoring and breathing pauses, both markers of sleep apnea.

Results: Prevalence of sleep apnea defined by AHI>5 was higher for Hmong (54%) vs WSCS (32%) (p<.01). In both Hmong and WSCS, BMI, male sex, and sleepiness were associated with habitual snoring. However, in the Hmong sample, sleep paralysis was also statistically significantly correlated with habitual snoring. More ethnic differences were found in exploring predictors of SR breathing pauses.In the WSCS,sex,age,and BMI were significant correlates of SR breathing pauses. Uniquely,in Hmong, the experience of a suffocating night spirit (OR=10), sleep paralysis (OR=8) and cataplexy-like symptoms (OR=39) (all p<.0001) were significant predictors of breathing pauses.

Conclusion: The prevalence of REM-like sleep problems are high in Hmong and associated with SR habitual snoring and breathing pauses. These markers of sleep apnea are strongly related to experiences of a night spirit (Dab Tsuam) that suffocates the sleeper (32% reporting frequent experiences). Ethnic differences in sleep problems and correlates of sleep apnea have importance in n screening Hmong and mandate both clinical and research attention.

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0356

PRELIMINARY REPORT: COGNITIVE IMPAIRMENT REFLECTED IN OBSTRUCTIVE SLEEP APNEA-HYPOPNEA AMONG MIDDLE-AGED KOREAN ADULTS

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Introduction: Patients with obsrtuctive sleep apnea-hypopnea (OSAH) suffer from repeated obstruction of upper airway, which consequently induces sleep fragmentation and nocturnal hypoxemia. As recent findings indicate ample evidences for cognitive impairment associated with sleep disturbances, we aim to investigate the resulting neurocognitive consequences of OSAH in a population-based level.
Methods: Ninety one participants in ages 52 to 75 (mean age = 58; 42% male), as part of an ongoing Korean Genome and Epidemiology Study (KoGES) underwent a neuropsychological test battery representing attention, executive function, verbal memory, visual memory, and verbal fluency. Presence of OSAH was evaluated by home portable polysomnography, and accordindg to the results, participants were divided into three different groups:48 in non-OSAH(AHI<5), 28 in mild OSAH (5≤AHI<15), and 15 in moderate-to-severe OSAH (AHI>15).
Results: There was no meaningful deviation of age, sex, and education levels between the three groups. Nonetheless, increasing severity of OSAH displayed significant differences in measures of executive function (F=3.930, P=0.023); the moderate-to-severe OSAH group presented the longest time of completion on the Trail Making Test (193.7±112.5 sec), followed by the mild group (134.4±82.6 sec) and lastly, the non-OSAH group (mean = 122.7±65.0), but no additional differences were observed in other neurocognitive domains thus far.
Conclusion: Based on these preliminary results, we found that severity of OSAH parallels with deficits in executive function defined by a neuropsychological test.

0357

CEPHALOMETRIC ANALYSIS OF OBSTRUCTIVE SLEEP APNEA SYNDROME IN ASIAN CHILDREN

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Introduction: Obstructive sleep apnea syndrome (OSAS) is a common disorder in childhood. The goal of this study is to analyze the relationship between the cephalometrics and the overnight polysomnography in Asian children.
Methods: We collected data from 50 children between 4 to 13 years old. In cephalometrics, we measured 9 angles, 10 lines and 2 ratios includ-

ing adenoid size. In addition, we separated these children into different groups according to their BMI (>= or < 17) and Apnea-hyponea index (AHI<1, 1=< AHI <5, AHI ≥5). The age was used as the covariance to further exclude the confounding of age in cephalometrics.
Results: Result showed significant main effect of AHI in PNSANS/GoGn (p = .02), MPH/GnGo (p = .04) and Tonsil grade (p = .01), indicating that these angles are significantly different between three AHI groups. For the group of AHI≥5, these cephalometric angles are larger than the other two groups.
Conclusion: Cephalometrics is a simple, objective technique for evaluation of bony and soft tissue structures with airway space in pediatric OSAS and might be useful to predict the effectiveness of surgical intervention. Furthermore, this present study might be able to show the similarity of the cephalometrics between Caucasian and Asian children.

0358

PREVALENCE OF SLEEP DISORDERED BREATHING (SDB) IN PATIENTS WITH TEMPOROMANDIBULAR JOINT DISEASE (TMD)

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Introduction: The purpose of this study was to determine the prevalence of SDB in patients with TMD. It has already been recognized that nocturnal bruxism (NB) is a common occurrence in patients with SDB and also TMD, but the occurrence of SDB in the TMD population has not been well established.
Methods: We reviewed all cases referred to the Center for Facial Pain and Dental Sleep Medicine, PC for evaluation of TMD during 2009. All patients filled out sleep questionnaires, were examined by a double boarded Facial Pain/Dental Sleep Dentist. When there were signs or symptoms suggestive of SDB, a referral for a NPSG study was initiated.
Results: A total of 429 patients were referred for evaluation of TMD. Of the 429 patients 309 had signs and symptoms of a SDB (72%) and were referred for NPSG testing. Only 65 of the 309 were complaint with the recommendation to undergo NPSG testing. Non-compliance was for various reasons. Of the 65 that had NPSG studies performed, 100% were found to be abnormal and demonstrated SDB in the form of obstructive respirations. Almost all of the studies were performed using esophageal pressure monitoring (Pes) in order reliably identify respiratory effort related arousals (RERA's) such not to miss the diagnosis of the UARS.
Conclusion: Our study demonstrated that 72% of all TMJ patients have clinical findings to suggest the presence of SDB. Of those who had NPSG testing, we found that clinical suspicion was correct 100% of the time in our group tested. This supports the fact that there is a high correlation between SDB and TMD. With these and previous results we postulate that the driving mechanism behind bruxing and clenching during sleep is a protective mechanism of an airway that has a propensity for collapsing, to prevent the obstruction from occurring. This protective phenomenon over time leads to TMD in many patients.

0359

PREVALENCE AND POLYSOMNOGRAPHIC CHARACTERISTICS OF CHINESE PATIENTS WITH COMPLEX SLEEP APNEA SYNDROME

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Introduction: Complex sleep apnea syndrome (CompSAS) is a form of central apnea specifically identified by the emergence of central apnea

or hypopnea during the application of CPAP. The prevalence of Comp-SAS is 5-20% among sleep apnea patients. We investigated CompSAS in Chinese patients with obstructive sleep apnea syndrome (OSAS) in this study.

Methods: In diagnostic night, the patients who were found to have apnea/hypopnea index(AHI) greater than 10 and central sleep apnea index less than 5 were recruited into the study. Consecutive 205 patients who met the criteria, received auto-CPAP titration. The CompSAS was considered when the patients had central sleep apnea index greater than 5 during the night of CPAP titration.

Results: Among 205 participants, 27 patients (males 86.8%) were diagnosed as CompSAS (13.2%). The age of CompSAS patients (42.9±11.8 years) was significantly (p<0.05) younger than rest of patients who were not CompSAS (OSA, 46.9±12.6 years). In diagnostic night, compared to OSA, CompSAS patients had greater AHI (57.3±21.6 vs. 49.3±21.8; p<0.01) and shortened latency to REM sleep, no differences in body mass index and score of Epworth sleepiness scale.

Conclusion: The results illustrate that the prevalence of CompSAS in Chinese patients is 13%, which appear to be higher than reported patients among Japanese and similar to that reported in American and Australia. CompSAS patients are possibly younger and more severe compare to OSA patients.

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0360

SIGNS AND SYMPTOMS OF SLEEP APNEA ASSOCIATED WITH CARDIOMETABOLIC OUTCOMES IN A NATIONALLY-REPRESENTATIVE SAMPLE

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Introduction: Sleep apnea is a major public health problem. Despite several well-described relationships with cardiometabolic risk factors, it remains largely undertreated. The present analysis leverages a nationally-representative sample to evaluate the association of the signs and symptoms of sleep apnea with self-reported and objectively-measured cardiometabolic outcomes.

Methods: Data in adults(18+) from the 2007-2008 National Health and Nutrition Examination Survey (NHANES) were used. Cardiometabolic measures included self-reported diagnoses of hypertension and diabetes, systolic and diastolic blood pressure, and the following blood test results: triglycerides, cholesterol (total, HDL, LDL), C-reactive protein, fasting insulin and glucose, impaired fasting glucose and 2-hour Oral Glucose Tolerance Test(OGTT). Apnea predictors consisted of self-reported previous sleep apnea diagnosis and frequency of daytime sleepiness, unrestful sleep, snorting/gasping during sleep and snoring. The analysis comprised those who provided complete data (N=4163 for all outcomes except for glucose(N=2008), LDL cholesterol(N=1968), OGTT(N=1522), triglycerides(N=2012) and insulin(N=1992)). Linear and logistic regression analyses corrected for age, gender, race/ethnicity, education, marital status, BMI (objective), general health, access to health insurance, depressed mood, alcohol use, current smoking and smoking history.

Results: After adjusting for demographic, socioeconomic and health-related covariates, each predictor was significantly related to cardiometabolic outcomes. Previous sleep apnea diagnosis was predictive of hypertension(p<.001), systolic BP(p<.05), and cholesterol(p<.001). Daytime sleepiness was predictive of systolic BP(p<.05), C-reactive protein(p<.001), and insulin(p<.05). Snorting/gasping during sleep was predictive of hypertension(p<.01), diabetes(p<.05), diastolic BP(p<.05), HDL cholesterol(p<.05) and triglycerides(p<.001). Unrestful sleep was predictive of C-reactive protein(p<.001) and triglycerides(p<.05). Snor-ing was predictive of hypertension(p<.01), diastolic BP(p<.05) and triglycerides(p<.001).

Conclusion: Previous sleep apnea diagnosis, as well as other self-reported predictors of sleep apnea, predict a variety of cardiometabolic outcomes when evaluated in a nationally-representative sample. Physicians might consider assessing these symptoms in cardiovascular screenings. Future research should explore whether these signs and symptoms confer cardiometabolic risk when measured objectively.

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0361

HOMOZYGOTIC TWINS AND OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA) has been shown to be a familial disorder. And search for genetic association has been performed.

Methods: We identified 12 pairs of homozygotic twins with symptoms of OSA. We performed a systematic study of each pair. Homozygocy was first demonstrated by DNA analysis. Each child had clinical pediatric evaluation, sleep/wake study including attended polysomnography with nasal cannula pressure transducer, oto-laryngological and cranial-facial anatomy evaluation by specialists including performance of frontal and lateral cephalometric evaluation . Tests for sleep/wake and cephalometric evaluation were first scored blind by specialists kept unaware of relationship and demographics.

Results: The mean age at time of study was 7.2 +3.6y/o, mean BMI19.25+4.22 kg/m2. All children had overall normal pediatric development for age, height and weight. None of them was overweight. All pairs of twins (8 girls) were discordant for OSA. Each pair was discordant for clinical symptoms, and polysomnographic results with discordant apnea-hypopnea-index (AHI). In 7 pairs out of 12, one twin scored with normal AHI while the other was abnormal. When all twins were tabulated together the twins with no SDB symptoms had significant AHI difference. Cephalometric evaluation showed that the SDB affected twin presented with difference at evaluation compared to the normal twin. The anatomical changes were not the same for all children but affected the primarily the mandible and nasopharynx airway about 80% of the cases. A pair by pair analysis was performed that showed variability in types of anatomical risk factor finding. A retrospective analysis showed that the affected twin was always the twin with smaller birth weight.

Conclusion: Pediatric homozygote twins are discordant for OSA symptoms , PSG, and anatomical risk factors . Environmental factors either in utero or early in life may have a strong influence on OSA occurrence in childhood.

0362

IS SLEEP APNEA A WINTER DISEASE? METEOROLOGICAL AND SLEEP LABORATORY EVIDENCE COLLECTED OVER ONE DECADE

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Introduction: Sleep apnea is associated with cardiovascular outcomes that are more frequent in winter. The hypothesis that apnea-hypopnea index (AHI) of patients undergoing polysomnography in the winter may be higher than in summer was tested.

Methods: The retrospectively analyzed database included 7,523 patients of both genders undergoing in-laboratory baseline polysomnography to investigate any complaint of disordered sleep, during one decade, between January 2000 and December 2009. Data on climate, air pollution, and mortality were obtained from official organs of Porto Alegre, Brazil. AHI was the main outcome variable.

Results: The cosinor analysis confirmed the existence of a circannual pattern for AHI, with acrophase in August, austral winter, and nadir during February, austral summer. The lowest oxygen saturation showed inverse pattern with acrophase in February and nadir in August ($p<0.0001$ and $p<0.005$, respectively). AHI in the six months with colder weather is 26.5 ± 25.2/h and in warm weather was 23.4 ± 24.1 ($p<0.0001$), even after adjusting for gender, age, body mass index. Among the 4,094 patients undergoing polysomnography in the colder months there were significantly more males. In women, but not in men, larger neck and waist circumferences, and higher systolic and diastolic blood pressure were seen in patients attending the sleep laboratory in colder months. Scores in Epworth sleepiness scale, heart rate, cardiac arrhythmias, snoring, sleep efficiency, and percentages of sleep stages N1, N2, and REM were significantly different among seasons. The AHI correlates inversely with ambient temperature and directly with atmospheric pressure, relative air humidity, precipitation, and carbon monoxide levels. Correlations with particulate air matter < 10 micrometers, sulfur dioxide, and ozone did not reach significance.

Conclusion: Patients undergoing polysomnography in wintertime present more sleep disordered breathing events than in other seasons. This finding generates the hypothesis that apnea-hypopnea index may be related to epidemiological phenomena such as the escalation in cardiac mortality in the winter.

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0363

EFFECTS OF AN EDUCATIONAL CAMPAIGN ABOUT SLEEP DISORDERED BREATHING ON HEALTHCARE COSTS

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Introduction: To determine if a sleep-disordered breathing (SDB) awareness and education campaign affects the costs and utilization associated with healthcare plan participants seeking diagnosis and positive airway pressure (PAP) treatment.

Methods: Retrospective 4-year review of claims data for a healthcare plan with 22,000+ enrollees: a 2-year period before the campaign (2005-2006) and 2 years after the campaign was implemented (2007-2008). SDB was diagnosed by polysomnography. Data were divided into three groups: plan participant members without SDB, plan participants with SDB not electing PAP treatment (SDB-NT), and plan participants with SDB electing PAP treatment (SDB-PAP). Primary outcomes compared the two SDB groups: total medical costs per member/per month (PMPM), in-patient hospital costs PMPM, and hospital admissions per 1,000 participants.

Results: Patients in the SDB-PAP group cost the plan 28% less during 2007-2008 than participants in the SDB-NT group. Participants in the SDB-NT group had in-patient hospital costs 82% higher than those in the SDB-PAP group. In-patient hospital costs are rising three times faster for SDB-NT participants. SDB-NT participants averaged 30% more hospital admissions than SDB-PAP participants from 2007 through 2008. The cumulative differential cost savings to the plan from 2007 through 2008 between the two SDB groups was about $4.7 million compared to a loss of $157,000 from 2005 through 2006.

Conclusion: Educating plan participants about SDB/treatment options resulted in lower medical expenditures and utilization for the health plan participants electing PAP treatment.

Support (If Any): ResMed Corp.

0364

COST OF DECREASED COGNITIVE FUNCTION IN A LARGE CORPORATION IN FLORIDA: BENEFITS OF OBSTRUCTIVE SLEEP APNEA SCREENING AND TREATMENT FOR HIGH-RISK PROFESSIONALS

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Introduction: Obstructive sleep apnea (OSA) affects an estimated 15 million adults in the United States. However, over 85% of people with OSA remain undiagnosed. Untreated OSA results in job performance deficiencies such as: excessive sleepiness, cognitive dysfunction, irritability, and reduced vitality. Over 30% of middle-aged men are obese and significantly at risk for OSA; coincidentally, 70% of OSA patients are obese. Research shows work performance can be decreased by 30% due to sleep fragmentation and repetitive hypoxia, characteristics of OSA. This analysis focuses on economic benefits of screening high-risk professionals (middle-aged, obese men) and treating those diagnosed with OSA.

Methods: This cost-effectiveness analysis applied epidemiological data related to OSA screening, diagnosis, and treatment to the specific demographics of a large corporation in Florida. All statistical estimates were conservative. The sensitivity analysis considered decreased work productivity loss as the variable of uncertainty and used half of its predicted value. The discount rate was calculated using the time value of money equation.

Results: Based on national statistics, 608 employees of this corporation were estimated to be at high-risk for OSA. Considering statistics that 70% of high-risk individuals are diagnosed with OSA and that 75% of those are compliant with continuous positive airway pressure treatment (CPAP), results in 319 employees treated for OSA. For each of the 319 employees treated, productivity was estimated at $150,000 per year. Recovering the 30% productivity loss from these employees yields a $14.4 million yearly gain. The cost of polysomnography screening and CPAP treatment over 10 years is calculated at $7.2 million, yielding a 10-year net savings of $136 million.

Conclusion: This analysis predicts substantial financial benefits in screening OSA high-risk professionals and treating those diagnosed. These benefits are potentiated for professionals responsible for million-dollar budgets. Increased work performance saves this company an estimated $136 million over ten years.

0365

MAKING SENSE OF THE CONVERSATION CONCERNING SLEEP APNEA ON THE INTERNET

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Introduction: Public discussion regarding sleep apnea has multiplied during the recent decade. The Internet posts by distinct individuals vary widely from academic statements to personal blog comments. We sought to characterize the current Internet conversation by analysis of unique publishers and their posts lexically over time.

Methods: All posts citing sleep apnea were counted and filtered to reduce the analysis of redundant websites simply posting copied material. These were plotted by date of posting over time. Websites were validated through inspection and contacted for classification regarding the purpose of the site. A lexical map was constructed that analyzed the proximity and frequency of words to the words 'sleep apnea'. This mapping was repeated at pre-specified 1-week and 3-month intervals to reveal consistent word relations.

Results: The English-language posts regarding sleep apnea rose nearly exponentially since 2005. Of 3240 total posts on October 12th, 2010, the filtering revealed 1095 unique posts. These unique posts were examined in detail. The top 200 meaningful words occurring multiple times in conjunction with sleep apnea were lexical-mapped. Validation of the websites classified them as self-help, personal, health professionals, news services, or commercial advertising. The words 'energy' and 'fatigue' occurred more often than 'sleepy' or 'sleepiness'. Lexical mapping revealed at least 6 discernible domains for these words: Sleep disorders; Associated conditions; Anatomy; Devices and makers; Feelings and body image; Wishes.

Conclusion: The blogosphere conversation regarding sleep apnea is rapidly growing. Nearly a thousand posts are found daily in 2010. The core symptoms discussed in these posts include fatigue and sleepiness. The 6 domains of lexical relationships describe practical, medical, and personal discussions.

Support (If Any): Nexalogy, Montreal, Canada

0366

BERLIN QUESTIONNAIRE PERFORMANCE FOR DETECTING SLEEP APNEA IN THE GENERAL POPULATION

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Introduction: Berlin questionnaire (BQ) has been proposed as a screening tool for identifying patients at risk for obstructive sleep apnea (OSA). The aim of our study is to evaluate the performance of this questionnaire for detecting OSA in a large sample of middle-aged general population.

Methods: 469 subjects (46.4% women, 50.6±7.4 years old, BMI 25.1±4.9 kg/m2) participating in an ongoing population-based cohort study (HypnoLaus, Lausanne, Switzerland) underwent a complete polysomnographic recording at home and an extensive clinical workup including BQ. This instrument includes 3 categories: 1) witnessed apnea and snoring 2) daytime sleepiness and 3) obesity or hypertension. A positive score in 2 or more categories was considered suggestive of OSA. This score was compared to apnea-hypopnea index (AHI) and 4% oxygen desaturation index (ODI) determined by PSG. AHI was scored according to 2007 AASM criteria

Results: Mean AHI was 6.3±10.6/h. Mean 4%ODI was 5.8±10.0. Prevalence of OSA defined as an AHI >5/h, >15/h and >30/h was 33.3%, 10.3% and 3.8%, respectively in our population. Prevalence of positive

BQ score was 24.4% (29.2% in men, 18.8% in women). BQ sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) to detect OSA were 36.1%, 82.4%, 51.8% and 72.9% respectively for an AHI >5/h; 52.1%, 78.8%, 21.9% and 93.5% for an AHI>15; and 72.2%, 77.6%, 11.4% and 98.6% for an AHI>30/h. Positive BQ was associated with higher 4% ODI (10.8/h vs 4.2/h p<0.001), higher Epworth score (8.3 vs 6.2 p<0.0001) and broader neck circumference (38.6 vs 35.7 cm p<0.0001).

Conclusion: BQ questionnaire performance for identifying OSA is lower in a middle-aged general population than previously reported in a clinical population. Our results do not support its use as a screening tool for OSA in an unselected population.

Support (If Any): Lancardis Foundation GSK CIRS Research Fund Swiss Pulmonary Society

0367

STOP-BANG QUESTIONNAIRE AS A SCREENING TOOL FOR OBSTRUCTIVE SLEEP APNEA IN THE GENERAL POPULATION

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Introduction: STOP-BANG (Snoring, Tiredness during daytime, Observed apnea, High blood Pressure, Body mass index >35, Age >50, Neck circumference >40 cm, Gender) questionnaire has been shown to be a useful tool to screen for obstructive sleep apnea (OSA) during preoperative evaluation. The aim of our study is to evaluate the sensitivity and specificity of this questionnaire for screening for OSA in a large sample of middle-aged general population.

Methods: 458 subjects (47.7% women, 50.6±7.5 years old, BMI 25.2±4.9 kg/m2) participating in an ongoing population-based cohort study (HypnoLaus, Lausanne, Switzerland) underwent a complete polysomnographic recording at home and an extensive clinical workup including STOP BANG parameters. A score of 3 or more out of a possible 8 was considered suggestive of OSA. This score was compared to apnea-hyponea index (AHI) determined by PSG. AHI was scored according to 2007 American Academy of Sleep Medicine (AASM).

Results: Mean AHI was 6.04±10.3/h. Prevalence of OSA defined as an AHI >5/h, 15/h and 30/h was 33.0%, 9.39% and 3.49%, respectively in our population. Mean STOP-BANG score was 2.16±1.37. 34.9% of the subjects had a score ≥3. To detect OSA with AHI thresholds of 5/h, 15/h and 30/h, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were respectively 55.6%, 75.2%, 52.5% and 77.5% for an AHI >5/h; 76.7%, 69.4%, 20.6% and 96.6% for an AHI>15; 93.8%, 67.2%, 9.4% and 99.7% for an AHI>30/h. The area under the ROC curve for whole STOP-BANG score was 0.7 for an AHI> 5/h, 0.775 for an AHI>15/h and 0.871 for an AHI >30/h.

Conclusion: STOP-BANG questionnaire appears to be a useful clinical tool to rule out severe OSA (AHI>30/h) with a high negative predictive value. However, it is not an adequate screening tool for mild to moderate OSA in the general population due to its poor sensitivity.

Support (If Any): Lancardis Foundation GSK CIRS Research Fund Swiss Pulmonary Society

0368

SCREENING FOR OBSTRUCTIVE SLEEP APNEA BY STOP AND BERLIN QUESTIONNAIRES IN CHINESE PATIENTS

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Introduction: STOP questionnaire is a newly developed screening tool for obstructive sleep apnea (OSA), which simply ask four questions concerning whether the subjects are snoring (S), tiredness (T) during daytime, observed (O) apnea, and high blood pressure (P). Compare to widely used Berlin questionnaire, which contains 11 original questions and is scored in three separate categories, STOP is easily used.

Methods: Consecutive 132 subjects who have suspicion of OSA and referred to full night polysomnography recording (PSG) for diagnosis, were asked to fill STOP and Berlin questionnaires before PSG. High risk OSA was considered when total STOP score was equal or greater than 2, and two categories at least were positive among three for Berlin questionnaire according to generally used criteria.

Results: Of 132 subjects, 87% and 61% subjects were distinguished as high risk for OSA patients by STOP and Berlin questionnaires according to the criteria that mentioned in above, respectively. The sensitivities and specificities detected by STOP vs. Berlin questionnaires were 90.7% vs. 64.8% and 34.8% vs. 56.5% [apnea/hypopnea index (AHI) >5], 96.3% vs. 72.5% and 29.4% vs. 56.9% (AHI>15), 96.4% vs.76.8% and 21.3% vs. 50.7% (AHI >30), respectively. Among individual subjects, scores of STOP (r=0.51, p<0.001) and Berlin (r=0.41, p<0.001) questionnaires were significantly correlated with values of AHI.

Conclusion: Our finding suggests that STOP has better sensitivity, whereas Berlin has better specificity with respect to PSG diagnosed OSA among mild, moderate and severe patients.

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0369

THE VALIDITY OF OBSTRUCTIVE SLEEP APNEA SCREENING QUESTIONNAIRES IN BARIATRIC SURGERY PATIENTS

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Introduction: Bariatric Surgery (BS) can reduce obesity-related mortality and health care costs. Obstructive Sleep Apnea (OSA) is very common and can be seen in up to 70% of patients undergoing bariatric surgery. Importantly, undiagnosed patients with OSA are at risk for peri-operative complications. The OSA screening questionnaires (the Berlin and STOP-bang) have not been validated in BS patients, hence, this study was undertaken to test the validity of OSA screening questionnaires in patients undergoing BS.

Methods: This is a retrospective cohort of consecutive subjects who were referred to the Tulane Sleep Center to rule out OSA prior to BS. All subjects answered the Berlin and STOP-bang questionnaires prior to their sleep study. Subjects with severely impaired intellectual capacity and those who were currently treated with positive airway pressure therapy were excluded. The demographic data and sleep study parameters were analyzed. The predictive parameters for each questionnaire were calculated for Apnea Hypopnea Index (AHI) cut-off values of 5, 15 and 30 events/hour.

Results: A total of 33 patients were included in the cohort. The average age was 39.8 ± 12.7 years, average BMI was 51.4 ± 10.1 kg/m2, and the average neck circumference was 42.28 ± 5.2 cm. The median AHI was 17.3 events/hour. The STOP-bang questionnaire sensitivities for AHI cut-off points of 5, 15, and 30 were 92%, 94% and 100% respectively.

The specificities for AHI cut-off points of 5, 15, and 30 were 14.2%, 15.3% and 13.6% respectively. The Berlin questionnaire sensitivities for AHI cut-off points of 5, 15, and 30 were 87.5%, 88%, and 77.8% respectively. The specificities for AHI cut-off points of 5, 15, and 30 were 14.3%, 15.4%, and 9.1% respectively.

Conclusion: The Berlin and STOP-bang questionnaires demonstrated a moderately high sensitivity for OSA screening in a population scheduled for bariatric surgery.

0370

CLINICAL UTILITY OF AN OSA MEASURE FOR ENGLISH AND SPANISH SPEAKERS

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Introduction: Population-based symptom questionnaires have been developed to assess obstructive sleep apnea (OSA) among English speakers. This investigation describes the construct validity and utility of the Spanish-translated Sleep Heart Health Study Sleep Habits Questionnaire (SHQ) for clinical and research use with Spanish speakers.

Methods: Principal axis factoring was used to confirm the five factors identified by Kump (1994). Logistic regression to determine predictors of OSA and confirmatory factor analysis using Structural Equation Modeling (SEM) were conducted to determine model fit. Receiver-operator curves (ROCs) assessed utility of the English and Spanish SHQ. Area under curve (AUC) was calculated using predictive and negative OSA values.

Results: Bilingual Hispanics (N=50) completed English/Spanish versions one week apart (randomized order). Five factors with total variance of 55% for English and 54% for Spanish were accounted for by sleep duration, snoring, apnea, sleep symptoms, driving impairment, restless legs and the Epworth scale; Kump's four and three factors were loaded on the same factors in the English and Spanish versions. Logistic regression showed participants with higher BMI to be 1.2 times more likely to develop OSA (p=0.02). SEM demonstrated that the OSA model fits the English (CFI=.976) and Spanish (CFI=.967) data. ROC analysis showed that snoring intensity and duration, witnessed apnea, driving impairment and BMI significantly differentiated participants with and without OSA for English (AUC of .924, p=0.005) and Spanish (AUC of .918, p=0.006).

Conclusion: Four variables (snoring, apnea, drowsy driving and BMI) show potential for identifying Spanish speakers with OSA in clinical and research settings. OSA can be diagnosed at 75% sensitivity and 96% specificity at mean score of 8.5 in English and Spanish.

Support (If Any): NIH NICHD Grant 1R03HD051678 "Spanish translation and validation of a sleep measure" (PI: CM Baldwin)

0371

BODY MASS INDEX, GENDER AND ETHNIC VARIATIONS INFLUENCE THE PERFORMANCE OF THE EPWORTH SLEEPINESS SCALE IN PREDICTING OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA) is a common disorder; cardiovascular and metabolic effects often complicate moderate to severe disease. The Epworth Sleepiness Scale (ESS) has been shown to distinguish OSA from primary snoring. Little is known about the effects of gender and ethnic differences on the performance of the ESS in predicting OSA.

Methods: Nineteen hundred consecutive patients referred for polysomnographic diagnosis of OSA completed questionnaires, including demographic data and ESS. These patients then underwent polysomnography, and OSA was determined based on a respiratory disturbance index (RDI) ≥15.

Results: The sensitivity of ESS in the diagnosis of OSA was 60% and the specificity was 50%. The positive (PPV) and negative (NPV) predictive values were 62% and 47%, respectively. In obese subjects, the sensitivity and specificity were 61% and 46%, compared with 53% and 56% in non-obese subjects. In males, the sensitivity and specificity were 62% and 50%, compared with 55% and 50% in females. The sensitivity was 57% and specificity was 50% in Caucasians; 62% and 50% in Hispanics; 58% and 41% in those of other ethnicities. In obese, Hispanic males, the sensitivity, specificity, and PPV were 65%, 43%, and 83%, respectively. In non-obese, Caucasian females, the sensitivity, specificity, and NPV were 49%, 55%, and 73%. ESS was significantly correlated with RDI ($r = 0.17$, $P < 0.0001$). This correlation was strongest in obese patients ($r = 0.17$, $P < 0.0001$), Hispanics ($r = 0.19$, $P < 0.0001$), and males ($r = 0.21$, $P < 0.0001$). Of all the subgroups, the weakest correlation was seen in females ($r = 0.09$, $P = 0.015$).

Conclusion: The ability of the ESS to predict OSA is modest, despite a significant correlation with the severity of OSA. The test characteristics improve substantially when applied to select populations, especially those at risk for OSA.

0372

OBSTRUCTIVE SLEEP APNEA: DOES SCREENING FOR TIREDNESS IN ADDITION TO SLEEPINESS IDENTIFY MORE PATIENTS AT RISK?

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Introduction: A literature search identified OSA screening tools with < 10 items and at least 1 item on tiredness. Of these tools, the STOP-Bang questionnaire had the highest sensitivity (SN) and area under the receiver operator characteristic curve (AUC) for identifying moderate-to-severe OSA (MS-OSA). This evidence-based practice project incorporated the STOP-Bang into the current OSA screening protocol, which used the Epworth Sleepiness Scale (ESS).

Methods: We compared the predictive abilities of the STOP-Bang and ESS/STOP-Bang combination to those of the ESS. The STOP-Bang responses were scored with two different body mass index (BMI) cut-offs: 35kg/m2 (STOP-Bang) and 30kg/m2 (STOP-Bang30). Sixty patients were assigned to OSA and sleep-disordered breathing (SDB) risk groups based on screening scores. We compared patients' OSA and SDB risks to their polysomnographic OSA and SDB results in 47 patients who also completed polysomnograms (PSGs).

Results: The STOP-Bang30 had the highest sensitivity (96.9%), positive predictive value (PPV, 75.6%), negative predictive value (NPV, 83.3%), and AUC (0.651, 95% CI [0.524, 0.778], d = .55) for OSA and SDB. The STOP-Bang shared the highest SN (94.7%) and had the highest PPV (45.0%), NPV (85.7%), and AUC (0.581, 95% CI [0.488, 0.674], d = 0.29) for MS-OSA and moderate-to-severe SDB (MS-SDB). The STOP-Bang30 AUC and STOP-Bang AUC were statistically higher than the ESS AUC for OSA/SDB (p = .019) and MS-OSA/MS-SDB (p = .042) respectively.

Conclusion: In this small sample, the STOP-Bang30 and STOP-Bang identified more patients at risk for OSA/SDB and MS-OSA/MS-SDB respectively than the ESS. The 95% CI for the STOP-Bang AUC included 0.500 for MS-OSA/MS-SDB, suggesting that larger studies are needed to further evaluate STOP-Bang screening in sleep clinic patients prior to PSGs. The STOP-Bang30 may identify more patients at risk for OSA than the ESS in sleep clinic settings.

0373

A SINGLE BLIND STUDY USING AN ELECTROCARDIOGRAM-BASED ANALYSIS TO SCREEN FOR THE PRESENCE OF A SLEEP DISORDER

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Introduction: This study investigates the clinical utility of a portable sleep monitoring device that utilizes an internet-based automated analysis compared to in-lab PSG in subjects with sleep disorders.

Methods: A pilot study in patients suspected of having a sleep disorder was conducted at National Jewish Health's sleep lab. Randomization was to use the M1 portable sleep monitor prior to (n=25) and after (n=25) PSG. 92% M1 studies were analyzed. PSG types were: full PSGs (n=25), CPAP titration (n=14) and split night (n=11) studies. Grouping was based on clinical diagnosis and the presence of elevated low frequency coupling narrow band (e-LFC nb): Normal (n=3), OSA (n=20), PLM (n=5), OSA + PLM (n=7) and e-LFC nb (n=8). RemLogic (Embla, Inc; Broomfield, CO) was used to calculate the cardiopulmonary coupling (CPC) values.

Results: MANOVA showed significant differences between group's CPC but not PSG variables (Wilks' Lambda, PSG: F = 1.058, p = 0.397; CPC: F = 2.786, p <0.001). High frequency coupling was significantly reduced in the e-LFC nb group (14.38 ± 11.68%) compared to normal, OSA and PLM groups (43.22 ± 9.23, 38.25 ± 15.41, 38.88 ± 14.83, respectively; p<0.05). Low frequency coupling was increased in the e-LFC nb group (63.65 ± 11.95%) compared to OSA and PLM groups (40.07 ± 11.61, 39.92 ± 15.74, respectively; p<0.05). All in-lab M1 and PSG CPC results correlated (p<0.05). The M1 CPC data (n=19) had a sensitivity = 84.2%, specificity = 100%, PPV = 100% and NPV = 25% to predict the presence of a sleep disorder. Mutual agreement was 91.4%.

Conclusion: The CPC data demonstrated high sensitivity and specificity identifying the presence of a sleep disorder.

Support (If Any): Embla Systems, Inc., Broomfield, CO

0374

VALIDATION OF AN AMBULATORY SCREENING DEVICE FOR SEVERE FORMS OF OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Obstructive sleep apnea syndrome (OSAS) is highly associated to other syndromes: type 2 diabetes, glaucoma, and hypertension with negative interactions. Therefore it would be crucial for non-sleep specialist medical doctors to faster and accurately identify patients with severe OSAS in order to give adapted treatment. Any appropriate diagnosis help could be interesting and RU SLEEPING system (PHILIPS-RESPIRONICS inc.) is one of the potential candidates.

Methods: 86 patients (59 men and 27 women; Age: 52.1 ± 16.8 years) were recruited from endocrinology and general medicine (ambulatory) services. All patients underwent a polysomnography and were equipped during a different night with this ambulatory screening device. This system gives us mean Respiratory Event Index (m-REI) the main criterion and maximum per hour Respiratory Event Index (max h-REI) the second criterion. These 2 criteria were compared to AHI, the gold standard.

Results: Our patients have AHI=27.4±22.7, m-REI=16±14.1 and max h-RE=34±23. We found a strong association between AHI and m-REI (Pearson correlation coefficient = 0.74 [0.62 0.82], p<.001) and max h-REI (Pearson correlation coefficient = 0.72 [0.61 0.81], p<.001). According to kappa criterion, best cutoff for m-REI with AHI>10 is m-REI>8 (sensitivity=0.73±0.05, specificity=0.80±0.08) and with AHI>30 is m-

REI>19 (sensitivity=0.71±0.08, specificity=0.89±0.04). Best cut-off for max h-REI with AHI>10 is max h-REI>17 (sensitivity=0.80±0.05, specificity=0.76±0.09) and with AHI>30 is max h-REI>26 (sensitivity=0.93±0.04, specificity=0.78±0.05)

Conclusion: Results show that best sensitivity for this ambulatory screening device is obtained for severe apnea with the second criterion max h-REI>26. Therefore this device seems to be appropriate to quickly send patients with supposed severe OSAS to sleep specialist.

Support (If Any): PHILIPS-RESPIRONICS for technical support

0375

ASSESSMENT OF A SIMPLE PIEZOELECTRIC SENSOR SYSTEM FOR APNEA/HYPOPNEA MONITORING

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Introduction: Polysomnography (PSG) is widely used for sleep analysis and also for monitoring of apnea/hypopnea during sleep. However, it is often unpleasant for patients because they must be attached with a respiratory flow sensor to their nose and belt sensors to their chest and abdomen. These uncomfortable sensor settings may induce a stress that might affect the quality of sleep and the result of PSG. Therefore, we designed a new piezoelectric transducer (PZT) sensor, which neither contacts to their skin nor binds their body, for the noninvasive monitoring of respiratory events, apnea/hypopnea.

Methods: A flat and thin PZT sensor ($30 \times 200 \times 1$ mm) was placed under a towel on a bed on which total of 44 cardiology inpatients underwent the simultaneous recording with the PZT sensor system and PSG. Patients were scored as having sleep disordered breathing (SDB) when they exhibited apneas/hypopneas of >30 times (AHI5 × 6h) in chain-stokes-like breathings in the PZT-sensor signal. Hypopneas were scored as obstructive apneas in the PZT-sensor-signal analysis because they were hardly distinguishable.

Results: In the PZT-sensor-signal analysis, we found SDB in 97% (34/35) of the patients with Apnea Hypopnea Index (AHI) of >10 judged by PSG, but no SDB was found in rest 9 patients with AHI <10 (sensitivity 97%, specificity 100%). Manually selected 107 obstructive and 88 central apnea events in the PZT-sensor signal of 44 patients were verified by PSG analysis. 86 and 88% of them were correct, respectively; 10 and 5% of them were inversely scored; rest 4 and 7% of them lacked decrease in SpO2 (<3%).

Conclusion: The present study demonstrated that the analysis of apnea/hypopnea in the chain-stokes-like breathing with our PZT-sensor system is likely to be practicable at least for the screening of SDB with AHI of >10 in patients with cardiac diseases.

0376

PHOTOPLETHISMOGRAPH DERIVED RESPIRATORY (PDR) - A SIMPLE METHOD FOR SLEEP DISORDERD BREATHING DIAGNOSIS USING A STANDARD PULSE OXIMETER

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Introduction: Photoplethysmograph (PPG) devices, known commonly as pulse oximeters, provide instantaneous and continuos in vivo measurements of arterial oxygenation. The objective of this study it to determine if an automatic algorithm techniques can be used to reliably determine respiratory events and especially AHI from the PPG signal measured during the night.

Methods: 60 subjects hospitalized in the cardiology department (Morristown Memorial Hospital; Morristown, NJ, USA) out of them 45 patients with heart failure and 14 patients referred to the sleep lab with suspected SDB were enrolled in the study. The study population included 20 females and 54 males. Subject's mean age was 64.63±14.34 and mean BMI was 30.85±8.74. Each subject went throuh a complete night sleep study. The sleep study included standard Polysomnography (PSG) signals with the PPG singal. The plethysmograph derived respiratory (PDR) signal that was calculated out of the PPG verified against gold standard of respiratory events detection and respiratory rate detected from the PSG.

Results: PDR respiratory events were defined and calculated as a reduction of at least 30% in the amplitude of PDR signal, lasting more than 10 seconds, accompanied by a reduction of at least 4% in saturation. An event based sensitivity of 85.5% (95% CI: [84.8%-86.1%]) versus the gold standard was observed when respiratory event detection was derived from the PDR signal. The agreement in respiratory rate reached 85%.

Conclusion: The study confirms that the respiratory signal and hence respiratory event detection can be adequately extracted from the PPG signal. Using a standard pulse oximeter and out of it the PPG and sturation signals for the detection of respiratory events and AHI will make this test available at home or at ambulatory enviroment to currently undiagnosed populations as heart failure patients that find it difficult to spend the entire night in the sleep lab.

Support (If Any): WideMed Ltd.

0377

ACCURACY OF AUTOMATED RESPIRATORY SCORING ALGORITHM USING PORTABLE MONITORING

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Introduction: Sleep Disordered Breathing (SDB) affects more than 40 million people in the US; yet, more than 80% of affected individuals are undiagnosed and/or untreated. Despite its reduced channel count, PM is expected to improve access to sleep medicine specialists by expanding sleep testing to the hospital room, the home, and other settings. However, the expected increase in sleep studies will intensify the burden of scoring for sleep technologists. Therefore, algorithms that accurately detect respiratory events will significantly assist in the implementation and ultimate success of PM.

Methods: A rules-based algorithm (RBA) that uses the minimum set of signals recommended by AASM for PM (pressure-based airflow, thoracic movement, and oxygen desaturation) was developed. Due to the lack of sleep state measurement, the algorithm was designed to rely on total recording time in contrast to total sleep time to calculate Apnea Hypopnea Index (RBA-AHI). The algorithm was applied to a subset of a 14 channel PSG acquired from 100 hospitalized patients. Manual scores (Manual-AHI) of the same dataset using the 14-channel PSG montage was performed, allowing for a direct comparison between manual and automated analyses.

Results: Correlation between RBA-AHI and Manual-AHI was 0.91 (R2=0.82), which is comparable to inter-rater reliability. An analysis to test the algorithm's accuracy on disease detection (AHI>5) revealed a sensitivity of 81% and specificity of 86% when compared to the 14-channel PSG.

Conclusion: A new algorithm for automated detection of respiratory events that uses PM signals was developed and tested with high correlation, sensitivity and specificity to a 14-channel PSG. Overall, this algorithm could serve as an effective tool to enhance data analysis of PM studies including home sleep evaluations.

0378

VARIABILITY AND CORRELATIONS IN AHI AND OXYGEN SATURATION OVER THREE NIGHTS OF PORTABLE MONITORING DISCLOSES THE IMPORTANCE OF BASELINE OXYGEN SATURATION

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Introduction: As portable monitoring is becoming increasingly utilized, it will be important to understand the reproducibility of the data, not only for AHI but also for indices of hypoxemia, in order to assess individual risk for morbidity. The hypothesis is that the night to night variability of percent time less than 90% (O2Sat90) will be similar to that of AHI, and correlate with AHI severity.

Methods: Retrospective review was performed from deidentified records from 1031 male patients age(>18yrs.) who underwent ambulatory monitoring with the NovaSom QSG™ sleep apnea diagnostic system (Palo Alto, CA). A software analysis algorithm defined the AHI using standard definition (Stepnowsky et al 2004) and O2Sat90. Values for 3 overnight portable studies were tabulated for night-to-night comparison, average AHI over all nights was placed into the severity categories (AHI<5, 5-15, >15-30, >30-75, and >75).

Results: Ninety-two patients (9%) were excluded due to incomplete data from all 3 nights. Of the 939 male patients (approx. age 56 ±12 yrs. M±SD: range 21-92), the average ESS was 9.5 ± 6.3, BMI 32.6 ± 7.3, AHI 18.5 ± 19.4/hr, and resting O2Sat 92.3 ± 2.8. The night to night variability by Pearson correlation for AHI was 0.88 for study 1vs2, 0.82 for study 1vs3, and 0.86 for night 2vs3, similar to the night to night variability in O2SAT90 (night 1vs2=0.84; 1vs3=0.79; 2vs3=0.82). However, correlations between AHI and O2SAT90 however were in a modest (range 0.27-0.35) within a given night. According to AHI severity categories, there were no significant differences in ESS or BMI or age. While values for O2Sat90 became higher with across increasing AHI severity, it was that baseline oxygen saturation which varied widely within a severity category that contributed to the mismatch between AHI and O2Sat90.

Conclusion: The night-to-night correlation in AHI and O2SAT90 are equally good; however, each appears to have only a weak correlation to the other indicating each could capture different risks. Across AHI severity, there baseline oxygen saturation plays a major role in O2Sat90, suggesting that oxygen saturation profiles will be an important in prospective studies of observation or intervention.

0379

USE OF CARDIOPULMONARY COUPLING IN CPAP EFFICACY STUDIES

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Introduction: To investigate the association between electrocardiogram (ECG)-based cardiopulmonary coupling algorithm and standard sleep-disordered breathing measures. New, less-invasive methods to assess sleep quality and breathing are needed to provide improved treatment tracking of treatment efficacy in OSA patients.

Methods: As part of a larger trial that investigates methods to improve CPAP adherence, we assessed "CPAP efficacy" in a subset of our partici-
pants. Data was obtained from a single night with patients simultaneous wearing CPAP (ResMed AutoSet S8; ResMed, Inc., San Diego, CA) and a Type III cardiopulmonary recording device (Embletta; Embla, Inc, Broomfield, CO). RemLogic software was used for manual respiratory scoring using the standard AASM 2007 criteria for apneas and the alternative definition for hypopneas (>50% drop in airflow from baseline and >3% desaturation). CPAP efficacy studies were indicated by the presence of either (a) high residual CPAP-measured AHI or (b) subjective report that was inconsistent with objective CPAP data.

Results: 13 CPAP efficacy studies were performed and all participants had been using CPAP on average for more than 1-month at the time of data collection. AHI was negatively associated with high-frequency coupling (HFC) (r=-.57; p=.04) and positively associated with low-frequency coupling (LFC) (r=.71; p=.007). e-LFCnb (nb=narrow band) was associated with the central apnea index (r=.88; p<.0001), but not with the obstructive apnea index (r=.41; p=.162). e-LFCbb (bb=broad band) was associated with the obstructive apnea index (r=.64; p=.018), but not with the central apnea index (r=-.09; p=.760).

Conclusion: These results suggest that CPC measures can provide insight into the sleep quality and residual sleep-disordered breathing that occurs in CPAP efficacy studies. Future work will investigate associations between patient's subjective assessment of treatment efficacy to PG and CPC variables. CPC has the methodological advantage of being based on ECG.

0380

DETECTION AND QUANTIFICATION OF SLEEP DISORDERED BREATHING USING ELECTROCARDIOGRAMS

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Introduction: Detection of sleep disordered breathing (SDB) using electrocardiograms (ECG) is non-invasive and inexpensive relative to conventional alternatives. Patient's sleep-wake cycle during SDB modulates instantaneous heart rate (IHR) which can be analyzed using HR variability (HRV). Furthermore, ECG-derived respiratory (EDR) information can be extracted from ECG morphology variation. We developed a SDB screening algorithm based on HRV and EDR techniques using single-channel ECG. This study is to demonstrate the algorithm's efficacy.

Methods: The algorithm was developed using 95 Polysomnography (PSG) recordings from the MIT/Physionet database and validated using 214 PSG recordings with expert annotation from an AASM-accredited sleep center. Hypopneas were detected by nasal pressure with a nasal cannula using the AASM alternate definition. The validation dataset included 105 normal-mild (AHI≤15), 49 severe apnea (AHI≥30), and 60 moderate apnea (15<AHI<30) PSGs. The algorithm first detects normal ECG beats and excludes ectopic beats to measure the IHR power in several frequency ranges. In parallel, the EDR values are calculated by measuring the maximum difference in normal QRS complexes. Final step is to combine HRV and EDR techniques to classify each epoch as apnea (at least 1 event), normal, or indeterminate.

Results: The first test was to classify every epoch in the evaluation database. The algorithm classified 17.2% of the epochs as indeterminate, and 82.8% of the epochs as normal or apnea with 97.8% accuracy. The second test was to determine if significant sleep apnea was present or not in each patient. The algorithm correctly classified 84.4% of severe apnea and normal-mild patients. For the second test, as recommended by PhysioNet, recordings with moderate apnea were excluded.

Conclusion: Our one-channel ECG-only SDB screening algorithm provides accurate detection and quantification. Since ECG is readily avail-

able, non-invasive, and low-cost, this algorithm has the potential for SDB screening in both hospital and home care environments.

0381

FEASIBILITY OF DETECTION OF PERIODIC BREATHING USING RESPIRATORY SINUS ARRHYTHMIA PATTERNS FROM SLEEP TIME AMBULATORY ECG RECORDINGS

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Introduction: Respiratory sinus arrhythmia (RSA), the response of the heart rate to autonomic changes during respiration, clearly tracks respiratory rate. RSA is especially prominent when subjects are supine. Periodic respiration is associated with a waxing and waning of the respiratory rate that should, in theory, be reflected in RSA and visible from a plot of instantaneous heart rate vs. time (HR tachogram).

Methods: HR tachograms from the ECG channel of recordings from older adults in the Sleep Heart Health Study were examined. ECGs had been extracted and scanned to research standards on a MARS PC Holter system. (GE Medical Systems, Milwaukee, WI). N=23 participants were selected as having been identified by the technician as having periodic breathing (PERGP) and also as having a central sleep apnea (>1/hr). These were matched by age and gender with participants without periodic breathing or central sleep apnea (NOGP). The presence of periodic breathing was blindly scored from HR tachograms. Participants were categorized as definite, possible or no periodic breathing based on the presence of RSA patterns suggesting cycles of increasing and decreasing respiratory rates. When discrepancies between SHHS and visual scoring occurred, the respiratory channels of the PSG were examined.

Results: Results: There were 38 interpretable recordings (9F,31M, age 78 SD 4 yrs). Of the 20 usable recordings in the NOGP, 3 were categorized as definite, 3 as possible and 14 as no periodic breathing. After examination of the PSGs, one of the 3 categorized as definite periodic breathing did have it, one had missing respiratory data at the time of the periodic RSA on ECG and one had respiration that was periodic in amplitude but not frequency. Of the 3 scored as possible, one had periodic amplitude but not frequency patterns, one had an abnormal heart rate pattern and one did not have any periodic breathing. N=16 of 18 usable recordings in the PERGP were categorized as having definite periodic breathing, one as possible and one as no. After examination of the PSGs, it was determined that the PER subject classified as no, had the wrong ECG file and the PSG ECG file for that person was not available.

Conclusion: Significant periodic respiration is clearly identifiable from RSA patterns on heart rate tachograms, suggesting that screening for this breathing pattern could be included in the information available from routine ambulatory ECG recordings.

0382

DELAYED CIRCADIAN PHASE AND THE TIMING OF THE POLYSOMNOGRAM TO DIAGNOSE OBSTRUCTIVE SLEEP APNEA

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Introduction: False negative polysomnograms could adversely affect the diagnosis and management of patients with obstructive sleep apnea (OSA). We hypothesize that false negative polysomnograms could occur from discordance between the patient's circadian phase and the routine sleep laboratory schedule.

Methods: Prospective study of seven patients with delayed circadian phase and high clinical suspicion for OSA. Patients were included if the first diagnostic polysomnogram, done according to the sleep laboratory

timing, was negative for OSA. These patients subsequently underwent a second polysomnogram performed in accordance with the patient's circadian phase. We evaluated differences between the two polysomnograms with respect to apnea hypopnea index (AHI), total sleep time (TST) and time spent in REM sleep. Data were analyzed with paired t test, $P < 0.05$ was considered statistically significant. Mean ± SD.

Results: There were statistically significant increases in all endpoints between the first and second polysomnograms. AHI and time spent in REM increased for all seven patients, while TST increased in six patients. AHI increased from 4.4 ± 1.7 events/hour to 14.3 ± 5.4 events/hour (P<0.01). TST increased from 283 ± 36 minutes to 429 ± 112 minutes (P<0.01).Time spent in REM sleep increased from 31 ± 19 minutes to 101 ± 60 minutes(P<0.05).

Conclusion: In patients with delayed circadian phase and clinical suspicion for OSA, there is an association between false negative polysomnograms and performing the study in discordance with the patient's circadian phase. If additional studies confirm this observation, it would indicate that polysomnogram should be performed in accordance with the patient's circadian phase to avoid false negative results.

0383

SLEEP FRAGMENTATION PHENOTYPES IN SLEEP APNEA SYNDROMES

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Introduction: Sleep quality varies widely in the presence of roughly similar sleep apnea severity. Excessive fragmentation may increase the probability of central apneas and reduce treatment compliance. Improved understanding of patterns and mechanisms of sleep fragmentation may be clinically useful.

Methods: We conducted an analysis of baseline polysomnographic (972 subjects) and ECG-spectrographic (617 subjects) data of the Apnea Positive Pressure Long-Term Efficacy study. Mild, moderate, severe and extreme OSA categories were defined based on respiratory disturbance indices of < 10, 10-30, 30-60, and > 60/ hour, respectively. Fragmentation phenotype thresholds were defined for sleep efficiency ≤ 70%, stage N1 ≥ 30%, and high frequency coupling ≤ 30%; consolidation phenotype thresholds were defined for ≥ 90%, ≤ 10%, and ≥ 50% respectively; the remaining subjects were considered "intermediate". Two further distinct types of fragmentation were identified: block (≥ 2 consolidated periods of wake during sleep period) and alternating (brief periods of alternating sleep and wake). Mathematical modeling approaches further explored mechanistic differences of block and alternating patterns.

Results: Mild, moderate severe and extreme categories consisted of 70, 394, 320 and 118 subjects for polysomnographic, and 54, 296, 209 and 112 subjects for spectrographic analysis. Each category included clear fragmented and consolidated phenotypes. For example, in the extreme group, 17.6% had stage N1 ≤ 10%, 14.4% a sleep efficiency ≥ 90%, only 40.4% N1 ≥ 30% and 25.5% a sleep efficiency ≤ 70%. Block and alternating fragmentation were seen in 57 (5.9%) and 198 (20.4%) subjects, respectively. "Alternators" had significantly more sleep apnea than other groups. Block and alternating sleep patterns could be reproduced by a mathematical model of human sleep.

Conclusion: In a sleep apnea dataset, sleep fragmentation and consolidation phenotypes could be readily recognized across all disease severities. The modeling implications and clinical consequences of these phenotypes deserve assessment.

0384

POLYSOMNOGRAPHIC ANALYSIS OF nREM CYCLIC ALTERNATING PATTERN (CAP) SLEEP MICROARCHITECTURE IN COMPLEX AND OBSTRUCTIVE SLEEP APNEA SYNDROMES

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Introduction: Complex sleep apnea syndrome (CompSAS) presumably involves unstable ventilatory control mechanisms, possibly including cortical brain arousal indexed by NREM cyclic alternating pattern (CAP) sleep microarchitecture. CompSAS has been associated with opiate use, but may also be idiopathic or associated with underlying cardiac disease. We aimed to determine whether CAP sleep rates differed between CompSAS subgroups (opiate users (OU) and non-opiate users (NOU)) and non-opiate user OSA controls.

Methods: 34 consecutive CompSAS patients (12 OU, 22 NOU) and 18 OSA controls matched for age, sex, BMI, and AHI were manually analyzed for CAP sleep rate during diagnostic polysomnography using Hypnolab scoring software (Verona, Italy). CAP sleep rate during diagnostic polysomnography in all patients was obtained. Group averages were compared utilizing Wilcoxon Rank Sum tests in JMP (Chicago, IL).

Results: CAP rate was significantly lower in CompSAS OU vs. NOU (62.1 vs. 79.3, p=0.01), and lower in CompSAS OU than OSA controls (62.1 vs. 74.0, p=0.079). There was no significant difference between CompSAS NOU and OSA controls.

Conclusion: CompSAS OU had a significantly lower CAP rate than NOU, and OU also trended toward a lower CAP rate than non-opiate user OSA controls. Since CAP sleep microarchitecture may reflect cortical infraslow oscillations, our findings suggest that cortical mechanisms associated with unstable ventilatory effort in CompSAS and OSA are similar, but that opiate use may induce central apnea through a different, likely subcortical mechanism. Further analysis of CompSAS patients including co-morbid cardiac disease influences may further clarify differences in cortical arousal potential for central apnea.

0385

IS THERE A DIFFERENCE IN CONTINUOUS POSITIVE AIRWAY PRESSURE REQUIREMENT OR DISEASE CONTROL BETWEEN NASAL AND ORONASAL MASKS IN THE TREATMENT OF OBSTRUCTIVE SLEEP APNEA?

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Introduction: The aim of this randomized controlled pilot trial was to investigate whether there is a difference in continuous positive airway pressure (CPAP) requirement or residual apnea-hypopnea index (AHI) between nasal and oronasal masks.

Methods: Adult patients (≥25 years) with severe obstructive sleep apnea (OSA) established on CPAP using a nasal mask within the previous three years were recruited. All were fitted with two oronasal masks (A and B) in addition to their own nasal mask, and were excluded if leak was >20 liters/minute at 8cmH2O while awake. Patients were randomized to CPAP at manually-titrated pressure, or auto-adjusting positive airway pressure (APAP) for seven nights each, with immediate crossover. Within each week, the two oronasal masks were used for two nights each and the nasal mask for three nights, in random order.

Results: Twelve patients (mean±SD body mass index 37.7±5.0 kg/m2, AHI 59.8±28.6 events/hour, CPAP 11.1±3.2 cmH2O) consented to the study. There was no significant difference in APAP 95th percentile pres-

sure between the three mask types (mean±SD 11.6±2.8, 11.5±3.7 and 11.6±3.2 cmH2O for nasal, oronasal A and oronasal B masks respectively, p=0.66). Six and five patients demonstrated a 95th percentile pressure difference of >1cmH2O with oronasal masks A and B respectively, compared with the nasal mask. The difference in 95th percentile pressure requirement was not strongly correlated with the difference in 95th percentile leak (nasal vs. oronasal A r=-0.36, p=0.12; nasal vs. oronasal B r=-0.29, p=0.18). The machine-interpreted residual AHI during CPAP use was significantly difference between the masks (mean±SD 1.3±1.5, 4.4±8.1 and 2.7±2.5 events/hour for nasal, oronasal A and oronasal B masks respectively, p=0.03).

Conclusion: This pilot randomized controlled trial found variation in pressure requirement between nasal and oronasal masks but was not statistically significant. This should be further investigated in an adequately powered trial.

0386

CLINICAL PREDICTORS OF EFFECTIVE CONTINUOUS POSITIVE AIRWAY PRESSURE IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA/HYPOPNEA SYNDROME

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Introduction: To identify standard clinical parameters that may predict the optimal continuous positive airway pressure (CPAP) in patients with obstructive sleep apnea/hypopnea syndrome (OSAHS) in Taiwanese.

Methods: One hundred twenty-nine OSAHS patients who underwent a completed physical examination, successful manual CPAP titration were included in this study. We recorded the severity of nasal obstruction, modified Mallampati grade (aka updated Friedman's tongue position (uFTP)), tonsil size, neck circumference and body mass index (BMI) and measured thyroid-mental distance and hyoid-mental distance (HMD) in the study population.

Results: When the physical parameters were correlated singly with the optimal CPAP, we found that uFTP, HMD and apnea/hypopnea index (AHI) were reliable predictors of OSA (P = 0.013, P = 0.002, P = 0.000, by Multiple Regression). When all important factors were considered in a stepwise multiple linear regression analysis, a significant correlation with optimal CPAP was formulated by factoring the uFTP, HMD and AHI (Optimal CPAP = 1.01 uFTP + 0.74 HMD + 0.059 AHI - 1.603).

Conclusion: This study has distinguished the correlation between updated Friedman's tongue position, hyoid-mental distance, and AHI with the optimal CPAP. The structure of upper airway (esp. tongue base obstruction) and disease severity may predict the level of optimal CPAP.

0387

THE EFFECTIVENESS OF TREATMENT APNEA-HYPOPNEA INDEX (ET-AHI): A NEW METHOD TO ASSESS THE THERAPEUTIC CONTROL OF OBSTRUCTIVE SLEEP APNEA

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Introduction: CPAP is highly efficacious, but the clinical effectiveness may be diminished due to non-adherence. In this study we assessed an innovative measurement instrument, the Effectiveness of Treatment Apnea-Hypopnea Index (ET-AHI). The ET-AHI is a weighted, composite measurement of the AHI both during adherence and non-adherence with CPAP therapy. ET-AHI = (CPAP Treatment AHI x % adherence to therapy) + (Untreated AHI x % non-adherence to therapy).

Methods: We retrospectively evaluated 37 adult (mean age = 44.2 ± 9.0 years) patients with moderate to severe OSA (baseline AHI = 56.3 ± 22.6), who subsequently underwent CPAP Titration (AHI = 4.3 ± 5.9).

No patient in the study group was adherent to CPAP therapy, and all individuals underwent Maxillomandibular Advancement Surgery (MMA). The Post-MMA PSG showed a significant reduction in the AHI (MMA Treatment AHI mean = 11.6 ± 7.4). We performed ET-AHI calculations using two assumptions: 1) the Untreated AHI for the CPAP group is equivalent to the Diagnostic AHI obtained during the Diagnostic PSG for the cohort (AHI=56.3), and 2) the CPAP Treatment AHI is equivalent to the CPAP Titration AHI obtained during CPAP Titration PSG for the cohort (AHI= 4.3).

Results: The ET-AHI calculations showed that an 85% adherence rate with CPAP would be necessary to achieve equivalence of treatment effectiveness with MMA (AHI=11.6). A CPAP adherence rate of about 98% would be required to achieve an ET-AHI of 5 and a rate of about 79% to reach an ET-AHI of 15.

Conclusion: The ET-AHI may provide a more accurate assessment of the true control of OSA than either the CPAP Titration AHI or rate of adherence to therapy because it accounts for both the level of AHI when the patient is adherent and non-adherent to therapy.

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0388
CPAP TREATMENT ADHERENCE IN SLEEP CLINICS

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Introduction: CPAP tracking technology allows sleep apnea therapy to be one of the first therapies with adherence documentation in a clinical setting. In a research setting, CPAP adherence has been reported to range from 30-60%. In addition to health implications, CPAP adherence in a clinical setting is now linked with ongoing payment coverage for many insurances. Since 2009, some insurances deny ongoing CPAP coverage for clinical patients who have not used CPAP > 4 hours for > 70% of 30 consecutive days (between days 1 to 90); and had a face-to-face visit documenting clinical benefits. With these criteria, half of new clinical CPAP patients may be at risk of losing their CPAP units.

Methods: CPAP data were retrospectively reviewed by 4 groupings of new CPAP users. All new PAP patients were included; patients were excluded only when there were technical problems. All unit types were included (as insurance requirements are standard for all new units: CPAP; BiPAP; Auto; ST/ ASV). The 4 new user groups were: Group 1 (06/2007 new PAP orders; n=32); Group 2 (06/2008 new PAP orders; n=84); Group 3 (06/2009 new PAP orders; n=88); Group 4 (01/2010 new orders; n=69). Using exported ResMed and Respironics data, for each of the 4 groups, PAP usage times were determined for the first 5 months following the request for new PAP. Outcomes measures were: percent PAP data cards returned; percent days used (any time); percent days used > 4 hours; average hours used (all days); average hours used (used days only).

Results: Problems using this method of data review were identified. Groups did not differ by gender or age. The percent of cards returned, the percent of any use days, and the average hours on days used did not differ for any groups. The percent days used > 4 hours (56% for Group 4) and the average hours used (all days; 4.0 hours for Group 4) improved for Group 4 when compared with the previous groups (p<0.01).

Conclusion: Despite changes in technology, clinical interventions, and insurance requirements, there were no differences in PAP usage over time, except for improved usage for Group 4 (01/2010), and only for percent days used > 4 hours and average hours (all days). Using current insurance criteria for ongoing CPAP coverage, many new PAP patients appear to be at risk of failing a 90 day PAP trial.

0389
PREDICTORS OF CPAP COMPLIANCE IN SPLIT NIGHT POLYSOMNOGRAMS

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Introduction: Split night polysomnograms are commonly performed. Predictors of CPAP compliance based exclusively on split night study data have not been sought. The aim of this study is to determine if sleep and oxygen parameters during a split night study correlate with CPAP compliance within the first 90 days of treatment.

Methods: We conducted a retrospective study of consecutive patients who had a split night polysomnogram from January through September, 2009 at Bridgeport Hospital. Demographic data, ESS, presence of hypertension, diabetes mellitus, depression, hypnotic use, sleep parameters, time of oxygen saturation < 90% during the diagnostic study (T90) and during CPAP (PAP T90), CPAP pressure, and CPAP compliance (average daily usage in hours) within the first 90 days of CPAP treatment were recorded. Pearson's correlations were determined for sleep and oxygen variables of interest and CPAP compliance. Variables that showed significant correlations with CPAP compliance were then evaluated in multivariable regression models.

Results: Analysis of the first 28 subjects' data showed the mean age, BMI, AHI, and ESS to be 48 ± 11 years, 38 ± 8 Kg/m2, 70 ± 36 events/hr, and 11 ± 6, respectively. We found a significant univariate correlation between PAP T90 and CPAP compliance (r = -0.43, p = 0.022). CPAP compliance was not associated with AHI, sleep efficiency, or sleep stages. In a multivariate regression model, PAP T90 (β = -0.628, p = 0.015), depression (β = -0.809, p = 0.017), and use of hypnotics (β = 0.452, p =0.032) were independently associated with CPAP compliance after adjusting for confounding factors.

Conclusion: Decreased hypoxemia while on CPAP during a split night sleep study is independently associated with increased CPAP compliance within the first 90 days of CPAP therapy and may be an early marker for increased tolerance and acceptance of therapy.

0390
COMPLIANCE WITH SHAM VERSUS THERAPEUTIC CPAP

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Introduction: Studies assessing the efficacy of CPAP for obstructive sleep apnea (OSA) often utilize sham CPAP as a control treatment. The ideal pressure and interface to institute sham CPAP is debated and few studies have reported the adequacy of blinding although many report hours of CPAP usage. A significant difference in hours of usage suggests lack of blinding due to perceived benefit of CPAP or adverse effects of sham CPAP. We performed a meta-analysis of CPAP usage in studies of OSA utilizing placebo CPAP to determine the effect size of hours of usage.

Methods: A literature search was performed using sleep apnea or related terms and positive airway pressure or related terms. Abstracts and papers were reviewed. If some form of sham or subtherapeutic CPAP was utilized and hours of CPAP compliance were published for both groups the data were included in the meta-analysis. Studies utilizing a crossover design were excluded given the chance of unblinding with crossover. CPAP usage hours were compared for the two groups and effect size was determined.

Results: Fifteen studies, with a total of 345 control and 373 active participants were included in the analysis. Mean duration of use of CPAP was 5.30 (SD 2.35) hours compared to 4.62 (3.67) hours for sham CPAP. Two of the studies demonstrated longer duration of use for sham CPAP

while 13 showed longer duration for CPAP. The difference was significant in favor of longer use of CPAP compared to sham CPAP (effect size using Hedge's d was 0.0117; 95% confidence interval 0.0071-0.0164; $p < 0.05$).

Conclusion: There was a significant difference in compliance with sham versus therapeutic CPAP suggesting potential unblinding of participants and/or investigators. Reasons for this difference in compliance rates should be investigated.

0391

ADHERENCE COMPARISON OF A NEW CPAP SYSTEM IN SLEEP DISORDERED BREATHING

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Introduction: Despite the efficacy of CPAP in the treatment of sleep disordered breathing, compliance remains suboptimal. In order to improve adherence numerous modifications have been undertaken to CPAP. To date, CPAP equipment modifications have had little impact on compliance. The latest design of a CPAP system, known as S9 (ResMed Ltd, Bella Vista, Australia), encompasses new features. The aim of this study was to examine if compliance on the new CPAP would be improved compared with the patient's usual CPAP system.
Methods: Fifty subjects with OSA, established on CPAP therapy (≥ 6 months) were recruited into this study (32 males, 18 females; 32 APAP users, 18 CPAP users; 49 with humidification). A retrospective download of the last 28 days from each participant's usual CPAP was taken at the beginning of the trial. Participants then trialled the new CPAP for 28 days and then returned to their usual device for an additional 28 days. Analysis was performed on compliance data downloaded from the devices.
Results: Average daily usage on the new CPAP significantly improved by 30 minutes from a mean of 6 hours 35 minutes on the patient's usual CPAP to 7 hours 5 minutes on the new CPAP ($p = 0.003$). Average daily usage then dropped significantly by 21 minutes when patients returned to their usual device ($p = 0.01$). There was no significant compliance difference with the patient's usual device before and after trialling the new CPAP ($p = 0.34$).
Conclusion: This study is one of only a small group to show a significant increase in compliance based on equipment changes. It is proposed that the combination of the improvements in humidification, comfort of breathing algorithm, and reduced noise are what have lead to the increase in compliance.
Support (If Any): This study was funded by ResMed Ltd.

0392

RETROSPECTIVE PERCEPTION OF SUBJECTIVE SLEEPINESS PREDICTS ADHERENCE TO PAP

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Introduction: Obstructive Sleep Apnea (OSA) is a serious medical condition with significant comorbidities. OSA can be debilitating for some, but as few as half of patients with significant OSA report subjective sleepiness outside of the normal range. This lack of reporting could be due to a true lack of sleepiness or to an accommodation to excessive sleepiness over time. We attempted to determine the degree to which baseline measures of subjective sleepiness would change in retrospect after successful treatment of OSA.
Methods: Ninety-eight adults with OSA were recruited into this study as a part of another study examining the effects of Continuous Positive Airway Pressure (CPAP) over time. Measurements of subjective sleepiness were obtained, using the Epworth Sleepiness Scale (ESS), at baseline and again after 3 months of CPAP. Participants were also asked at 3 months to reflect back to their baseline assessment and to rate their sleepiness, retrospectively, before CPAP.

Results: Participants averaged 9.73 (5.34) on their baseline assessment and 7.19 (4.08) on their follow-up assessment. Retrospective assessments of baseline ESS scores were generally higher than true baseline scores (10.30 ± 5.79). Of particular interest, participants who were good adherers to CPAP also demonstrated a greater change between true and retrospective assessments of baseline sleepiness, with retrospective assessments being higher than true baseline assessments (r = .283, p<.005). High adherers (≥ 4 hrs/night) rated their baseline sleepiness as 1.4 points higher than they had originally. Poor adherers rated their sleepiness as -0.37 points lower than they had originally. The difference between these groups was significant (t = 16.6, p <.001).
Conclusion: Retrospective assessments of baseline sleepiness, after CPAP, might reflect a changed perception in baseline sleepiness based upon the efficacy of CPAP. This change may be most demonstrated most prominently in good adherers to CPAP.
Support (If Any): This project was supported by a grant from the NHLBI (2R01 HL 67209).

0393

EFFECT OF CHIN STRAP ON AHI, LEAK AND CPAP COMPLIANCE

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Introduction: A number of factors influence PAP compliance. The role of chin-strap on outpatient PAP compliance is not known. We evaluated the effect of addition of chin strap during PAP use on air leak, PAP compliance, and symptoms in patients with obstructive sleep apnea (OSA) in an accredited sleep center at a VAMC.
Methods: 121 patients diagnosed with OSA by PSG (AHI 48.8 ± 37.2, BMI was 36.6 ± 6.6 kg/m2) were followed after 1 month and again after an additional 1 - 3 months of PAP use. Chin strap was dispensed during PAP initiation after PSG or at follow-up visits to prevent air leak. Compliance card data was downloaded to determine hours of PAP use, air leak, and residual estimated AHI. Compliance with chin strap and ESS were recorded. We evaluated data from chin strap users vs. non-users and data from non-users who became chin strap users (n=23) after their first clinic visit. Nonparametric tests were used for statistical analysis.
Results: At the first visit there 35 chin strap users vs. 86 chin strap non-users. The mean estimated AHI from the compliance card at first follow up was 4.7 ± 5.2/hr. There were no significant differences in leak, residual AHI, compliance or ESS at the first visit (p=ns). However, on the next follow-up visit the addition of chin strap significantly reduced duration of residual leak (22.5 ± 26.1 vs 61.1 ± 52.1 min, p=0.003, mean ±sd), improved residual AHI (5.6 ± 7.9 vs. 7.1 ± 9.1/hr, p=0.051), percent days of PAP use ($90.8\pm0.2\%$ vs $79.5\pm0.3\%$, p=0.02), percent compliance ≥ 4 hr per night ($83.7\pm23.7\%$ vs $69.5\pm35.3\%$, p=0.02), and total minutes of PAP usage/night (423.7 ± 121.4 vs 347 ± 139.2 min, p=0.00). ESS scores were not significantly different (8.5 ± 5.1 vs 5.4 ± 5.9, p=0.08).
Conclusion: Addition of chin strap to PAP significantly improves PAP compliance probably by reducing air leak. Further studies are needed to confirm these findings and expand on the results.

0394

THE UTILITY OF USING THE APNEA-HYPOPNEA INDEX AND COMPUTER ADMINISTERED NEUROPSYCHOLOGICAL TESTING TO PREDICT CPAP TREATMENT ADHERENCE: A RETROSPECTIVE ANALYSIS

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Introduction: Executive functioning (EF) and cognitive flexibility (CF), as measured by neuropsychological (NP) testing, have been shown to be

significant predictors of compliance with various medical treatments. Our goal was to evaluate the utility of pretreatment cognitive status, as represented by EF and CF, for predicting adherence to continuous positive airway pressure (CPAP).

Methods: Thirty five subjects (17 men, 18 women; M(age) = 46.5, SD = 14.0 years) were selected from archival data collected from 2008-2010. Inclusion criteria were: a diagnosis of OSA by overnight polysomnography, pretreatment completion of the Central Nervous System Vital Signs (CNS-VS) computer administered NP test battery, and having objective CPAP adherence data for at least 1 month. NP variables were reported as Standard Score (M=100; SD=15) and CPAP adherence was defined as average minutes of nightly use over the first 30 days of treatment.

Results: Using EF, CF and apnea-hypopnea index (AHI) as predictors and CPAP adherence as the criterion, results from a linear regression analysis revealed that the scores of EF and CF, when combined with the AHI, contributed significantly to the variance of CPAP adherence, R = .556, F(3) = 4.61, p = .009. EF scores alone are inversely predictive of CPAP adherence, b* = -1.35, t(31) = -3.51, p < .05. CF scores alone were also significantly predictive, b* = 1.13, t(31) = 2.89, p < .05, but the AHI alone was not significantly predictive, b* = .151, t(31) = .948, p > .05.

Conclusion: Consistent with findings for other medical therapies, when combined with AHI, EF and CF are useful predictors of CPAP adherence. Further investigation of EF and CF in OSA patients can determine if knowledge of pretreatment cognitive status can help identify patients at risk for subtherapeutic adherence to CPAP.

0395

THE ROLE OF PATIENT PERCEPTIONS IN COMPLIANCE WITH CONTINUOUS POSITIVE AIRWAY PRESSURE

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Introduction: The high efficacy of continuous positive airway pressure (CPAP) in treating obstructive sleep apnea (OSA) is limited by poor CPAP compliance. The lack of data regarding predictors of CPAP compliance has hindered the development of tailored interventions that can be implemented before or during the critical first weeks of CPAP initiation. The primary objective of this study was to determine whether patient perceptions (perceived benefit of using CPAP, subjective knowledge of the operating features of the CPAP machine, and perceived support from the patient's bed partner) predict CPAP compliance.

Methods: Adults diagnosed with OSA who initiated fixed CPAP after undergoing a titration study were eligible to participate. Subjects completed an anonymous questionnaire that encompassed both objective and subjective experiences with CPAP as well as demographic and medical history information. CPAP compliance was defined as ≥ 4 hours of use per night for ≥ 6 nights per week.

Results: A total of 483 subjects (55.1% male) have been enrolled thus far. Using logistic regression, perceived benefit was found to be an independent predictor of CPAP compliance after adjusting for gender, comorbidities, and potential adverse effects of CPAP (adjusted OR 1.70 (95% CI 1.16-2.25), p <.0001). Neither subjective knowledge of the operating features nor perceived support from the patient's bed partner were found to predict CPAP compliance (adjusted OR 0.43 (95% CI -0.17-1.03) and 0.14 (95% CI -0.36-0.64), respectively).

Conclusion: These data suggest that perceived benefit of using CPAP predicts compliance. Characterizing this factor can lead to tailored patient education programs that may result in improved compliance and, ultimately, improved long-term outcome of patients with OSA.

0396

ETHNIC DISPARITIES IN CPAP COMPLIANCE IN NEW ZEALAND: EFFECTS OF SOCIOECONOMIC DEPRIVATION, HEALTH LITERACY AND SELF-EFFICACY

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Introduction: Preliminary New Zealand research suggests that the ethnic difference in CPAP compliance is significant after controlling for area-based socioeconomic deprivation. We aimed to perform a prospective study of patients referred for CPAP treatment, investigating compliance, socioeconomic status, health literacy and self-efficacy.

Methods: Consecutive CPAP-naïve patients ≥18 years of age referred for treatment at WellSleep clinic were approached for inclusion. All received a standardized educational package before CPAP titration and were followed for one month. Objectively-measured CPAP compliance was compared with self-identified ethnicity, Epworth Sleepiness Scale, Self-Efficacy Measure for Sleep Apnea, Rapid Estimate of Adult Literacy in Medicine, the area-based New Zealand Deprivation Index (calculated from residential address), New Zealand Individual Deprivation Index (validated 8-item questionnaire), educational history, income and employment. Multivariate logistic regression was undertaken using significant univariate predictors of CPAP compliance ≥4 hours per night, as well as ethnicity (Māori/non-Māori).

Results: Compliance data were available for 126 patients (mean±SD apnea-hypopnea index 57.8±38.8 events/hour). Māori (n=25) demonstrated significantly lower compliance than non-Māori (median 4.68 interquartile range 2.24 hours/night compared with median 5.33 interquartile range 2.61 hours/night; p=0.05), and were significantly over-represented in areas of high socioeconomic deprivation (p=0.05). There were no significant relationships between compliance and subjective sleepiness, self-efficacy or health literacy. After controlling for ethnicity, not completing tertiary education and high individual deprivation were significant independent predictors of not reaching ≥4 hours/night compliance (odds ratio 0.25, 95% CI 0.08-0.83, p=0.02; odds ratio 0.10, 95% CI 0.02-0.86, p=0.04 respectively). The overall model explained approximately 23% of the variance in CPAP compliance.

Conclusion: The disparity in CPAP compliance demonstrated between Māori and non-Māori can be explained in part by lower education levels and higher levels of individual socioeconomic deprivation. Self efficacy and health literacy using an American measurement were not significantly related to compliance in this sample.

Support (If Any): This study was funded by a Lotteries Health Research Grant, Ministry of Internal Affairs, New Zealand Government.

0397

EFFECT OF AUTO-TITRATION ON COMPLIANCE WITH CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP)

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Introduction: CPAP verified by attended polysomnography is a standard treatment for Obstructive Sleep Apnea Syndrome (OSAS). Compliance with CPAP, defined as ≥ 4 hours use 70% of nights, ranges between 29-83%. The initial experience with CPAP reportedly affects future compliance. Auto-titrating positive airway pressure (APAP) devices may be initiated and used for home titration and treatment of uncomplicated patients with moderate to severe OSA. However, it is unknown if the lack of supervision during home titration affects compliance.

Methods: OSAS patients >18 years old, CPAP naive, and with a compliance report within 3 months of initiating CPAP between 1/1/08 and 11/30/09 were eligible for inclusion. This was a retrospective chart review recording demographics; OSAS severity; medical, psychiatric and upper airway surgical history; Epworth score; presence of witnessed ap-

neas or nighttime gasping; insurance; presence of bed partner; physician visits during first 3 months of treatment; titration method; and attended titration quality. The association of adherence with categorical variables was evaluated using the chi-square test; continuous variables were compared with the t-test.

Results: Fifty-five patients (37 males), ages 30-83, 35% Caucasians, 27% Hispanic, 18% African-American, 18% unknown, 2% Asian were identified. The average body mass index was 33.1 kg/m2. Twenty-six (47%) had severe, 11(20%) moderate, and 13 (24%) mild OSAS. Five (10%) had upper airway resistance syndrome. Seventeen (31%) were compliant. Attended titrations were successful in 59%. No variable was significantly associated with compliance. A trend toward significance was seen for increased compliance in 11 patients on APAP, with 6 /11 being compliant (p=0.07), 5/11 (45%) with severe OSAS, 1/11(10%) with moderate OSAS and 5/11 (45%) with mild OSAS. Average # of visits for APAP patients was 1.9; for attended titration patients was 0.8. Medicaid insured 7/11 APAP patients.

Conclusion: No factors reviewed were significantly associated with CPAP adherence. Autotitration devices may not adversely affect compliance.

0398

RELATIONSHIP OF APAP ADHERENCE IN COMMERCIAL TRUCK DRIVERS AT THE INITIATION OF TREATMENT AND AFTER 270 DAYS

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Introduction: Obstructive Sleep Apnea (OSA) screening, testing, and treatment of commercial drivers is not only recommended, and is anticipated to become an upcoming requirement of the Department of Transportation. Given its morbidity and mortality, as well as its link to fatal crashes, it is of critical importance to identify and treat drivers who have OSA. To effectively do so treatment adherence must be maintained.

Methods: Recruited drivers were administered screening questionnaires (Berlin, Epworth Sleepiness Scale, SF-36 and the Functional Quality of Sleep Questionnaire), followed by history and physical. Drivers with a high pre-test probability for OSA underwent in-cab type 3 portable monitoring that followed by APAP titration during their 34-hr restart. In-lab polysomnography was performed for AHI < 15 and when portable test results were technically suboptimal. Drivers were assessed for adherence within the first 14 days of treatment and every 90 days for 270 days. Adherence for 14 day was defined as use of APAP for 10 or more days for 4 hours or more. Adherence for 90 days used the Medicare standard.

Results: Twenty-six drivers were included in the study. Fifteen of the subject completed the full 270 days and were used for analysis. Of the 7 (47% of subjects) that did not meet adherence during the 14 day start, 2 (13%) did not meet adherence during the last 90 day period and 5 (33%) did. Of the 8 (53% of the subjects) that did meet adherence during the 14 day start, 1 (7%) did not meet adherence during the last 90 day period and 7 (47%) did. Ten of the subjects (66%) were in adherence every 90 days for 270 days based on Medicare, with 3 of the drivers not being in adherence during the first 14 day period.

Conclusion: Adherence during the first 14 days of treatment is a good indicator of long term compliance, but not for all drivers. Detailed analysis can give guidance for maintaining adherence in initially adherent and in converting non-adherent drivers to become adherent drivers. Continuous monitoring and timely intervention are essential to successfully manage drivers with OSA.

0399

VARIATIONS IN AUTOCPAP RECOMENDED CPAP PRESSURES

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Introduction: AutoCPAP (APAP) devices are frequently used to determine optimal CPAP pressure for home OSA therapy, although optimal parameters and accuracy require further validation. We investigate these issues by using APAP devices to perform in-lab CPAP titrations and compare device generated data to physician assessment.

Methods: Four REMStarAuto with A-Flex (Respironics, "R") and two S8 AutoSet II (ResMed, "RM") APAP devices were interfaced with the Sandman (Embla) acquisition system and randomly assigned to perform in-lab CPAP titrations in OSA patients; APAP range was set to 4-20cmH20. Technicians temporarily switched to manual titration if APAP failed to increase for obstructive apneas/hypopneas/persistent flow limitation or if intermittent flow limitation was absent with APAP pressure "step-down" procedures. Device recommended pressure (Device Pressure-based on 90th percentile for R and 95th percentile for RM) was compared to pressure recommended by the interpreting physician blinded to the APAP generated data (Physician Pressure).

Results: 146 OSA patients underwent in-lab APAP titration (103 R, 43 RM). Mean Device Pressure (11.7±3.5cmH20) was higher than Physician Pressure (10.1±3.3cmH20) by an average of 1.6±2.2cmH20 (1.2±2.2 R, 2.2±2.1 RM, p=0.009). Device Pressure was equal to Physician Pressure in 19.2%; It was over by ≥2cmH20 in 43.8% (37.9% R vs 58.1% RM, p=0.02) and over by ≥4cmH20 in 4.1% (5.8% R vs 14.0% RM, p=0.10); It was under by ≥2cmH20 in 6.3% (8.7% R vs 0.0% RM, p=0.05). Median polysomnography derived residual AHI4% were similar and normalized with both devices.

Conclusion: Compared to physician recommended pressures, using APAP recommended pressures results in a low under-titration rate; Under-titration was seen only with R devices while RM devices had a higher over-titration rate. Clinical follow-up is important to identify treatment with insufficient pressure and manage potential pressure-related discomfort. However, the gold standard method of determining optimal pressure is still yet to be determined.

0400

COMPARISON OF EXHALATION PRESSURE RELIEF TO STANDARD PRESSURE DELIVERY AMONG OSA SUBJECTS ON AUTO-ADJUST THERAPY

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Introduction: CPAP represents the gold standard in the treatment of OSA. Expiratory pressure relief (EPR) and Auto-Adjust devices were developed to improve patient comfort but may result in sub-therapeutic pressure settings. The aim of this study was to determine if the Smart-Flex™ technology (DeVilbiss Healthcare Inc, Somerset, PA) is "at least as good as" standard delivery of PAP among subjects receiving Auto-Adjust Therapy

Methods: Two center, randomized, prospective, double-blinded, crossover study compared outcomes (AHI and Epworth scores [ES]) between flexible EPR (flx, at a setting of 3) and standard (std) Auto-Adjust therapy (6-15 cm H2O.IRB approval was obtained. Subjects age≥18, AHI ≥15, CPAP naïve with ESS ≥10 and no other sleep co-morbidity or acute medical condition, and adequate response to in-laboratory CPAP titra-

tion were eligible to participate. Subjects used each treatment arm for 2-weeks; AHI and ESS data was collected at the end of each treatment period. Paired t-tests were used to test for differences between standard and flx modes.

Results: Results: Data on nine (of 28) subjects (5 male), age 43.2 (± 15.1), BMI 35.6 (± 6.2) and baseline ES 14.9(±3.4) is presented. Both groups achieved comparable use (flx: 4.95±1.28; std 5.22±1.01 hrs; p 0.56). Auto-Adjust derived AHI on flx was 6.4 ±3.2 and on std 5.4±2.9 (p 0.38). ES on flx was 10.3±3.6 and on std 9.6±3.5 (p 0.49).

Conclusion: Conclusions: Interim analysis shows comparable outcomes on respiratory event indices among OSA subjects treated with an Auto-Adjust device with EPR or with standard pressure delivery. Consistent with these results is the comparable improvement in daytime alertness documented during the therapeutic trial.

Support (If Any): This study was supported by DeVilbiss Healthcare. Inc

0401

SLEEP DISORDERED BREATHING (SDB) IS SIGNIFICANTLY MORE DIFFICULT TO TREAT WITH POSITIVE AIRWAY PRESSURE AT ALTITUDE

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Introduction: Based on clinical concerns as to the difficulty of treating SDB with increasing elevation in the Mountain West, split night polysomnography results were compared between three sites differing primarily as to altitude: (site a) 4662 feet (1421 meters), (site b) 5930 feet (1808 meters) and (site c) 7100 feet (2165 meters).

Methods: Patients included in this retrospective study were individuals living at the altitude of study between the ages of 40 & 79 completing a split night study with a diagnostic AHI > 15. (site a - #150) (b -#150) (c - #142). Mean age - 58.6, mean BMI - 33.2, 33.6% female - no significant demographic differences noted between sites. The three locations utilize the same interpreting medical director, and diagnostic/treatment protocols. The quality of PAP titration obtained was rated as 1-optimal, 2-good, 3-adequate, or 4-unacceptable based on AASM clinical guidelines (Kushida et. al. 2008).

Results: Rated titration quality at site a was 1.437 (sd 0.821), site b 1.569 (sd 0.96), and site c 1.772 (sd 1025). Titration quality at site c is significantly worse than at site a (t=3.22, p > 0.01) and at site b (t=2.55, p>0.02). Analysis of covariance comparing titration across three altitude levels, controlling for age, was significant for the effect of altitude p=0.017. At site a (4/150 - 2.7%) of patients required repeat pap titration while at site b (12/150 - 8%) and at site c (15/142 -10.6%) of patients returned for repeat titration due to inadequate titrations during initial split night studies (P=.025). Mean numbers of central apneas/hr developing on treatment with PAP varied from 4.8/hr. at site a, to 9.79/hr. at site b, to 19.25/hr. at site c (significant at P < .000). At site a 16/150 (10.6%) a central apnea index CAI > 5.0 on PAP therapy, while at site b, 33/150 (22%), and at site c, 52/142 (36.6%) of patients met this criteria for the development of "complex" apnea.

Conclusion: The results demonstrate that increasing altitude has a negative effect on the quality of SDB treatment obtained during pap titration for patients living at altitude. This finding is apparently secondary to the development of central apnea on treatment with PAP (complex apnea) significantly more common with increasing altitude.

0402

COMPLEX SLEEP APNEA IN OSA PATIENTS FIRST TIME TREATED WITH CPAP

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Introduction: Some patients develop central apneas during the attempt to treat obstructive events with continuous positive airway pressure (CPAP). This is called complex sleep apnea (CompSA). The aim of this study was to evaluate the occurence of CompSA and characterize relevant patients during first two nights of CPAP treatment in a retrospective study in our sleep lab.

Methods: We included 150 patients (age 58.6 ± 10.9 years; BMI 30.9 ± 5.84kg/m2; (117 male, 33 females) with a first time diagnosis of moderate to severe OSA and underwent CPAP titration for two nights. An inclusion in the group of patients with CompSA required a central apnea index of more than 5 per hour. The AHI was determined using polysomnography before treatment and under CPAP. CPAP was titrated using standard criteria (range 4 - 15 cmH2O).

Results: We found CompSA in 27 patients (18%). Compared with the group with no CompSA there were more mixed apneas (35.4 ± 61.6 vs. 11.5 ± 27.1/h, p = 0.011) before treatment. More men were affected (92.6 vs. 74.8%, p = 0.011), a tendency that the patients with CompSA were older (60.4 ± 10.9 vs. 58.2 ± 10.9 years, p = 0.268) and they had a higher severity of OSA (AHI 39.7 ± 19.8 vs. 36.2 ± 19.3 /h, p = 0.377). The events predominantly occured in light NREM sleep and in the first night with CPAP (CAI in the CompSA group first night 9.1 ± 4.8 vs. second night 6.6 ± 2,6/h).

Conclusion: We found a high prevalence of CompSA in our group of patients. CompSA may lead to residual symptoms and intolerance to CPAP therapy. Some patients with CompSA may benefit from other modes of PAP therapy. Our data support that in most patients CompSA is limited to first night with CPAP and is already reduced in the second night of treatment.

0403

TREATMENT OF COMPLEX APNEA WITH SUPPLEMENTAL OXYGEN AND PAP

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Introduction: Complex apnea [CpxA] (defined for this study as the development a cental apnea index (CAI) > 5.0/hr. during split-night PAP titration) occurs frequently among patients being treated for obstructive sleep apnea at altitude. In this study of the effects of altitude on PAP titration, > CAI > 5.0 on treatment with PAP was present in 107/444 OSA patients evaluated with split-night polysomnography(24.1%). This finding is significantly more common with increasing altitude, and has significant negative effects on PAP titration quality (Pagel et. al. APSS Abstract 2011).

Methods: Because of the frequency of central apneas occring with PAP titration at altitude, the medical director of these sites has developed a treatment protocol for such patients described clinically as an 02>cpap/bipap titration: PAP is discontinued, low flow oxygen is administered for 30 min and PAP titration is restarted with 02. Patients (107) included in this retrospective study were between the ages of 40 & 79 being clinically evaluated with split night polysomnography for suspected OSA with a diagnostic AHI > 15 and developing a component of CpxA (CAI > 5.0) on treatment with PAP.

Results: For patients with CpxA - means: age 61.7, BMI 30.8, AHI 47.9, and low SaO2 - 75.6. For non- CpxA patients - means: age 57.8, BMI 34.1, AHI 44.8, and low SaO2 - 74.3. Using the above protocol in CpxA patients, an optimal or good titration (AASM criteria - Kushida et. al. 2008) was attained during the initial split night study in 55/107 (51%), and attained for 20/24 additional patients when they returned for a full night 02>cpap/bipap titration. 4/79 (5 %) of CpxA patients could not be adequately treated using this protocol. 28/52 (54%) did not return for their recommended repeat titration to these laboratories (this return rate was consistent for all laboratories). Overall treatment success using this protocol was 75/107 (72%). Excluding non-returning patients, this protocol achieved an optimal/good titration in 75/79 (95 %) of CpxA patients.

Conclusion: The above described 02>cpap/bipap titration protocol can be utilized to achieve an optimal/good titration in 95% of OSA patients living at altitude and developing central apneas (CpxA) on treatment with PAP.

0404

THERAPY-EFFICACY OF A NEW MODE OF AUTOMATIC SERVO VENTILATION IN SUBJECTS WITH COMPLICATED BREATHING PATTERNS DURING SLEEP

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Introduction: Cheyne-Stokes respiration (CSR) is a form of sleep disordered breathing (central apnea, periodic breathing) seen in approximately 40% of congestive heart failure patients with a left ventricular ejection fraction less than 40%.CSR is an independent risk factor for death. Auto SV is a mode of pressure support to treat obstructive, central and complex breathing patterns during sleep which may be seen in patients with CHF. The aim of the study was to determine if the Auto SV device adequately treated CSA and CSR. We evaluated the efficacy of an enhanced AutoSV algorithm in previously untreated patients with heart failure and central apnea

Methods: After providing consent, participants had a diagnostic polysomnography followed by a full night of treatment on the enhanced BiPAP autoSV ADVANCED (Respironics, Murrysville, PA USA)algorithm to determine the effect of treatment on the respiratory disturbance index (RDI), central apnea index (CAI), CSR, apnea-hypopnea index (AHI) during both REM and non-REM sleep, hypopnea index (HI) and respiratory arousals. The device was set to automatically determine expiratory and inspiratory pressures and a minimum respiratory rate with maximum pressures limits available. A maximum expiratory pressure relief setting of 3 was provided. Data were analyzed with paired t-tests.

Results: Data (mean ± SD) are presented on eight male participants. The average age was 67±12.4 years, BMI was 29.2± 5.8 Kg/m2 and the ejection fraction was 25.3% ± 5.6. Sleep time and sleep efficiency were not significantly different. The RDI on the treatment night (5.2±4.9 events per hour) was significantly lower (p=0.0001) than that on the diagnostic night (45.4±13.6 events per hour). The enhanced AutoSV also lowered the CAI (0.5±1.0 vs. 20.9±16.7, (p=0.01)), the CSR Index (1.0±3.0 vs. 26.1±17, (p=0.002)). The AHI during REM with treatment (2.8± 3.3) was significantly lower than that during the diagnostic PSG(21.6±19.9. (p=0.032)). There was a significant reduction in the AHI during non-REM as well (AHI with treatment = 5.7±5.7 and 48.3±13.8 without treatment, p=0.0001). The HI was 4.3±3.9 with therapy compared to 17.1±10.8 on the diagnostic night (p=0.018) and the respiratory arousal index (5.3±5.8 vs. 95.8±69, (p=0.007)) decreased significantly.

Conclusion: These data indicate that the enhanced Auto SV algorithm successfully treats central apnea and Cheyne-Stokes respiration in patients with severe heart failure.

Support (If Any): Support provided by Philips Respironics.

0405

THE IMPACT OF CPAP ON OBSTRUCTIVE SLEEP APNEA ON THE FIRST POSTOPERATIVE NIGHT: A PILOT STUDY

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Introduction: Obstructive Sleep Apnea (OSA) is considered a risk factor for perioperative complications. Limited data suggests that CPAP may be protective in the perioperative setting. However, little is known about the postoperative sleep in patients with OSA who use their CPAP following surgery. This pilot study describes the effects of CPAP on sleep and OSA on the first night after surgery.

Methods: Patients with known OSA on fixed pressure CPAP therapy at home admitted for elective extremity and lower abdominal surgery were enrolled. Patients were randomized to their fixed pressure CPAP vs. autoadjusting CPAP (ACPAP) for the night after surgery and underwent full attended PSG. Descriptive statistics, t-tests and Fishers exact test were used where appropriate.

Results: Eleven patients were enrolled. Demographics: 9 women, age 51.2 years old, BMI 37.6 kg/m2 (range 20.4-54.0), baseline AHI 42.9 (range 5.7-116.4), and baseline CPAP setting of 10.0 cm H2O (range 6-14). Three of the 11 slept 10 minutes or less (all on fixed pressure CPAP) and were excluded from analysis. Due to logistical issues, only 3 of the remaining 8 patients were randomized to ACPAP. All 8 of these patients slept at least 2 hours (average 300 minutes, range 136-446 minutes) with average sleep efficiency 60%. Slow wave sleep was seen in 3 patients (average 8.5%) and REM sleep in 4 patients (average 8.6%). The average residual AHI (while on CPAP or ACPAP) was 1.5 (range 0 to 5.5, infrequent central apneas). There were no significant differences on the postoperative PSG between CPAP or ACPAP patients. Due to persistent hypoxemia during sleep, 4 patients (50%) required nocturnal supplemental oxygen. There were no significant differences between those requiring oxygen and those not in terms of severity of baseline OSA, known pulmonary disease, tobacco use history, BMI or age.

Conclusion: In this small pilot study, patients with OSA undergoing elective surgery slept poorly while on CPAP the night after surgery. Despite this, OSA appeared well-controlled with either fixed pressure CPAP or ACPAP. However, significant hypoxia still occurred in half the patients and suggests monitoring is warranted.

Support (If Any): Support provided by ResMed and CleveMed.

0406

PREDICTABLE FACTORS OF RESIDUAL SLEEPINESS IN OBSTRUCTIVE SLEEP APNEA PATIENTS WHO WERE TREATED WITH NASAL CPAP

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Introduction: Some patients with obstructive sleep apnea (OSA) remain sleepy despite adequate use of continuous positive airway pressure (CPAP). The aim of this study was to investigate the clinical and polysomnographic determinants of residual daytime sleepiness in CPAP-treated OSA patients more than 6 months.

Methods: We enrolled consecutively 70 patients, who were diagnosed with OSA by polysomnography and prescribed nasal CPAP therapy. Among them, 36 patients continued to wear CPAP adequately (≥ 70% of nocturnal sleep time, ≥ 5 days a week) for more than 6 months. They were divided into Sleepy (Epworth sleepiness scale, ESS ≥10) or Non-

Sleepy group (ESS < 10) after CPAP therapy. Clinical and polysomnographic variables were compared between two groups.

Results: All patients in Sleepy and Non-Sleepy groups were considered to have adequate CPAP therapy. Twenty-two patients (57.9%) were included in Sleepy (mean ESS 14.1±4.2 → 12.4±2.3) and 16 (42.1%) were in Non-Sleepy group (13.5 ±3.2 → 6.9±1.5). There were no differences in mean duration of CPAP (10.0 ± 10.2 vs. 17.9 ± 22.8 months and 4.7 ± 1.7 vs. 4.7 ± 1.3hr/d), the mean frequency of CPAP use (71.8 ± 22.0 vs. 71.5 ± 18.9 %), and mean CPAP pressure during the therapy (9.1 ± 1.8 vs. 10.0 ± 1.7 mmH2O) between two groups (p > 0.05). Patients in Sleepy group were more depressive (higher Beck depression index), lower body weight, and higher % of slow wave sleep (N3) on initial polysomnography than patients in Non-Sleepy group. Other demographics and polysomnography parameters were not different between groups. Moreover, depression score and lower proportion of N2 sleep in Sleepy group were the independent predictable factors of residual sleepiness after adequate CPAP therapy (p < 0.05).

Conclusion: Our findings showed that remnant sleep apneas are not the principal cause of residual sleepiness in CPAP users. Depressive mood mainly seems to contribute to remaining sleepiness in patients with adequate CPAP therapy.

0407

LONG-TERM EFFECTS OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE THERAPY ON SLEEP-DISORDERED BREATHINGS AND SLEEP QUALITY IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Nasal continuous positive airway pressure (CPAP) therapy is the most effective treatment option in obstructive sleep apnea syndrome (OSA). However, the long-term benefits of CPAP on sleep-disordered breathings or sleep structures have not been determined.

Methods: We selected 37 subjects (32 men, mean age 53.2 yrs) who were diagnosed with OSA by 1st PSG and treated for more than 2 years with adequate nasal CPAP. They underwent follow-up 2nd PSG (without CPAP on the study night) to evaluate whether nasal CPAP therapy itself improve OSA or sleep quality such as sleep structures, arousal index, and wakefulness after sleep onset . Epworth sleepiness scale (ESS) and Stanford sleepiness scale (SSS) were checked before and after CPAP therapy (the same days with PSG studies).

Results: Mean duration of CPAP therapy was 50.0 ± 26.6 months (5.3±1.9 hr/d), thus the mean frequency of CPAP use was 86.4±14.3 %. Mean CPAP pressure during the therapy was 9.5 ±1.9 mmH2O. After long-term CPAP therapy, daytime sleepiness was much improved (ESS 10.8±5.1 → 7.8±4.6, p <0.001). Body weight did not change significantly during CPAP therapy (73.1±8.2 →72.9±8.3kg, p > 0.05). Compared to 1st PSG, some parameters showed a significant improvement on 2nd PSG data. Sleep latency was reduced (sleep latency, 14.5±23.6 → 6.7±6.6 min), total sleep time was increased (total sleep time 268.7±72.8→ 316.7 ± 97.3 min), the lowest oxygen saturation was increased (76.5±15.6 → 82.6 ± 5.1%). The severity of sleep-disordered breathing (Apnea-Hypopnea Index, 48.4±28.6 → 33.5±18.6/hr), arousal index (42.9±19.9 → 33.0±15.4/hr) and N1 portion (N1 38.3±19.3 → 30.9±16.6%) were also reduced, but still remained in the abnormal range.

Conclusion: Some patients with long-term CPAP use report subjective improvement of daytime sleepiness, sleep quality, and the severity of sleep-disordered breathings even if they skipped wearing CPAP mask for a considerable time. Our study showed that long-term CPAP therapy improved subjective sleepiness of patients and some PSG parameters to a degree, but this improvement was not satisfactory from a clinical point

of view. These findings suggested the necessity of CPAP therapy to OSA patients for the duration.

0408

SLEEP STAGE DYNAMICS REFLECT REDUCED SLEEP FRAGMENTATION WHEN OSA IS TREATED WITH CPAP

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Introduction: Sleep stage dynamics, as reflected by number and probability of sleep stage transitions, and by mean durations of contiguous sleep and sleep stage bouts, provide a measure of sleep fragmentation, but are rarely applied in clinical settings. We examined how sleep dynamics change when obstructive sleep apnea is treated with CPAP.

Methods: Retrospective analysis of polysomnographic baseline and CPAP titration data for adult patients referred for OSA (respiratory disturbance index [RDI]≥5). Procedures and scoring followed AASM 2007 criteria.

Results: Among 50 subjects, 23 were male; mean age was 47±11 years; and mean RDI was 32±25. During CPAP titration, the number of sleep stage transitions decreased from baseline in 37 subjects, the number of stage 1 bouts decreased in 38; stage 2 bouts decreased in 32; and mean stage 2 bout time increased in 33. Among all subjects, on average the mean number of sleep stage transitions decreased from 174±70 to 133±48 (t-test p<.0001); the number of stage 1 bouts from 64±31 to 44±21 (p<.0001); and stage 2 bouts from 55±26 to 43±17 (p=.0016). The mean stage 2 bout time increased from 283±168 to 338±155 sec (p=.02), and the probability of transitioning from stage 2 back to stage 1 decreased from .52±.18 to .40±.21 (p=.0018). Mean bout lengths for other stages, and numbers of other specific stage transitions, did not change significantly.

Conclusion: The numbers of sleep stage transitions, numbers of some sleep stage bouts, and durations of uninterrupted stage 2 sleep changed with CPAP in a manner likely to be informative, despite less than ideal CPAP levels for much of a typical titration night. Analysis of sleep dynamics may well be useful in clinical practice to help characterize the extent to which sleep improves when OSA is treated.

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0409

ONE YEAR IMPACT OF CPAP THERAPY ON HEALTH-RELATED QUALITY OF LIFE (QOL) IN PATIENTS WITH OSA AND COPD (OVERLAP SYNDROME)

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Introduction: COPD and OSA confers a high risk of disability and impaired health-related QoL. This study is designed to measure the impact of CPAP treatment on health-related QoL in patients with overlap syndrome after 1 year.

Methods: This is a prospective observational study of patients with overlap syndrome started on CPAP therapy. A control group of patients with OSA alone is recruited for comparison. All participants completed baseline polysomnography. Patients with COPD had spirometry at baseline. BMI and health-related quality of life was measured using St George's Respiratory questionnaire (SGRQ), SF-36 questionnaire and Epworth Sleepiness Scale (ESS) at baseline, 4 months and 12 months. CPAP adherence downloads were obtained at 4 months, and 12 months. Univariate analysis, ANOVA, and Friedman's test will assess impact of different variables; Pearson's or Spearman's correlation will analyze relationships.

Results: 33 subjects are currently enrolled. One year follow-up information is available for 14 patients: 4 with overlap syndrome and 10 with OSA only. Patients with overlap syndrome were slightly older than those with OSA alone (61.8 years vs. 55.7 years). At baseline, both group of patients had similar weight (BMI 34.5kg/m2 vs. BMI 36.9kg/m2, respectively). After 1 year, BMI remained unchanged in both groups (36.3 kg/m2 vs BMI 34 kg/m2, respectively). At baseline, the OSA patients compared to patients with overlap syndrome had more severe apnea (AHI 42 vs. 29.5) and reported similar sleepiness (ESS 11.3 vs.11). After 1 year of CPAP treatment, ESS improved in OSA group (ESS 7.8) and remained unchanged in overlap group (11.7). After 12 months, mean adherence was worse in the overlap group (53.2% vs. 72.6% nights use for greater than 4 hours) and hence, there was no improvement in the ESS score. As expected, at baseline respiratory-related quality of life measured by SGRQ was better in the OSA only group vs. overlap syndrome (18.5 in the 51.95, respectively). After 1 year of treatment, both groups exhibited no change in SGRQ total symptom score 17.2 vs. 50.5 respectively. Similarly, there was no change in overall health-related quality of life measured by the SF -36 questionnaire.

Conclusion: Patients in overlap group had more EDS with lower AHI. However their CPAP compliance was worse compared to OSA only group. CPAP therapy does not result in significant improvement in health-related QoL measured by SGRQ and SF36 questionnaires in patients with overlap syndrome.

0410
CPAP USE AND CHANGE IN BLOOD PRESSURE IN OBSTRUCTIVE SLEEP APNEA

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Introduction: Studies assessing effects of continuous positive airway pressure (CPAP) therapy on blood pressure (BP) in obstructive sleep apnea (OSA) have produced conflicting results.

Methods: We reviewed the charts of 316 patients with newly-diagnosed OSA who were started on CPAP. Systolic BP (SBP), Diastolic BP (DBP), Mean BP (MBP) and Body Mass Index (BMI) at the time of CPAP initiation were compared to that obtained 1-66 (average 21) months later. CPAP adherence (average daily CPAP use and usage index, i.e. percentage of nights CPAP was used for >4 hours) was assessed 2-6 weeks after the CPAP therapy was initiated.

Results: The mean age of the 316 patients (297 men and 19 women) was 61.1±10.3 years (range 29-90 years). The mean initial SBP was 133±14 mm Hg, DBP was 78±10 mm Hg, MBP 96±10 mm Hg and BMI was 36.47±7.04 kg/m². Paired t-test revealed small decreases in SBP (2mm Hg, P=0.02), DBP (4mm Hg, P<0.001) and MBP (3mm Hg, P<0.001) but no significant change in BMI (increase by 0.12kg/m², P=0.39) at follow up. MBP decreased in 63% of the subjects at follow up. Logistic regression revealed that the odds that MBP would decrease were higher in participants with higher initial MBP (OR=1.10, CI 1.06-1.15, P<0.001). The magnitude of decrease in MBP correlated significantly with initial SBP (R=0.49, P<0.001), initial DBP (R=0.42, P<0.001), hours of daily CPAP use (R=0.16, P=0.01) and decrease in BMI (R=0.22, P=0.001). Linear regression revealed that age, initial MBP, daily hours of CPAP use and change in BMI were independent determinants of decrease in MBP. Conversely, those using CPAP > 4 hours a night had a greater decrease in SBP (5.0 mm Hg vs. 0.5mm Hg, P=0.02) and MBP (4.9mm Hg vs. 1.5mm Hg, P=0.02) than those using it <4 hours a night. There was no correlation between the absolute Epworth Sleepiness Scale Score (ESS) or presence or absence of daytime sleepiness (ESS>10) and decrease in MBP. To assess whether CPAP decreases MBP in both the young and the elderly, we subdivided all participants into those above (n=176) or below (n=140) age 60 years. A significant decrease in MBP was seen in both groups.

Conclusion: We found a small decrease in BP with long-term CPAP use in this predominantly male population with OSA. The BP decreased in sleepy and non-sleepy individuals as well as in the elderly. Age, initial BP, CPAP use and change in BMI determined the magnitude of decrease in BP.

0411
INCREASE IN CARDIAC OUTPUT BY BI-LEVEL POSITIVE AIRWAY PRESSURE VENTILATION IN PATIENTS WITH CONGESTIVE HEART FAILURE

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Introduction: Noninvasive positive pressure ventilation has been widely used in the treatment of patients with chronic and severe congestive heart failure (CHF). Recently, pressure support type noninvasive positive airway pressure (PAP) ventilation like adaptive servo ventilation has been highly evaluated as an effective treatment modality in this setting. Major concern in treatment is deterioration of cardiac function by PAP itself. Though decrease in cardiac output (CO) by a fixed level of positive airway pressure (CPAP) has been reported in healthy subjects as well as in some condition of CHF patients, there is no study so far where the effects of one level PAP and bi-level PAP to cardiac function, which is widely prevailing recently as adaptive servo ventilation, are compared in CHF patients.

Methods: In 11 stable CHF patients, we performed stepwise CPAP (0, 4, 8, 12cmH2O, 5 minutes each step) and bi-level PAP (4/4, 4/9, 0/0 cmH2O) while continuously monitoring intra-cardiac pressures and CO using Swan-Ganz catheter.

Results: Stepwise increase in single level of PAP from 4 to 12 cmH2O significantly increased PAWP and tended to decrease CO in the patients with PAWP<12 mmHg (p=0.07). On the other hand, all of 3 patients with PAWP>12mmHg showed increase in CO. Bi-level PAP (EPAP/IPAP: 4/9cmH2O), however, increased CO (3.32±0.58 L/min) significantly compared with single level of PAP (4/4cmH2O) (3.09±0.69 L/min, p=0.02) irrespective of the level of PAWP or basal CO of the patients. HR did not show any consistent change during bi-level pressure ventilation.

Conclusion: Our result implies that bi-level ventilation may be more effective in treating severe CHF patients compared with same averaged level of positive pressure. This effect to severe CHF patients may be caused by unknown non-mechanical mechanisms.

0412
SYMPTOMS OF AEROPHAGIA ARE COMMON IN PATIENTS ON CONTINUOUS POSITIVE AIRWAY PRESSURE THERAPY AND RELATED TO THE PRESENCE OF NOCTURNAL GASTROESOPHAGEAL REFLUX

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Introduction: Continuous positive airway pressure (CPAP), the mainstay treatment for obstructive sleep apnea (OSA), involves administration of air under pressure to the upper airway. A well-known but poorly understood side effect of positive airway pressure therapies is air passage into the esophagus and stomach, rather than the lungs. It is possible that the aerophagia-induced gastric distension may increase gastroesophageal reflux (GER) by increasing transient lower esophageal sphincter relaxations, the most common cause of reflux. This study aimed to determine i) the prevalence of aerophagia symptoms in a large group of

OSA patients on CPAP therapy and ii) whether they were related to an increase in prevalence of GER symptoms.

Methods: Consecutive OSA patients undergoing overnight polysomnography for the purpose of optimizing their CPAP therapy completed a validated questionnaire regarding GER symptoms (heartburn or acid regurgitation) and aerophagia symptoms (increased stomach noise, belching, bloating, decreased appetite, diahorrea, or flatulence). On average patients had been on CPAP between 1 and 6 months at the time they completed the questionnaire.

Results: Complete data was available for 259 individuals (203 males). The group with aerophagia symptoms had a greater (p<0.05) prevalence of frequent (once a week or more) GER symptoms (29% vs 10%) and nighttime GER symptoms (9% vs 2%) than those without aerophagia. The group with nighttime GER symptoms had a greater prevalence of aerophagia symptoms than those without nighttime GER symptoms (63 vs 23%, respectively).

Conclusion: In a large patient sample, we have shown a higher prevalence of GER and nighttime GER symptoms in individuals with symptoms of aerophagia; Aerophagia as a side effect of CPAP therapy may precipitate GER, particularly nighttime GER. We speculate this is due to exacerbation of transient lower esophageal relaxations, precipitated by gastric distension.

0413

PSYCHOSOCIAL AND PAIN OUTCOMES OF SLEEP APNEA TREATED WITH POSITIVE AIRWAY PRESSURE IN VETERANS FOLLOWED IN MENTAL HEALTH CLINICS

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Introduction: Sleep apnea is associated with a higher prevalence of psychiatric comorbidities. Research on the effects of sleep apnea treatment on psychosocial functioning in patients followed in mental health clinics is limited. This study looks at effect of treatment on Global Assessment of Function (GAF) scores and pain scores in this population.

Methods: Retrospective, observational study. Electronic records were reviewed at VAMC Milwaukee for data downloads from January 2009 to July 2009. Inclusion criteria were: (1) Positive airway pressure (PAP) initiated within preceding 12 months, and (2) active follow up in mental health clinic, and (3) documented GAF and pain score (0-10)within 6 months prior and 6 to 12 months after treatment. High compliance was defined as PAP usage >=4 hours for >=70% of days. Wilcoxon Rank Sums for correlations based on high versus low compliance, and Spearman correlation for associations between outcome and confounding variables were used for analysis.

Results: N=26. Male: female= 22:4. Mean number of psychiatric comorbidities: 3.08(SD1.67). Mean baseline GAF score: 59.22(SD5.97). Mean baseline pain score: 2.97(SD2.40). Number of psychiatric comorbidities positively correlated with mean (p=0.0248) and median (p=0.008) pain scores. 7(27%) patients had high compliance; 19(73%) had low compliance. There was a significant decrease in lowest GAF score in the high compliance group compared to the low compliance group(p=0.0396). There was no significant difference in change in pain scores between low and high compliance groups.

Conclusion: 1.Psychiatric disorders requiring follow-up in mental health clinics are associated with higher rates of poor PAP compliance. 2.High compliance is associated with poorer psychosocial function 6-12 months after therapy compared to the low compliance. Results need confirmation with a larger sample size.

0414

EFFECTS OF ARMODAFINIL ON SIMULATED DRIVING AND SELF-REPORT MEASURES IN OBSTRUCTIVE SLEEP APNEA PATIENTS PRIOR TO TREATMENT WITH CONTINUOUS POSITIVE AIRWAY PRESSURE

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Introduction: Obstructive sleep apnea (OSA) has been associated with an increased risk of motor vehicle crashes. This driving risk can be reduced (≥ 50%) by treatment with continuous positive airway pressure (CPAP). However residual excessive daytime sleepiness (EDS) can persist for some patients who regularly use CPAP. The current study was designed to assess the effect of armodafinil on simulated driving performance and subsequent CPAP treatment compliance in newly diagnosed OSA patients with EDS during a 2-week "waiting period" prior to initiation of CPAP.

Methods: Sixty-nine newly diagnosed OSA patients, awaiting CPAP therapy, were randomized (1:1) to placebo or armodafinil (150 mg/day) treatment. Simulated driving tests and self-report measures were completed at baseline, after 2 weeks of drug treatment, and following 6-weeks of CPAP treatment. CPAP compliance was evaluated at the end of 6 weeks of CPAP.

Results: Compared to placebo, armodafinil improved simulated driving safety performance in OSA patients awaiting CPAP therapy (p=0.03). Improvement was seen in lane position deviation (p= 0.002) and number of lane excursions (p=0.02). Improvement was also observed on measures of sleepiness using the Epworth Sleepiness Scale (ESS) and sleep related quality-of-life. Following 6 weeks of CPAP, there was also significant improvement observed on multiple measures of simulated driving performance. CPAP compliance did not differ between armodafinil-treated and placebo-treated patients (p=0.80).

Conclusion: These results suggest that armodafinil may reduce the risk of motor vehicle crashes in OSA patients awaiting CPAP therapy. Treatment with armodafinil showed no effect on subsequent CPAP compliance.

Support (If Any): This was an investigator initiated research study supported by Cephalon, which provided no role in the conception and production of this study.

0415

CAFFEINE CONSUMPTION IN SLEEP-DISORDERED BREATHING (SDB): RESULTS OF A COMMUNITY-BASED STUDY

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Introduction: Caffeine is a countermeasure used to circumvent sleepiness. However, the association between caffeine consumption and the severity of SDB is not well defined. The current study aimed to examine whether SDB severity and sleepiness were associated with caffeine consumption.

Methods: Data from the Sleep Heart Health Study were analyzed to correlate SDB, as assessed by the apnea-hypopnea index (AHI) to daily caffeine consumption. Participants were surveyed for caffeinated tea, coffee, and soda use. SDB severity was assessed with overnight polysomnography. The Epworth Sleepiness Scale (ESS) was used to assess daytime sleepiness. Negative binomial regression was used to model the association between caffeine consumption, AHI, and ESS given caffeine consumption was assessed as cups/day.

Results: The sample consisted of 3036 men and 3405 women (median age: 62yrs). Coffee consumption was associated only with smoking. Former and current smokers reported consuming 1.37 and 2.14 times the number of coffee cups than non-smokers (p<0.001). Caffeinated soda use was associated with SDB severity. Women with mild (AHI:

5.0-14.9), moderate (AHI: 15.0-29.9) and severe sleep apnea (AHI>30) reported consuming 1.20, 1.46, and 1.67 times the number of soda cups, respectively, than women with an AHI<5 events/hr (p<0.0001). In contrast, men with an AHI>30 events/hr reported consuming 1.44 times the number of soda cups than men with an AHI<5 events/hr (p<0.0001). The association between SDB severity and soda consumption was stronger in the younger than older age participants. Tea consumption was associated SDB severity in women but not in men. Finally, ESS was associated with tea, but not coffee or soda, consumption in women only.

Conclusion: SDB severity is associated with greater amounts of caffeinated soda consumption, an association that was stronger in younger but not older age groups. Caffeine use in SDB may be harmful particularly in those prone to hypertension and cardiovascular disease.

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0416

DONEPEZIL IMPROVES OBSTRUCTIVE SLEEP APNEA AND SLEEPINESS

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Introduction: The literature has addressed the importance of cholinergic mechanisms in respiratory regulation and the contribution of cholinergic systems to state-dependent modulation of respiratory control. Previous publications have shown beneficial effects of cholinergic medication on OSA (obstructive sleep apnea) in AD (Alzheimer's disease) patients. We hypothesized that cholinergic medication could also improve OSA in non-AD patients. The present study evaluated the effects of donepezil on OSA in non-AD patients.

Methods: A randomized, double-blind, placebo-controlled study was conducted. Twenty-four male patients with mild to severe OSA and AHI >10 were divided into two groups, a donepezil-treated group (n=13) and a placebo-treated group (n=11). Polysomnography, sleepiness, and fatigue evaluations were performed at baseline and after 1 month of treatment

Results: There were significant improvements in the obstructive apnea/hypopnea index and the desaturation index, and reductions in the time spent with an oxygen desaturation level lower than 3% and in the Epworth Sleepiness Scale Scores (ESS), after donepezil treatment (p<0.05). Sleep efficiency decreased (p<0.01) after 1 month of donepezil treatment. Donepezil treatment did not change fatigue scores.

Conclusion: Donepezil treatment improved obstructive sleep apnea and sleepiness. Our findings support the concept that cholinergic transmission may influence breathing regulation in OSA patients.

Support (If Any): AFIP FAPESP

0417

CHANGES IN DAYTIME FUNCTIONING FOLLOWING EXERCISE TRAINING IN ADULTS WITH UNTREATED OBSTRUCTIVE SLEEP APNEA: A RANDOMIZED CONTROLLED TRIAL

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Introduction: Impairments in daytime functioning, including excessive sleepiness, reduced vigor and increased fatigue, and impaired cognition and quality of life (QOL), are common for individuals with obstructive sleep apnea (OSA). Although exercise training has been shown to improve many of these problems in other populations, there has been little

investigation into whether exercise training improves daytime functioning in individuals with OSA.

Methods: Forty-three sedentary adults with an apnea-hypopnea index ≥ 15 were randomly assigned to 12 weeks of moderate-intensity exercise training (EX; n=27) or stretching control treatment (STR; n=16). Before and following the intervention, questionnaires assessing sleepiness (Epworth Sleepiness Scale; ESS), daytime impairment due to sleepiness (10-item Functional Outcomes of Sleepiness Questionnaire; FOSQ-10), depressive symptoms (Center for Epidemiologic Studies Depression Scale; CES-D), mood (Profile of Mood States; POMS), and QOL (Medical Outcomes Study Short-form 36; SF-36) were administered, and cognitive function was evaluated with a neurobehavioral performance battery (Psychomotor Vigilance Task, Stroop Color-Word Test, Trail-making Test).

Results: Significant reductions in depressive symptoms (CES-D; P=0.03) and increases in vigor (POMS; P=0.02) and SF-36 measures of physical functioning (P=0.04), vitality (P=0.03), and mental health (P=0.04) were noted following EX compared to STR. Additionally, despite not reaching statistical significance, perhaps due to the small sample size, moderate effect size improvements (Hedges' g>0.50) were noted for sleepiness (ESS, FOSQ-10), POMS fatigue, and SF-36 physical health and role limitations due to physical problems following EX relative to STR. No improvement was found for any neurobehavioral performance measure. Improvements in fatigue following EX were mediated by improvements in OSA severity, but all other daytime functioning improvements were independent of changes in OSA severity.

Conclusion: The results suggest that exercise training may be an important therapy for the management of daytime functioning for individuals with OSA, but better powered studies are necessary to fully evaluate these effects.

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0418

EXERCISE TRAINING SIGNIFICANTLY REDUCES OBSTRUCTIVE SLEEP APNEA SEVERITY AND IMPROVES SLEEP QUALITY IN UNTREATED ADULTS: A RANDOMIZED CONTROLLED TRIAL

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Introduction: Although previous epidemiologic and small-scale experimental research has suggested that exercise training may significantly reduce obstructive sleep apnea (OSA) severity independent of changes in body weight, the efficacy of exercise training has been scarcely explored for the management of OSA.

Methods: Forty-three overweight/obese (body mass index > 25) and sedentary adults aged 18-55 years with at least moderate-severity untreated OSA (screening apnea-hypopnea index [AHI] ≥ 15) were randomized to 12 weeks of an exercise training treatment (EX; n=27) or a low-intensity stretching control treatment (STR; n=16). Participants assigned to EX met 4 days/week for 150 min/week of aerobic activity at 60% of heart rate reserve and 2 days/week of resistance training involving 2 sets of 10-12 repetitions for 8 exercises. Participants assigned to STR met 2 days/week to perform a ~30-min program designed to increase whole-body flexibility. At baseline and post-intervention, a single night of laboratory polysomnography (PSG) assessed OSA severity, home-based objective sleep quality was assessed with 7-10 days of

actigraphy, and subjective sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI).

Results: EX resulted in a significant reduction in AHI relative to STR (EX: 32.2±5.6 [mean±standard error] to 24.6±4.4, STR: 24.4±5.6 to 28.9±6.4; P<0.01) as well as a significant reduction in the oxygen desaturation index (P=0.03). The only PSG sleep variable to improve was NREM stage 3 sleep (P=0.03). Reductions in OSA severity were achieved without a significant body weight reduction (EX: -0.9±0.6 kg; STR: -0.6±0.5 kg). Improvements in actigraphic sleep onset latency, sleep efficiency, and fragmentation index, as well as improvements in PSQI global score, were also noted following exercise training.

Conclusion: These data suggest that exercise training without weight loss results in a statistically significant, albeit modest, reduction of OSA severity in overweight adults, with additional improvements in actigraphic and subjective sleep quality.

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0419

AVOIDING SLEEPING SUPINE, WHO BENEFITS AND BY HOW MUCH. THERAPEUTIC AND PUBLIC HEALTH IMPLICATIONS

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Introduction: Position effects on apnea-hypopnea index (AHI) are recognized. We quantify the degree that position contributes to diagnosis and therapy in patients/groups with clinical characteristics.

Methods: Diagnostic polysomnograms of 195 patients of GSF are analyzed by sleeping position (supine: AHIs, non-supine: AHIn, and for all sleep: AHIa) and sex, age, BMI and clinical characteristics. For four groups (severe, moderate, mild, not-OSAHS), differences in AHIa and AHIn allow reassignment to a (lower) severity group. Effects of sleep time, N3 sleep, and clinical characteristics were examined.

Results: 56 of 195 individuals were in the severe group and had AHIa >= 30, and the AHIn for 4(7%) was in the moderate group and for 5 (9%) in the mild group and 5(9%) in not-OSAHS group. For 40 in the moderate group, 17 (43%) had AHIn in the mild category and 7 (18%) were in the not-OSAHS group. For 58 in the mild group, 32 (55%) had AHIn in not-OSAHS category.

Conclusion: Individuals with OSAHS based on AHI >= 5, having slept both supine and in other positions, overwhelmingly show a higher prevalence of obstructive events while supine. Our data suggest that by avoiding the supine position, 2 out of 5 individuals with mild or moderate OSAHS (including over half with mild) no longer would meet criteria for diagnosis. One in 4 with severe OSAHS would come to a lower severity designation. Accordingly, avoiding sleeping supine could be expected to benefit well over half of individuals with mild to moderate OSAHS and remove the diagnosis entirely from one in three with mild severity. Awareness of these data may be helpful in treating patients and in supporting public health advisories about OSAHS.

0420

OBSTRUCTIVE SLEEP APNEA IN ADULTS: BODY POSTURES AND WEIGHT CHANGES INTERACTIONS

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Introduction: Body postures changes as well as weight changes have a major influence on the severity of Obstructive Sleep Apnea (OSA). The aim of the present study was to assess the interactions between changes in body posture and body weight changes in adult OSA patients.

Methods: For the purpose of this study, we analyzed demographic and polysomnographic data of 112 non-treated adults with OSA who under-

went two polysomnographic (PSG) evaluations at our Sleep Disorders Unit. The average time interval between the first and the second PSG was 6.2±3.7 years.

Results: Positional Patients (PP) - having most of their breathing abnormalities in the supine posture, who became Non Positional Patients (NPP) - having apneas and hypopneas unrelated to body posture, had a significant weight gain and a significant increase in Apnea Hypopnea Index (AHI), but mainly in Lateral AHI. On the contrary, NPP who became PP had a significant decrease in weight (but less than the increase in weight of PP who became NPP) and showed a significant improvement in AHI, again mainly in Lateral AHI. These NPP who became PP had initially a less severe disease as judged by AHI, Lateral AHI and minimum SaO2 during NREM sleep and were less obese than NPP who remained NPP. The later were the patients who showed initially the worst condition and were more obese than the rest of the patients. After 5 years on average their condition did not change significantly.

Conclusion: NPP who became PP showed a decrease in body weight and improvement of OSA while PP who became NPP showed an increase in body weight and worsening of OSA. It appears that weight changes have a modulatory effect on positional dominance, and Lateral AHI seems to be a sensitive parameter of these changes.

0421

THE INFLUENCE OF SLEEP POSITION ON GLUCOSE INTOLERANCE IN POSITIONAL OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: It is well known that patient with positional obstructive sleep apnea-hypopnea syndrome(OSAHS) have less severe respiratory disturbance and less obesity than in patient with nonpositional OSAHS and obstructive sleep apnea-hypopnea syndrome (OSAHS) is associated with impaired glucose intolerance. We investigated that pattern of impaired glucose intolerance differs among patient with non-positional OSAHS and positional OSAHS.

Methods: We diagnosed OSAHS by overnight polysomnography study. And we assessed severity apnea-hypopnea index (AHI) and positonal apnea-hypopnea index difference. We defined positional OSAHS when supine-lateral index [(supine AHI- lateral AHI)/supine AHI] is more than 0.5. Insulin resistance was assessed with fasting plasma blood glucose, plasma insulin and homeostatic model assessment of insulin resistance index (HOMA-IR), leptin.

Results: 72 OSAHS patients included. Positional OSAHS were 50 and nonpositional OSAHS 22. The body mass index, respiratory disturbance index, waist circumference, glucose were higher in severe OSAHS. Compared with positional and nonpositional OSAHS group, there were noted that impaired glucose tolerance and HOMA-IR were significantly increased in non-positional OSAHS group.

Conclusion: We found that that severe OSAHS is associated with glucose intolerance and non-positional OSAHS has a poor control of glucose than positional OSAHS group. It is suggest that the positional change during sleep in OSAHS could compensate the aggravation of metabolic consequence by OSAHS.

0422

CLINICAL EFFICACY OF A NASAL EXPIRATORY POSITIVE AIRWAY PRESSURE (EPAP) DEVICE FOR THE TREATMENT OF OBSTRUCTIVE SLEEP APNEA

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Introduction: PROVENT® Therapy (Ventus Medical Inc.) is a novel and effective nasal EPAP treatment for patients with OSA. It is well tolerated, easy to use and less cumbersome than traditional therapies.
Methods: Eligible patients in this community based sample had OSA and were treatment naive, or they had tried and failed CPAP. A total of 123 patients were offered nasal EPAP. Polysomnography was recommended if patients intended to use nasal EPAP as a primary treatment, OSA severity was moderate to severe, or OSA severity was mild and accompanied by medical co-morbidities.
Results: Of the 123 patients offered nasal EPAP, 64% were CPAP failures, 32% were treatment naive and 4% had tried therapies other than CPAP. There were no differences in age (51 yrs ± 10), gender (72% men) or BMI (32 ± 6) between the entire sample and those patients with PSG data. Follow-up is pending for 53 patients. In the analysis of the remaining 70 patients, 41 (59%) accepted therapy after an initial trial. Eleven are continuing with nasal EPAP therapy based on physician evaluation and subjective symptom relief. Polysomnographic data were available for 30 patients. Treatment success was defined as a reduction in AHI ≥ 50% or an AHI < 10. Twenty four patients (80%) were effectively treated. The median AHI was reduced from 17.1 to 4.9 (p < .0001). There was a trend toward lower mean Epworth scores [7.2 to 5.5 (p=0.07)].
Conclusion: Nasal EPAP is an effective and well tolerated initial treatment option for patients with mild to moderate OSA or for patients who cannot tolerate CPAP.
Support (If Any): This study was supported in part by Ventus Medical Inc.

0423

NASAL EPAP THERAPY FOR SLEEP APNEA: ESTIMATION OF TREATMENT RESPONSE

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Introduction: Studies of a novel EPAP device (PROVENT™, Ventus Medical) have shown improved sleep disordered breathing in OSA patients overall but the number of patients with meaningful treatment response is unclear. The current analysis was undertaken to better estimate the proportion of patients meeting a standard definition of treatment response and to investigate predictors of response across five studies.
Methods: Data from studies involving 199 subjects with AHI > 5 (AASM scoring) or > 10 (Chicago scoring) who had 1 baseline and 1-3 EPAP PSGs were evaluated. Treatment response was defined as a decrease in AHI ≥ 50% and AHI < 10 (AASM scoring) or < 20 (Chicago scoring).
Results: EPAP decreased AHI (29.9 ± 24.9 to 16.9 ± 21.0), percent stage N1 (24.0 ± 16.4 to 21.6 ± 15.1), and arousal index (26.5 ± 24.3 to 19.3 ± 21.0; P < .007 for all). Forty-seven percent met treatment response criteria (Responders) and an additional 11% showed a decrease in AHI ≥ 50%. Mean AHI with EPAP was 4.7 ± 3.3 for Responders and 27.8 ± 24.0 for all others. At baseline, Responders had lower AHI (21.3 ± 12.4 vs 37.6 ± 30.3, P < .001) and BMI (31.7 ± 6.4 vs 33.6 ± 6.4, P = .03) and a trend for a higher REM/nonREM AHI ratio (4.1 ± 10.4 vs 2.2 ± 3.0, P = .07). Responders did not differ from other subjects in sex, age, neck size, Mallampati rating, CPAP pressure requirements, or baseline Epworth, FOSQ, or supine/non-supine AHI ratio. Regression analysis found that AHI was the only significant predictor of treatment response. Responders comprised 54% of subjects with mild, 68% with moderate, and 25% with severe OSA.
Conclusion: EPAP produced a meaningful treatment response in 47% of OSA patients and decreased AHI at least 50% in an additional 11%. Lower baseline AHI was associated with a positive treatment response.

0424

RETROSPECTIVE CASE SERIES ANALYSIS OF A NASAL EXPIRATORY POSITIVE AIRWAY PRESSURE (EPAP) DEVICE TO TREAT OBSTRUCTIVE SLEEP APNEA IN A CLINICAL PRACTICE

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Introduction: Continuous positive airway pressure (CPAP) is considered the gold standard treatment for patients with obstructive sleep apnea (OSA). However, other treatment alternatives for OSA are needed to provide increased compliance and additional choices for patients and prescribing physicians. Prior studies have reported that a nasal expiratory positive airway pressure (EPAP) device (PROVENT® Therapy, Ventus Medical, Inc) significantly reduced the apnea-hypopnea index (AHI) as well as improved oxygenation and subjective daytime sleepiness. This retrospective analysis was conducted to evaluate real-world patient acceptance and outcomes of this new therapeutic option in a clinical setting.
Methods: Patients with a diagnosis of obstructive sleep apnea (AHI > 10/hour) were approached to try nasal EPAP. 97% of the patients were either CPAP failures or current CPAP users. Patients received 10 nights of sample devices for in-home acclimation evaluation. Patients that acclimated were asked to return for efficacy confirmation using standard in-lab polysomnography (PSG). During the PSGs, adjunctive therapy (e.g. chin straps, positional therapy) was used, when necessary, to achieve optimal efficacy. Patients with demonstrated efficacy were given a prescription for nasal EPAP.
Results: At a single center, 151 patients sampled nasal EPAP and 131 are in the analysis group (16 patients pending follow up and 4 status unknown). Of the analysis group, 98 patients (75%) acclimated to the device. Effectiveness (AHI < 10) was achieved in 80.7% of all patients and 90.6% of mild/moderate OSA patients. AHI was reduced to < 5 in 56.3% of all patients (63.9% of mild/moderate OSA patients). The median AHI was reduced from 25.8 to 4.2 (p<0.001).
Conclusion: The nasal EPAP device provided a statistically significant and clinically meaningful reduction in AHI in a group of clinical practice patients. Acceptance of the therapy was excellent.

0425

NASAL EPAP AS A MAJOR OSA THERAPEUTIC OPTION IN A CLINICAL SLEEP CENTER SETTING

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Introduction: Nasal EPAP (PROVENT® Therapy, Ventus Medical, Inc) is a novel OSA therapeutic device. Research has validated its efficacy but data regarding real-world experience is required. We report

here our clinical sleep center experience using nasal EPAP (nEPAP) as a major therapeutic option. Treatment efficacy, predictors of response and acceptance are also assessed.

Methods: Patients with OSA intolerant of CPAP were eligible for nEPAP evaluation. They underwent a clinic orientation session, in-home acclimation assessment, and portable monitoring to evaluate effectiveness (nEPAP "post-test"). Treatment response was defined as ≥50% AHI4% improvement and AHI4%<10. AHI4%, ODI4%, %SpO2<90%, minimum oxygen saturation, positional effect, optimal CPAP pressure, height, weight, BMI, age, and gender were compared between responders and non-responders.

Results: 94 patients with OSA underwent nEPAP orientation; 86 (91.5%) proceeded with in-home evaluation. 36 (41.9%) returned for a nEPAP post-test. Among those completing a post-test, improvement in OSA indices were seen (AHI4% 22.7±19.4 vs. 8.9±9.9, p<0.00001; ODI4% 21.8±13.0 vs. 12.1±10.3, p=0.002). 19 (52.8%) patients met response criteria with a mean nEPAP AHI4% of 2.6 and a median AHI4% improvement of 91.0%. Response rate stratified for OSA severity was 63.6%, 70.0%, and 38.5% for mild, moderate, and severe patients respectively. No other significant differences in baseline characteristics were seen between those that did and did not meet response criteria. 6 additional patients had partial response with ≥50% AHI4% improvement but AHI4%≥10. 22 of 25 (88.0%) of patients offered ongoing therapy accepted prescriptions. No significant difference in OSA severity and sleepiness was seen between those that underwent or declined the nEPAP post-test (18 declined for nEPAP discomfort, 2 for cost).

Conclusion: Nasal EPAP is feasible as a major therapeutic OSA option. Efficacy is validated and comparable to previous data. There is a high rate of accepted prescriptions in responders.

0426

ARE TREATMENT ACCEPTABILITY AND HEALTH VALUE ASSOCIATED WITH ADHERENCE TO TREATMENTS FOR OBSTRUCTIVE SLEEP APNEA?

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Introduction: Mandibular advancement devices (MAD) offer an alternative to Continuous Positive Airway Pressure (CPAP), the standard treatment for obstructive sleep apnea, yet our understanding of which phenotype may be more suitable for either treatment is limited. Some evidence is available regarding the disease phenotype (e.g. AHI, upper airway physiology), though it is still unclear what psychological variables might predict adherence. The aim of the present study was to examine psychological variables that might be associated with adherence.

Methods: Thirty-four individuals were conveniently sampled from a large randomised controlled cross-over study (n=108) evaluating the effectiveness of MAD versus CPAP. Treatment Acceptability for both MAD and CPAP, and Health Value (high vs. low with median split) and general self efficacy were measured. We examined the effects of these variables on adherence to both treatments.

Results: There was a trend for the effect of treatment acceptability on adherence levels in the CPAP phase; mean adherence for the high scoring acceptability group (mean = 4.9, SD = 2.5) was higher than for the low scoring acceptability group (m=3.4, SD=2.0), t (30) =-1.7, p=0.08, representing a medium effect, d=0.6. This effect remained robust after controlling for self-efficacy. Health value had a large effect (d=0.8) on compliance in the CPAP phase; higher mean adherence was evident in those that viewed their health as important (m=4.8, SD=2.1) as compared to those who viewed it as less important (m=2.9, SD=2.5), t (31)

=-2.4, p<0.05. Interestingly the relationship between adherence and psychological variables was not observed in the MAD phase.

Conclusion: Treatment Acceptability and health value had a moderate to large effect on CPAP, but not MAD adherence. The results provide preliminary information on the psychological variables that might differentially impact adherence to two different treatment modalities. This could potentially provide us with the possibility to tailor treatment choice for different OSA phenotypes.

0427

A PRELIMINARY STUDY ON THE SHORT-TERM OUTCOMES OF A TITRATABLE PREFABRICATED MANDIBULAR ADVANCEMENT DEVICE IN THE TREATMENT OF PATIENTS WITH OBSTRUCTIVE SLEEP APNEA-HYPOPNEA SYNDROME

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Introduction: Non invasive therapy through the use of an intraoral mandibular advancement device (MAD) is a common therapeutic option for obstructive sleep apnea-hypopnea syndrome (OSAHS). A prefabricated monoblock MAD has been associated with a poor clinical outcome compared with a custom made device, but evidence lacks regarding the beneficial role of titrable prefabricated devices. The aim of this prospective study was to assess the short-term effect on sleep apneas, sleep structure and daytime sleepiness from a titratable, prefabricated mandibular advancement device (TP-MAD) in patients with mild to moderate OSAHS.

Methods: Nine patients diagnosed with OSAHS were treated with TP-MADs. Polysomnographic and questionnaires-based control was done at baseline and after a mean of 10±3 weeks.

Results: Snoring was abolished or became inaudible in all patients as witnessed by their bed partners. Six of the 9 patients (67%) had treatment success and one patient had partial therapeutic response from TP-MAD. Slow-wave sleep increased from 14% of total sleep time at the baseline to 21% after therapy with TP-MAD. Arousal index was lower after therapy (6/hr) than at the baseline (16/hr). All sleepiness scales scores and sleep complaints as well as sleep quality improved (p<0.05).

Conclusion: In this preliminary study, a titratable prefabricated mandibular advancement device was effective on sleep apneas and sleep in the short term. The results encourage more studies of this type of device in larger samples and during longer follow-up times.

0428

EFFICACY OF AN ORAL APPLIANCE COMPARED TO CPAP UPON HEART RATE VARIABILITY PARAMETERS IN OBSTRUCTIVE SLEEP APNEA PATIENTS

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Introduction: The mechanisms underlying the association between OSA and cardiovascular disease are not well defined. The autonomic nervous system plays a role in the cardiovascular consequences of OSA, and altered heart rate variability (HRV) may represent a fundamental link in this context. However, the impact of CPAP and OA over the potential mechanisms involved in the cardiovascular consequences of OSA remains unknown.

Methods: Twenty-nine moderate-to-severe OSA patients were selected to evaluate the effect of Oral Appliance (OA) treatment compared to CPAP on HRV in a randomized, crossover, double-blind and controlled trial. All patients were submitted to one month of each treatment: BRD oral appliance (OA), CPAP and placebo oral appliance (POA). Poly-

somnography, Epworth Sleepiness Scale (ESE) and HRV were assessed at baseline and after one month of each treatment. Diaries were used to evaluate compliance. Repeated measures ANOVA model was applied.

Results: Both active treatments led to a decrease in the AHI and ESE, although CPAP had a greater effect. For HRV, there was a decrease in the total power at night with CPAP (14608.6±960.9 ms2/Hz) and OA (15576.9±1123.3 ms2/Hz), both compared to placebo (19108.8±1759.1 ms2/Hz); ($p<0.05$). The LF/HF ratio (night) was reduced with OA (3,7±0,4) compared to placebo (4,6±0,7) and CPAP (4,7±0,4); ($p<0.05$), and LF/HF ratio (REM) was reduced with OA (5,1±0,6) compared to CPAP(9,3±2,1); ($p<0.05$). The Index of Sleep Autonomic Variation (ISAV = LF REM-LF SWS) was reduced with OA (1491.0±328.6) compared to baseline (2854.9±580.0); ($p<0.05$). The compliance rate was higher during OA treatment than during CPAP (86.3±3.0% versus 72.0±4.2%; $p<0.05$).

Conclusion: Even though CPAP was more effective, the better compliance with OA favored the autonomic modulation during sleep.

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0429

SURGICAL TREATMENT FOR ADULT OBSTRUCTIVE SLEEP APNEA: A SYSTEMATIC REVIEW OF HIGH-LEVEL EVIDENCE

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Introduction: The treatment effect of surgery on obstructive sleep apnea is controversial. Recent systematic reviews of surgical treatment effect focus on surrogate outcomes in primarily level 4 evidence (case series). This systematic review and evidence grading will complement those evaluations by assessing the surgical treatment effect on multiple clinical outcomes in level 1-3 evidence (controlled studies).

Methods: Relevant articles were located using PubMed and limited to 1/1/1994 - 6/1/2010, English language, human studies, adults 19+ years, and studies with ≥10 patients. Abstracts were screened for controlled studies, and full articles reviewed for relevant outcomes and evidence level 1-3 criteria per Sackett et al. Studies were grouped by outcome category and assigned an overall recommendation grade (Sackett et al.) based on the strength of evidence. Due to variation among surgical techniques, all sleep surgical procedures were included and judged as a unit for treatment effect. Review of articles dating from 1970 and an analogous Embase search are ongoing.

Results: The PubMed search produced 2144 abstracts. Seventy-six abstracts met screening inclusion criteria, and the complete articles were systematically evaluated. Thirty studies provided level 1-3 evidence. Detailed extraction produced 12 clinical outcome categories, such as mortality risk, cardiovascular disease risk, quality of life, and others. Grade A and B recommendations support the positive impact of surgical treatment on multiple clinical outcomes. The high-level evidence is most robust for improvement of daytime sleepiness and mortality risk after surgery as compared to conservative treatment and equivalence between surgical and CPAP treatments. Higher-level studies reveal mixed effects of surgery on surrogate polysomnography parameters.

Conclusion: Published high-level 1-3 evidence supports a positive effect of surgical treatment on multiple clinical outcomes for obstructive sleep apnea. Lack of high-level evidence evaluating a specific procedure or outcome does not rule out an important beneficial effect but rather leaves the question open prompting further evaluation.

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0430

SURGICAL OUTCOMES OF MAXILLARY MANDIBULAR ADVANCEMENT FOR OBSTRUCTIVE SLEEP APNEA IN ACTIVE DUTY SOLDIERS

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Introduction: Obstructive Sleep Apnea (OSA) is an increasingly common diagnosis in Soldiers. Currently soldiers with more severe OSA, defined by apnea-hypopnea index (AHI) >30, are not deployable without an extensive waiver process. Maxillomandibular advancement (MMA) is reported as a surgical cure for OSA by increasing the diameter of the upper airway and can potentially remove the requirement for CPAP, resulting in a fully deployable Soldier. To our knowledge MMA and its surgical outcomes have not been reported in an active duty population.

Methods: We performed a retrospective review of all MMA procedures performed at our institution between 2006 -2009 for the treatment of OSA. Only Soldiers who underwent both a pre-operative and post-operative polysomnogram were included in our review. A surgical cure was defined as a 50% reduction and post-operative AHI less than 15/hour. The pre and post operative AHI and minimal nocturnal oxyhemoglobin saturation were our primary study outcomes.

Results: We identified 37 Soldiers who underwent MMA during the study period. Data obtained at the time of preoperative polysomnogram included a mean BMI of 29 (range = 19.3-36.9) and AHI of 50.5 events/hour (SD=32.1). Following MMA the post-operative AHI dropped by 36.8 to 13.8 (SD = 15.5; ($p<0.001$). Twenty-two Soldiers (59.5%) met criteria for surgical cure . Sixteen Soldiers (43%) had no residual disease defined as a postoperative AHI of less than 5 events/hour. The mean minimal nocturnal oxyhemoglobin saturation increased from 85% (SD=6.8%) to 86% (SD=7.0%, p-value=0.21) following MMA.

Conclusion: Most Soldiers in this study had severe OSA at baseline. Almost all experienced a significant reduction in their AHI following MMA and many were cured. MMA represents a viable surgical treatment option for patients in whom CPAP is either not tolerated or desire a fully deployable status.

0431

ATTITUDES REGARDING PERIOPERATIVE CARE OF PATIENTS WITH OSA: A NATIONAL SURVEY STUDY OF FOUR SPECIALTIES

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Introduction: Obstructive Sleep Apnea (OSA) is felt to be a risk factor for perioperative complications. However, the perioperative management of patients with known or suspected OSA remains controversial. This national survey study sought to determine attitudes of physicians involved in the perioperative care of OSA patients.

Methods: This was a mixed-modality national survey sent to 3000 physicians in the United States practicing in the following specialties (750 of each specialty): Anesthesiology (A), Primary Care (Family Practice or Internal Medicine) (PC), Sleep (SM), and Surgery (S). Physicians were mailed a modified version of the Turner et al. survey utilized in a 2004 survey of Canadian Anesthesiologists. The questionnaire was sent with a $1 incentive, followed by a series of 2 email blasts inviting those who had not completed the survey to complete it on-line. This is an interim report. Statistical analysis was performed using chi-square analyses.

Results: To date, 588 questionnaires (20%) have been returned. Return rate by specialty; A=26%, PC=17%, SM=21%, S=12%. Overall, 94%

feel OSA is a risk factor for perioperative complications (no difference by specialty). Of these, 29% feel it is major risk factor for perioperative complications (A=34%, PC=23%, SM=35%, S=10%, p<0.001) and 90% feel it is a major or moderate risk factor (A=91%, PC=81%, SM=94%, S=72%, p<0.001). Despite this, only 71% screen for OSA preoperatively (A=89%, PC=52%, SM=88%, S=49%, p<0.001). In patients suspected of having OSA, 32% would delay surgery pending a sleep study (A=4%, PC=41%, SM=54%, S=27%, p<0.001), while 20% would proceed with surgery without any special precautions (A=22%, PC=21%, SM=5%, S=31%, p<0.001). 52% reported personal experience with an adverse outcome related to OSA in the perioperative setting. Only 27% of respondents reported their hospital had a written policy for perioperative care of OSA patients.

Conclusion: The majority of physicians in this survey feel OSA is a significant risk factor for perioperative complications. Despite only 29% of physicians feeling that OSA is a major risk factor for perioperative complications, 52% report experience with adverse outcomes related to OSA in the perioperative setting. Perioperative management guidelines for OSA are not available at most institutions. Further work is needed to help physicians identify and intervene on patients with OSA in the perioperative setting before adverse events develop.

Support (If Any): Cephalon, Inc.

0432

TREATMENT OF OBSTRUCTIVE SLEEP APNEA WITH HYPOGLOSSAL NERVE STIMULATION: INTERIM FEASIBILITY TRIAL RESULTS

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Introduction: This study examined the safety and effectiveness of a novel hypoglossal nerve stimulation (HGNS™; Apnex Medical, Inc.) system for the treatment of obstructive sleep apnea (OSA) that is designed for unilateral hypoglossal nerve stimulation during inspiration while asleep.

Methods: Twenty-one subjects (67% male, mean age 53.6 ± 9.2 years) with moderate to severe OSA and unable to tolerate positive airway pressure underwent surgical implantation of the HGNS system. OSA severity was defined by the apnea-hyponpea index (AHI) during laboratory polysomnography (PSG) at baseline and at 3 and 6 months post-implant. AHI was scored utilizing the 1999 American Academy of Sleep Medicine criteria. Therapy compliance was assessed by evaluating nightly use hours and percentage of nights therapy was used. Symptoms were assessed using validated questionnaires: Epworth Sleepiness Scale (ESS), Functional Outcomes of Sleep Questionnaire (FOSQ) and Pittsburgh Sleep Quality Index (PSQI).

Results: HGNS was used on a median of 96% of nights, with a mean use of 6.0±1.4 hrs per night. Nineteen/21 subjects had baseline and 6 month PSGs. With HGNS therapy, there was a significant improvement (p<0.05) from baseline to 6 months in (mean ± SD): AHI (41.7±17.8 to 15.5±9.7), ESS (11.9±5.0 to 8.0±4.6), FOSQ (14.4±2.1 to 16.9±2.1), and PSQI (10.4±2.1 to 8.4±3.9). Body mass index was unchanged. Two procedure/system-related serious adverse events occurred: one pocket infection that required device removal and one stimulation lead cuff dislodgement that required lead replacement. These events resolved without sequelae.

Conclusion: HGNS therapy demonstrated a favorable safety and effectiveness profile, with high compliance. Subjects experienced a significant decrease in OSA severity as measured by AHI as well as showing a reduction in OSA-associated symptoms.

Support (If Any): Apnex Medical

0433

SELECTION FOR SUCCESS IN UPPER AIRWAY NERVE STIMULATION IN OBSTRUCTIVE SLEEP APNEA

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Introduction: Electrical stimulation of the hypoglossal nerve can improve obstructive sleep apnea syndrome (OSAS). Factors that predict success would be important to define before instituting it effectively. Initial results from a Phase II trial of a second generation Upper Airway Stimulation system (Inspire Medical Systems, Inc) were used to predict success in a second smaller cohort.

Methods: 22 patients (20 completed) with symptomatic, moderate-to-very severe OSA who had failed, or were intolerant of, continuous positive airway pressure were enrolled using broad selection criteria. Apnea hypopnea index (AHI) and oxygen saturation index (ODI) were collected using polysomnography at before and at 2, 4 and 6 months post-implant(Inspire Medical Systems device). Based on factors predictive of therapy response (AHI < 20 and 50% reduction from baseline as FDA-approved criteria) from this experience, a second set of patients were enrolled and underwent the same protocol based on a narrowed selection criteria with outcomes currently available in 8 patients at 2 months.

Results: In the first cohort the baseline BMI and AHI were 29.8±2.7 (M±SD) and 43.6±18.4/hr, respectively, and the overall response rate was 35%, and parameters predictive of an FDA responder were a BMI ≤ 32 and AHI ≤ 50/hr, without apparent palatal airway collapse. In the test cohort selected on these three criteria, baseline values for BMI and AHI were 29.2 ± 2.1 and 38.9 ± 9.8/hr, respectively. In this group, the average reduction of AHI and ODI from baseline was 62% and 60%, respectively. 7 (88%) met the responder criteria; of these, 3 patients exhibited AHI values ≤5, and 2 others AHI values <10.

Conclusion: Prediction parameters improved the responder rate from 35% to 88%, and more consistently achieved AHI values that indicate acceptable responses. Going forward, the site of obstruction and BMI, along with AHI are features to assess and address in this therapeutic pathway for moderately severe to severe OSA.

Support (If Any): Inspire Medical Systems

0434

SELECTIVE STIMULATION OF THE HYPOGLOSSAL NERVE IN OBSTRUCTIVE SLEEP APNEA - EARLY SUBJECTIVE AND OBJECTIVE RESULTS

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Introduction: Reduced pharyngeal muscle tone is considered to be an important cause for upper airway obstruction in adult obstructive sleep apnea (OSA). Electrical stimulation of the hypoglossal (XII) nerve is a potential therapy for these subjects by activation of genioglossus muscles, which causes tongue protrusion and increases retroglossal airway. This case study describes the early experience of implantation of an Upper Airway Stimulation (UAS) system (Inspire Medical Systems, Inc) and clinical outcome in four subjects up to 6-month post-implantation.

Methods: Between February and August 2010, Inspire(tm) UAS system was implanted in four subjects. All four patients were male, age between 33 and 61 years, BMI between 26 and 28 kg/m2 and baseline AHI between 30/h and 38/h. The implanted system was placed under general anesthesia, and consisted of a pressure sensor in the intercostal muscles, a stimulation electrode around the medial branch of the hypoglossal

nerve, and a pulse generator in an infraclavicular pocket on the right side of the patient. Selection of the hypoglossal nerve fibers responsible for best tongue protrusion was confirmed using an intraoperative nerve integrity monitoring (NIM®, Medtronic) system. The stimulating pulses were delivered synchronously during the inspiratory phase of breathing during sleep.

Results: Despite of the anatomical variety of the protruding fibers within the hypoglossal nerve, placing the stimulation electrode was successful in all four cases. There were no serious adverse events reported. One patient had a postoperative submental hematoma treated conservatively. In the polysomnography study, an acute effect of stimulation to stabilize airflow was observed in all four subjects. The overall AHI reduced from 33 ± 3.4 to 5.1± 3.3 at the latest follow-up. In one patient the AHI decreased from 38/h to 10/h in the first and increased to 27/h in the second follow-up, and finally 7.2/h at the 6-momth visit. Interestingly, this patient gained 5 kg bodyweight between the first two follow-ups, which suggesting a relation between BMI and the reduction of apneas. No apparent BMI changes in the other patients implanted.

Conclusion: Selective stimulation of the protruding fibers of the hypoglossal nerve is feasible and lead to predictable introperative and post-operative results.

Support (If Any): Inspire Medical Systems, Inc.

0435

CLINICAL AND POLYSOMNOGRAPHIC DATA OF POSITIONAL SLEEP APNEA AND ITS PREDICTORS

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Introduction: In Asian population, facial structure has effect on obstructive sleep apnea more than body mass index (BMI). We hypothesized that sleep position may have more effect on obstructive sleep apnea in Asians compared to Western population. If this hypothesis is accurate, positional therapy will have a major impact on treatment of obstructive sleep apnea among Asians.

Methods: We reviewed polysomnographic studies from our laboratory from Jan 1st, 2010 to June 30th, 2010. Each polysomnographic studies required at least 30 minutes each for recorded supine and recorded non-supine sleep to be included in our study. Criteria for positional and non-positional sleep apneas were (1) supine RDI/non-supine RDI >=2 and total RDI ≥5 and (2) supine RDI/non-supine RDI <2 and total RDI ≥5; respectively. We aim to determine the difference in baseline characteristics, polysomnographic findings, and predictors for positional sleep apnea.

Results: We found 144 patients with obstructive sleep apnea (RDI≥5), and 96 patients met criteria for positional sleep apnea (67%). Almost half of these patients (47%); RDI was normalized (<5) in non-supine position. Snoring intensity and snoring frequency were significantly lower among positional sleep apnea patients. Obstructive sleep apnea was also less severe in positional sleep apnea group indicated by lower RDI and arousal index, higher mean and nadir oxygen saturation, and higher %NREM3. There was no difference in BMI between two groups. We also found that low snoring frequency (≤50% of total sleep time) and

high mean oxygen saturation (≥95%) were significant predictors for positional sleep apnea. Among obstructive sleep apnea patients, low snoring intensity (can only be heard when getting closed to the patient), low RDI (5-14), and high mean oxygen saturation were significant predictors for normalization of RDI in non-supine position (non-supine RDI<5) (p=0.022, p=0.009, p=0.001; respectively).

Conclusion: Positional sleep apnea is very prevalent and noted in almost 70% of our patients. Low snoring frequency and high mean oxygen saturation were noted to be predictors for positional sleep apnea. This finding is encouraging that positional therapy can be very beneficial as the treatment modality for obstructive sleep apnea among Asians.

0436

METABOLIC CHANGES IN REM SLEEP RELATED DESATURATION IN NON OSA NON OBESE INDIVIDUALS

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Introduction: OSAS and obesity hypoventilation syndrome are well known sleep related breathing disorders. However, more subtle types of respiratory abnormalities during sleep may be recognized in sleep clinics. Oxygen desaturation associated with OSAS is linked to important metabolic changes; however it is not know if oxygen desaturation in non OSAS non obese subjects without obesity hypoventilation syndrome has clinical consequences. The purpose of this study was to evaluate the metabolic consequences of REM sleep related desaturation in non OSA non obese individuals.

Methods: A population-based survey adopting a three-stage randomized cluster sampling of Sao Paulo city was used to represent the population according to gender, age (20-80 years), and social class. Questionnaires and in lab full night PSG using nasal pressure cannula and thermistor were done. We classified as "desaturators" individuals who presented lowest oxygen saturation below 90%.

Results: From 1101 questionnaires, 1042 volunteers underwent to PSG (refusal rate=5.4%). From the total group, 644 (61%) had AHI< 5. From this group, 138 (21,4%) had lowest oxygen saturation < 90%. Most desaturation events were associated to short lasting hypopneas during REM sleep. Mean age: 43,5± 12, 65,7% was women. From this group, 32.1 % had normal weight, 49.6% were overweight (BMI > 25< 28Kg/m2) and 18.2% were obese (BMI> 28). Overweight non obese "desaturator" group presented significantly more complaints of snoring, anxiety and agitated sleep compared to control. Regarding metabolic markers, we observed a significant increase in cholesterol and LDL values in this group compared to control group ("non desaturator").

Conclusion: Oxygen desaturation during sleep not associated with OSAS, not associated with obesity, seen in 81.2% of non-obese patients (<28 kg/m2) is not recognized as a sleep related breathing disorder. Our results demonstrated that it is a frequent condition and that may be considered as a disease, since it is already associated with clinical complaints and metabolic changes.

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0437

SNORING AS AN INDEPENDENT RISK FACTOR FOR CARDIOMETABOLIC DISORDERS AFTER ADJUSTING FOR OTHER SIGNS AND SYMPTOMS OF SLEEP APNEA

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Introduction: Snoring is a highly prevalent, well-described risk factor for sleep-disordered-breathing, which is associated with cardiometabol-

ic disorders. The independent contribution of snoring to these disorders, over and above other signs and symptoms of sleep apnea, has not been explored at the population level.

Methods: Adult(18+) data from the 2007-2008 National Health and Nutrition Examination Survey (NHANES) were used. Cardiometabolic measures included self-reported diagnosis of hypertension and diabetes, systolic and diastolic BP, and blood test results: triglycerides, cholesterol(total, HDL, LDL), C-reactive protein, fasting insulin and glucose, impaired fasting glucose, and 2-hour Oral Glucose Tolerance Test(OGTT). Sleep apnea predictors consisted of self-reported sleep apnea diagnosis and frequency of: daytime sleepiness, unrestful sleep, and snorting/gasping during sleep. Snoring frequency was measured with: "How often do you snore?" Reponses were 0,1-2,3-4 or ≥5 nights/week. Linear and logistic regression analyses corrected for age, gender, race/ethnicity, education, marital status, BMI (objective), general health, health insurance, depression, alcohol intake, current smoking, and smoking history. The analysis comprised those who provided complete data (N=4163 for all outcomes except for glucose(N=2008), LDL cholesterol(N=1968), OGTT(N=1522), triglycerides(N=2012), and insulin(N=1992)).

Results: When adjusting for other apnea predictors, but not covariates, snoring ≥5 nights/week was a significant independent predictor of: hypertension, diabetes, impaired glucose, systolic-BP, diastolic-BP, total-cholesterol, HDL-cholesterol, LDL-cholesterol, OGTT, triglycerides, insulin and glucose. Snoring 3-5 nights/week was a predictor of: hypertension, diabetes, systolic-BP, diastolic-BP, HDL-cholesterol, OGTT, triglycerides, insulin and glucose. Snoring 1-3 nights/week was a predictor of: OGTT, LDL-cholesterol, and triglycerides. After adjusting for all other apnea predictors and covariates, snoring ≥5 nights/week was associated with increased risk of hypertension (OR=1.48;95%CI=1.12-1.95,p<.01).

Conclusion: Although self-reported sleep apnea predictors may not have separated snorers from patients with undiagnosed sleep apnea, the results suggest that snoring ≥5 nights/week is an independent risk factor for hypertension. Future efforts should explore whether this finding is replicated with objective sleep-disordered-breathing measurements.

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0438

S OBSTRUCTIVE SLEEP APNEA A PREDICTOR FOR PROTEINURIA? A DECISION TREE ANALYSIS

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Introduction: Proteinuria or obstructive sleep apnea (OSA) was associated with cardiovascular events and mortality in community-based cohorts. Whether OSA is a predictor for proteinuria is still controversial. We conducted a data-driven analysis to delineate a potential categorical classification algorithm of protienuria to exam if OSA a potential predictor.

Methods: 300 male adults shift workers in central Taiwan were recruited this cross-sectional community-based cohort study. Demographic data and evening blood pressure were measured before; while morning blood pressure, serum biochemical study, single dipstick urinalysis, af-

ter an overnight polysomnography (PSG) study in hospital sleep center. Where proteinuria was defined as trace or greater. Modeling proteinuria as a hierarchical multiple dimensional models, we employed decision tree analysis to identify a model that best "fitted" the relationships between the correlates and proteinuria, post multivariate logistic regression analysis.

Results: Of all participants (42.7 ± 7.4 yrs, mean±SD), 20.3% (n=61) had proteinuria. Logistic regression showed age, body mass index (BMI), glycated hemoglobin (HbA1c), desaturation index (DI), and apnea-hypopnea index (AHI) could predict proteinuria. Decision tree shows the subjects, aged older than 49 years ($\chi2df = 1 = 15.267$, P = 0.001) and of their AHI value>21 event/hour ($\chi2df = 1 = 10.076$, P < 0.029) had the highest risk for proteinuria (61.5%). In junior group, HbA1c>7 ($\chi2df = 1 = 19.725$, P < 0.001) and BMI >27.4 ($\chi2df = 1 = 8.79$, P = 0.027) was another two discriminating factors, where the former one dominant over the latter.

Conclusion: Our results indicate that a variety of age, AHI, HbA1c, BMI can predict proteinuria. Furthermore, AHI the sole determinant in senior workers, whereas HbA1c and BMI are responsible in younger ones for proteinuria. By categorical classification algorithm analysis, this study provides a comprehensive model for better understanding the correlates of proteinuria.

0439

OSA AND REFLUX - RETROSPECTIVE CHART REVIEW EXPLORING RELATIONSHIP BETWEEN OSA SEVERITY AND ESOPHAGEAL INJURY SEVERITY

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Introduction: Medical researchers have long suspected a relationship between OSA and esophageal reflux. Both these conditions have a deleterious effect on patient quality of life. However the associations still remain controversial. There has been conflicting studies recently exploring the relationship of OSA and reflux disease. We aimed to determine whether there is any correlation between severity of sleep apnea based on AHI and severity of esophageal injury based on EGD.

Methods: Retrospective chart review of 51 patients with concurrent diagnosis of OSA and esophageal disease. OSA defined as AHI >5, esophageal injury was characterized by EGD results and diagnosis in chart. Various parameters like age, gender, AHI, desaturations, BMI, sleep stages and esophageal injury were recorded in an excel sheet. Esophageal injury was assigned numbers from 1 to 5 based on severity of injury. Reflux was #1 and Esophageal cancer #5. Patients with major confounders like smoking and alcohol were removed from the review. Correlation coefficient was calculated.

Results: Data evaluation revealed a coefficient correlation of 0.421 and had a positive linear trend. Although the correlation was slight, greater sample size lead to a stronger correlation coefficient. It was also noted in 2 cases that esophageal injury reversed after compliance with PAP therapy.

Conclusion: Based on our data it can be concluded that there is a positive linear correlation between AHI and severity of esophageal Injury. Our data indicate as severity of OSA increases, the severity of esophageal injury increases. Multiple patients lacking EGD data may limit the correlation of esophageal injury with OSA. Causality cannot be established because of the nature of the study and further investigation is warranted.

0440

MILD OBSTRUCTIVE SLEEP APNEA: A QUANTITATIVE EEG ANALYSIS

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Introduction: Obstructive sleep apnea (OSA) results in sleep fragmentation, which can lead to changes in the EEG power spectrum. On the other hand, spectral analysis can also be affected by age leading to a decline in slow wave activity (SWA) and sleep deprivation, which is known to enhance SWA. The aim of our study was to study EEG spectral power in young subjects with mild obstructive sleep apnea.

Methods: Polysomnography recordings from 20 subjects, 10 healthy control subjects and 10 apnea patients, were studied. EEG channels included F1-A2, C3-A2, O1-A2, F2-A1, C4-A1, O2-A1 and A2-A1. After manual artifact removal (including EEG arousals) relative spectral power was examined in the following EEG bands: delta, theta alpha and sigma (fast and slow). Fourier transform (FFT) analysis was conducted with Brain Analyzer 2.

Results: OSA patients and Controls showed no significant difference in age (31.9 ± 1.7 [OSA] versus 29.0 ± 1.7 [Controls], $p=0.48$) and BMI (29.7 ± 1.9 [OSA] versus 27.9 ± 1.53 [Controls], $p=0.24$). Analysis of polysomnograms demonstrated no significant difference in total sleep time, sleep efficiency or sleep stage distribution between groups. Significant differences were only observed in AHI (17.1 ± 2.6/h vs. 3.7 ± 0.4/h, $p<0.001$), oxygen nadir ($87.4\pm1.1\%$ vs. $91.1\pm0.7\%$, $p=0.004$) and arousal index (25.0/h±3.0 vs. 16.7 ± 1.2/h, $p=0.020$). EEG power analysis revealed a significant increase in alpha power over C3 ($p=0.048$) and a trend increase over F3 ($p=0.078$) during NREM sleep in OSA patients. Analysis of spectral power at delta, theta and sigma frequencies did not reveal significant group differences. Regression analysis showed a significant correlation between alpha power and arousal index ($p=0.012$) as well as AHI ($p=0.005$), but not oxygen nadir.

Conclusion: Our data demonstrates signs of reduced central and frontal sleep depth in OSA patients and suggests ongoing disruption of the sleep homeostasis beyond EEG arousals during NREM sleep even in mild disease.

Support (If Any): NIH/NIHLB K23 HL103850-01 and American Board of Sleep Medicine Junior Faculty Research Award

0441

COLD SENSORY TESTING IN SNORING AND OBSTRUCTIVE SLEEP APNEA SYNDROME - EVIDENCE FOR PROGRESSIVE NERVOUS LESIONS

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Introduction: Obstructive sleep apnea syndrome (OSAS) in many cases is a progressive disorder, but the reason(s) for this is not fully understood. One hypothesis is that longstanding snoring vibrations cause a local neuropathy in the upper airway, in turn causing partial paresis and defective dilating reflexes in the surrounding muscles. Previous studies have indicated upper airway peripheral neuropathy in OSAS. The oropharyngeal sensation of cold has been shown to be compromised in patients with sleep apnea and, to a lesser extent, habitual snoring. We aimed at establishing a quick, safe and reliable temperature testing method suitable for longitudinal studies, and to use this method to compare non-snorers, snorers and untreated subjects with OSA.

Methods: 40 non-snoring subjects underwent quantitative cold sensory testing with Method of Limits (MLI) and Method of Levels (MLE) at the soft palate and the lip on two separate occasions, using a Medoc

TSA - 2001 equipment with an intra-oral thermode. Thereafter, non-snorers (n=25), snorers (AHI<10, n=32) and OSA subjects (AHI≥10, n=33) were tested.

Results: MLI showed a better test-retest repeatability (r= 2.2 vs. 2.6) for the soft palate. The performance of this method is also faster. There were no significant differences concerning lip sensory function between groups. Non-snoring controls had lower thresholds for cold (i.e., better sensitivity) in the soft palate compared to both other groups (p<0.01). Snorers had lower thresholds than OSA subjects (p< 0.05). There were significant correlations between decreased sensory function and AHI (r= 0.41) and also to duration of snoring (r=0.47).

Conclusion: MLI should be used in longitudinal studies with quantitative cold sensory testing. The degree of sensory neuropathy in the upper airway correlates with degree of obstructive sleep disorder. Our results strengthen the hypothesis that snoring vibrations may cause a neuropathy in the upper airway which contributes to the progression and development of OSA.

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0442

DOES INSPIRATORY FLOW LIMITATION WITHOUT OXYGEN DESATURATION OR CORTICAL AROUSAL ALTER SYMPATHOVAGAL BALANCE?

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Introduction: Sympathetic activation, associated with obstructive sleep apnea (OSA), may lead to cardiovascular morbidity and mortality. However, whether isolated inspiratory flow limitation (IFL) i.e. non-apnea/hypopnea flow limited breathing, without associated cortical arousals or oxygen desaturation, contributes to sympathetic activation is unclear. We hypothesized that IFL contributes to sympathetic activation as assessed by autoregressive (AR) estimates of heart rate variability spectra.

Methods: All subjects underwent continuous positive airway pressure (CPAP) titration polysomnography for treatment of OSA. IFL was defined as flattening of the inspiratory limb of the flow-time signal without associated oxygen desaturation or cortical arousal. We excluded subjects with known cardiac disease, diabetes, or use of medications that alter cardiac conduction or autonomic activity. AR spectral analysis was performed on two non-contiguous 5-minute ECG segments: one during IFL and the other during non-flow limited (NFL) breathing during CPAP titration.

Results: Data (mean ± SD) were obtained from 7 subjects (4 males, 3 females): age 51 ± 4.6 years; BMI 32.8 ± 1.8 kg/m^{2}; AHI 41.1 ± 11.3/h. No statistically significant differences were found between IFL and NFL breathing in the relative distributions of power across the primarily sympathetic modulated low frequency (LF) (0.04 - 0.15 Hz) region and the primarily parasympathetic-modulated high frequency (HF) (0.15 - 0.4 Hz) region. LF and HF powers, expressed as percentages of total spectral area, were during IFL: 37.7 ± 13.7% and 61.5 ± 13.3%; during NFL breathing: 34.9 ± 9.5 and 63.5 ± 8.6 respectively, p=ns.

Conclusion: We did not demonstrate alteration of sympathovagal balance due to IFL without associated cortical arousals or oxygen desaturation. These data raise questions regarding the need to titrate CPAP to completely eliminate flow limited breathing.

0443

DEPRESSION ATTENUATES CEREBRAL AND PERIPHERAL VASCULAR RESPONSES TO THE VALSALVA MANEUVER IN OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA) patients show high levels of depression and cardiovascular dysfunction, possibly resulting from neural injury in regions regulating those functions. Since depression is predictive of worsening cardiovascular outcomes in other chronic conditions, depression in OSA may be associated with compromised peripheral and cerebral vascular function.

Methods: We studied 47 recently-diagnosed, untreated, moderate-to-severe OSA patients (AHI = 32.9 ± 21.1 events/hour; age = 46.7 ± 9.1 years; female:male = 12:35), with no history of mental illness. We classified subjects with the Beck Depression Inventory-II (BDI) into "lowBDI" (BDI ≤ 9; N = 25), "mildBDI" (10 ≤ BDI ≤ 19; N = 7) and "mod-severeBDI" (BDI > 19; N = 5) groups. We collected functional magnetic resonance imaging (fMRI) and heart rate measurements while subjects performed a Valsalva maneuver, an 18 second forcible exhalation against a closed glottis, which normally elicits substantial transient blood pressure and heart rate changes. Relative changes in cerebral blood flow were calculated from the global fMRI (blood-oxygen level dependent; BOLD) signal. We assessed between-group differences by repeated-measures ANOVA.

Results: Group-by-time differences in heart rate appeared ($p < 0.05$), with the lowBDI group showing the greatest heart rate responses, followed by mildBDI, and with mod-severeBDI group the lowest (e.g., increases at time 17 s by group: lowBDI = 22%, mildBDI = 13%, mod-severeBDI = 7%). The lowBDI group showed the greatest extents of post-release overshoot (4 s post) and subsequent dip (11 s post), followed by the mildBDI and mod-severeBDI groups; BOLD responses also were reduced in the mildBDI and mod-severeBDI groups, with the greatest impairment in the mod-severeBDI group; differences emerged 3 seconds into the challenge, and after release at 1-4 s and 14-24 s.

Conclusion: Depressive symptoms in OSA are accompanied by reduced cardiovascular and cerebral blood flow responses to a blood pressure challenge. The cardiovascular effects likely result from the increased tissue injury in insular and cingulate areas, which are excessively damaged in OSA patients with depression. Depressed mood in OSA, as in other disorders, may worsen cardiovascular outcomes, and the reduced cerebral blood flow responsiveness may contribute to further brain injury in OSA during momentary challenges.

0444

36 HOURS OF SLEEP DEPRIVATION REDUCES GENIOGLOSSUS MUSCLE ACTIVITY DURING HYPERCAPNIA AND INSPIRATORY RESISTIVE LOADS DURING WAKEFULNESS

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Introduction: Sleep fragmentation/deprivation has been associated with multiple detrimental effects and has been proposed to induce or worsen OSA severity. Genioglossus is the largest upper airway dilator muscle and is important in maintaining upper airway patency in OSA. However, the effect of sleep deprivation on genioglossus muscle function and minute ventilation has been minimally studied. We hypothesized that 36 hours of sleep deprivation would reduce genioglossus muscle responsiveness and minute ventilation to chemical and mechanical stimuli.

Methods: A nasal mask and pneumotachograph were fitted to measure ventilation in 11 healthy subjects (2 women) aged 19-50 years. Fine wire intramuscular electrodes were inserted per orally into genioglossus to create a bipolar EMG recording. Genioglossus EMG activity (% maximum activity obtained during either a tongue protrusion maneuver or a swallow; whichever yielded the highest value), and minute ventilation were measured in the evening during wakefulness before and after 36 hours of sleep deprivation during the following conditions: 1) quiet breathing, 2) hypercapnia (CO_2 5 and 10mmHg above baseline $PETCO_2$), and 3) inspiratory resistive loading (15cmH_2O/L.s^{-1}). Additional measurements including reflex responses to negative pressure, data during sleep transitions, and stable sleep before and after sleep deprivation were also obtained. Sleep deprivation was accomplished by constant human interaction and documented by ambulatory EEG.

Results: Compared to pre-deprivation, peak genioglossus EMG activity was reduced across all conditions following acute sleep deprivation (quiet breathing: 5.5±1.5 vs. 3.1±0.7 %max; hypercapnia 5mmHg above baseline: 8.2±1.9 vs. 3.5±0.7 %max; hypercapnia 10mmHg above baseline: 13.2±3.7 vs. 5.3±1.1 %max; inspiratory resistive loading: 11.7±3.3 vs. 4.4±1.0 %max, ANOVA main effect p=0.01). Similar reductions were observed in tonic genioglossus activity. However, minute ventilation during wakefulness across the various conditions did not differ during pre- versus post sleep deprivation. Analysis for the sleep data remains ongoing.

Conclusion: During wakefulness, acute sleep deprivation results in substantial reductions (approximately 30-40%) in genioglossus muscle responsiveness to chemical (hypercapnia) and mechanical (resistive loads) stimuli but minute ventilation is preserved. These data suggest that sleep deprivation may initiate or perpetuate OSA, at least in part, via impaired genioglossus muscle function.

0445

NOCTURNAL SLEEP DETERMINANTS FOR EXCESSIVE DAYTIME SLEEPINESS IN OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: There are large variation to determine excessive daytime sleepiness (EDS) between two often-used manners, subjective evaluation of Epworth sleepiness scale (ESS) and objective evaluation of multiple sleep latency test (MSLT), in obstructive sleep apnea syndrome (OSAS). This may significantly affect the exploration of nocturnal sleep determinants for EDS in OSAS. EDS determined with combined ESS and MSLT scores is supposed to be useful way to more reliably distinguish EDS.

Methods: One hundred eighty-two consecutive patients who had AHI greater than 5 were used in this study. EDS (n=32) was considered present whenever ESS score was >10 and the MSLT score <5 min. Absence of EDS (No-EDS, n=48) was diagnosed in those patients with an ESS score of <10 and an MSLT score of >10 min.

Results: Compared to No-EDS patients, EDS patients exhibited 1) greater AHI and time length of SaO2 < 95%, and lower nocturnal SaO2 during separate REM and NREM periods, and total mean and minimum SaO2; 2) shortened latency to sleep and REM, and increases in total sleep and sleep efficiency; 3) increases in brief arousal index, N1 time and a trend of decrease in N3 percentage (p<0.081). In addition, stepwise logistic regression analysis showed that arousal index, time length of SaO2 < 95% and REM sleep latency to be independent predictors of EDS.

Conclusion: Utilizing clear cutoff criteria to diagnose EDS by combined subjective and objective evaluation, the results suggest that EDS patients in OSAS patients are characterized by at least following different aspects of nocturnal sleep: 1) severe sleep apnea/hypopnea and hypoxemia, 2) fragmented sleep, 3) low quality of sleep, and 4) high pressure of sleeping drive.

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0446

UNCONVENTIONAL CORRELATES OF MSLT-DEFINED SLEEPINESS IN OBESE PATIENTS

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Introduction: MSLT-defined sleepiness shows only modest relationships to measures of impaired respiration in sleep. In this study, we examined polysomnographic correlates of MSLT-defined sleepiness in a group of obese patients (all BMI $\geq$ 30), most of whom showed substantial levels of sleep apnea.

Methods: We studied 90 obese patients (34 women, 56 men), BMI (mean$\pm$SD) = 42.7$\pm$9.3 (range 30.1-68.8) who were attended at INCMNSZ Sleep Clinic. The mean$\pm$SD age was 40.9$\pm$10.9 and mean$\pm$SD AHI was 36.7$\pm$34.2. All underwent two nights of nocturnal polysomnography and daytime testing (MSLT).

Results: Mean$\pm$SD MSLT was 5.4$\pm$3.9, range 0-17.3 and was weakly correlated with AHI (Spearman rho= -0.24, p < 0.03). However, among these obese patients, greater levels of sleepiness were associated with higher sleep efficiencies (rho = -.024, p < .03), lower N1% (rho = -0.24, P < .03), a higher number of desaturations per hour (rho = -0.31, p < .005) and a greater number of PLMS per hour (rho = -.0.27, p < .02).

Conclusion: Among these very obese patients, the severity of daytime sleepiness was related marginally to markers of greater breathing disorder in sleep, but also appeared to be related to higher levels of sleep continuity. The positive association to PLMS severity, in the absence of associations with conventional measures of fragmentation, warrants further attention either as a) a better measure of sleep fragmentation or b) a unique correlate of sleepiness in this population.

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0447

DAYTIME SLEEPINESS IN REM DEPENDENT OBSTRUCTIVE SLEEP APNEA PATIENTS

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Introduction: Obstructive sleep apnea (OSA) is usually worse in rapid eye movement (REM) sleep than non-rapid eye movement (NREM) sleep. It was reported that duration of apnea is longer in REM than NREM and the degree of hypoxemia is more severe in REM sleep than NREM sleep. Apnea-hypopnea index, arousal index and the degree of hypoxemia has been previously suggested parameters that affect the daytime sleepiness in OSA patients. . In a small group patients, obstructive respiratory events occur more frequently in REM than NREM sleep. In this study, we aimed to investigate the daytime sleepiness in REM sleep dependent sleep apnea patients in comparison to the non-stage dependent OSA patients.

Methods: Twenty one subjects with REM sleep dependent OSA were identified among 860 patients referred to sleep disorders center in teaching hospital with an apnea-hypopnea index (AHI) >or= 5 events per hour. REM sleep dependent OSA was defined as non-REM (NREM) AHI <or= 15/h and REM AHI/NREM AHI ratio >or= 2. For comparison, 22 subjects with non-stage dependent OSA were selected with an AHI <or= 15/h. We determined the age, sex, body mass index (BMI), AHI, duration of apnea-hypopnea, minimum oxygen saturation and oxygen desaturation index, arousal index, sleep latency, REM latency, total sleep time, percentage of sleep stage and wakefullness. Epworth sleepiness scale was used to determine the daytime sleepiness. Student t test was used for statistical analysis.

Results: Epworth sleepiness scale was found 7.9$\pm$3.9 in REM sleep dependent OSA patients and 9.6 $\pm$5.2 in non-stage dependent OSA group. There was no any statistical difference between two groups in terms of daytime sleepiness. The other sleep and respiratory patterns did not show any difference between two groups.

Conclusion: Obstructive respiratory events that are seen predominantly in REM sleep did not affect daytime sleepiness.

0448

THE ASSOCIATION OF OXIDATIVE STRESS WITH CENTRAL OBESITY IN OBSTRUCTIVE SLEEP APNEA

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Introduction: Previous studies have presented contradictory results concerning oxidative stress and antioxidant status in obstructive sleep apnea (OSA). This study was done to compare concentrations of multiple oxidative stress and antioxidant status markers among normal controls and patients with OSA. We also tried to examine the correlations between oxidative stress markers and various clinical characteristics.

Methods: A total of 76 subjects were enrolled in this study. All subjects underwent overnight polysomnography. Subjects were divided into normal control (n=21), mild-to-moderate OSA (n=32) and severe OSA (n=23). Blood was withdrawn from subjects, and parameters of glucose metabolism, markers of oxidative stress and antioxidant status were assessed.

Results: There was no significant difference in the concentration of either oxidative stress or antioxidant status markers among three groups. There was no significant correlation between oxidative stress markers and OSA variables. However, there were correlations between waist-to-hip ratio (WHR)-oxidized LDL cholesterol (OXLDL) (r = 0.430, P < 0.01), WHR-glutathione peroxidase (GPX) (r = 0.331, P < 0.01), WHR-total antioxidant status (TAS) (r = -0.327, P < 0.01) and WHR-superoxide dismutase (SOD) (r = -0.337, P < 0.01). When we divided the subjects into 3 groups by waist-to-hip ratio value, there were significant differences of OXLDL, GPX and SOD among three groups. WHR was a significant independent variable of OXLDL, GPX, TAS and SOD in multiple linear regression analysis.

Conclusion: The oxidative stress in OSA was related to central obesity rather than intermittent hypoxia or respiratory disturbances. To control cardiovascular complications in OSA, weight reduction should be a component in the treatment strategy of OSA.

0449

INTERINDIVIDUAL DIFFERENCES IN ENDOTHELIAL FUNCTION IN OTHERWISE HEALTHY OSA SUBJECTS

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Introduction: The aim of this study was to measure endothelial function in otherwise healthy obstructive sleep apnea (OSA) patients compared to controls from the general population and changes following 3 months of continuous positive airway pressure (CPAP) treatment. Endothelial dysfunction reflects cardiovascular risk and has been found in OSA subjects with cardiovascular disease.

Methods: Participants underwent a full-night polysomnography. Measurements of endothelial function were performed in the evening and morning, measuring reactive hyperemia peripheral arterial tone (RH-PAT) index. Blood samples were collected for interleukin-6 and leptin determinations and nocturnal urine for catecholamine measurements.

Results: 35 male subjects (mean age±SD, 48.4±8.6 years, mean BMI 33.2±6.1 kg/m2) were recruited. 17 subjects had mild-to-moderate OSA (apnea-hypopnea index, AHI =10-30, mean 20.1±6.6), 10 severe OSA (AHI >30, mean 50.1±14.2) and 8 were controls (AHI <10, mean 3.8±2.0). No significant difference was found in RH-PAT index between controls, mild-to-moderate OSA and severe OSA. Most subjects did not have endothelial dysfunction (RH-PAT index <1.67). No change in RH-PAT index was observed in the 14 subjects who completed 3 months of CPAP treatment. However, OSA subjects with low RH-PAT index while untreated were more likely to have an increase in RH-PAT index with CPAP treatment (r= -0.73, p=0.003).

Conclusion: Endothelial function in otherwise healthy OSA subjects is similar to that of controls. Interindividual variability in endothelial function was high in OSA subjects both at baseline and follow-up but the majority did not have endothelial dysfunction. Those subjects with more impaired endothelial function while untreated were more likely to have improved endothelial function with CPAP.

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0450

OBSTRUCTIVE SLEEP APNEA INCREASES EXPRESSION OF APOPTOSIS-RELATED PROTEINS IN FEMALE PLATELETS

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Introduction: Obstructive sleep apnea is associated with increased risk of stroke and cardiovascular events. Dysregulated platelet function may also contribute to thrombotic risk. In vitro analyses demonstrate enhanced platelet activation and aggregation in OSA compared to control subjects. However, molecular mechanisms mediating platelet abnormalities have not been investigated. Therefore, we sought to evaluate expression of low abundance platelet proteins using proteomics in patients with and without sleep apnea.

Methods: Platelets were obtained from 8 subjects (4 males, 4 females) with severe obstructive sleep apnea (apnea-hypopnea index greater than 30 events per hour) and 8 subjects free of OSA measured by overnight polysomnography. Subjects were matched for age, gender, and body mass index. Platelet proteomics were measured using antibody micro-array. Relative expression of platelet proteins were compared between OSA and controls and gene ontology analysis was done for proteins with differential expression.

Results: Hierarchical cluster analysis revealed that platelet proteins clustered by matched male and female pairs rather than clustering by OSA or control categorization. For the most part, low-abundance platelet protein expression was not different between OSA and control subjects. Gene ontology analysis demonstrated that apoptosis was a biological process significantly represented in proteins increased in female OSA (p=1.5 e-05) but not control subjects (p=NS). Furthermore, a greater frequency of apoptosis-related proteins included in the microarrays had higher relative expression in female OSA compared to control subjects (24.2% vs 4.8%, respectively, (p=0.004).

Conclusion: OSA has less influence on platelet protein expression compared to age, gender, and BMI. Expression of apoptosis proteins was higher in female but not male OSA subjects when compared to control subjects. Since the apoptosis pathway may produce a procoagulant state, enhanced apoptosis in platelets may represent a previously unknown contributor to thrombosis risk in OSA.

0451

NEW SIGNIFICANCE OF MEASURING PLASMA VASPIN LEVELS IN OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Obesity is an important etiologic factor for OSAS. OSAS is suggested to be associated with factors common to the development and pathophysiology of metabolic syndrome. Vaspin is a protein identified within a gene cluster increasingly expressed in visceral fat of OLETF rats, an animal model of obesity with visceral fat accumulation or type 2 DM. Like leptin, vaspin has been suggested to be associated with metabolic syndrome. However, factors affecting and mechanisms regulating plasma vaspin levels remain unclear. Thus, we investigated, in OSAS patients considered to have leptin and insulin resistance, whether plasma vaspin levels are as associated with the severity of sleep-disordered breathing as is leptin.

Methods: The subjects were patients who visited Iwate Medical University Hospital, with chief complaints of snoring, apnea, EDS, and who were diagnosed with OSAS by PSG. The study enrolled 22 OSAS patients and 6 non-OSAS volunteers as controls. Moreover, the subjects consisted of 7 patients who had been diagnosed as having OSAS by PSG . All the patients had received the nCPAP treatment for a period of 3-6 months. Plasma vaspin levels(PVLs) were measured using a Human Vaspin ELISA Kit.

Results: PVL in the 22 OSAS patients was 0.9 ± 0.20 ng/ml and level in the OSAS was significantly higher than that in the control (0.3 ± 0.02ng/ml). The data obtained by PSG showed no correlation between PVL and sleep stages in any of the subjects, but a significant positive correlation was detected between these levels and the AHI. Moreover, PVL correlated significantly with the arousal index(AI), a sleep disorder severity index. The nCPAP treatment significantly decreased AHI and AI, and significantly increased the percentages of stage 3+4 sleep and stage REM sleep. The PVL in the 7 OSAS patients before the nCPAP treatment was 06 ± 0.2 ng/ml and after the nCPAP treatment was 0.3 ± 0.1 ng/ml. PVLs were significantly lower after the nCPAP treatment than before the nCPAP treatment.

Conclusion: While past reports have suggested a correlation between vaspin and BMI, this investigation limited to OSAS patients found no correlation between vaspin and BMI. However, strong correlations were recognized between vaspin and AHI and AI. Thus, vaspin, considered to be a new biomarker of visceral fat, is associated with respiratory

and sleep disorders rather than BMI in OSAS patients, suggesting that plasma vaspin level is a potential biomarker of the pathophysiology associated with OSAS.

0452

EFFECTS OF OBSTRUCTIVE SLEEP APNEA ON LEUKOCYTES PROFILE: A POPULATION-BASED SURVEY

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Introduction: Accumulating evidence suggests that sleep loss can impact the immune profile in experimental conditions. However, investigations focusing whether sleep disorders are associated with host defense alterations in epidemiological studies are still limited. Aim: This study was undertaken to evaluate whether obstructive sleep apnea syndrome (OSAS), one of the most prevalent sleep disorder, was associated with hematologic changes in a sample representative of the population of Sao Paulo, Brazil.
Methods: A sample of 1042 subjects was used to represent the population of Sao Paulo city according to gender, age (20-80 years), and socioeconomic status. Hematological analysis of venous blood and a full polysomnography were carried out.
Results: It was found significant increased leukocytes number in OSAS subjects. Further analysis considering sex-differences demonstrated that the leukocytes number was increased only in premenopausal women. Linear regression analysis using backward method showed the following factors that independently predicted the leukocytes alterations: neutrophils, TNF-α, estradiol, age, current smoker, cortisol, body mass index and oxyhemoglobin saturation.
Conclusion: The results showed that sleep apnea was associated with an exclusive increase of leukocytes in women during the young ages. The data highlighted that several outcomes induced by OSAS were determinants in the altered immune profile, indicating the influence of sleep disruption on immunity. Finally, sleep fragmentation induced by OSAS seems to be involved in the bidirectional relationship between sleep quality and immune response.
Support (If Any): FAPESP (#07/55445-6 to FSR and CEPID #98/14303-3 to ST), Associação Fundo de Incentivo à Psicofarmacologia (AFIP) and CNPq

0453

ASSOCIATION BETWEEN URIC ACID LEVELS, HYPOXIA AND SLEEP APNEA: A POPULATION-BASED SURVEY

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Introduction: Recurrent hypoxia associated with obstructive sleep apnea syndrome leads to an increase in the degradation of adenosine triphosphatase into xanthine, which in turn increases uric acid concentrations. The current study aimed to determine whether a correlation exists between uric acid levels in the peripheral blood and the arterial oxyhemoglobin saturation (SpO2) from a representative population of Sao Paulo.
Methods: A population-based survey adopting a probabilistic three-stage cluster sample of Sao Paulo was used to represent the population according to gender, age and socioeconomic class. A total of 1,021 volunteers underwent polysomnography recordings, blood pressure assessment and biochemical blood analysis.
Results: The results indicated that 30.3% of women and 48.3% of men with an apnea-hypopnea index (AHI)>5 had higher uric acid levels compared with normal gender-matched individuals. Men presented higher levels of uric acid than women, independent of AHI. Uric acid levels were significantly correlated with AHI, systolic blood pressure,

SpO2, arousal index, percentage of slow-wave sleep, creatinine, sodium, cholesterol, triglycerides and glucose levels. A linear regression model revealed that the predictors for uric acid concentration were gender, creatinine, triglycerides, systolic blood pressure, SpO2 and HDL. However, when the model was controlled for body mass index, the influence of SpO2 decreased in the model.
Conclusion: Uric acid levels were positively correlated with the number of obstructive respiratory episodes during sleep and present a possible marker for sleep apnea. Nevertheless, this association seems to be influenced by a confounding factor: obesity.
Support (If Any): This work was supported by grants from AFIP, FAPESP and CNPq.

0454

QUALITY OF LIFE, DEPRESSION AND ANXIETY SCORES IN SLEEPY AND NON-SLEEPY OSA SUBJECTS

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Introduction: Excessive daytime sleepiness, a common symptom of OSA, negatively impacts QoL in these patients. It is not clear however whether non-sleepy OSA patients have similar impairments in QoL, and if mood or anxiety scores are affected independently of daytime sleepiness. The objective of this study was to compare the Quality of Life, depression and anxiety scores in sleepy and non-sleepy OSA subjects.
Methods: One hundred and two consecutive patients referred to a tertiary sleep disorders clinic for evaluation of OSA completed SF-36, CES Depression Scale, State-Trait Anxiety Inventory (STAI), ESS, and underwent an in-lab PSG. Patients diagnosed with OSA (AHI > 5) were classified based on subjective sleepiness scores as sleepy (ESS ≥ 10) and non-sleepy (ESS < 10). Groups were matched for age, sex and BMI. We compared SF-36, PSQI, STAY-1 and STAY - 2 as well as CES depression scores between sleepy and non-sleepy patients prior to initiating CPAP therapy.
Results: The sleepy OSA group had significantly worse depression (17.44 ± 10.16 vs. 10.86 ± 7.30, p = 0.02) and STAI anxiety scores (35.92 ± 9.95 vs 30.26 ± 6.87, p = 0.04) than the non-sleepy OSA patients. Non-sleepy and sleepy OSA patients had similar impairments in SF-36 Vitality and MCS scores. There was no significant correlation between ESS and SF-36 Vitality scores. There was a weak correlation between ESS and depression and anxiety scores.
Conclusion: Sleepy OSA patients demonstrate worse depression and anxiety scores than non-sleepy subjects. Non-sleepy and sleepy OSA patients have similar decrements in general health QoL scores as measured by SF-36. Furthermore ESS scores do not correlate with SF-36 QoL scores in OSA subjects.
Support (If Any): The study was supported by Lung Association of Saskatchewan, Kelsey Trail Health Region and Saskatoon Health Region.

0455

EFFECTS OF TRAZODONE ON THE RESPIRATORY AROUSAL THRESHOLD AND UPPER AIRWAY DILATOR MUSCLE RESPONSIVENESS DURING SLEEP IN OBSTRUCTIVE SLEEP APNEA

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Introduction: Cessation of respiratory events occurs via 1) arousal from sleep or 2) sufficient recruitment of upper airway (UA) dilator muscles to restore airflow without arousal. Thus, a low respiratory arousal threshold (awaken easily to respiratory stimuli) is likely to be important in the pathogenesis of OSA for some patients. Increasing the arousal threshold with a hypnotic to enable UA muscle recruitment and restore airflow without arousal may be a therapeutic option in appropriately selected pa-

tients (those with a low arousal threshold and recruitable UA muscles). However, to be effective, the hypnotic selected must increase the arousal threshold without major impairment of UA dilator muscle function as can occur with benzodiazepines. This study aimed to determine the effect of the hypnotic agent, trazodone, on the arousal threshold and UA dilator muscle responsiveness during sleep.

Methods: OSA patients estimated to have a low arousal threshold (nadir epiglottic pressure immediately prior to arousal 0 to -15cmH$_2$O) were studied overnight on therapeutic CPAP on two separate occasions 1) without and 2) following 100mg of trazodone. Patients were instrumented with fine wire EMG electrodes into genioglossus and tensor palatini, an epiglottic pressure (Pepi) catheter via the nares, and a nasal mask. During non-REM sleep, transient CPAP reductions were performed to induce flow-limitation for assessment of 1) UA collapsibility; Pcrit (estimated mask pressure where flow ceases), 2) UA dilator muscle responsiveness (%max EMG activity per -cmH$_2$O Pepi), and 3) the arousal threshold (nadir Pepi just prior to arousal).

Results: To date, we have measured these 3 variables on and off trazodone in 7 OSA patients (1 female). Pcrit ranged from 0 to 5cmH$_2$O. Compared to baseline, trazodone significantly increased the arousal threshold (-11.3±1.5 vs. -15.2±2.3cmH$_2$O, p<0.01). In the data analyzed thus far, genioglossus and tensor palatini muscle responsiveness were not different during baseline vs. trazodone (0.15±0.9 vs. 1.2±0.9, p=0.29 and 0.27±0.20 vs. 0.42±1.3 %max EMG per -cmH$_2$O Pepi, p=0.44 respectively).

Conclusion: Trazodone increases the respiratory arousal threshold to mechanical stimuli (transient CPAP reductions) in OSA patients estimated to have low arousal thresholds. While data collection and analysis is ongoing, these preliminary results suggest that trazodone does not impair UA dilator muscle responsiveness during sleep and thus, may be of therapeutic benefit in patients with low arousal thresholds.

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0456

A PILOT STUDY ON THE EFFECTS OF OPIATES ON BREATHING IN SLEEP DISORDERS PATIENTS

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Introduction: Respiratory suppression during sleep is a concern in patients on chronic narcotic therapy. We hypothesized that sleep and medical conditions such as sleep apnea and diabetes mellitus may increase adverse effects of opiates on respiration.

Methods: After IRB approval, we compared 59 consecutive patients taking opiates (opiate group-OG) with 52 consecutive patient controls (PC). These patients presented to the Division of Sleep Medicine from January 2009 through March 2010. We included patients between 18 and 85 years completing a first night diagnostic polysomnogram. From history and physical examination, we excluded patients with cardiac, pulmonary, and neurological disease leaving 34 OG and 36 PC participants. Ten patients taking opiates (29%) and eight opiate free patients (22%) had diabetes mellitus. We used an analysis of variance (ANOVA) with two factors (opiate use and diabetes mellitus) to examine effects on apnea duration, longest apnea duration, baseline and nadir oxygen saturation.

Results: Apnea duration was longer in those diabetics taking opiates (Mean = 18.5s versus non-diabetic PC group, 16.0s, p=<0.023). Opiates did not affect the other measures. Overall, diabetics had the longest maximum length apnea events (Mean = 43.4s, SD = 16.4s versus 29.6s, SD = 14.4s, p=<0.001), and the lowest nadir O2 saturation (Mean = 83.5%, SD = 7.24% versus 86.9%, SD = 4.94%, p=<0.023). There was no effect on baseline O2 saturation in diabetics (94.1%) versus non-diabetics (95.0%). Respiration rate and apnea frequency were unaffected.

Conclusion: Diabetic mellitus patients regularly using opiates have longer apnea events suggesting that they may be at greater risk from opiate therapy. Overall, diabetes mellitus rather than opiates was associated with the longest apnea events and the lowest oxygen desaturations. These results may be due to differences in diabetics' sensitivity to blood gases, impairment in arousability, or differences in autonomic control.

0457

ASSOCIATION OF NARCOTICS AND BENZODIAZEPINES WITH APNEA SEVERITY AND SLEEPINESS IN VETERANS UNDERGOING A SLEEP STUDY

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Introduction: Over the last decade, narcotic and benzodiazepine use has increased dramatically in general and amongst those being referred for sleep studies for excessive somnolence. Because of their respiratory effects, there is concern that these medications may complicate sleep disordered breathing.

Methods: Retrospective review of 2730 patients who underwent a sleep study at the JAHaley Veteran's Hospital between 2001-2006. In order to exclude one-time prescriptions for acute events, a narcotic or benzodiazepine user was identified by prescriptions totaling 91 tablets or more in the 4 month period beginning three months before the patient's last sleep study date and ending one month after. Logistic regression was used to compare OSA parameters between narcotic or benzodiazepine users and others undergoing a sleep study.

Results: 316 (11.6%) and 131 (4.8%) patients used narcotics and benzodiazepines respectively. The most prevalent narcotics were oxycodone (5.4% of patients), morphine and codeine. The most prevalent benzodiazepines were alprazolam, clonazepam and diazepam. We divided the sleep study population into four groups: Group 1: neither drug (N=2324); Group 2: narcotics only (N=275); Group 3: benzodiazepines only (N=90); Group 4: both (N=41).An Epworth Sleepiness Score (ESS) ≥ 18 was associated with drug use (Odds ratio (OR)=1.39, OR =1.60 and OR=2.07 for groups 2, 3 and 4 respectively vs Group 1), but these patients were also less likely than Group 1 to have OSA (AHI ≥5) or low trough SpO2 ≤ 78. Results were most pronounced for Group 3 (OR for OSA = 0.25, p<0.001; OR for low SpO2 =0.48, p=0.007). Similar results remained after adjustment for age, race, BMI and Charlson morbidity index.

Conclusion: Patients presenting with excessive daytime sleepiness on narcotics or benzodiazepines may be misidentified as having a high pretest probability of OSA. Care should be taken to assess and monitor these medications in these patients.

0458

CENTRAL MECHANISM OF PERIODIC APNEAS WITHOUT CHF: COMPENSATORY (SET) HYPOTHESIS

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Introduction: The aim of this paper is to present data in favor of the "central" hypothesis explaining periodic breathing (PB) as an active CNS modulation of ventilation.

Methods: PSG by eighteen patients with PB without CHF were analyzed by the power-spectrum-density (PSD) correlations of different physiological parameters in different sleep stages. On a model of a patient with PB without CHF regulatory CNS influences were demonstrated.

Results: Mathematical analysis of PSG records revealed clear indicators of large peaks in a low frequency range of f equal 0.02 Hz. Data demonstrated entertainment of the cerebral and cardiac activities with respiration highly pronounced in NREM, and much less in REM sleep. Correlations between EEG and respiration attain maximum at negative lag times which favors the central hypothesis of generation of PB. In 11 patients (61.1%) PB in NREM was alternated by PLM with similar frequency.

Conclusion: Our data supports the "central" hypothesis of PB: in a subgroup of patients with PB without CHF. The fact PB might be "substituted"by PLM suggests that PB and PLM might be compensatory ("set") physiological disorders in a framework of control system theory. Initial positive results of experimental application of periodic vibro stimulations with the frequency of apneas supports the idea of the CNS origin of some form of PB. Clinical applications of these findings, if confirmed, may lead to emergence of some forms of "substitution therapy" for PB.

0459

IMPACT OF PULMONARY HYPERTENSION (PH) ON SHORT- AND LONG-TERM OUTCOMES IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME (OSA)

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Introduction: Obstructive Sleep Apnea (OSA) has several cardiovascular consequences. Pulmonary hypertension (PH) is a less appreciated complication of OSA. We studied short- and long-term outcomes in OSA patients with PH.

Methods: Sleep center and right heart catheterization (RHC) databases were queried. Patients with a polysomnographic (PSG) diagnosis of OSA (apnea-hypopnea index[AHI]>5) between January 2004 and August 2010, who underwent RHC within 6 months of PSG were included. PH was defined as resting mean pulmonary arterial pressure (mPAP) > 25 mmHg. Data on demographics, PSG, characteristics, and hemodynamics were collected.

Results: 113 patients with complete data were analyzed (no PH, n=38 [33.6 %]; PH, n=75 [66.4 %]). No significant differences were observed between the PH and non-PH groups regarding demographics, body mass index, or AHI. Compared to patients without PH, those with PH had greater percent time spent with oxygen saturation < 90% (%TST <90) (p=0.008), were more likely to have pericardial effusion (p=0.017), and had lower cardiac output (p=0.001) and pulmonary capacitance (PCap) (p<0.001). Compared to patients without PH, those with PH had reduced survival at 1, 2, and 5 years (97.3%, 86.5%, 77.8% versus 89.6%, 82.7%, 51% respectively). Factors associated with increased mortality were increased %TST < 90% (p=0.042), decreased left ventricular diastolic filling (P=0.046), increased mean RAP (p=0.020), decreased stroke volume (p=0.047), and decreased PCap (p=0.021).

Conclusion: In patients with OSA, PH results in more nocturnal oxygen desaturation. Degree of oxygen desaturation and abnormal pulmonary hemodynamics are important predictors of survival in patients with OSA.

0460

HEART RATE CHANGES ASSOCIATED WITH MICROAROUSAL IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Recent studies have reported an age-related reduction in the amplitude of heart rate changes (normally calculated by R-R intervals) associated with microarousal (MA) in health subjects. The aim of the present study was to explore heart rate changes associated with MA at termination of sleep apnea in different sleep stage and in different ages of severe obstructive apnea (OSAS) patients.

Methods: The subjects were 7 young (32.1±5.2 yrs), 7 middle-aged (45.1±5.9 yrs) and 7 elderly (70.7±5.9 yrs) male patients with severe obstructive sleep apnea syndrome (AHI>30). R-R intervals were calculated for 10 intervals of heart beats prior to and 25 intervals after onset of apnea event related MA. We randomly selected 10 artifact-free MA during sleep stage 2 (N2) and 10 during REM sleep for analysis in each subject. Repeated measures analysis of variance were used in data analysis (p<0.05).

Results: In both N2 and REM, three groups of patients showed similar patterns for amplitude of heart rate changes during totally analyzed 35 intervals of heart beats, which were increased at onset of MA, compared to the prior to onset of MA. The increase lasted approximately 20 intervals of heart beats and reached peak level at around 10th heart beat after onset of MA. The ranks of amplitude of increase were young > middle aged > elderly groups for both N2 and REM. Three groups of patients had greater increased amplitude during REM than during N2. Only elderly patients exhibited a decrease of heart rate after increase during N2, but not during REM.

Conclusion: The results illustrated that the patterns of heart rate changes associated with MA at the termination of apnea events in severe OSA patients are similar to those have been reported in heath subjects with no sleep apnea. Compared to older patients, greater increases of heart rate changes after onset of MA in young patients may implicate that they have stronger autonomic activity in responses to sleep apnea. Autonomic reaction reflected by heart rate change during MA may vary among different sleep stages in OSAS patients.

0461

INCREASE IN HEART RATE IS ASSOCIATED WITH RERAS

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Introduction: A respiratory effort-related arousal (RERA) is a sequence of breaths lasting at least 10 seconds characterized by increasing respiratory effort or flattening of the nasal pressure waveform leading to a cortical arousal. This sequence must not be associated with a significant blood oxygen desaturation, else it would be called a hypopnea. To understand further the episodic increase in heart rate and its relationship to RERAs, an analysis of relevant polysomnograms was conducted.

Methods: Three hundred thirty-eight (338) consecutive diagnostic polysomnograms during a six month period in 2010 at an AASM accredited sleep disorders center were evaluated. A RERA index ≥ 15 and an Epworth Sleepiness Scale ≥ 10 were used for inclusion. The study excluded patients with the following: PSGs with AHI ≥ 5 (139); PSGs with RERA Index < 15 (29), patients with ESS < 10 (68); patients with concurrent cardiac medications or history of cardiac disease or stroke (6); patients with significant arrhythmia (7) and PSGs with technical difficulties (3). This allowed the analysis of the diagnostic polysomnograms of 26 patients.

Results: A striking correlation was found between RERA's and a sudden increase in heart rate of at least 10 bpm and lasting 15 to 30 seconds. Additional breathing-related increase in heart rate sometimes occurred without a scorable arousal. There was a strong relationship between the RERA Index, Arousal Index and a sudden increase in heart rate of ≥ 10 bpm (Heart Rate Increase Index) as measured by EKG occurring within 30 seconds of a scorable arousal.

Conclusion: Increase in heart rate can be used as a scoring tool in the identification of RERA's. However, an episodic breathing-related increase in heart rate may be seen as an episodic increase in sympathetic tone. This may have health implications beyond those currently appreciated for Upper Airway Resistance Syndrome (UARS).

0462

VARIABILITY IN THE PATHOPHYSIOLOGICAL PHENOTYPIC CAUSES OF OBSTRUCTIVE SLEEP APNEA: TARGETS FOR NOVEL THERAPEUTIC APPROACHES

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Introduction: OSA pathophysiology is multifactorial and the influence of the various causes likely varies substantially between patients. Key traits include: 1) upper airway collapsibility/anatomy (Pcrit), 2) upper airway dilator muscle responsiveness during sleep, 3) respiratory arousal threshold, and 4) respiratory control stability (loop gain). The purpose of this study was to measure and characterize the contribution of each of these traits in a large cohort of OSA patients. The ultimate goal is to develop targeted novel therapeutic approaches according to underlying pathophysiology in individual patients.

Methods: CPAP compliant men and women with OSA aged 20-65ys were studied overnight on 3 occasions, ~1 week apart. Initially, the AHI was determined via PSG. During subsequent nights, patients were studied supine on therapeutic nasal CPAP. On one night, progressive CPAP drops were used to induce varying degrees of airway collapse for measurement of Pcrit (estimated mask pressure where flow ceases), muscle responsiveness (intramuscular genioglossus EMG vs. negative epiglottic pressure) and the arousal threshold (minimum epiglottic pressure immediately prior to arousal). Steady-state loop gain was measured on a separate night also using CPAP drops.

Results: To date, we have enrolled 69 OSA patients and obtained data in 58 (AHI 11-112events/h). Non-REM sleep values for the 4 key traits measured in the first 30 patients analyzed thus far, varied substantially between patients. Pcrit ranged from -5 to 5 (-1±3) cmH$_2$O, muscle responsiveness from 0 to 2.2 (0.33±0.47) %max EMG per -cmH$_2$O epiglottic pressure, arousal threshold from -8 to -28 (-16±5) cmH$_2$O and steady state loop gain from 0.9 to 8.6 (3.9±2.0) dimensionless. A substantial proportion (59%) had negative Pcrit values (<0 cmH$_2$O) and loop gain tended to be higher in patients with negative vs. positive Pcrit values (5.2±0.6 vs. 2.9±0.4).

Conclusion: Preliminary findings show substantial between-subject variability in these 4 key pathophysiological traits. Pcrit/anatomy remains an important determinant of OSA. However, there are a significant proportion of OSA patients with negative Pcrit values suggesting that other traits (e.g. loop gain) importantly contribute to the presence of OSA within this group. Individualized strategies based on pathophysiological characterization to manipulate muscle responsiveness, arousal threshold, or loop gain may be a novel and effective therapeutic approach for a substantial proportion of carefully selected patients.

0463

THE RELATIONSHIP BETWEEN VENTILATORY DRIVE AND UPPER AIRWAY FUNCTION IN OBESE ADOLESCENTS WITH AND WITHOUT OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: The prevalence of obstructive sleep apnea syndrome (OSAS) in adolescents is increasing in conjunction with the rising prevalence of childhood obesity. However, the mechanisms leading to OSAS in obese adolescents are not fully understood. Central ventilatory drive may play a role. We hypothesized that obese adolescents with OSAS would have blunted hypercapnic ventilatory responses (HCVR), and that this would correlate with upper airway function during sleep.

Methods: Adolescents (aged 12-16 years; 15 obese with OSAS, 16 obese without OSAS and 24 lean controls) underwent HCVR during wakefulness using the rebreathing technique. During sleep, they underwent measurement of the upper airway pressure-flow relationship (PFR). Comparisons among groups were performed using ANCOVA.

Results: The HCVR slope was 2.37±1.21, 2.46±1.23, 1.51±0.64 ml/s*cmH2O in the OSAS, obese without OSAS and lean control groups, respectively. Significant differences in HCVR (p=0.007), HCVR/height (p=0.009) and HCVR/forced vital capacity (p=0.05) were found among groups. Post hoc testing showed lower HCVR for lean controls vs OSAS and obese controls. However, no significant difference was found among the groups when controlling HCVR for either weight or body mass index (BMI). HCVR correlated with the slope of the PFR (r=0.351, p=0.011) and there was a trend for correlation with the critical closing pressure (Pcrit; r=0.272, p=0.051). However, when controlled for weight or BMI, these relationships were no longer significant.

Conclusion: Obese adolescents with and without OSAS have a normal ventilatory drive compared to lean controls when HCVR is controlled for weight. Similarly, HCVR does not contribute to upper airway dynamics during sleep when controlled for weight. We speculate that ventilatory drive does not play a major role in the pathophysiology of OSAS in obese adolescents.

0464

RELATIONSHIP BETWEEN THE UPPER AIRWAY RESPONSE TO LOADING IN NREM SLEEP AND APNEA SEVERITY IN REM SLEEP

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Introduction: On suboptimum CPAP during NREM sleep, an increase in ventilatory drive can dilate/stiffen the pharynx and increase ventilation in some individuals (Positive Responders). In others, ventilation may actually decrease over successive breaths despite increasing ventilatory effort (Negative Responders). Compared to NREM sleep, pharyngeal muscles are more hypotonic in REM. We hypothesized that Positive Responders would have significantly more OSA in REM sleep compared to NREM sleep. Also, the ventilatory drive/effort response to CO2 is lower in REM. We hypothesized that Negative Responders would have less OSA in REM sleep compared to NREM sleep, due to less negative effort dependence (defined as ventilation decreasing despite increasing effort).

Methods: 15 subjects were studied. During supine NREM sleep, CPAP was dropped from an optimum to various suboptimum levels for 3-5

minute intervals. On suboptimum CPAP, ventilation is less than eupnea (due to airway narrowing) and therefore CO2 and ventilatory drive increase. In order to determine how much ventilatory drive has increased, CPAP was returned to the optimum pressure (opening the airway) and the ventilatory overshoot above eupnea was measured. The upper airway response (UA response) was calculated by dividing the increase in ventilation across the drop (ventilation at the end of the drop minus ventilation at the beginning of the drop) by the corresponding increase in ventilatory drive across the drop (as determined by the height of the ventilatory overshoot minus eupneic ventilation). The UA response ratio is a measure of the ability of ventilatory drive to open the airway and permit more ventilation (e.g. if the airway is completely open, UA response = 1; if the airway is closed, UA response = 0).

Results: 8 individuals were Positive Responders (UA response ≥ 0.2), 5 were Negative Responders (UA response ≤ -0.2), and 2 were neither ($-0.2 <$ UA response < 0.2). In the Positive Responders, AHI increased from 9 ± 7 episodes/hr in NREM sleep to 26 ± 16 episodes/hr in REM sleep (p = 0.02). In the Negative Responders, AHI decreased from 76 ± 34 episodes/hr in NREM sleep to 52 ± 19 episodes/hr in REM sleep (p = 0.07).

Conclusion: REM predominant OSA may be a marker for patients with effective upper airway compensatory mechanisms. Negative effort dependence may play an important pathophysiologic role in OSA patients that improve during REM sleep.

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0465

HYPOPNEA - HYPOXEMIA INTERVAL: IMPLICATIONS FOR BETTER SCORING CRITERIA FOR THE HYPOPNEAS

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Introduction: AASM guidelines do not lay down the criteria for the time interval between the end of airflow reduction in hypopnea and the $\geq 4\%$ oxygen desaturation (per "recommended" criteria). We sought to estimate this Hypopnea-Hypoxemia Interval (HHI).

Methods: We analyzed 865 events in 31 patients (all with predominant hypopneas) scored as hypopneas based on the "recommended" criteria laid down in the AASM Manual for the Scoring of Sleep and Associated Events. We calculated the hypopnea duration (HD) and HHI, for hypopneas. HHI was defined as the interval between the end of airflow reduction and the $\geq 4\%$ desaturation. If the $\geq 4\%$ desaturation occurred during the hypopnea and prior to the end of airflow reduction, HHI was recorded as a negative value. It was recorded as positive if it occurred after the end of airflow reduction.

Results: There were 31 patients with a mean age of 50.6 years, 20 females and 11 males. Median Apnea -Hypopnea index (AHI) was 4.130. Median HHI was 11.9 seconds [95% CI (10.719 - 12.600), IQR (5.400 - 17.025)] .There was a weak but statistically significant inverse correlation between HD and HHI [correlation coefficient, r = -0.1399 (95% CI = -0.2046 to -0.07389); p=<0.001)]. There was no statistical difference in HHI between REM and NREM hypopneas.

Conclusion: Majority of patients develop hypoxemia at a median of 12 seconds [IQR (5.400 - 17.025)] after the end of airflow reduction in hypopnea. Our findings suggest that HHI should be better defined and incorporated in the interpretation & definition of hypopnea.

0466

QUANTITY OF RESPIRATORY EFFORTS IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA SYNDROME COMPARED IN ADULTS

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Introduction: In the diagnosis of child obstructive sleep apnea syndrome (OSAS) in the second edition of the International Criteria of Sleep Disorders, views with continuance of upper airway narrowing such as snoring and respiratory efforts other than apnea hypopnea index (AHI) in polysomnography (PSG) are included. This means that detection of respiratory efforts is regarded as important than adults in children.We quantified respiratory efforts using the esophageal pressure (Pes) measurement and, about relationships with AHI, performed comparison with child and adult.

Methods: Twelve child and 39 adult OSAS patients are enrolled in this study. We have measured Pes simultaneously with PSG. It was calculated each Pes maximum during apneas(Pes Max in apnea) and that during hypopneas(Pes Max in hypopnea) for respiratory effort quantity. In addition, it was estimated correlations of AHI as Pes Max in apnea/hypopnea on both child and adult.

Results: AHI, PesMax in apnea/ in hypopnea of child subjects were 24.3+35.3/hr, -19.6±13.9cmH2O ,-19.5±13.2 cmH2O, and these of adult subjects were 54.2 ± 30.6/hr, -23.3±15.7 cmH2O, -16.3±25.9 cmH2O. The significant correlation was not recognized in PesMax in apnea/hypopnea and AHI in child OSAS, but correlation (r=-0.504, r=-0.350) which was significant in whichever of Pes Max in apnea and Pes Max inhypopnea and AHI was found in adult OSAS. Even if AHI was a low with a child, a high of PesMax was present.

Conclusion: It was confirmed that quantity of respiratory efforts of a child did not depend on AHI. It was thought that not only AHI but also quantity of respiratory efforts were useful in evaluation of child OSAS.

0467

REM RELATED BREATHING DISORDERS

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Introduction: We report clinical features of REM related breathing disorders in a sleep disorders clinic population and their impact on treatment decisions.

Methods: The study involves retrospective chart review at our accredited sleep center. Baseline polysomnograms (PSG) were reviewed. Patients with REM Apnea hypopnea index (AHI) of at least two times NREM AHI were included. REM AHI had to be greater than five per hour. REM hypoxemia was defined as non-apneic hypoxemia occurring only in REM sleep.

Results: 115 patients met criteria. 81/115(70.4%) were females and 34/115(29.6%). Average age was 48.6 years (range 25-76y). Average BMI was 40.2 (range 23-80). Snoring (81/115), excessive day time sleepiness (52/115), fatigue (28/115) and apnea (36/115) were the most common presenting complaints. Mean total AHI was 8.56 (range 0.4-27), REM AHI was 34.30 (6.6-87) and NREM AHI was 4.06 (0 - 20.6). 8/115 had REM hypoxemia, 11/115 combination of REM hypoxemia and REM OSA. 96/115 had REM OSA.

Conclusion: 34% of OSA population is reported to have REM related OSA. Our study results conformed the previous observation that this entity is seen mainly in obese women with mild disease (mean BMI 40.2; mean total AHI 8.56). Presenting complaints included snoring, excessive daytime sleepiness, fatigue and apnea. However, clinical features cannot reliably differentiate between REM OSA and NREM OSA. High REM AHI compared to NREM AHI reiterates the importance of studying REM sleep in PSGs. REM AHI can provide high contribution to to-

tal AHI. It is necessary to perform all night PSGs as percentage of REM sleep increases in morning. In addition it is important to consider that night to night variability in REM sleep proportion may affect total AHI. The study has implication in redefining of the criteria for diagnosis and treatment of obstructive sleep apnea. This invokes the need for studies that evaluate the benefit of offering treatment to symptomatic patients with significant REM-only OSA even if the total AHI does not meet the criteria for PAP therapy (AHI < 5).

0468

OBESITY BUT NOT OSA ALTERS FUNCTIONAL CAPACITY

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Introduction: There is evidence in the literature that OSA patients have impaired functional capacity compared to controls. Our previous study in lean subjects showed similar functional capacity in OSA and control groups. However, it is known that obesity may impair exercise performance. Therefore, the role of OSA and obesity in exercise capacity is still unclear. The aim of this study is to evaluate the exercise performance, blood and echocardiographic parameters in obese, sedentary OSA patients compared to matched controls.

Methods: Fifty obese subjects (25 OSA patients) were selected from database of Sleep Institute of Sao Paulo city, Brazil. The control group was matched by age, gender and BMI. Inclusion criteria were: both gender, age between 35 and 65 years, BMI > 30 and < 40 Kg/m2 and sedentarism. Severe systemic disease, pulmonary or cardiac disease, smoking, pregnancy and patients receiving treatment for OSA were excluded. All subjects underwent clinical evaluation, polysomnography, a maximum limited symptom cardiopulmonary exercise test, 2D-transthoracic echocardiography, spirometry and blood withdraw. Satistical Analysis: One-Way ANOVA, Repeated measures ANOVA, Chi-Square; $p \leq 0.05$

Results: There were no differences in baseline characteristics between groups. The mean age were 48.6 ± 6.8 years in OSA patients and 48.7 ± 6.9 years in controls (p=0.9) As expected, there were statistical differences in the AHI (33.6 ± 24.4 events/h vs. 3.2 ± 1.4 events/h; p < 0.01), arousal index (25.6 ± 20.6 events/h vs. 11.7 ± 7.2 events/h; p < 0.01), minimal oxygen saturation (82.1 ± 8.7 % vs. 89.8 ± 3.1 %; p < 0.01), and saturation time below 90% (43.6 ± 85.9 min vs. 0.51 ± 0.9 min; p < 0.01) in the obese OSA patients and obese controls. There were no differences between obese OSA and control groups in the peak oxygen consumption (28.6 ± 10.0 ml/Kg/min vs. 25.9 ± 7.7 ml/Kg/min; p=0.3), anaerobic threshold (21.9 ± 6.9 ml/Kg/min vs. 19.9 ± 6.4 ml/Kg/min; p=0.4), respiratory exchange ratio (1.03 ± 0.2 vs. 1.03 ± 0.1; p=0.9), and, blood pressure and heart rate behavior. In a similar fashion, echocardiographic and blood samples variables were not different between groups.

Conclusion: OSA did not significantly affect exercise cardio-respiratory function, and blood and echocardiographic parameters in obese patients.

0469

EXERCISE TESTING IN PATIENTS WITH SLEEP DISORDERED BREATHING

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Introduction: Sleep disordered breathing (SDB) is associated with several adverse cardiovascular outcomes. Few studies have examined exercise capacity or cardiovascular responses to maximal exercise testing and recovery, and results from these studies are conflicting.

Methods: In this large cross-sectional study, we identified 1425 adults who underwent comprehensive exercise testing between 1/1/2005-1/1/2010 and within six months prior to first-time diagnostic polysomnography (PSG). Subjects were categorized by apnea-hypopnea index (AHI) quartiles: <5, 5-14, 15-29 and ≥30. A logistic regression model incorporated age, gender, BMI, smoking, hypertension, diabetes, beta-blocker use, and cardiopulmonary disease as covariates.

Results: The mean age was 56.4 +/-12.4 years; 75% were male. On multivariate analyses, AHI was significantly associated with increased resting and peak diastolic blood pressure (DBP) (p=0.005), and chest pain index (p=0.03). Peak oxygen consumption (VO2) data (collected on a subset of 499 patients in whom it was measured) correlated negatively with AHI (p=0.008, R^2 adj 0.44). When comparing patients with severe sleep apnea (AHI≥30) with those without sleep apnea (AHI<5), heart rate recovery (HRR), resting, peak, post-exercise DBP, peak VO2 and respiratory rate (RR) were significantly more abnormal in the severe apneics (all p<0.05). The former group also had significantly more chest pain, dysrhythmias and inability to complete protocol (all p<0.05). Analyses repeated on those with sleep efficiency greater than 85% and excluding central sleep apnea did not reveal any different results.

Conclusion: SDB severity is independently associated with increased resting/peak DBP and decreased peak VO2. After accounting for several confounders, HRR, resting/peak/post-exercise DBP, peak VO2, peak RR, occurrence of chest pain, dysrhythmias and ability to fulfill protocol differed significantly in those with severe SDB compared to those without SDB.

0470

DURATION RESPONSE CURVE TO BRIGHT LIGHT IN HUMANS

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Introduction: Light exposure at night has been shown to induce a phase delay of the melatonin rhythm in humans. Previous studies have investigated the effect of timing, intensity, wavelength, and pattern of light stimuli on the human circadian timing system. Here we present results from a study of the duration-response relationship to phase-delaying bright light.

Methods: Thirty-seven healthy adults (18-30 years of age; 14 F) who completed a 9-day inpatient protocol were included in this analysis. The protocol consisted of 3 baseline days (16h wake/8h sleep) followed by a 50h constant routine (CR) to assess circadian phase. The dim light melatonin onset (DLMO25%) was determined from hourly blood samples collected throughout the CR. Following an 8h sleep episode, the next 16h wake episode included an experimental bright light exposure (LE) which was scheduled during the early subjective night. This timing was chosen because it is at a time when plasma melatonin levels are high and when maximal phase delays of the endogenous circadian melatonin rhythm occur. Subjects were assigned to receive an LE of 0.2h, 1.0h, 2.5h, or 4.0h in duration (n = 9, 10, 10, and 8, respectively). A 36h CR on the following day was performed to reassess the DLMO25% so that the phase shift induced by the LE could be determined.

Results: Mean ± SD phase delays induced by the 0.2h, 1.0h, 2.5h, and 4.0h LE were: 1.07 ± 0.36h, 1.37 ± 0.52h, 2.29 ± 0.28h, and 2.65 ± 0.25h, respectively. The magnitude of the phase delay shifts increased as the duration of the LE increased; 0.44h of phase delay per hour of light and R=0.984.

Conclusion: Brief exposure to bright light (0.2h) in humans can substantially shift endogenous circadian melatonin phase, resetting the circadian pacemaker much more efficiently per minute of light exposure than longer durations of light.

0471

NIGHTLY MELATONIN SUPPLEMENTATION IMPROVES TOTAL SLEEP TIME, SLEEP EFFICIENCY AND SLEEP ONSET LATENCY IN HYPERTENSIVE PATIENTS TREATED WITH β-BLOCKERS

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Introduction: β-Blockers are often used in the treatment of hypertension, angina, arrhythmia, and heart failure. However, β-blockers also lower the levels of the soporific hormone melatonin, which may explain some of the reported side-effects including nighttime insomnia and daytime fatigue. Therefore, we tested whether or not nightly melatonin supplementation improves sleep in hypertensive patients treated with β-blockers.

Methods: Sixteen hypertensive patients (45-64 years of age; 9 women) treated with the β-blocker Atenolol or Metoprolol were enrolled in a randomized, double-blind, placebo-controlled, parallel-group trial. The study included two 4-day in-laboratory visits during which their sleep was assessed by polysomnography in a private, sound-attenuated, and completely dark room during 8-h sleep opportunities. After the baseline assessment during the first visit, patients were randomized to receive melatonin 2.5 mg or placebo nightly for 3-4 weeks, after which their sleep was assessed again during the second 4-day visit. One subject was excluded from analysis due to unstable medication dose. Baseline-adjusted values are reported.

Results: 3-4 Weeks of melatonin supplementation increased total sleep time (placebo: 387 min vs. melatonin: 424 min; P=0.046), increased sleep efficiency (81% vs. 88%; P=0.046), and decreased sleep onset latency (16 min vs. 5 min; latency to Stage 1; P=0.007) as assessed by polysomnography in the laboratory. Melatonin did not significantly affect durations of different sleep stages, although the increase in Stage 2 approached significance (232 min vs. 271 min; P=0.051). Also throughout the 3-4 weeks while on melatonin and sleeping at home, melatonin significantly improved actigraphy-estimated total sleep time (377 min vs. 390 min; P=0.011) and sleep efficiency (78% vs. 81%; P=0.007), but not sleep onset latency.

Conclusion: In hypertensive patients treated with β-blockers, nighttime melatonin supplementation significantly improves sleep quality as assessed by polysomnography in the laboratory and as estimated by actigraphy at home.

0472

STAYING UP LATE AND EATING IN THE EVENING: RECIPE FOR OBESITY?

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Introduction: Alterations in circadian timing have been associated with dysregulation of appetite hormones and insulin metabolism. Few studies have evaluated the role of sleep timing and circadian rhythms on feeding patterns and obesity. The goal of this study was to evaluate the associations between sleep timing, timing of caloric intake, and BMI in adults.

Methods: Participants included 52 individuals (27 males, mean age 31 SD= 12). Diet was measured by a 7-day food diary. Caloric intake was calculated through publicly available nutrition databases. Sleep timing was defined a average midpoint of sleep based on 7 days of wrist actigraphy. Data were analyzed using t-tests, correlations, and multivariate regression. In categorical analyses, normal sleepers (n=23) were defined as an average midpoint of sleep earlier than 5:30 am and late sleepers were defined as a midpoint of sleep at or after 5:30 am.

Results: Late sleepers had later bedtimes (p<.001) and wake times (p<.001) and later times for breakfast (p<.001), lunch (p<.01), dinner (p<.05), and last snack or meal of the day (p<.001). Only the duration between breakfast and lunch was different, with a shorter duration in late sleepers (p<.01). Later sleep timing was associated with shorter sleep duration (r= -.33, p<.05), higher BMI (r= .41, p<.01), more calories consumed after 8 pm (r= .56, p<.001), and fewer daily servings of fruits and vegetables (r= -.49, p<.01). Calories consumed after 8 pm were associated with shorter sleep duration (r= -.57, p<.001), higher BMI (r= .37, p<.01), and greater caloric intake (r= .59, p<.001). In multivariate analyses controlling for age and sleep duration, later sleep timing was associated with more calories consumed after 8 pm (β = .45, r2Δ= .18, p=.001) and fewer servings of fruits and vegetables (β = -.51, r2Δ= .22, p=.002). Sleep timing did not predict BMI after controlling for covariates. Calories after 8 pm remained a significant predictor after controlling for age, sleep duration, and sleep timing (β = .44, r2Δ= .09, p=.03).

Conclusion: Results suggest that sleep timing plays a role in the pattern of caloric consumption and diet quality. However, timing of caloric intake was associated with BMI above and beyond sleep timing and duration.

0473

CHRONIC SLEEP RESTRICTION COMBINED WITH CIRCADIAN MISALIGNMENT LEADS TO INADEQUATE INSULIN SECRETION RESPONSE TO MEALS IN YOUNG AND OLDER HEALTHY ADULTS

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Introduction: Aging is generally associated with reduced sleep and increased obesity. Sleep deficiency (insufficient sleep quantity or quality) and circadian misalignment impair glucose metabolism in young adults. We tested whether a history of ~ 17 days of circadian disruption combined with sleep deficiency lead to metabolic disturbances in older adults, predisposing them to greater risk of obesity and diabetes.

Methods: 11 healthy, non-obese, older adults (6F, mean age 59 y) completed a 39-day study with three conditions: (1) 'Sleep Replete' (>2 weeks of >10 h/day time in bed [TIB]/day); (2) 'Circadian Disruption and Sleep Deficiency' (achieved via recurring 28 h sleep/wake cycles for ~2.5-weeks with 6.5h TIB/28h cycle; ≡5.6h TIB/24h); (3) 'Recovery Sleep' (1 week of 10h TIB/24h). Metabolic assessments were made across conditions at similar circadian phases following standardized breakfasts (58-60% CHO). Results were compared to data from 12 healthy, non-obese, younger adults (6F, mean age 23 y).

Results: In the older group, prolonged 'Circadian Disruption and Sleep Deficiency' significantly increased post-prandial plasma glucose by 16.3% (AUC across 90 min; p=0.04). This effect was likely caused by an inadequate pancreatic beta cell response because post-prandial plasma insulin decreased by 23.7% (AUC across 90 min; p=0.02). Glucose and insulin responses to meals returned to baseline 'Sleep Replete' levels after 'Recovery Sleep'. These results in elderly subjects were statistically indistinguishable from those in the young adults; both younger and older adults exhibited similar, reversible metabolic disturbances.

Conclusion: Circadian disruption combined with sleep deficiency for 2.5 weeks caused a notable increase in the glucose response to a meal due to inadequate insulin secretion. The metabolic disturbances were reversible in the short-term but may underlie the elevated risk of diabetes in conditions of chronic circadian disruption or sleep deficiency.

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0474

LABORATORY VALIDATION OF AN IN-HOME METHOD FOR ASSESSING CIRCADIAN PHASE USING THE DIM LIGHT MELATONIN ONSET (DLMO)

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Introduction: Methods for assessing circadian rhythm timing typically require lengthy procedures in highly controlled laboratory conditions, and thus are impractical for use in patients. This study addressed whether an accurate circadian phase assessment can be obtained from saliva samples collected by patients in their home.

Methods: Twenty-four individuals reporting sleep timing difficulties were recruited for the study. For 1-2 weeks, each wore an activity monitor and recorded their sleep-wake times. On the last day, participants were instructed to remain in dim light at home beginning 7h before their usual bedtime and to collect hourly saliva samples until 1h after their usual bedtime (8 samples). Participants spent 9h on the following evening in a laboratory room with controlled dim (<20 lux) light, beginning 8h before usual bedtime (9 hourly samples were collected). Samples were frozen and later assayed (Solidphase, Inc., Portland ME) using a commercially-available radioimmunoassay kit (Bühlmann Direct Saliva Melatonin RIA, ALPCO Diagnostics, Windham NH). DLMO was defined using both an absolute threshold of 3pg/mL and a relative threshold of 2 standard deviations (2SD) above the mean of 3 baseline values. The at-home and in-lab DLMOs were then compared using a Pearson Correlation.

Results: Neither method for determining DLMO worked well on either night for 2 subjects (8%) who were 'low-secretors'. In three cases (12.5%) the participant's in-lab melatonin levels differed greatly from their at-home levels, and one participant appeared to take the samples out of order, indicating that these four (16.7%) did not follow the instructions. For the remaining 18 participants, at-home and in-lab DLMO values were significantly correlated (3pg/mL: n=18, r=0.854, r2=0.73, p<0.0001; 2SD: n=22, r=0.64, r2=0.41, p=0.0013).

Conclusion: The at-home assessment procedure was able to determine an accurate DLMO in 75% of the participants. Thus, an at-home procedure for assessing circadian phase could be practical for evaluating patients for circadian rhythm sleep disorders.

Support (If Any): The study was supported by an investigator-initiated research grant from Philips-Respironics, and was conducted at the BWH Center for Clinical Investigation, part of the Harvard Catalyst (the Harvard Clinical and Translational Science Center), supported by UL1 RR025758.

0475

DELAYED SLEEP PHASE DISORDER RISK IS ASSOCIATED WITH ABSENTEEISM AND IMPAIRED FUNCTIONING

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Introduction: Delayed Sleep Phase Disorder (DSPD) is a primary (circadian rhythm) sleep disorder with reported prevalence of 7-16% in adolescents and young adults. Its classic manifestations include markedly delayed sleep onset and wake times that are intractably later than desired. Absence of a questionnaire screening tool for the disorder remains a barrier to its detection and diagnosis. The present study aimed to develop a new questionnaire to identify those at risk for DSPD, and to assess the impact of DSPD symptoms on self-reported absenteeism and functioning in work/school, social and family life.

Methods: 13,844 individuals were recruited by an internet survey provider. Those aged 18-65 years, in schooling or full-time employment during the daytime/evening, not employed in market research, advertising or pharmaceutical industries, and self-identifying as evening type completed questionnaires assessing DSPD risk based on International Classification of Sleep Disorders (2nd edition) criteria, and degree of functional impairment (Sheehan Disability Scale) (n=979 complete responses).

Results: 483/979 (49.3%) of the evening type individuals were at high risk for DSPD. Compared to those not at high risk for DSPD, those at high risk showed significantly higher odds of missing more than half of the last school/work week (odds ratio 2.67; 95% confidence interval 1.90, 3.75) and having reduced productivity during more than half of the last school/work week (OR 2.84; 95% CI 2.15, 3.75). High risk DSPD was also associated with increased odds of at least moderate level of disruption to work/school (OR 2.77; 95% CI 2.19, 3.51), social/leisure activities (OR 2.55; 95% CI 1.99, 3.26) and family life/home responsibilities (OR 2.60; 95% CI 2.03, 3.33).

Conclusion: DSPD risk is associated with increased absenteeism and impaired functioning in work/school, social and family life.

Support (If Any): This study was funded by Vanda Pharmaceuticals Inc.

0476

HEALTH AND PSYCHOLOGICAL VARIABLES RELATED TO INSOMNIA IN SHIFT WORKERS

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Introduction: The contribution of insomnia in the context of shift work on physical and psychological health is poorly documented. The present study aims at assessing the contribution of insomnia on perceived health, psychological variables, and life style habits of night and rotating shift workers compared to day workers.

Methods: 418 adults (51% of women; age, M = 41.4 years old) including 50 night workers, 163 rotating night shift workers, and 213 day workers were selected from an epidemiological study. Each rotating shift worker and night worker was paired with a day worker based on gender, age, income, and presence of insomnia. The three groups of workers were further classified into presence or absence of insomnia symptoms groups. Participants completed self-reported questionnaires about sleep, psychological, and health variables.

Results: Among the no insomnia group, night and rotating shift workers presented a poorer sleep quality than day workers ($F_{(2,412)}$ = 6.2, p = .002). Apart from sleep quality, night and rotating shift workers with insomnia were not significantly different than day workers with insomnia on all psychological and health-related variables. Indeed, individual with insomnia slept significantly less ($F_{(1,407)}$ = 27.7 , p < .001), had more wake time ($F_{(1,403)}$ = 77.1 , p < .001), more severe insomnia ($F_{(1,412)}$ = 201.6 , p < .0001), and more dysfunctional beliefs about sleep ($F_{(1,411)}$ = 25.4, p < .001) than good sleepers regardless of their work schedule. Moreover, individuals with insomnia presented higher levels of anxiety, depression, and lower quality of life than individuals without insomnia. Life style habits were similar among the three groups of workers, except for alcohol and cigarettes. Day workers reported drinking more alcohol ($F_{(2,348)}$ = 5.7, p < .01), while night workers with insomnia reported smoking more ($F_{(2,409)}$ = 5.0, p = .007). Last, workers with insomnia were more at risk of suffering from chronic pain independently of their work schedule (OR = 3.1, p = .002).

Conclusion: This study suggests that insomnia, rather than shift work, may better explained several negative consequences usually associated with shift work. Sleep quality seems directly related to shift work. These results underline the importance of addressing insomnia symptoms in shift work. Further research remains warranted to specify the contribution of sleepiness for each group of workers.

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0477

CIRCADIAN PHASE DIFFERENCES IN PATIENTS WITH SHIFT WORK DISORDER RELATIVE TO ASYMPTOMATIC SHIFT WORKERS

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Introduction: Simulated shift work studies have demonstrated a relationship between light induced delays in circadian phase and enhanced adaptation to a shift work schedule including improvements in performance and sleep. It is not know if individuals with shift work disorder (SWD) have phase differences relative to asymptomatic shift workers.

The present study used 24-hr dim light melatonin profiles to test for phase differences between patients diagnosed with SWD compared to asymptomatic shift workers.

Methods: All subjects were currently working the night shift (~1900-0800). Five patients diagnosed with SWD (2M; mean age: 35.6±8.6 yrs; mean yrs on shift = 8.4) and 5 asymptomatic shift workers (2M; mean age: 39.2±12.6 yrs; mean yrs on shift = 9.3) were screened for other sleep disorders and studied under dim light (< 10 lux) conditions during a 25-hr (1700-1800) modified constant routine. Salivary melatonin (30 minute intervals), multiple sleep latency test (13 trials, 2 hour intervals), and driving simulator performance (5 trials) were assessed. Dim light melatonin onset (DLMO) was determined using the method of Lee et al., 2006.

Results: Asymptomatic shift workers had a significantly (p < .001) delayed DLMO (09:34±3:33) relative to patients with SWD (22:48±2:21). The MSLT was lower in the SWD patients during night shift hours 2300-0900 (3.95±2.30 vs 7.45±2.76; p = .06). Nocturnal driving simulator performance was worse in the SWD patients, but did not reach statistical significance (p > .1).

Conclusion: These findings in workers currently on night shift suggest a failure to delay the circadian pacemaker in response to shift work contributes to symptoms of SWD and the presence of physiological sleepiness. Future studies should explore both intrinsic circadian factors (e.g., tau, light sensitivity) and external factors (e.g., light exposure) that may account for differences in circadian phase between workers with SWD and asymptomatic shift workers.

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0478

INFLUENCES OF SHIFT WORK ON SLEEP - INDUSTRIAL HEALTH AND SLEEP DISORDERS

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Introduction: Industrial health promotion shall detect the factors in an organisation which have a positive effect on health and how they can be used preventively. Aim of this study is the identification of such company health potentials, which have influences on health and on the sleep-wake-rhythm of shift workers in different companies and shift systems.

Methods: Questionnaires of sleep medicine and work psychology with the items "work situation", "exposure/stress", "health", "personal attitude", "insomnia", "narcolepsy", "chronotype" and "Restless-Leg-Syndrome" ascertained the sleep-wake rhythm of 372 employees and the individual working conditions in different companies and shift systems. For the demonstration of the objective effects on sleep we examined the sleep efficiency (fraction of total sleep time to total time in bed beginning from turning off the light and final uprising), the length of sleep and the sleep latency on a subgroup of 137 persons by actigraphy for a period of 14 days - 24 hours continously - together with a sleep-wake-diary.

Results: In the first interim analysis variables for every person could be detected, like professional appreciation, possibilities of learning, positive contact to customers and high identification with work, which can influence the effects of shift work on health in a positive way. Employees who are working only in night shifts reported lower tenseness, depletion and physical impairment than workers in a different shift system. The sleep latency, total sleep time (in average 6 hours) and sleep efficiency (< 85%) is for all tested persons lower than in normal population. 46% showed a clinic prominent fatigue and 30% reported from sleep disorders and insomnia. Furthermore the persons with insomniac symptoms showed correlations with more negative perception of working conditions than persons without these symptoms.

Conclusion: The results leads to the conclusion, that most of the workers have an objective chronic sleep deficit. Despite a low number of test

persons variables could be found which have a positive effect on negative results of shift work. Out of this individual industrial strategies of prevention can be deduced and implemented.

0479

SLEEP DISORDERS AND DEPRESSION IN SHIFT WORKERS IN COMPARISON WITH DAY WORKERS

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Introduction: Shift work refers to a job schedule in which employees work hours other than the standard hours or a schedule other than the standard workweek. To evaluate the effect of shift work on Iranian workers' health we studied the workers of Granite Behseram Company.
Methods: A cross sectional study was performed to identify frequency of psychosomatic and sleep disorders in day workers and shift workers in Granite Behseram Company. The information on 156 workers about sleep disorders was gathered using Epworth Sleepiness Scale (ESS), CCNY (for insomnia), and SDQ. We also used Beck Questionnaire for evaluation of depression. Specific chart was designed to determine if gastrointestinal problems existed. Data was analysed using Chi-square test.
Results: Of 156 workers with a mean age of 33.0 ± 5.3, 65 workers (41.7%)were day workers and 91 (58.3%) were shift workers. All the workers were male. Sleep disorders, insomnia, excessive daytime sleepiness and depression were more prevalent in shift workers although it was not significant. Occupational accidents were significantly higher in shift workers (p=0.01). Among gastrointestinal problems, abdominal cramps was the only symptom significantly higher in shift workers (p=0.03).
Conclusion: Although psychosomatic and sleep disorders were not significantly higher in shift workers, more prevalent accidents necessitate new strategies to prevent injuries.

0480

PHYSIOLOGICAL CHARACTERISTICS OF PATIENTS WITH CIRCADIAN RHYTHM SLEEP DISORDER (FREE-RUNNING TYPE)

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Introduction: Most behavioral and physiological function in living organisms on earth exhibit 24-hour period. The central circadian pacemaker in mammals resides in the suprachiasmatic nuclei (SCN) of the anterior hypothalamus. The intrinsic period (τ) generated by the pacemaker is not exactly 24 h and the biological clock therefore needs to be entrained to the 24-hour day. Disorganized circadian system could cause various diseases including sleep disorders. Circadian rhythm sleep disorder, free-running type (CRSD-FRT) is one of the CRSD characterized by the sleep timing that occur 30min-1h delay each day. Little is known about the mechanism underlying CRSD-FRT. In this study, we examined rhythmic characteristics of physiological functions in CRSD-FRT patients and controls.
Methods: Rhythmic characteristics of physiological functions (core body temperature and plasma melatonin etc.) of six CRSD-FRT patients diagnosed according to ICSD-2 criteria (mean age 34.17(SD 12.59), range 17-56 yrs, 66.7 %female) were examined under a 28-h forced desynchrony protocol. The intrinsic circadian period was estimated by temperature minimum (nadir) and corticosteroid maximum (acrophase)

and dim-light melatonin onsets (DLMO) between CRs before and after FD.
Results: Patients with CRSD-FRT showed the longer intrinsic circadian periods than healthy subjects with the intermediate chronotype, the period length of CRSD-FRT was similar to that of some evening chronotype.
Conclusion: These findings indicate that not only the intrinsic circadian period but also other functions (ability of entrainment to the environment, homeostatic sleep regulation) might have pathogenic significance in CRSD-FRT.

0481

BLIND FREE-RUNNERS CAN SPONTANEOUSLY ENTRAIN TO UNKNOWN ZEITGEBERS FOR UP TO 345 CONSECUTIVE DAYS

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Introduction: The biological clock is no longer synchronized to the 24-hour day in the majority blind individuals lacking light perception, resulting in recurrent insomnia and daytime somnolence as the timing of the clock (circadian phase) drifts in and out of synchrony with the timing of sleep. We have previously described a pattern of relative coordination (RC) in such blind free-runners (BFRs) wherein the drift in phase to a later, or earlier, time regularly slows and accelerates in response to weak time cues, but entrainment to the 24-hour day does not occur. We describe here four BFRs who, after a period of free-running with RC, spontaneously had circadian periods that were indistinguishable from 24-hours which we define as transient entrainment.
Methods: Subjects were 20 BFRs lacking conscious light perception (11 F, 9 M; 9-78 y.o.). Saliva samples were collected every 1-2 h for 14-25 h at the Oregon Health & Science University Clinical and Translational Research Center (CTRC) or at home approximately every 2 weeks. Melatonin concentrations were measured by radioimmunoassay (ALPCO) and the salivary melatonin onsets (MOs) were assessed using a 3 pg/ml threshold. Circadian period was calculated by linear regression through a series of MOs. As we have done previously, entrainment was defined as a period, based on at least 4 MOs, $>= 23.96$ h and $<= 24.04$ h with 95% CI that overlap 24.00 h. Free-running periods were calculated across an integral number of circadian beat cycles.
Results: Four of the twenty subjects demonstrated entrainment for 42, 71, 98 and 345 days with periods ($\pm$ 95% CI) of 23.96 ± 0.12 h, 24.02 ± 0.02 h, 24.02 ± 0.02 h and 24.00 ± 0.01 h, respectively. Their average period ($\pm$ SD) during entrainment was 24.00 ± 0.02 h. While free-running the subjects had periods ($\pm$ 95% CI) of 23.81 ± 0.08 h, 24.25 ± 0.11 h, 24.17 ± 0.05 h and 24.30 ± 0.05 h, respectively.
Conclusion: Transient entrainment in BFRs has diagnostic and treatment implications: phase must be assessed over a long enough period of time to prevent individuals from being misdiagnosed as entrained and to ensure treatment with oral melatonin; individuals who are sufficiently responsive to weak zeitgebers to demonstrate transient entrainment may require lower doses of melatonin.

0482

DELAYED SLEEP PHASE DISORDER AND CO-MORBID CONDITIONS IN AN ACADEMIC SLEEP CENTER

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Introduction: Circadian rhythm disorders have been so far characterized primarily as sleep disorders, resulting in sleep loss, circadian mismatch, and clinical symptoms of sleepiness, fatigue, dysphoric mood, and attentional difficulty. Delayed sleep phase syndrome (DSPS) is the

most common circadian rhythm disorder encountered in the sleep clinic and has been associated with depression and attention deficit hyperactivity disorder. This analysis explored associations between DSPS and co-morbid conditions such as sleep apnea, diabetes and cardiovascular disease.

Methods: In a retrospective cohort analysis, we reviewed the demographic data, medical histories, sleep schedules, and polysomnograms of the DSPS patients (n=861) evaluated in our multidisciplinary academic sleep disorders clinic from 1998 through 2008.

Results: The onset of DSPS was 2.6% in childhood, 13% in adolescence, and 84.4% in early adulthood. Depression, the most common co-morbid psychiatric disorder, occurred in 51.5% of subjects. Sleep disorder breathing (SDB), characterized as AHI $\geq$ 5 or RDI $\geq$ 20 events/hours, was seen in 43.32% and 86.76%, respectively. Hypertension co-existed in 25.2% and type 2 diabetes (T2DM) in 17.1%. A minority (< 10%) were able to use light / melatonin therapy to provide sustained entrainment.

Conclusion: Co-morbid conditions including SDB, T2DM, cardiovascular disease, and depression are extremely common in the DSPS population. The disease does not remit with age, and sustained successful treatment is exceptionally difficult. The high prevalence of T2DM is reminiscent of the known cardiometabolic effects of circadian misalignment in experimental models of shift work. The standard recommendation of not performing polysomnograms in those with clinical delayed sleep phase syndrome may need to be reconsidered.

Support (If Any): This work was conducted with support from KL2 Medical Research Investigator Training (MeRIT) grant awarded via Harvard Catalyst / The Harvard Clinical and Translational Science Center (NIH grant #1KL2RR025757-01 and financial contributions from Harvard University and its affiliated academic health care centers).

0483

ARMODAFINIL IMPROVES SEVERE SLEEPINESS, AS MEASURED BY SLEEP LATENCY TIME, COMPARED WITH PLACEBO IN PATIENTS WITH SHIFT WORK DISORDER

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Introduction: Armodafinil significantly improves wakefulness in patients with excessive sleepiness associated with shift work disorder (SWD), as measured by the Multiple Sleep Latency Test (MSLT) given at night. This *post-hoc* analysis examined the effect of armodafinil on improving severe nighttime sleepiness based on MSLT sleep latency time.

Methods: In this multi-center, 12-week, randomized, double-blind, parallel-group study, permanent or rotating night shift workers with nighttime sleep latencies of $\leq$6 minutes (MSLT) and diagnosed with moderate-to-severe SWD received 150 mg armodafinil or placebo 30-60 minutes before a night shift after 3 consecutive night shifts. Patients were administered the MSLT at 2400, 0200, 0400, 0600, and 0800 hours at baseline and at Week 12. Severity of sleepiness was characterized using MSLT sleep latency time as follows: <5 minutes (severe), 5 to 10 minutes (diagnostic grey area), and 10-20 minutes (normal).

Results: A total of 226 patients were included (armodafinil, n=112; placebo, n=104). At final visit, 38% of armodafinil-treated patients had sleep latencies >5 minutes (17% for placebo). The percentage of patients with sleep latency >5 minutes at 2400 hours was 49% in the armodafinil group and 30% in the placebo group. These percentages decreased throughout the night for armodafinil (42% at 0200, 33% at 0400, 22% at 0600) and for placebo (27% at 0200, 12% at 0400, 7% at 0600). There was a slight increase at 0800 for both treatment groups (26% armodafinil; 12% placebo).

Conclusion: Armodafinil improved sleep latencies versus placebo in patients with SWD and severe excessive sleepiness. Armodafinil resulted

in sustained improvements in sleep latencies and attenuated the decline of sleep latency throughout the night shift. A percentage of patients in both groups had sustained sleep latency times that remained <5 minutes.

Support (If Any): This research was sponsored by Cephalon, Inc., Frazer (NCT00080288).

0484

SLEEP PROBLEMS IN A COLLEGE POPULATION: WHAT ROLE CIRCADIAN RHYTHMS MAY PLAY AND RELATIONS TO DEPRESSION AND ANXIETY

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Introduction: The relations among sleep habits, depression, and anxiety are far from fully understood, and surprisingly little research has specifically examined college students. Brown, Soper, and Buboltz (2001) found an 11.5% college student prevalence of DSPS in their sample. In addition Lund et al. (2010) found low sleep quality along with short sleep and irregular schedules among college students. Thus, the present study was designed to explore the relations among depression, anxiety, and sleep problems, specifically delayed sleep phase syndrome (DSPS), as indicated by individual differences in morningness-eveningness, in a general sample of college students.

Methods: Undergraduates aged 18 to 44 years old (M= 20, SD= 9.58) completed a series of questionnaires, including the Pittsburgh Sleep Quality Index, Epworth Sleepiness Scale, Insomnia Symptom Questionnaire, Composite Scale of Morningness, Sleep Timing Questionnaire, Zung Self-Rating Depression Scale, and the Zung Self-Rating Anxiety Scale.

Results: Approximately 13% of the participants classified as evening types on the Composite Scale indicating DSPS. Sleep latency, later night times during the week, later night times on the weekends, and later morning times on the weekends were all significant independent predictors of lower scores on the Composite Scale of Morningness, which indicates the evening type. The Composite Scale of Morningness total score was also significantly correlated with both depression and anxiety as measured by the Zung Self-Rating Depression Scale and the Zung Self-Rating Anxiety Scale (all p's < 0.05).

Conclusion: The findings of this study add to research describing poor college student sleep habits, specifically poor sleep/wake scheduling that is typical of DSPS. Furthermore, depression and anxiety appear to be significant, unique predictors of the sleep/wake scheduling typical of DSPS. Implications and the need to explore in depth the prevalence of DSPS and how it relates to depression and anxiety will be further discussed.

0485

DEPRESSIVE SYMPTOMS AND DESYNCHRONIZATION OF CIRCADIAN ACTIVITY RHYTHMS IN COMMUNITY-DWELLING OLDER WOMEN

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Introduction: Aging is associated with changes in circadian rhythms and there is evidence to support a role for circadian rhythms in the pathophysiology of depression. However, little is known about the relationship between depressive symptoms and circadian activity rhythms in older adults. We examined this association in a large sample of community-dwelling older women.

Methods: Cross-sectional analysis of 3020 older women (mean age 83.55 ± 3.79 years) enrolled in an ongoing prospective study was performed. Depressive symptoms were assessed with the Geriatric Depression Scale categorizing participants as "normal" (0-2; n=1961), "some depressive symptoms" (3-5; n=704), or "depressed" (≥ 6; n=355). Circadian activity data were measured using wrist actigraphy. Circadian activity rhythm parameters were computed by fitting activity data to a 5-parameter extended cosine model. Circadian variables were expressed as dichotomous outcomes (acrophase > 1.5 SD above mean (advanced) vs. remainder sample and > 1.5 SD below mean (delayed) vs. remainder sample; amplitude, mesor, pseudo-F: lowest quartile vs. remainder sample). Association of level of depressive symptoms with circadian parameters was examined using logistic regression. Tests for linear trend were performed.

Results: After adjusting for multiple confounders, the odds of being in the lowest quartile for amplitude (less rhythmicity) were greater for women with some depressive symptoms (OR 1.32, CI 1.04-1.67) and depressed women (OR 1.51 , CI 1.11-2.05; p-trend < 0.003). The odds of being in the lowest quartile for mesor (lower mean modeled activity) were increased for women with some depressive symptoms (OR 1.55, CI 1.24-1.94) and depressed women (OR 1.62, CI 1.20-2.18, p-trend < 0.001). The odds of being in the lowest quartile for pseudo-F (less robustness) were increased for women with some depressive symptoms (OR 1.30, CI 1.03-1.63) and depressed women (OR 1.26, CI 0.93-1.71, p-trend = .045). No association was found between level of depressive symptoms and earlier or later occurring acrophase.

Conclusion: These data provide evidence to support an association between greater level of depressive symptoms and more desynchronization of circadian activity rhythms in older women. Future research should investigate whether longitudinal associations exist.

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0486

THE IMPACT OF EXCESSIVE SLEEPINESS ASSOCIATED WITH SHIFT WORK: RESULTS FROM SHIFT WORKERS AND PATIENTS WITH SHIFT WORK DISORDER PARTICIPATING IN AN INTERNET SURVEY

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Introduction: To investigate the impact of excessive sleepiness associated with shift work (SW) on the lives of shift workers (SWs).

Methods: SWs (with and without shift work disorder [SWD]) completed an online market research survey in 2009. Respondents must have spent ≥21 hours per week working shifts in the previous 2 weeks, reported SWD or had excessive sleepiness (score of ≥10 of the Epworth Sleepiness Scale), and scored ≥5 on any of the subscales of the Sheehan Disability Scale.

Results: 260 respondents completed the internet survey and reported anxiety (50%) and depression (45%) as their most common comorbidities. On a 10 point scale, where 1="not serious at all" and 10="extremely serious," respondents scored excessive sleepiness and insomnia due to SW as 7.43 and 7.15, respectively. SW negatively impacted respondents' lives by affecting energy level, social life, mood, ability to get sufficient sleep, irritability, motivation, weight, alertness/ability to stay awake, quality of life, concentration, sex life, emotional health, and physical health. As a result of their excessive sleepiness, in the past month, 87% reported a loss of concentration/lapses of attention at work, 69% made mistakes at work, 37% dosed off while driving, 34% almost caused a

car accident while driving, and 11% had an injury at work. Respondents reported using over-the-counter remedies coffee/tea and caffeinated soda. 57% of SWs received prescription medication to treat SWD symptoms (buproprion 52%, other anti-depressants 52%, anxiolytics 45%, modafinil 42%, and zolpidem 36%).

Conclusion: SWs suffered a number of comorbid conditions including anxiety and depression. Respondents reported that both excessive sleepiness and insomnia associated with SW seriously impacted their lives, both at home and at work. Respondents have used over-the-counter remedies and pharmaceutical interventions to treat SW-related symptoms.

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0487

EFFECT OF LIGHT THERAPY ON SLEEP TECHNOLOGIST FUNCTIONING

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Introduction: Shift work, although essential in the medical environment, is known to result in morbidity for the worker, including sleep disorders and mood and eating habits changes. Additionally, it also contributes to sleepiness and increased accidents in the workplace. Bright light therapy has been used to shift circadian rhythms and treat shift workers. We, therefore, hypothesized that bright light therapy would result in improvements in subjective sleepiness, quality of life, mood, eating habits and increased off-shift sleep, with a longer consolidated sleep period.

Methods: Sleep laboratory technologists underwent two weeks of bright light therapy during work hours, compared to two weeks of normal light exposure, in randomized order separated by a one-week wash-out period. Depression (CESD), overall health (SF36), Epworth sleepiness scale (ESS), Visual analog scale (VAS) and functional outcomes of sleep (FOSQ) questionnaires were completed at baseline (T1) and at the end of each light cycle (T2=bright, T3=normal). Actigraphy and food diary data were obtained at the end of the bright and normal light periods.

Results: Eighteen sleep technologists (eleven females, age 32.6 ± 8 years) participated in the study. CES-D (p<0.00001), SF-36 Physical Functioning scale (p=0.0005), and FOSQ (p= 0.0077) were significantly different between the three periods. Specifically, bright light exposure resulted in a trend towards less depression and better physical functioning. The SF-36 General Health scale trended towards significance (p=0.0843). No significant VAS, ESS, food diary, and sleep consolidation differences were observed.

Conclusion: Bright light therapy during work hours results in a trend towards less depression and better physical functioning in sleep technologists. A bigger sample size may be necessary to detect potential differences in caloric intake, sleepiness, and sleep consolidation.

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0488

CHRONOTYPE AS A PREDICTOR OF PERFORMANCE IN MAJOR LEAGUE BASEBALL BATTERS

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Introduction: Previous reports have suggested that chronotype may influence athletic performance at different times during the day. The

Morningness Eveningness Questionnaire (MEQ) is a method for assessing chronotype. Because Major League Baseball (MLB) players play games both during the day and night, it was hypothesized that chronotype might predict optimal batting performance times.

Methods: MEQ data from 16 MLB batters representing 7 teams was collected. A modified 7 question MEQ (mMEQ) was obtained by adding the score of question 7 (subject global impression) to the total score. Statistical performances from the 2009 and 2010 seasons were logged with game start times adjusted for travel using the convention that for every time zone traveled, it takes 24 hours to adjust. Games were divided into two groups. 'Early' games featured start times prior to 14:00, 'Mid' games between 14:00-19:59, and 'Late' games began at 20:00 or after. This produced 2149 early innings, 4550 mid inning, and 750 late innings. 16 players were divided into two groups: 9 'evening type' players [E-types] (mean age = 29.0, SD = 3.4, mMEQ score of 12-23), and 7 'morning type' players [M-types] (mean age = 29.0, SD=4.1, mMEQ of 24-33).

Results: In early games, M-type batters had an average of .267 compared with an E-type average of .259. In mid games, M-type batters had an average of .252 and E-type batters an average of .261. In late games, M-type batters had an average of .252 and E-type batters an average of .306.

Conclusion: Other investigations have shown tendencies for M-type athletes to perform significantly better in the morning versus the evening. Our results showed a similar trend. Because of the small magnitude of the effect we are studying, we plan on looking at more players and precise batting times to better understand this effect.

0489

NATURAL CIRCADIAN PHASE-SHIFTS DURING SUMMER NIGHTWORK IN POLICE OFFICERS ASSIGNED TO ROTATING SCHEDULES

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Introduction: It is often reported that night shift workers usually do not adapt to the night schedule due to the resynchronising effect of light during the commute home combined with low light exposure at night in the workplace. However, police officers who are patrolling at night do experience some natural light towards the morning especially in summer time. It is unclear if this light which may starts as early as 4AM may cause phase-delay or if it would be counterbalanced by light received later in the morning. This study investigated the phase-shift experienced by patrol police officers with DLMO obtained before and after a series of 4 night shifts in summer time in Quebec city (latitude 46°49.2'N).

Methods: Salivary samples were obtained before and after 4 consecutive night shifts in 13 officers (mean age 28.5±2.67). Pre-night shifts (hourly) collection went from 19h00 to 23h00 whereas post-night shifts collection went from 21h00 to 04h00 (in order to detect an expected phase-delay). Elisa was used to assay melatonin concentration. Police officers were assessed between May and October and wore a wrist photometer to measure ambient light. Work schedule was 23h00-07h00.

Results: DLMO before the night shift range from 20h00 to 23h00 with a mean of 21h10±0h41. Phase-shift ranged from 1 to 7 hours with a mean of 3h02±1h46. There was no correlation between the amount of phase-shift experienced and sunrise which varied (during the experiment) from 04h50 in June and 07h15 in October. Interestingly the police officer tested in October showed a 3h30 phase-delay.

Conclusion: Preliminary analysis revealed that substantial phase-shifts could observe in some patrol police officers whereas very small phase-shifts are observed in others. Light exposure analysis shall provide more information regarding the possibility that light intensity received in morning or evening (before the night shift) could explain this variability.

0490

OBSTRUCTIVE SLEEP APNEA AND NON-DIPPING NOCTURNAL BLOOD PRESSURE

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Introduction: The relationship of obstructive sleep apnea (OSA) and the absence of normal physiologic sleep-related blood pressure (BP) dipping has not been specifically characterized in those with cardiovascular (CV) risk. We hypothesize that increasing OSA severity is associated with non-dipping BP during sleep in those with increased CV risk.

Methods: Data are from participants of the baseline visit of a multi-center randomized controlled trial (Heart Biomarker Evaluation in Apnea Treatment: HeartBEAT). OSA severity was assessed using the apnea hypopnea index (AHI). BP dipping from 24-hour ambulatory BP monitoring was defined as a sleep-related BP reduction of > 10% (i.e., sleep-wake BP ratio of <0.9) of systolic BP (SBP), diastolic BP (DBP) and mean arterial pressure (MAP). Logistic regression models were used to assess AHI (per 5-unit increase) with BP dipping status.

Results: Subjects (n=158) were: 62.6±8.8 (mean ± SD) years, 69% men, 75% Caucasians with body mass index (BMI) 34.0±5.8 kg/m2, 80% hypertension, 56% coronary artery disease (CAD). The AHI was 24.8±8.8 (15 to 50). The baseline SBP and DBP (mmHg) were 123.6±15.3 and 70.4±7.8 respectively. Non-dipping SBP, DBP and MAP prevalence was 53%, 44% and 48% respectively. For each 5-unit AHI increase, there was a 27% increased odds of non-dipping SBP in unadjusted analyses, which persisted when adjusted for age, sex, race, BMI, hypertension or antihypertensive medications, diabetes, CAD and smoking status (OR=1.27, 95% CI: 1.03-1.58). The relationship between AHI and non-dipping systolic BP was similar in those with CAD (OR=1.20, 95%CI: 0.95-1.52) versus without CAD (OR=1.35, 95%CI: 0.97-1.89). AHI was not associated with non-dipping DBP or MAP.

Conclusion: In a sample of patients with moderate to severe OSA and CV risk or known CV disease, increasing AHI was associated with SBP (but not DBP) non-dipping. These relationships were similar irrespective of CAD status and despite anti-hypertensive medication use and acceptable BP control.

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0491

EEG POWER DURING WAKING AND NREM SLEEP IN PRIMARY INSOMNIACS AND HEALTHY CONTROLS

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Introduction: The hyperarousal theory of insomnia is supported by increased activation of the neuroendocrine and neuroimmunological axes, as well as increased high frequency EEG activity during NREM sleep. Because increased arousal in primary insomnia (PI) is thought to be a 24-hour phenomenon, it is possible that the waking EEG of PI would also show evidence of hyperarousal. The aim of this study was to compare EEG power during the waking EEG in PI and good sleeper controls (GSC), and to examine associations between waking and NREM sleep EEG power in PI.

Methods: Subjects include 59 PI and 26 GSC similar in age and sex distribution. Five minutes of eyes closed waking EEG were collected 60-90 min prior to usual bedtime in the evening, followed by PSG at habitual sleep times. An automated algorithm and visual editing were used to remove artifacts from waking and sleep EEGs, followed by power spectral analysis to estimate power from 0.5 - 32 Hz. Subjects also completed self-reports including Pittsburgh Sleep Quality Index and sleep diary.

Results: Waking EEG power was significantly higher in PI than GSC in theta (4Hz-8Hz; p=0.045) and low beta (16Hz-20Hz; p=.044) frequencies. Power in these two bands was significantly correlated (whole group r=0.70,n=86, p<0.001). The group difference in theta persisted after controlling for age and sex, but the beta difference became marginally significant (p=.076). Waking and NREM power in PI were significantly correlated: theta (r=0.65, n=55, p<0.001, and low beta (r=0.67,n=55, p=0.001).

Conclusion: Elevated theta power in the waking EEG of PI compared to GSC suggests increased homeostatic sleep drive, and increased beta power suggests increased arousal during wakefulness, similar to previous findings with NREM EEG power. The correlation between waking and NREM EEG power raises the possibility that waking EEG could be used as a simpler physiological marker of insomnia.

0492

ALTERED REGIONAL BRAIN GABA IN PRIMARY INSOMNIA: A MAGNETIC RESONANCE SPECTROSCOPY STUDY AT 4 TESLA

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Introduction: Prior work from our laboratory using proton magnetic resonance spectroscopy (1H-MRS) demonstrates reductions in global brain GABA in primary insomnia (PI) versus healthy sleepers, supporting the hyperarousal model of PI. However, previous studies utilized a 2D chemical shift imaging (CSI) acquisition combined with J-resolved Echo-Planar Spectroscopic Imaging (JEPSI), with limited spatial resolution. The primary aim of this study was to extend prior findings by again using 1H-MRS at high field, but now examine single-voxels in specific regions of interest, utilizing J-difference editing using Point Resolved Spectroscopy with MEGA suppression (MEGAPRESS), which has become the most commonly used spectroscopic method for quantifying GABA in vivo.

Methods: Unmedicated PI subjects (n=20) and healthy sleeper controls (n=19) were recruited from the greater Boston, MA area. After evaluation for psychiatric, sleep and medical disorders, subjects completed two weeks of sleep diaries supplemented by actigraphy. 1H-MRS acquisitions were conducted on a 4-Tesla MR scanner operating at 170.3 MHz for proton, using a single-tuned, birdcage design whole-head coil. Using MEGAPRESS for GABA editing, integrated GABA to creatine ratios (GABA/Cr) were determined in the thalamus, anterior cingulate cortex (ACC) and occipital cortex (OCC). Unpaired t-tests were used to compare GABA/Cr between groups in regions of interest. Post hoc correlations of GABA/Cr to psychometric insomnia severity measures were additionally performed.

Results: GABA/Cr was significantly decreased in OCC (0.00125±0.0006 vs. 0.00158±0.0004, p=0.005) and trended towards decrease in ACC (0.00104±0.0003 vs. 0.00119±0.0003, p=0.08) in PI relative to controls. GABA/Cr in the thalamus did not differ between groups. Post hoc correlations revealed no significant correlation between OCC GABA/Cr and ISI, PSQI, or DBAS-16 scores among PI subjects.

Conclusion: This study extends our findings of decreased GABA/Cr in PI. Given demonstrations of GABA reduction in major depressive disorder, further evaluation of the relationship between GABA, insomnia and mood disorders is indicated.

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0493

A GENOME-WIDE ASSOCIATION ANALYSIS OF INSOMNIA: THE CHARGE CONSORTIUM

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Introduction: Insomnia is a common sleep disorder characterized by difficulties in initiating or maintaining sleep. The genetics of insomnia are poorly understood and many of the genes related to sleep initiation and maintenance are unknown. The discovery of novel pathways responsible for insomnia may lead to a better understanding of the disease process and more effective therapeutic targets.

Methods: Through the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium, single-nucleotide polymorphism genome-wide association analyses were pooled from the Age, Gene/Environment Susceptibility Reykjavik Study, the Atherosclerosis Risk in Communities Study, the Cardiovascular Health Study, the Framingham Heart Study, the Rotterdam Study, and the Study of Health in Pomerania. The phenotypes were obtained by self report, and included sleep latency, frequency of difficulty initiating sleep or difficulty in maintaining sleep. An additive model was used with adjustments for age, sex and relatedness and filtered for minor allele frequency >5%, and availability of genotyping in at least three cohorts.

Results: Up to 15,664 individuals were included in the meta-analysis for difficulties in initiating or maintaining sleep. Sleep latency was available in 12,503 individuals. We identified a number of genes associated with difficulty in initiating sleep (SORCS1, p=3.57e-7; SOX5, p=3.93e-7), maintaining sleep (EXT1, p=1.19e-7; ME3, p=1.23e-7), and sleep latency (POU1F1, p=1.24e-7; FLJ20160, p=2.77e-7). Several of the candidate genes possess biological plausibility in the neurophysiology of sleep. For example, SORCS1 is involved in central nervous system neu-

ropeptide signaling, while POU1F1 is involved in pituitary regulation which has been implicated in the development of insomnia.

Conclusion: In a large meta-analysis of six population cohorts, we identified promising novel gene associations to traits important in the characterization of insomnia. Further work is needed to confirm these findings, including additional in-silico replication with larger population cohorts.

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0494

CORTISOL RESPONSIVITY TO A COLD PRESSOR CHALLENGE IN INSOMNIACS

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Introduction: Stress can elicit insomnia in predisposed individuals. The autonomic (ANS) and hypothalamic-pituitary-adrenal (HPA) axis are important systems involved in the stress response. In contrast to previous studies comparing basal levels of cortisol in insomnia, the present study assessed HPA and autonomic reactivity during two cold pressor test (CPT) challenges in insomniacs and controls.

Methods: 52 subjects (18 insomniacs and 34 controls) were recruited to assess reactivity to a CPT. We are reporting the data on 39 subjects (11 insomniacs and 28 controls), who kept their hands in cold (4C) water for at least 45 seconds. The age of the insomnia group (7M, 4F) was 31.7+ 10.1 and 27.4+7.9 years for controls (17M, 11F). Subjects with sleep, psychiatric and medical disorders were excluded. ANS measures (SBP, DBP and HR) and salivary cortisol level (6 assays in 10 min intervals) were collected before, during, and following the CPT on two days. ANOVAs were used to test for group differences in ANS and HPA reactivity.

Results: No group differences were observed in baseline levels of SBP, DBP, HR or cortisol. Cortisol peak reactivity across the CPT days was higher ($p < 0.05$) in the insomnia group (5.98+4.6 nm/L) relative to controls (3.23+3.12 nm/L). SBP was increased after CPT ($p < 0.01$) but there were no group differences in reactivity ($p > 0.05$). No differences in DBP or HR were observed in response to CPT.

Conclusion: Cortisol response to stress is greater in insomniacs relative to controls. The lack of group differences in ANS response suggests differences in physiological responsivity may be more specific to the HPA axis.

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0495

MSLT AND TOTAL SLEEP TIME IN PRIMARY INSOMNIACS

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Introduction: Studies have reported elevated, relative to normals, MSLTs in persons with insomnia, supporting the hypothesis that insomnia is a condition of hyperarousal. Some reports from small samples indicate MSLTs of insomniacs do not relate to total sleep time (TST). In contrast, in normal population based samples shorter TST is associated with shorter MSLTs. This study assessed the relation of MSLT and TST in insomniacs qualifying for a large hypnotic treatment trial.

Methods: Primary insomniacs (N=88), ages 32-64, meeting DSM-IVR criteria and additional screening sleep efficiency (sleep time/bed time) criteria of <85% and no other primary sleep disorders on an 8-hr sleep recording were recruited. They were without psychiatric diseases or drug dependency and in good general health. On the day following the screening NPSG all participants received a standard MSLT (1000, 1200, 1400, and 1600 hr). No MSLT inclusion criteria were applied for study entry.

Results: The MSLT scores ranged from 3-20 min and were normally distributed (Shapiro-Wilk test statistic: 0.95, p<.001). The mean MSLT was 13.5+/-4.5 min and the median 14.2 min. The mean MSLT of the highest quartile of the distribution was 18.2+/-1.5 min and the lowest quartile 7.3+/-2.6 min with the two intermediate quartiles collapsed being 13.6+/-1.4 min. The TST of the highest MSLT quartile (344.4+/-51.2 min) was significantly shorter than that of the lowest quartile (374.4+/-28.6 min) (F=3.15, p<.05). The TST of the two intermediate quartiles was 350.2+/-45.9 min and not different from either extremes. The age and sex distribution did not differ among the MSLT quartiles.

Conclusion: The shortest sleeping insomniacs have the highest MSLTs, a relation the reverse of that seen in healthy normal sleepers. This finding is further supportive of the hypothesis that insomnia is a disorder of hyperarousal, with increased drive for wake expressed both at night and during the day.

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0496

DO OLDER ADULTS WITH INSOMNIA HAVE IMPAIRED WORKING MEMORY PERFORMANCE?

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Introduction: Older individuals suffering insomnia typically report subjective declines in their cognitive performance beyond what they consider to be normal changes due to the aging process. Recent neuro-imaging studies have demonstrated frontal lobe hypo-activation among insomniac populations when compared to healthy, good sleepers. However, research is yet to confirm whether frontal lobe hypo-activation translates into objective declines when performing tasks hypothesized to draw upon this brain region. This study aimed to objectively identify if older insomnia sufferers demonstrate significantly impaired performance on a working memory task when compared to age-matched good sleepers.

Methods: To date, forty-nine (male=22) older adults (M=64.59, SD=7.29) suffering from sleep maintenance insomnia have been compared with 49 age and gender matched good sleepers. Cognitive performance was assessed using the Double Span Memory Task, a computer-based working memory task which asks participants to indicate the names and/or spatial locations of increasingly longer sequences of visually presented objects.

Results: Results indicate that after controlling for general intelligence, the individuals suffering from insomnia did not perform differently when compared to good sleepers on either the simpler or more cognitively demanding components of the task.

Conclusion: Older individuals with insomnia do not display an observable impairment on working memory process relative to good sleepers. This may be an indication that mechanisms, such as chronic hyperarousal, may assist insomniacs in maintaining performance at a level similar to good sleepers.

Support (If Any): NHMRC

0497

UNDERESTIMATION OF N-BACK PERFORMANCE COMPARED TO INSOMNIA SEVERITY

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Introduction: A diagnosis of primary insomnia (PI) requires significant daytime complaints. PIs typically report performance deficiencies at work, school, or in day-to-day activities. However, PIs typically show

no objective deficits when tested in-lab. This discrepancy may relate to different domains of inquiry: day-to-day function vs in-lab. Here, we further examine this phenomenon by comparing objective-subjective discrepancies on the same in-lab test and examining if insomnia severity influences this discrepancy.

Methods: 16 PIs (age=33 ±7.27yrs, 6F) were studied. After the n-back task was administered during an fMRI scan, subjects estimated the percent of correct responses achieved for each task level. A discrepancy score was calculated as Objective-Subjective score. Insomnia severity on the ISI was examined as a predictor of objective-subjective discrepancy. Knowing that people with insomnia do mention having cognitive deficits, and that hyper-arousal is an aspect of insomnia, we would expect subjects with a worse insomnia to more accurately estimate their performance.

Results: Insomnia severity was significantly associated with objective-subjective discrepancy scores for 0-back (r=.588), 1-back (r=.643), and 3-back (r=.606), but not 2-back (r=.379). Insomnia severity was generally not correlated with either objective performance or subjective performance separately, (r= -.336 to .475) with the exception of subjective 1-back performance (r=.515, p=.041).

Conclusion: This data suggest those with worse insomnia are attuned to their cognitive performance and can more accurately estimate their score, while those with a more mild insomnia tend to show the more traditional underestimation of performance. This may help explain why there is such a difference with various subjects between objective scores (PSG sleep data, actiwatch activity data) and their subjective complaints (waking up during the night multiple times, for long periods of time). Future studies should try to incorporate subjective ratings or scores for each task, in order to further support how insomnia severity can influence the objective-subjective discrepancies.

0498
COGNITIVE MECHANISMS IN INSOMNIA: A COMPARISON OF COMORBID AND PRIMARY INSOMNIA

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Introduction: Different cognitive mechanisms are hypothesized to play a critical role in maintaining insomnia and some of them may also be implicated in maintaining anxiety and depression. This study examined whether individuals with insomnia comorbid with a mood or anxiety disorder differed from individuals with primary insomnia on different measures of cognitive processes.

Methods: Participants were 205 adults (mean age = 50.2 years; 60% women) with an insomnia disorder, including 47 with a comorbid mood or anxiety disorder and 158 without comorbidity. They were enrolled in a CBT trial aimed at assessing mechanisms underlying therapeutic change. This study focused on baseline data and included the following measures: Anxiety and Preoccupation about Sleep Questionnaire (APSQ), Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS), Thought Control Questionnaire for Insomnia (TCQ-I), Sleep Associated Monitoring (SAMI), Sleep Behaviors Rating Scale (SBRS), and the Insomnia Severity Index (ISI).

Results: The two insomnia groups did not differ with respect to gender, age, insomnia duration, or sleep-incompatible behaviors. However, they differed on the ISI, with the comorbidity group showing higher insomnia severity (M= 19.5 vs. 17.2; p < 0.001). Significant group differences were also observed on the APSQ (p < 0.001), DBAS (p < 0.001), TCQI worry (p < 0.001) and cognitive distraction (p= 0.056) subscales, and most of the SAMI subscales (all ps < 0.05), with higher scores in the comorbidity group, suggesting these patients were more preoccupied, engaged more often in worry and monitoring and had more sleep-related dysfunctional beliefs. All differences remained significant after controlling for insomnia severity. On the other hand, the SAMI calculation and

TCQ-I suppression subscales were positively correlated with insomnia severity but not related to comorbidity.

Conclusion: These results suggest that the presence of a comorbid mood or anxiety disorder increases insomnia severity and support the hypothesis that some cognitive mechanisms may be shared across these disorders. These findings have implications for tailoring CBT interventions.

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0499
DEMOGRAPHIC, BEHAVIORAL AND CLINICAL RISK FACTORS FOR INCIDENT POOR SLEEP

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Introduction: Poor sleep is very prevalent in the general population and is considered to precede the development of chronic insomnia. However, none of the available population-based, longitudinal studies have examined risk factors for the development of poor sleep in the general population. In this study we examined the demographic, behavioral and clinical factors that increase the risk of developing poor sleep.

Methods: From a random, general population sample of 1741 adults of the Penn State Cohort, 1395 were followed-up after 7.5 years. In this study we included those with normal sleep at baseline (n = 590) and those with normal sleep at baseline who developed into poor sleep (n = 188). Poor sleep was defined as a moderate to severe complaint of difficulty falling asleep, difficulty staying asleep, early morning awakening, or non-restorative sleep. Medical and sleep history, 8-hour PSG, and personality testing were obtained at baseline, and sleep history also at follow-up.

Results: Ulcer (OR=7.00; p=.0001), depression (OR=2.04; p=.012), obesity (OR=1.70; p=.010), number of alcoholic drinks/day (OR=1.02; p=.0001), and AHI ≥ 15 (OR=1.83; p=.074) significantly increased the odds of incident poor sleep, whereas number of cigarettes/day (p=.159) did not remain significant in the multivariate model. Individuals with incident poor sleep showed higher elevations in all personality scales, except hysteria, at baseline as compared to normal sleep even after adjusting for obesity and depression.

Conclusion: Physical and mental health problems are strong predictors of the development of poor sleep. These data suggest that poor sleep is a symptom of underlying medical and psychological conditions and the primary focus of prevention and treatment of poor sleep complaints should be the underlying health conditions rather than sleep per se.

0500
SEVERE INSOMNIA SYMPTOMS PREDICT INCIDENT CARDIOMETABOLIC DISEASE

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Introduction: Accumulating evidence suggests that short sleep duration is linked to cardiometabolic risk and disease course. Fewer studies have evaluated the cardiometabolic health consequences of insomnia, which is the most common primary sleep disorder and differs functionally from short sleep duration.

Methods: The present study evaluated prospective associations among insomnia symptoms and three indices of cardiometabolic disease: hypertension (HTN), diabetes and ischemic heart disease (IHD). Participants were drawn from the longitudinal Finnish Public Sector Study of government and hospital employees (n=39,724, mean age 44.7 ±9.4 yrs, 18.5% male). Insomnia symptoms were measured by self-report

according to diagnostic criteria, including a minimum symptom duration of greater than 1 month. Participants were categorized as follows: No Insomnia (symptoms less than or equal to 1 night/week), Moderate Insomnia (symptoms 2-4 nights/week) or Severe Insomnia (symptoms greater than or equal to 5 nights/week). National register and medical records were used to identify incident cases of HTN, diabetes and IHD at least one year following the insomnia assessment (mean follow-up duration = 4.4 ±0.6 yrs). Only participants with a negative history of all 3 cardiometabolic outcomes at baseline were included in the analyses. Logistic regression was used to predict the odds of incident disease according to insomnia symptom categories, after adjusting for age, sex and occupational status.

Results: Severe insomnia was associated with an increased risk for all 3 outcomes (HTN OR=1.35, CI: 1.23-1.49; diabetes OR=1.42, CI: 1.04-1.94; and IHD OR=1.57, CI: 1.08-2.27). Severe insomnia remained prospectively associated with increased risk for incident hypertension (OR=1.20, CI: 1.08-1.33) after additional adjustment for health behaviors and medical co-morbidities.

Conclusion: These results suggest that severe insomnia may be a novel biobehavioral risk factor for cardiometabolic disease, especially hypertension. If this relationship is shown to be causal, effective treatment of insomnia may represent a promising therapeutic target for primary prevention of cardiometablic disease.

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0501

PHYSICAL AND MENTAL HEALTH FACTORS ASSOCIATED WITH INSOMNIA PERSISTENCE, PARTIAL REMISSION AND FULL REMISSION IN THE GENERAL POPULATION: A LONGITUDINAL STUDY

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Introduction: Few population-based, longitudinal studies have examined the rates of insomnia persistence and remission, whereas there is no study that has examined risk factors associated with persistent insomnia. We examined the rates and risk factors of persistent, partially remitted and fully remitted insomnia in a sample of the general population.

Methods: From a random, general population sample of 1741 adults of the Penn State Cohort, 1395 were followed-up after 7.5 years. In this study we included those with normal sleep at baseline and follow-up (n = 590) and those who were insomniacs at baseline (n = 149) and developed into persistent (n = 65), partially remitted (n = 47), or fully remitted insomnia (n = 37). Medical and sleep history and MMPI-2 testing were obtained at baseline, and sleep history also at follow-up.

Results: The rates of persistent insomnia, partial remission, and full remission were 44.0%, 30.0%, and 26.0%, respectively. Mental health problems at baseline were strongly associated with persistent insomnia as compared to normal sleep (OR =12.2) and to a lesser degree compared to remitted insomnia (OR=3.10), whereas physical health problems predicted full remission. Persistent and partially remitted insomniacs showed higher elevations in all personality scales when compared to normal sleepers, whereas in remitted insomniacs only two scales were significantly higher.

Conclusion: Insomnia is a chronic and persistent disorder with a rather low rate of full remission. Mental health problems are strong predictors of insomnia persistence or partial remission. Early detection of insomnia should be a focus of our public health policies.

0502

NATURAL HISTORY OF POOR SLEEP: A POPULATION-BASED, 7.5 YEARS LONGITUDINAL STUDY

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Introduction: Poor sleep is thought to precede the development of chronic insomnia. However, none of the available population-based, longitudinal studies have examined risk factors of the natural history of poor sleep.

Methods: From a random, general population sample of 1741 adults of the Penn State Cohort, 1395 were followed-up after 7.5 years. In this study we included those with poor sleep at baseline (n = 403) who remained poor sleepers (n = 155), switched to normal sleep (n = 180), or developed chronic insomnia (n = 68). Medical and sleep history, 8-hour PSG, and MMPI-2 testing were obtained at baseline, and sleep history also at follow-up.

Results: The rates of persistent poor sleep, remitted poor sleep, and poor sleep with incident insomnia were 39%, 44%, and 17%, respectively. Male gender, middle-age, allergy/asthma, heart disorder, ulcer, and depression increased significantly the odds of persistent poor sleep as compared to remission, whereas female gender, family history of sleep problems, young age, and caffeine consumption increased the odds of poor sleepers developing insomnia. Poor sleepers who developed insomnia also showed higher elevations in 6 personality scales when compared to remitted poor sleepers, whereas in persistent poor sleepers only 2 scales were significantly higher.

Conclusion: These data suggest that the large majority of poor sleepers either get better or stay the same, whereas only a small percentage of them develop chronic insomnia. Persistent poor sleep is associated with physical and /or mental health problems, whereas emotional distress is of primary importance in those developing into chronic insomnia. Treatment of underlying health problems may reduce persistent poor sleep, whereas addressing maladaptive personality traits may prevent the development of chronic insomnia.

0503

THE EFFECTS OF INSOMNIA TREATMENT ON SLEEP INSTABILITY: IS SLEEP STABILIZATION AN IMPORTANT TREATMENT TARGET?

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Introduction: Night-to-night sleep variability is considered a frustrating component of the insomnia experience. Therefore, stabilization of sleep could be regarded as a desirable insomnia treatment endpoint. However, few studies have addressed whether sleep instability decreases with behavioral or pharmacologic treatments or whether reduced variability relates to other clinically important outcomes. This study evaluated the effects of cognitive-behavioral therapy (CBT) on sleep instability across primary (PI) and comorbid (CI) insomnia subgroups, and explored the relationship of sleep instability and perceived sleep quality at the post-treatment time point.

Methods: Participants were insomnia sufferers (n=41, 6 women, mean(SD) age 54(14) years) randomized to CBT in a larger clinical trial. Twenty individuals met criteria for PI, whereas 21 had CI associated with psychiatric disorders. Before and after treatment, intra-individual instability of sleep onset latency (SOL), wake after sleep onset (WASO), total sleep time (TST) and sleep efficiency (SE), derived from diary as well as from actigraphy, was assessed by squaring the differences between successive nights over a 2-week period. Treatment effects on

resultant sleep instability measures were tested with generalized multi-level models. We used Pearson's correlations to examine the relationship between post-treatment instability estimates and Pittsburgh Sleep Quality Index (PSQI) scores.

Results: Four biweekly CBT sessions produced statistically significant reductions in all four diary-derived instability measures, as well as in actigraphy-derived SE instability for the total sample (all Ps<.05). By contrast, the decrease in actigraphy-derived SOL instability was significant only in the CI group (p<.01). Correlational analyses revealed that higher post-treatment scores on the PSQI were associated with more unstable diary TST (r=.40, p=.03) and actigraphy SOL (r=.50, p<.01).

Conclusion: CBT is effective for reducing subjective and objective sleep instability indices, although its "stabilizing" effects may vary across insomnia subtypes. Moreover, our correlational findings suggest that reduced sleep variability across nights might itself be perceived as clinically important to insomnia sufferers.

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0504

DEVELOPING A NEW BEHAVIORAL TREATMENT FOR INSOMNIA: ACCEPTING BEHAVIORAL CHANGES TO TREAT INSOMNIA (ABC-I)

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Introduction: Insomnia affects 9-20% of adults and 33% of the elderly population, with even higher prevalence when psychiatric and/or medical comorbidities are present. While cognitive-behavioral therapy for insomnia (CBT-I) is the gold standard treatment, patient acceptance of CBT-I and adherence remain a challenge, particularly among complex patients such as older adults with comorbidities. We developed a behavioral treatment for insomnia, the ABC of Insomnia (ABC-I: Accepting Behavioral Changes to Treat Insomnia), utilizing components of an evidence-based treatment aimed at increasing adherence to and acceptance of treatment while decreasing hyperarousal.

Methods: The study followed the NIH model for development of behavioral treatments (stage 1-a and b). The ABC-I treatment incorporates principles of Acceptance and Commitment Therapy (ACT; Values, Committed Action, Acceptance, Mindfulness, Defusion, Self as Context) with the behavioral components of CBT-I (Sleep Restriction, Stimulus Control). After developing the manual and gathering qualitative data on comprehensibility of the manual, acceptability and effectiveness of the treatment on 6 clinical patients, we further piloted the ABC-I on 3 older veterans with comorbidities. Insomnia Severity Index (ISI), Glasgow Sleep Effort Scale (GSES), and actigraphy variables were assessed at three time points: before treatment, after treatment, and at 3-month follow-up.

Results: 3 male veterans (aged 60, 77, and 81 years) with severe psychiatric and medical comorbidities (e.g., PTSD, GAD, Diabetes, Legal Blindness) completed the study. One individual had previously attempted CBT-I in our sleep disorders center without success. Following the ABC-I program, all three patients' insomnia severity decreased from before to after treatment and follow-up (ISI means=15.0+/-7.0, 9.3+/-5.1, 8.9 +/- 6.9, respectively). Sleep effort was also reduced (GSES means=9.3+/- 4.0,3.0+/-1.7,3.0+/- 2.6, respectively). Actigraphic variables also confirmed improved sleep after treatment.

Conclusion: ABC-I is a promising new behavioral treatment for insomnia in complex patients with medical and psychiatric comorbidities. Randomized controlled trials are underway to test its efficacy.

0505

EFFECTS OF CBT FOR INSOMNIA ON RELATIVE REGIONAL CEREBRAL METABOLIC RATE OF GLUCOSE DURING NREM SLEEP AND MORNING WAKEFULNESS IN ADULTS FROM PRIMARY INSOMNIA

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Introduction: Insomnia is a prevalent, debilitating disorder that is thought to arise from hyperarousal. Preliminary neuroimaging studies showed that the persistence of heightened brain activity from wakefulness to NREM sleep in arousal-regulating regions characterizes primary insomnia. In this study, we explored whether cognitive-behavioral therapy for insomnia (CBT-I) is associated with reductions in relative regional cerebral metabolic rate of glucose (rCMRglc) in brainstem arousal-regulating regions, hypothalamus, thalamus, limbic structures, and frontal cortical regions.

Methods: Five adults with primary insomnia received CBTI over 8 weeks, and completed in-lab sleep and 18F-FDG positron emission tomography (PET) studies. Participants completed PET scans during wakefulness and during NREM sleep. Sleep and PET studies were repeated after CBTI. Statistical analysis of imaging data was performed using SPM8.

Results: Four of the 5 participants responded to CBTI, defined as decreases of 3 points or more on the Pittsburgh Sleep Quality Index and of more than 6 points on the Insomnia Severity Index. Post-CBTI, a greater reduction in relative rCMRglc from morning wakefulness to NREM sleep was observed in portions of the left temporal, occipital lobes, and cerebellum (p = 0.01) compared to between-state reductions observed pre-treatment. Post-hoc analysis revealed that relative rCMRglc was reduced post-CBTI during both wakefulness and NREM sleep in areas of the left and right frontal lobe, thalamus, and right hippocampus, temporal lobe and cerebellum (p < 0.05), relative to pre-CBTI.

Conclusion: This pilot study suggests that CBTI is associated with significant reductions in relative rCMRglc during both wakefulness and NREM sleep in the thalamus and frontal cortex. This pattern is consistent with a reduction of cerebral metabolic activity post-treatment in the thalamocortical network involved in maintenance of arousal. Future directions for investigation include replication in a larger sample, and comparison of the effects of CBT-I and hypnotic medication on relative rCMRglc.

0506

A RANDOMIZED CONTROLLED TRIAL OF A COMBINED TREATMENT OF COGNITIVE BEHAVIOUR THERAPY AND EVENING BRIGHT LIGHT THERAPY FOR INSOMNIA IN OLDER ADULTS

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Introduction: Insomnia is a prevalent public health problem, particularly for older adults. The treatment of choice for insomnia is currently cognitive-behaviour therapy. However, recent research suggests sleep maintenance and early morning awakening insomnia, typically observed in the older population, is associated with advancement of the circadian phase, which can be effectively treated using evening bright light thera-

py. The present study evaluated the efficacy of a combined treatment of cognitive-behaviour therapy and evening bright light therapy.

Methods: One-hundred and nine adults (n= 48 male, mean age=63.91, SD=6.47) with sleep maintenance and/or early morning awakening insomnia were selected from community-based sample. Participants were randomly allocated to receive either a four-week, group-based treatment program of cognitive-behaviour therapy and evening bright light therapy (n=42)(CBT+EBL), cognitive-behaviour therapy alone (n=37) (CBT only) or to a wait-list control condition (n=30). The efficacy of the therapy program was assessed using one-week sleep diaries, actigraphy and a comprehensive battery of questionnaires to evaluate quality of life and other psychological variables. All participants completed these outcome measures at pre-treatment, post-treatment, and 3-month follow-up. Participants allocated to the treatments groups (CBT+EBL and CBT only) also completed these measures at 6-month follow-up.

Results: Participants in the treatment groups (CBT+EBL and CBT only) had significantly less wake after sleep onset and higher sleep efficiency, when compared to waitlist at post-treatment and 3-month follow-up. Treated participants averaged a reduction of 78 minutes of wakefulness from pre-therapy to post-therapy. This improvement corresponded with a gain of 17% in sleep efficiency from pre-therapy to post-therapy. These improvements were maintained at 3-month follow-up. Following treatment, participants also reported a significant reduction in insomnia severity and fatigue relative to the wait-list group. Results indicate outcomes related to sleep quality and quantity, psychological variables, and daytime functioning, do not differ between the two treatment groups. Potential explanations for this finding will be discussed and other outcome data will be presented.

Conclusion: A four-week program of cognitive behaviour therapy with or without evening bright light is an effective treatment for sleep maintenance and early morning awakening insomnia in the older population.

Support (If Any): NHMRC

0507

GREATER TOTAL SLEEP TIME IS ASSOCIATED WITH LOWER PRE-SLEEP SALIVARY CORTISOL DURING CHRONIC ZOLPIDEM USE

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Introduction: Some studies have reported enhanced nocturnal cortisol levels in insomniacs. The question arises as to whether insomnia treatment impacts cortisol levels. We evaluated the relation of pre-sleep salivary cortisol to total sleep time during chronic zolpidem use.

Methods: Individuals 21-70 years old (N=39) met DSM IV-TR criteria for primary insomnia. Participants additionally had a sleep efficiency of <85% on a screening NPSG and no other primary sleep disorders. This report is part of a larger study conducted as a mixed design, double-blind, placebo-controlled, experiment comparing primary insomniacs randomly assigned to zolpidem 10 mg (n=21) or placebo (n=18) nightly for 12 months. During the 12 months, participants were assessed in the sleep laboratory for treatment efficacy after 7 nights and 8 months of zolpidem or placebo use. Pre-sleep salivary cortisol samples were collected just prior to nightly administration of zolpidem or placebo (30 min prior to bedtime) on night 7 and night 2 of month eight.

Results: Total sleep time (TST) was greater in the zolpidem group compared to the placebo group on night 7 (413+/-48.4 vs 381+/-61.6 min) (t=2.87, p<.01) and again in month eight night 2 (410+/-39.6 vs 362+/-58.7 min) (t=2.99, p<.005). There was a statistically significant negative correlation between pre-sleep salivary cortisol and TST in the zolpidem group (r= -0.522, p<0.05) that was not demonstrated in the placebo group (r=-0.30, NS). On night two of month eight, once again there was a statistically significant negative correlation between pre-sleep salivary

cortisol and TST in the zolpidem group(r=-0.430, p<0.05) , not seen in the placebo group (r=0.02, NS).

Conclusion: Zolpidem improved sleep relative to placebo in months one and eight and lower pre-sleep cortisol levels were significantly correlated with greater total sleep times. Importantly, this relation was found in the the zolpidem, but not the placebo group.

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0508

IS THE TREATMENT OF INSOMNIA IMPAIRED WHEN OSA IS ALSO PRESENT?

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Introduction: A high prevalence (20-60%) of obstructive sleep apnoea (OSA) has been found in those referred for the treatment of insomnia. The aim was to determine if the OSA is left untreated, it impairs the effectiveness of the insomnia treatment.

Methods: Of 344 consecutive insomnia patients (65%F) referred for treatment 31% had mild to moderate OSA (AHI<30) and another 12% had severe (AHI>30) OSA as determined by a full PSG. They all attended an outpatient cognitive/behavioural treatment program for insomnia. Treatment response was determined from 7-day sleep/wake diaries and questionnaires for sleepiness, fatigue, depression, and anxiety administered at pre-treatment and at 3 month follow-up.

Results: At pre-treatment there were no differences between these three groups in any of the sleep or questionnaire measures. The treatment effects for the entire group as a whole showed a significant decrease in sleep latency (from 63 min to 27 min), decrease in wake time after sleep onset (from 111 min to 49 min), and increases in total sleep time (from 5.3 to 6.0 hours) and sleep efficiency from 62% to 80% with all changes significant at p<0.001 and moderate to large effect sizes. All groups showed decreases of fatigue, depression and anxiety across treatment (all p<0.001) with large effect sizes. Improvements for all measures were similar in the three groups with no interaction effects between groups across treatment (p>0.10).

Conclusion: In this moderately large study more than a third of patients referred for the treatment of insomnia had at least mild OSA with 12% showing severe OSA. Following a non-drug treatment program for insomnia, those with co-morbid OSA (both mild and more severe) showed improvements in sleep and daytime functioning variables at least as great as those without OSA. The presence of co-morbid OSA did not impair the treatment of insomnia in this study.

0509

SELF-EFFICACY ENHANCEMENT STRATEGIES CAN FACILITATE HYPNOTIC TAPERING IN PATIENTS WITH PRIMARY INSOMNIA

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Introduction: Clinical guidelines suggest that hypnotic use should be time-limited. However, many patients with chronic insomnia use hypnotics for prolonged periods of time and have difficulty discontinue hypnotic use. Systematic tapering schedule has been shown to be an efficacious approach to assist the reduction of hypnotic use. Previous studies have also shown that self-efficacy for discontinue medication is associated with the outcome of medication tapering. The present study compared the efficacy of systematic tapering programs with and without a self-efficacy enhancement component in assisting the reduction of hypnotic use.

Methods: Forty-eight patients with primary insomnia (31 females; mean age = 46.8; mean duration of hypnotics use = 66.7M) were assigned to two groups: a self-efficacy enhancement (SEE) group (n=24) and a Control group (n=24). Patients in the SEE group underwent a two-week self-efficacy enhancement program by providing case examples and verbal persuasion prior to an eight-week gradual tapering program. Patients in the Control group underwent the gradual tapering program only.

Results: Patients in SEE group showed significantly greater percentage of dose reduction than those in Control group (78.62% vs 64.10%; t =1.92, p<.05). The percent of drug-free patients at the end of the programs, however, was not different in the two groups (SEE: 29.2%; Control: 16.7%). In addition, hierarchical regression showed that, after controlling for baseline self-efficacy, the increase of self-efficacy following the first 2 weeks of self-efficacy enhancement strategy can explain the variation of percent of dose reduction up to 21.9%.

Conclusion: Self-efficacy enhancement strategies in a systematic hypnotic tapering program can increase reduction of hypnotic use. The increase of self-efficacy by the strategies was found to be associated with the magnitude of dose reduction. This approach can be applied in clinical settings to enhance the efficacy of hypnotic tapering.

0510

PATIENT-REPORTED SYMPTOM IMPROVEMENT IN SLEEP MAINTENANCE ENDPOINTS IN ADULT AND ELDERLY PATIENTS WITH INSOMNIA TREATED WITH DOXEPIN 3 AND 6 MG

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Introduction: This report reviews patient-reported (PR) efficacy data from two trials evaluating doxepin (DXP) in insomnia patients.

Methods: In two double-blind placebo-controlled trials, patients meeting DSM-IV-TR criteria for primary insomnia were randomized for treatment. Study A was a 12-week trial in elderly [N=240; DXP 3mg vs placebo (PBO)]; Study B was a 5-week trial in adults (N=221; DXP 3mg and 6mg vs PBO). PR endpoints included subjective wake after sleep onset (sWASO) and total sleep time (sTST). These endpoints were analyzed with a mixed-effect model repeated measures (MMRM) approach, using a model that included fixed effects for treatment group, time, the treatment-by-time interaction, and the baseline value of the endpoint.

Results: There was a main effect for treatment, with no significant interaction, for both sWASO and sTST in both studies. For both sWASO (Study A: DXP 3mg p=0.0052; Study B: DXP 3mg p=0.0213; DXP 6mg p=0.0014) and sTST (Study A: DXP 3mg p=0.0114; Study B: DXP 3mg p=0.0469; DXP 6mg p=0.0042) treatment effects were significantly different from PBO in both trials. In Study A, the estimated difference from PBO in sWASO for DXP 3mg was -18.3 minutes (SE=6.49). In Study B, the difference in sWASO for DXP 3mg was -10.2 minutes (SE=4.41), and was -14.2 minutes (SE=4.41) for DXP 6mg. In Study A, the difference in sTST for DXP 3mg was 18.9 minutes (SE=7.41). In Study B, the estimated difference in sTST for DXP 3mg was 11.9 minutes (SE=5.97), and was 17.3 minutes (SE=5.96) for DXP 6mg.

Conclusion: In both an adult (3 and 6mg) and an elderly trial (3mg), DXP 3 and 6mg produced significant improvements in PR sleep maintenance and duration endpoints. These data parallel the significant improvements previously reported in polysomnographic endpoints, providing further evidence for the efficacy of DXP 3 and 6mg for the treatment of sleep maintenance insomnia.

Support (If Any): This study was funded by Somaxon Pharmaceuticals.

0511

A POSTHOC ANALYSIS OF ESZOPICLONE EFFECTS ON CARDIOMETABOLIC INDICES OF HYPERAROUSAL IN THE TREATMENT OF PRIMARY INSOMNIA

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Introduction: Despite considerable evidence that chronic insomnia may be associated with underlying hyperarousal, little is known about the potential impact of pharmacologic insomnia therapy on measures of hyperarousal. The current study examined the effects of eszopiclone treatment on cardiometabolic indices of hyperarousal in insomnia patients.

Methods: Data were analyzed from two double-blind, placebo-controlled eszopiclone trials in patients diagnosed with primary insomnia: (1) a 2-week study in the elderly; and (2) a 6-week study in adults. Mean change±SD from baseline to Week 2 (elderly) or 6 (adults) in evening (adult only) and morning heart rate (HR), systolic and diastolic blood pressure (SBP; DBP) were assessed in a subset of these insomnia patients (elderly: n=78; adults: n=68) potentially enriched for hyperarousal via stratification by a 25th percentile split on HR, SBP, and DBP for each variable separately. Stratification was necessary because this population excluded patients with significant medical comorbidity.

Results: In the adult study, the eszopiclone group demonstrated a trend in mean reduction of morning HR and evening SBP vs placebo (HR: -10.02±1.44 vs. -5.90±1.68; p=.053; evening SBP: -11.4±2.41 vs. -4.68±3.19; p=0.08). In the elderly study, the eszopiclone group demonstrated a significant reduction in morning HR (-9.79±1.24 vs. -4.12±1.32; p=0.002) and a trend towards reduction in morning SBP (-11.52±2.46 vs. -4.19±3.12; p=0.06) There were no significant differences between treatment groups for the bottom 75th percentile subgroup in either study.

Conclusion: In this exploratory analysis, treatment with eszopiclone was associated with a tendency to decrease morning HR which was statistically significant in older insomnia patients. Trends for eszopiclone to decrease SBP but not DBP were also noted. These results suggest that eszopiclone treatment may lead to a decrease in sympathetic tone in insomnia patients with potential markers of hyperarousal. Future research should prospectively study insomnia patients selected for evidence of hyperarousal.

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0512

CBT-I TREATMENT INITIATION IS PREDICTED BY PAIN, MOOD, GENDER AND AGE

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Introduction: Cognitive-behavior therapy for insomnia (CBT-I) has been established as an efficacious treatment for both primary and co-morbid insomnia. While research has demonstrated that patients prefer psychological or behavioral insomnia treatments to pharmacological interventions, few studies have examined the clinical and demographic factors associated with initiation of CBT-I.

Methods: Thirty patients presenting to an outpatient psychiatric practice for an evaluation and treatment initiation for insomnia complaints were included in the analysis. Of the 30 patients completing the evaluation, 24 began CBT-I treatment. Demographic information and self-report measures were collected at the initial evaluation.

Results: Discriminant function analysis was used to examine whether baseline measures of mood, pain, age, and sex predicted which patients initiated CBT-I treatment. The overall function accurately predicted

92.3% of group membership. The Wilks' lamda for the discriminant function was 0.45, $\chi2(4)=17.51$, p<.01. The predictors were ranked in the following order reflecting the magnitude of correlation with the discriminant function: average pain rating, QIDS total score, gender, and age.

Conclusion: These findings suggest that clinical factors, such as the presence of pain and mood difficulties, contribute to patients' decisions about whether to initiate CBT-I treatment. Additionally, while gender and age contributed to whether patients initiated treatment, these demographic factors were less influential than the presence of pain or mood difficulties. These findings provide important preliminary information about potential factors that influence treatment decision making in insomnia.

0513

EFFECTS OF AURICULAR THERAPY ON AUTONOMIC ACTIVITY AND SLEEP IN ADULTS WITH SLEEP DISTURBANCES

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Introduction: Insomnia is associated with decreased parasympathetic nervous activity and increased sympathetic nervous activities. Auricular therapy, based on the Chinese Meriadian theory, stimulates parasympathetic nerve area in the auriculae to counterbalance the autonomic nervous system, hence may improve sleep and sleep quality in adults. This study examined effects of a 3-week auricular therapy on autonomic activity, polysomnography and sleep quality in adults with sleep disturbances.

Methods: Sixteen adults with sleep disturbances (7 in control and 9 in auricular therapy, aged 25-58 years) completed this study. Sleep disturbance was assessed by the global score of the Pittsburg Sleep Quality Index greater than 5. Auricular therapy (AT) was performed by taping magnetic pearls on seven auricular points. Autonomic activity was estimated by the heart rate variability of low frequency- high frequency ratio (LF/HF, normal 1.5-2). Two consecutive overnight polysomnography (PSG) were performed before and at the end of therapy. PSG results obtained on the second night were analyzed. Subjective sleep quality was assessed by the Insomnia Severity Scale.

Results: There was a trend that total sleep time increased 23.2±64.3 minutes (t=-1.98, p=.069) after the auricular therapy. The increased sleep time shifted to stage 2 (t=-2.09, p=.076) and slow wave sleep (t=-2.37, p=.034). There was also a trend of improved subjective sleep quality (F=4.64, p=.002) and insomnia severity (F=2.02, p=.078). However, LF/HF did not change in control (2.89±2.20 to 3.03±1.38) or AT (2.36±1.57 to 1.93±1.08) groups (F=0.59, p=.456).

Conclusion: Chinese auricular therapy is a potential intervention for adults with poor sleep of unbalanced autonomic nervous system. Findings from this study provide reference for application of Chinese auricular therapy in adults with sleep disturbances.

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0514

EFFECT OF COGNITIVE BEHAVIORAL THERAPY(CBT) FOR PATIENTS WITH BOTH INSOMNIA AND OBSTRUCTIVE SLEEP APNEA(OSA)

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Introduction: Patients with both insomnia and OSA remain to be a difficult group for clinicians since they have difficulty adapting to continuous positive airway pressure(CPAP). This is to evaluate the difference between these groups.

Methods: 139 patients(age 15-84) who visited the clinic with symptoms of insomnia were selected to see underlying sleep disorders and had done polysomnography. 6 patients had severe OSA and were recommended to use CPAP for their sleep problems. 36 patients(5<RDI<30) who refused or failed to use CPAP or to have surgery and insomnia only patients had gone through 5 sessions of CBT. Total sleep time(TST), sleep latency(SL), sleep efficiency(SE) were collected from sleep log data. Mixed model ANOVA with Bonferroni correction was used for analysis.

Results: Mean SL was improved from 60.52 to 20.61min, SE from 62.55 to 88.78%, TST from 298.76 to 346.37min. SL, SE improvement was significant from 1st to 2nd CBT session(p<.0001, p<.0001) and 2nd to 3rd session(p<.0001, p=0.0208). TST difference was most significant from 4th to 5th session(p=0.0156). Insomnia with RDI<5 group showed gradual improvement in their SE, whereas, insomnia with OSA(RDI>5) group showed their improvement from 1st to 2nd session most significantly(p<.0001). SL difference between sessions were not significantly different, however TST between these two groups (insomnia only vs insomnia+OSA) were different initially(mean 307.87 vs 242.29min) and could not be compensated even after 5 sessions of CBT(mean 362.25 vs 295.42min)(p=0.0032).

Conclusion: Patients with insomnia and OSA could gain benefit from CBT, but their improvement through CBT is partially limited due to underlying OSA. Physiological problem could not be overcome completely by CBT only and should be emphasized to improve their sleep problems.

0515

A CONTROLLED STUDY OF LY2624803 IN OUTPATIENTS WITH CHRONIC INSOMNIA

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Introduction: LY2624803, an inverse agonist at H1 receptors and antagonist at 5-HT2a receptors, has previously been reported to promote sleep in rats and in phase-advanced human volunteers. We report now on I2K-MC-ZZAD(b), a Phase 2 study of LY2624803 in the treatment of patients with insomnia.

Methods: Each of 419 patients aged 18-85 with the diagnosis of insomnia disorder and sleep maintenance complaints was randomized to one of 16 possible treatment sequences in a 3-period crossover design study, following completion of a placebo baseline period. Four treatments were compared in each treatment period: P=placebo, LY1=LY2624803 1 mg, LY3=LY2624803 3 mg, and Z=zolpidem (10 mg if age 18-64, 5 mg if age 65-85). Each baseline and treatment period was nominally 14 days long with study drug taken each night. Patients completed morning sleep diaries and evening questionnaires on a daily basis and completed questionnaires at the conclusion of each treatment period. Actigraphy measurements will be reported elsewhere.

Results: Morning diary: Z and LY3 improved total sleep time and overall sleep quality (visual analog scale) more than P did. Z, LY3, and LY1

improved sleep latency, wake after sleep onset, and proportion of nights on which "Did you sleep well last night?" was answered with "Yes" more than P did. Z and LY3 improved the Assessment of Sleep Questionnaire (ASQ) sleep experience domain more than P did. Z improved the ASQ Feeling Upon Awakening domain more than P did. Evening questionnaires: no treatment differences were found with the Daytime Consequences of Insomnia Questionnaire. End-of-period questionnaires: only Z improved the Insomnia Severity Index more than P did. Safety: all treatments were tolerated well.

Conclusion: LY2624803 improved subjective impression of sleep, sleep quantity, and measures of sleep initiation and sleep maintenance in outpatients with chronic insomnia.

0516

THE EFFECT OF ESZOPICLONE ON STAGE 2 SLEEP: RESULTS FROM STUDIES IN ADULT AND ELDERLY PATIENTS WITH PRIMARY INSOMNIA

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Introduction: It is understood that sleep architecture varies across the life span. Sleep architecture changes are a pharmacological signature of GABAergic hypnotic drugs. This analysis aimed to compare the effect of eszopiclone on the polysomnographic (PSG) profile of adult and elderly patients with primary insomnia.

Methods: For comparative purposes, absolute (mean minutes) and percent of total sleep time (TST) in each stage of sleep were analyzed from PSG data captured at Week 2 from 2 double-blind, placebo-controlled studies of eszopiclone with different durations: a 6-week study in adult patients aged 18-64 (3 mg; n=204) and a 2-week study in elderly patients aged 64-86 (2 mg; n=264).

Results: Relative to placebo, eszopiclone increased absolute time (minutes) in stage 2 in both patient groups at the Week 2 time point (Adults: Day 15: 22.5 minutes, p=0.002; Elderly: Day 14: 21.43 minutes, p<0.0001). With the exception of a transient (Day 1) increase on stage 1 in the elderly, there were no significant drug-placebo differences in absolute time in stages 1, 3/4, and REM. Significant increases in percent time spent in stage 2 were also observed in both populations (all p<0.03). Small but statistically significant decreases in percent time spent in REM were observed for the adult group at the Week 2 time point (Day 15: p=0.01), but not the elderly group (Day 14: p= 0.183).

Conclusion: In this analysis, eszopiclone treatment resulted in sustained increases in stage 2 sleep in adult and elderly patients with primary insomnia. Despite changes in sleep architecture associated with advancing age, eszopiclone's effect on sleep architecture does not appear to vary with age.

0517

TREATMENT WITH ESZOPICLONE IN ADULTS WITH PRIMARY INSOMNIA: PREDICTORS OF RESPONSE

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Introduction: Predictors of response to pharmacologic treatment of insomnia have not been systematically evaluated. This analysis aimed to identify predictors of response to treatment with eszopiclone in adults with insomnia.

Methods: A post-hoc, multivariate logistic regression analysis was performed on ITT LOCF (endpoint) data at 6 months comparing eszopiclone 3 mg to placebo in a group of previously studied adult patients diagnosed with insomnia (n=828). Insomnia treatment response was defined as ≥50% reduction from baseline in sleep latency (SL) or wake

time after sleep onset (WASO); or >30 minute increase from baseline in total sleep time (TST). Covariates included demographic and baseline clinical variables, and odds ratios (OR) with confidence intervals were calculated for each potential predictor.

Results: Treatment group (eszopiclone 3 mg vs placebo) was the only factor found to influence all 3 response variables (range OR=2.3 to 3.3; p<0.0001). Significant predictors of eszopiclone response were the following: for SL, baseline SL (OR=1.01; p<0.0001), baseline Short Form-36 Health Survey (SF-36) Social Functioning Scale (OR=0.98; p<0.002), and baseline SF-36 General Health Scale (OR=1.03; p<0.0001); for WASO, baseline WASO (OR=1.01; p<0.001); and for TST, baseline TST (OR=0.99; p<0.0001).

Conclusion: In this analysis, the only factor that influenced insomnia treatment response was assignment to eszopiclone 3 mg. In the eszopiclone treatment group, greater baseline severity of SL, WASO, and TST were identified as significant predictors of improvement in SL, WASO, and TST, respectively. However, none of the significant predictors were of sufficient magnitude to be considered clinically relevant. Overall, the likelihood of subjective clinical response was largely independent of patient characteristics.

0518

CAN A TWO-DAY SLEEP 101 EDUCATION PROGRAM DECREASE DYSFUNCTIONAL BELIEFS AND ATTITUDES ABOUT SLEEP AMONG COLLEGE STUDENTS?

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Introduction: Dysfunctional beliefs and attitudes about sleep have long been theorized to contribute to the perpetuation of insomnia symptoms. Morin and colleagues (1993) found that those with chronic insomnia endorsed significantly stronger negative beliefs about the consequences of insomnia as well as expressed more hopelessness and lack of control over their sleep relative to their "good-sleeper" counterparts. This study, along with a series of others, suggests that treatments for insomnia include a focus on the alteration of these maladaptive cognitions. Since cognitive behavioral therapy for insomnia (CBT-I) is an efficacious treatment for decreasing such cognitions and insomnia severity, we sought to examine the effect of a two-workshop sleep education program (Sleep 101). One of the goals of Sleep 101 was to reduce maladaptive sleep behaviors and cognitions for college students because of their vulnerability for the manifestation of insomnia.

Methods: A group of college students were randomly assigned to either a Sleep 101 psychoeducational intervention group or a Sleep Monitoring group (control). Participants in both groups were asked to fill out a series of self-report sleep and quality of life questionnaires (including the Dysfunctional Beliefs and Attitudes Scale Short-Form; DBAS-SF) at baseline and post-intervention as well as complete sleep diaries for four weeks. In addition, participants in the Sleep 101 group were asked to attend two separate Sleep 101 Workshops. These workshops included information on sleep hygiene, behavioral strategies (i.e., stimulus control and sleep restriction), and cognitive therapy.

Results: Preliminary analyses showed that baseline and post-intervention DBAS-SF scores were significantly, positively correlated with insomnia severity (r=.39, p=.001 and r=.52, p< .001, respectively). Participants in the Sleep 101 group endorsed significantly lower DBAS-SF scores relative to participants in the Sleep Monitoring group, t(65)= -2.84, p = .046, after completing the Sleep 101 workshops.

Conclusion: Participants in the Sleep 101 group endorsed significantly less dysfunctional beliefs and attitudes about sleep relative to those in the Sleep Monitoring group. While the results of this investigation are preliminary, they garner support for the use of a brief intervention to decrease dysfunctional beliefs and attitudes about sleep among college students and further help to target the perpetuating factors of insomnia.

0519

TWELVE MONTHS OF NIGHTLY ZOLPIDEM DOES NOT PRODUCE WITHDRAWAL SYMPTOMS ON DRUG DISCONTINUATION: A PROSPECTIVE PLACEBO CONTROLLED STUDY

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Introduction: Animal studies have demonstrated physical dependence with benzodiazepine receptor agonists (BzRAs). In patients chronic use of therapeutic doses of BzRA anxiolytics is associated with withdrawal, but reports of withdrawal with BZRA hypnotics are less conclusive. This study prospectively tested for withdrawal symptoms after 12 months of nightly use of the BzRA hypnotic, zolpidem 10mg.

Methods: 29 DSM-IVR defined primary insomniacs, ages 32-64 yrs, with a sleep efficiency (sleep time/bed time) of <85% and no other primary sleep disorders on a 8-hr sleep recording, without psychiatric disorders, drug dependency and in good general health participated. Participants received 10 mg zolpidem or placebo, double-blind, nightly for 12 months. Weekly information regarding medication compliance and sleep was collected via IVRS. On two laboratory nights in Months 1, 4, and 12, placebo was administered to both groups and the Tyrer Benzodiazepine Withdrawal Symptom Questionnaire (a 20 symptom rating scale,0-2) was completed in the morning.

Results: On the IVRS participants reported taking 73-89% of nightly capsules and the groups did not differ (placebo: 81+0.04% vs zolpidem: 84+0.03%). At month 12 the total Tyrer score (mean night 1 and 2 of discontinuation) did not differ between the placebo and zolpidem groups: 1.2+/-1.7 vs 1.6+/-1.7 (a score >20 is considered clinically significant). The number of severe symptom ratings (2) given for any one of the 20 symptoms was 3/15 in the placebo group and 1/14 in the zolpidem group. Placebo and zolpidem groups did not differ in their ratings on any of the 20 symptoms individually.

Conclusion: In insomniacs, zolpidem 10 mg was not associated with withdrawal after chronic nightly administration, suggesting with hypnotics, a condition in which receptors are unoccupied for 16 hours a day, there is no withdrawal. This contrasts with BzRA anxiolytics, where receptors are occupied all day, and withdrawal is reported.

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0520

THE EFFICACY OF COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA ON FATIGUE SYMPTOM

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Introduction: Fatigue is one of the most common daytime complaints in patients with insomnia. Cognitive behavioral therapy for insomnia (CBT-I) has been proved to decrease fatigue in patients with insomnia comorbid with cancer. However, it is still not clear if CBT-I is effective in decreasing fatigue among patients with primary insomnia. The goals of this study are to: 1) investigate the effect of CBT-I on fatigue complaint, and 2) explore the association between the improvement in fatigue and changes in sleep-related psychological factors, including sleep beliefs, sleep habits, and arousal symptoms in patient with primary insomnia.

Methods: 67 patients with primary insomnia were recruited for the study. Before and after a 6-week CBT-I program, they completed a package of questionnaires including situational fatigue scale (SFS), dysfunctional beliefs and attitudes about sleep scale (DBAS), sleep hygiene practice scale (SHPS), pre-sleep arousal scale (PSAS), insomnia severity index (ISI).

Results: Prior to the CBT-I, physical fatigue (PF) and mental fatigue (MF) correlated significantly with ISI. PF decreased significantly following CBT-I (F=7.33, p < .01), while MF did not (F=1.13, n.s.). The decrease of PF correlated significantly with the decrease of score on Cognitive Arousal subscale of PSAS (r=0.24, p <.05). On the other hand, the decrease in MF showed significant correlations with changes on Sleep Requirement subscale of DBAS (r=0.26, p <.05), Arousal-Related Behavior subscale of SHPS (r=0.26, p <.05), and Cognitive Arousal subscale of PSAS (r=0.25, p <.05).

Conclusion: CBT-I is helpful for the symptom of fatigue in insomnia patients, especially for the physical fatigue. The decrease of cognitive arousal along the process of CBT-I may be the most prominent factor related to the treatment efficacy of fatigue symptom. Changes in sleep-related beliefs and sleep habits, on the other hand, are more associated with decrease in mental but not physical fatigue.

0521

PHARMACOKINETIC PROFILE OF A MODIFIED RELEASE FORMULATION OF ZALEPLON (SKP-1041) 10.0 MG, 15.0 MG, AND 20.0 MG IN ADULTS WITH PRIMARY SLEEP MAINTENANCE INSOMNIA

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Introduction: A novel formulation of zaleplon (SKP-1041) that releases active drug via proprietary Geoclock® technology has a pharmacokinetic profile consistent with drug release during the middle hours of the night. The present study evaluated the pharmacokinetics of a single dose of SKP-1041 10.0, 15.0, and 20.0 (2x10.0) mg in adults with insomnia characterized by middle-of-the-night awakenings.

Methods: This was a phase II, multicenter, randomized, double-blind, double-dummy, placebo-controlled study. For pharmacokinetic testing, patients received a single dose of SKP-1041 10.0, 15.0, or 20.0 (2x10.0) mg at bedtime; to maintain the double-blind, patients who received the 10.0- or 15.0-mg dose also received a placebo capsule. Blood was drawn for determination of plasma zaleplon concentrations predose and hourly to 10 hours postdose. Pharmacokinetic parameters were determined by standard non-compartmental methods. Statistical analyses were done using SAS General Linear Models.

Results: Pharmacokinetics were evaluated for 45 patients (15 males, 30 females; age 24 - 64 years). Dose distribution was 10.0 mg, n=17; 15.0 mg, n=13; 20.0 mg, n=15. Median time to maximum zaleplon plasma concentration (Tmax) was 4 hours postdose and was not different among doses. Mean elimination half-life of zaleplon was 1.52, 1.65, and 1.47 hours for the 10.0, 15.0, and 20.0 mg doses, respectively. Maximum plasma concentration (Cmax) was dose-proportional: 17.9, 25.3, and 34.4 ng/mL for the 10.0, 15.0, and 20.0 mg doses, respectively. Total area under the plasma concentration curve (AUC) was also dose-proportional (56.5, 77.4, and 135.3 ng/mL x hr). Normalization of Cmax and AUC for dosage eliminated these differences.

Conclusion: All three doses of SKP-1041 produced essentially identical delayed release of zaleplon, with median Tmax at 4 hours postdose. Cmax and AUC were dose proportional, indicating linear pharmacokinetics of zaleplon from SKP-1041 in this dose range.

Support (If Any): Supported by Somnus Therapeutics, Inc.

0522

TREATMENT OF PRIMARY INSOMNIA IN THE ELDERLY: PREDICTORS OF RESPONSE TO ESZOPICLONE

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Introduction: Chronic sleep disturbance is highly prevalent in the elderly. This analysis aimed to identify predictors of response to treatment with eszopiclone in elderly patients (65-85 years of age) with insomnia.
Methods: A post-hoc, multivariate logistic regression analysis was performed on ITT week 12 LOCF (endpoint) data comparing eszopiclone 2 mg to placebo for insomnia in a cohort of previously studied elderly outpatients diagnosed with insomnia (n=388). Treatment response was defined as ≥50% reduction from baseline in sleep latency (SL) or wake time after sleep onset (WASO); or >30 minute increase from baseline in total sleep time (TST). Covariates included demographic and baseline clinical variables, and odds ratios (OR) with confidence intervals were calculated for each potential predictor.
Results: Treatment group (eszopiclone 2 mg vs placebo) was the only factor found to influence all 3 response variables (range OR=2.31 to 3.14; p<0.001). Significant predictors of eszopiclone response were the following: for SL, baseline SL (OR=1.02; p<0.01), baseline TST (OR=1.01; p<0.01) and Short Form-36 Health Survey (SF-36) Bodily Pain Scale (OR=0.94; p<0.001); for TST, female gender (OR=2.9; p<0.01), baseline TST (OR=1.01; p<0.01), and baseline SF-36 General Health Scale (OR=0.95; p<0.03). No significant predictors were identified for WASO.
Conclusion: In this analysis, the only factor that consistently influenced treatment response was assignment to eszopiclone 2 mg. In the eszopiclone treatment group, greater baseline severity of SL and TST were identified as modest but significant predictors of improvement in SL and TST, respectively. Female gender was also identified as a significant predictor of improvement in TST. Overall, the likelihood of clinical response was largely independent of patient characteristics.
Support (If Any): Funded by Sunovion Pharmaceuticals Inc.

0523

QUETIAPINE THERAPY AND MONITORING IN ACTIVE DUTY PATIENTS

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Introduction: Quetiapine is an atypical antipsychotic medication with FDA indications for treatment of schizophrenia, bipolar I disorder, and as an adjunctive agent in the treatment of major depression. Quetiapine is associated with numerous side effects including weight gain, onset of diabetes mellitus, and prolongation of the QT interval. Off-label use of quetiapine is common but has not been characterized in active duty Soldiers. The purpose of this study is to identify the indications for use of quetiapine in active duty soldiers, measure weight change while on treatment, and monitor for compliance with screening for drug-induced diabetes and QT prolongation.
Methods: We performed a retrospective review of all active duty soldiers who received initial prescriptions for quetiapine which were filled at a pharmacy within the Madigan Healthcare System between 1 January 2007 and 31 December 2008. Charts were reviewed to abstract descriptive data about the subjects, indication for quetiapine prescription, and for presence of recommended screening tests including weight changes, incident diabetes mellitus within 6 months of receipt of first prescription, and measurement of QTc interval within 3 months of receipt of first prescription. Number of tablets received from the pharmacy was also calculated and served as a surrogate marker for duration and intensity of treatment

Results: 692 Active Duty Soldiers received initial prescriptions for quetiapine during the study period. The most common indications for quetiapine prescription were insomnia (60%), anxiety (19%), mood disorders (12%) and PTSD (8%). Only 3.4% received quetiapine for an FDA-approved indications. The average Soldier experienced a 9 pound weight gain at 24 months. Compliance with screening for diabetes and QTC prolongation was poor at 52% and 18%, respectively. None of the Soldiers who received screening met criteria for diabetes. 126 underwent an EKG after staring quetiapine, eleven (9%) had prolonged QTc durations.
Conclusion: Quetiapine is most commonly prescribed for non-FDA approved indications with insomnia and anxiety as the most frequently associated diagnoses. The majority of soldiers gained weight while on this medication. Prolonged QTc was a common finding. Prescribers of quetiapine should adhere to the recommended screening parameters to minimize risks associated with this medication and ensure their patients undergo appropriate counseling regarding side effects.

0524

USE OF RELAXATION TECHNIQUES BY ADULTS WITH INSOMNIA: RESULTS OF A NATIONAL SURVEY

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Introduction: AASM recommends relaxation training as standard treatment for insomnia. While nearly one in six adults in the United States use some form of relaxation annually, little is known about current patterns and reasons for use of relaxation techniques by adults with insomnia.
Methods: We analyzed data from the 2007 National Health Interview Survey (n=23,393). We defined relaxation techniques as use of progressive muscle relaxation, guided imagery, meditation, or deep breathing exercises within the past 12 months. We estimated prevalence of use of relaxation techniques among adults by self-reported insomnia status. Among respondents with insomnia (n=4,415), we further examined use of relaxation techniques for treatment of specific medical conditions, additional reasons for use, and disclosure to conventional medical providers. We performed multivariable logistic regression to determine the association between relaxation technique use and insomnia adjusting for sociodemographics, health care access, medical conditions, and health behaviors. SAS-callable SUDAAN was used to account for the complex sampling design, and results were weighted to reflect national estimates.
Results: More than one in four adults with insomnia, representing an estimated 10 million Americans, use relaxation techniques annually, and have higher likelihood of use compared to adults without insomnia (adjusted OR 1.5, 95% CI 1.3,1.7). Deep breathing exercises is the most common relaxation technique used by adults with insomnia. Only 4% of adults with insomnia used relaxation techniques to treat their insomnia. General wellness/disease prevention was the most frequently cited reason for use. Forty percent of adults with insomnia did not disclose use of relaxation techniques to conventional providers.
Conclusion: Adults with insomnia commonly use relaxation techniques, yet despite current guidelines, use specifically for treatment of insomnia is low. Improved provider and patient communication regarding the benefits of relaxation techniques for insomnia may help facilitate more targeted use of these practices for treatment of insomnia.

0525

A PILOT PROGRAM TO EXAMINE ALTERNATIVE APPROACHES TO CBT-I

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Introduction: There is overwhelming evidence of the benefits of cognitive behavior therapy for insomnia (CBT-I); however, there continues to be only a scarcity of providers of CBT-I. We developed a CBT-I program to be delivered in a group session by trained physicians and nurses in sleep and CBT. The purpose of this pilot program was to determine feasibility of a group approach, outcomes of CBT-I using physicians and nurses as providers, and payment mechanisms of CBT-I through insurance.

Methods: Patients were screened at the Tuscaloosa Lung & Sleep Clinic using inclusion/exclusion criteria. The program consisted of 4 sessions beginning with basic information related to sleep, then introducing basic concepts and components of CBT-I. Subjective data was collected at each session (4 times) using the Epworth Sleepiness Scale, Generalized Anxiety Disorder (GAD)-7, Quick Depression Assessment Score, Insomnia Severity Index, Fatigue Inventory, and Sleep Quality Inventory. If needed, participants were referred to a mental health care provider (social workers, psychiatric nurse practitioners, psychologists or psychiatrists). Participants completed sleep diaries between sessions.

Results: There were 6 participants (one male) in the study with 3 Caucasians and 3 Blacks (mean age = 55.5 years). Simple t-test compared total mean scores of each of the variables at each of the 4 times. Significant differences were reported in insomnia severity (p=0.04), sleep quality (p=0.03), time in bed (p=0.01), and average number of awakenings (p=0.01). One participant asked to see a mental health care provider.

Conclusion: Board-certified sleep physicians, nurses trained in CBT and nurse practitioners can effectively provide CBT-I. Limitations include a small, purposive sample and no objective measures of sleep (actigraphy). The group therapy approach was effective in improving insomnia. Participants' evaluations were positive and identified the group format as very helpful. No reimbursement for the program was received through any of the insurance providers.

Support (If Any): Tuscaloosa Lung & Sleep Consultants, PC Resperonics

0526

INFLUENCE OF SLOW OSCILLATING TRANSCRANIAL DIRECT CURRENT STIMULATION (SO-TDCS) ON ELECTROENCEPHALOGRAMM AND SLEEP PARAMETERS

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Introduction: Transcranial stimulation has an impact on EEG oscillations characteristics (e. g. power), memory performance as well as on sleep architecture. It was shown that so- tDCS increased slow oscillation (0.4-1.2Hz) power as well as theta (4-8Hz) and beta (15-25Hz) power. Enhancing the excitability of the prefrontal cortex (PFC), by means of anodal tDCS, is proposed to result in improved working memory function. Primary endpoint is an increase in slow oscillation power, at F7, F8 and Fz, as well as on theta and beta power across electrode sites. Secondary it is hypothesized that stimulation enhances cortical excitability in PFC, resulting in increased cognitive performance (indicated in improved Digit Span, DSST and PVT test results).

Methods: In a randomized, sham-controlled, double-blind cross-over-trial 30 healthy individuals are stimulated during daytime with anodal so- tDCS of 0.75Hz and 250μA at EEG position F3/ F4. Subjects are divided into 3 groups and receive different numbers of stimulation sessions per day from one up to five sessions according to their group. One stimulating session includes 30min of stimulation, EEG recording during rest (eyes closed vs. eyes open) as well as several cognitive tests (PVT, Digit Span, DSST) and a subjective sleepiness questionnaire (KSS). Subjects assigned to group 3 will additionally receive polysomnography the night before and after daytime stimulation.

Results: Data analysis suggests that so- tDCS increases slow oscillation power at central sites (Cz) but not at frontal EEG position (F7). Moreover EEG theta power increased by means of stimulation on Cz and F7. Concerning cognitive performance tests visual short term memory and reaction time was enhanced, indicated by improved results in DSST and PVT tests. Furthermore subjective sleepiness decreased, assessed by means of KSS.

Conclusion: These results indicate that it is possible to awaken subjects through anodal so- tDCS. For definite conclusions final data collection and analysis needs to be completed. It is conceivable that short term memory improvement is mediated through theta oscillations power increase.

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0527

HELPFUL COMPONENTS OF GROUP COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA (CBTI) FOR PATIENTS WHO PERCEIVED PAIN TO INTERFERE WITH SLEEP

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Introduction: Past literature has indicated that CBTI is effective for patients with chronic pain, improving insomnia and reducing pain levels. This study aimed to identify the components of CBTI that patients with chronic pain found to be particularly helpful.

Methods: Participants were 183 patients (55% male, mean age 43.4) who completed group CBTI. Participants rated their perception of pain interfering with sleep on a 6-point scale from "I don't have pain" to "all of the time" at baseline. Groups were dichotomized with 73 participants classified as pain interfering with sleep (Pain group) and 110 without pain interfering with sleep (NonPain group). All patients rated 24 therapeutic elements on how helpful each was (using a scale of 0 - 3). The patients also completed a questionnaire asking about how difficult it was to follow treatment components.

Results: The therapeutic elements were organized by four conceptual categories: behavioral (eg, anchoring wake-up time), cognitive components (eg, changing the way I think about not sleeping), sleep hygiene (eg, reducing caffeine) and non-specific therapeutic elements (eg, trusting treatment provider). Category scores were the average of its individual items. The patients in the Pain group identified the behavioral components as the most helpful (X=2.62), followed by cognitive components (X=2.18), non-specific therapeutic elements (X=2.17), and sleep hygiene (X=1.67). Compared to the NonPain group, patients in the Pain group had significantly more difficulty decreasing time in bed [F(1, 80)=9.599, p=0.003] and changing thoughts about not sleeping [F(1, 73)=5.22, p=0.03].

Conclusion: These results suggest that patients who perceive pain to interfere with their sleep found behavioral components most helpful but also had the most difficulty restricting time in bed, a key behavioral component. They also found it more difficult to change their beliefs about sleep. Future studies should focus on identifying specific cognitions that hinder adherence with time in bed restriction.

0528

A PILOT RANDOMIZED CLINICAL EFFECTIVENESS TRIAL OF GROUP COGNITIVE-BEHAVIORAL THERAPY FOR INDIVIDUALS WITH PERSISTENT INSOMNIA FROM THE WISCONSIN SLEEP COHORT STUDY

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Introduction: Cognitive-behavioral therapy (CBT) for insomnia has been shown to be effective for primary and co-morbid insomnia. However, studies have mainly used clinic-based samples. The current study examined the effectiveness of CBT for individuals with persistent insomnia from the Wisconsin Sleep Cohort Study (WSCS), a 20+ year epidemiological study of sleep.

Methods: 17 participants (mean age=64.1;SD=7.1) were enrolled from a sub-sample of 179 participants endorsing insomnia symptoms and recruited by letter from the WSCS. Patients underwent screening, met research diagnostic criteria for insomnia, completed baseline questionnaires and sleep logs, were randomized to either group CBT (n=8) or treatment as usual (TAU;n=9), and completed post-test questionnaires and sleep logs. Outcomes included questionnaire assessment of insomnia symptoms, dysfunctional sleep-related beliefs, sleep inhibitory behaviors, depression, and worry. Sleep log outcomes were sleep onset latency, wake time after sleep onset, and total sleep time. Group CBT included stimulus control, sleep restriction, relaxation, and cognitive strategies in 6 1-hour-long sessions over approximately 6 weeks. Analyses included repeated measures ANOVA and chi-square analysis for continuous and categorical variables, respectively.

Results: The CBT group demonstrated significantly greater improvement in insomnia symptoms than the TAU group (F(1,15)=6.4,p=.02). Moreover, 50% of the CBT group reached an Insomnia Symptom Severity cut-off of <7 at post-test compared to 0% of the TAU group (χ2(1,N=17)=5.9,p=.02). Finally, the CBT group had a greater decrease in dysfunctional sleep-related beliefs (F(1,14)=5.9,p=.03), sleep inhibitory behaviors (F(1,15)=4.7,p=.047), and worry (F(1,15)=6.6,p=.02) than the TAU group. There were no treatment effects for the sleep log outcomes or depressive symptoms.

Conclusion: In a sample of mostly older and retired adults recruited from an epidemiological sample, group CBT appears to improve insomnia severity and insomnia-related variables like dysfunctional sleep-related beliefs, sleep inhibitory behaviors, and worry. Similar future research may provide crucial information regarding dissemination of insomnia treatments more broadly.

Support (If Any): This study was supported by the Wisconsin Partnership Program (133JT72) as well as NIH (1UL1RR025011 and R01HL62252).

0529

SLEEP LATENCY RESPONSE RATES ARE INCREASED WITH RAMELTEON 8 MG TREATMENT COMPARED WITH PLACEBO IN ADULTS WITH CHRONIC INSOMNIA USING STRICT DEFINITIONS OF RESPONSE: COMBINED ANALYSIS OF 2 CLINICAL TRIALS

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Introduction: Ramelteon is an MT1/MT2 melatonin receptor agonist approved for the treatment of sleep onset insomnia. The current analysis combined data from 2 clinical trials to assess response rates for ramelteon 8 mg using latency to persistent sleep (LPS) in order to identify a population of responders according to a strict definition of response.

Methods: Data were collected from 2 randomized, placebo-controlled trials of ramelteon in adults diagnosed with chronic insomnia. The primary endpoint of both trials was mean LPS measured by 2-night polysomnography in the sleep lab. Response rates for LPS were calculated at Visit 1 (Nights 1 and 2 from both studies) and Visit 2 (equivalent visits at Week 5 and Month 1) using 3 definitions of response ([1] LPS <=30 min, [2] percent decrease in LPS from baseline >=50%, and [3] percent decrease in LPS from baseline >=50% and LPS <=30 min). Logistic regression, including study and treatment as explanatory variables, was used to test for differences in response rates between ramelteon and placebo.

Results: Data from 715 subjects (mean age 43.5 yrs, 65.0% women) were analyzed. LPS response rates for the ramelteon group were significantly increased at Visit 1 using all 3 definitions of response (n=362; [1] 62.4%, [2] 61.6%, [3] 51.7%; p<0.001) compared with the placebo group (n=353; [1] 43.1%, [2] 39.7%, [3] 32.3%) Response rates were sustained at Visit 2 and remained significantly higher for the ramelteon group (n=336; [1] 64.6%, [2] 64.9%, [3] 55.4%; p<0.005) than the placebo group (n=330; [1] 52.7%, [2] 51.5%, [3] 39.7%).

Conclusion: In this combined analysis, LPS response rates were significantly increased with ramelteon 8 mg compared with placebo even when using the strictest definition of response (percent decrease in LPS from baseline >=50% and LPS <=30 min).

Support (If Any): Takeda Pharmaceutical Company, Ltd.

0530

EFFICACY OF A TELEPHONE INTERVENTION FOR INSOMNIA: PRELIMINARY RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Introduction: Chronic insomnia is a prevalent condition with associated medical, psychiatric, and economic consequences. Cognitive behavioral treatment for insomnia (CBT-I) is the most effective non-pharmacological intervention to treat chronic insomnia, but its availability to the general population is limited. We therefore compared the efficacy of CBT-I, delivered by telephone, to that of a minimal treatment control.

Methods: Twelve participants (mean age 41.0±11.4 years, 2 males, mean Insomnia Severity Index [ISI] at baseline 17.9±2.4) with a DSM-IV diagnosis of chronic insomnia were randomized to receive CBT-I via either telephone (4-8 sessions, n=6) or written pamphlet (n=6) over 8 weeks. Primary sleep outcomes included sleep efficiency (SE) and total sleep time (TST) from sleep diaries, the ISI, and the Pittsburgh Sleep Quality Index (PSQI). Measures of daytime functioning included the Dysfunctional Beliefs and Attitudes about Sleep scale (DBAS-16), the Quick Inventory of Depressive Symptomatology (QIDS-SR), the State-Trait Anxiety Inventory Trait Subscale (STAI-T), and the Multidimensional Fatigue Inventory (MFI-20). Participants completed outcome measures via mail at baseline, immediately following treatment, and at 3-months post-treatment.

Results: All participants completed treatment; two control participants failed to complete the 3-month follow-up. Just after treatment, and in comparison to baseline, self-reported sleep and daytime functioning had improved in both groups, but telephone participants had improved more on the PSQI (F=10.59, p<.01) and ISI (F=6.14, p<.05). Effect sizes for the remaining interactions were large (Cohen's f >.40) for SE, DBAS-16, QIDS-SR, and MFI-20, and moderate (.20 < Cohen's f <.40) for TST and STAI-T. Telephone participants also showed PSQI improvement at 3-month follow-up, in comparison to post-treatment (t=4.72, p<.01), while maintaining gains on all other measures.

Conclusion: Self-reported sleep and daytime functioning improved more with CBT-I via telephone than with a written pamphlet. Treatment gains were sustained at 3-month follow-up. An effective telephone-

based CBT-I could greatly expand access to non-pharmacological treatment for chronic insomnia.

0531

IMPROVEMENT IN SLEEP MAINTENANCE AND EARLY MORNING AWAKENINGS IN ADULT AND ELDERLY PATIENTS WITH INSOMNIA TREATED WITH DOXEPIN 3 AND 6 MG

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Introduction: This report reviews the effects of doxepin (DXP) 3 and 6mg on sleep maintenance (SM) and early morning awakenings (EMA).
Methods: SM and EMA endpoints from four double-blind placebo-controlled trials are reported. Study A was a 12-week trial of elderly insomnia patients [N=240; DXP 3mg]. Study B was a 5-week trial of adult insomnia patients (N=221; DXP 3mg and 6mg). Study C was a 4-week trial of elderly insomnia patients (n=255; DXP 6mg). Study D was a transient insomnia trial (N=565; DXP 6mg). The primary method of evaluating efficacy was polysomnography (PSG) in Studies A, B, and D, and patient-reports in Study C. SM endpoints included polysomnographic wake after sleep onset (WASO) and subjective WASO (sWASO). EMA was assessed with PSG Sleep Efficiency% in the last quarter-of-the-night (SE-LQ). Data from the first and final assessment point [Study A=Night (N) 85; Study B=N29; Study C=WK4] of the study are reported.
Results: DXP 3 and 6mg significantly improved WASO on N1 in all PSG trials (p<0.0001), with improvements vs placebo (PBO) ranging from 25 (Study B, 3mg) to 40 minutes (Study D, 6mg). DXP 3mg (Study A and B; p≤0.0008) and 6mg (Study B and D; p<0.0001) significantly improved SE-LQ on N1 in all trials, with improvements vs PBO ranging from 8% (Study B, 3mg) to 15% (Study A, 3mg). DXP 6mg (Study C; p<0.0001) significantly improved sWASO in Week 1, with improvement vs PBO of 23 minutes. The significant improvements in SM and EMA were maintained in all studies, excepting SE-LQ on N29 (Study B, 3mg p=0.07).
Conclusion: DXP 3 and 6mg demonstrated significant improvements in WASO, sWASO and SE-LQ that were consistent across trials and maintained at the final timepoint for all but one assessment. These data suggest DXP is effective at treating both SM (WASO and sWASO) and EMA (SE-LQ) in transient and chronic insomnia populations.

0532

INDIVIDUAL DIFFERENCES IN THE LIKELIHOOD OF REBOUND INSOMNIA

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Introduction: While therapeutic hypnotic doses have not been associated with rebound insomnia, a worsened sleep relative to baseline following drug discontinuation, some individuals do show rebound. This study evaluated the reliability of producing rebound insomnia with repeated tests (i.e., placebo substitution) during 12 months of nightly use of zolpidem (10mg).
Methods: Primary insomniacs (N=16) ages 32-64, meeting DSM-IVR criteria and a baseline sleep efficiency (sleep time/bed time) of <85% with no other primary sleep disorders on a 8-hr sleep recording, without psychiatric diseases or drug dependency and in good general health were recruited. Participants received 10 mg zolpidem (n=16), double-blind, nightly for 12 months. On two laboratory nights in Months 1, 4, and 12 placebo was administered. Eight-hour sleep recordings were collected and rebound was assessed by comparing change in total sleep time from baseline on the two placebo subsitution nights.
Results: Within the zolpidem group, on both nights of month 1, 2 participants had shorter total sleep times (TST) than baseline. Their TSTs were consistently shorter than baseline both nights in months 4 and 12 (F=7.22, p<.02) than those with no month 1 rebound (n=9), or 1 night of rebound (n=3). The rebound did not worsen from month 4 to 12 (no nights or nights by drug interactions). One of the 2 was a female. Relative to the others (n=14), the 2 were similar in age (42 and 58 vs 52.3+11.2 yrs) , but tended to have a shorter duration insomnia (7 and 10 vs 14.5+12.1 yrs) and to have better screening total sleep times (386 and 403 vs 351.8+38.5 min).
Conclusion: Twelve percent of insomniacs showed consistent rebound insomnia during placebo substitution of zolpidem (10 mg), which did not worsen from month 1 to 12, appearing to be a reliable individual difference in drug discontinuation response.

0533

CBT FOR INSOMNIA, PERCEPTION OF PAIN INTERFERING WITH SLEEP AND DEPRESSIVE SYMPTOM SEVERITY

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Introduction: 56 million Americans complain that nighttime pain interferes with their sleep. Cognitive behavioral therapy for insomnia (CBT-I) improves insomnia among patients with chronic pain. Depression and insomnia can exacerbate pain. To the best of our knowledge, no study has compared the efficacy of CBT-I among patients with insomnia disorder who perceive pain to interfere with sleep versus those who do not.
Methods: One hundred and eighty three participants (55% male, average age=43.4) completed group CBT-I and rated the extent to which pain interfered with their sleep on a 6-point Likert scale from "I don't have pain" to pain interferes with sleep "all of the time." Groups were dichotomized with 73 participants classified as pain interfering with sleep (Pain group) and 110 did not or occasionally perceived pain interference with sleep (NonPain group). Participants also completed the Insomnia Severity Index (ISI) and Beck Depression Inventory pre and post CBT-I.
Results: At baseline, ISI scores were higher among patients in the Pain group than the NonPain group. Repeated measures ANOVA with pain perception grouping as between-subjects variable and ISI pre-post CBT-I as the within-subjects variable revealed a significant main effect for time, F(1,73)=177.8, p<.001 and group, F(1,73)=4.96, p=.03, but no significant interaction effect. One-way ANOVA revealed that patients with pain were significantly more depressed at baseline, F(1,53)=4.11, p=.004. When depressed mood was controlled for in repeated measures ANCOVA, the main effect for group was no longer significant F(1,63)=2.57, p=0.11.
Conclusion: CBT-I was equally effective in both groups but those in the Pain group had greater insomnia severity at pre- and post-treatment. This suggests that depressive symptoms may explain the greater severity of insomnia pre- and post-treatment among patients who perceive pain to disrupt their sleep and that attending to depressive symptoms in these patents may be needed.

0534

FRONTAL CEREBRAL THERMAL TRANSFER AS A TREATMENT FOR INSOMNIA: A DOSE-RANGING STUDY

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Introduction: A reduction in frontal metabolism from waking to sleep is associated with restorative sleep. Frontal cerebral metabolism during sleep correlates positively with insomnia severity. Can reducing frontal metabolism during sleep treat insomnia? Previously, frontal cerebral thermal transfer (FCTT) at a cool setting reduced frontal metabolism during sleep in insomnia patients. The current study aimed to determine if all-night FCTT in insomnia patients had a dose-dependent effect on improving sleep onset and sleep efficiency.

Methods: In a crossover study, order randomized between patients, subjects received all-night FCTT via a soft plastic cap fitted on the scalp and filled with circulating water. Conditions varied in temperature of the circulating water, and therefore, in thermal transfer intensities, and included: no device, and device with either neutral, moderate or maximal cooling thermal transfer intensity. 110 subjects were screened, 12 met criteria for Primary Insomnia (9 women, mean age + s.d. = 44.6 + 12.5 years) and completed the study. Healthy age- and gender-matched subjects (n=12) served as a reference.

Results: A repeated measures ANOVA revealed linear effects of thermal transfer intensities (2-night means) on sleep latency (p = .02; effect size = .45) and sleep efficiency (p = .05; effect size = .36). Sleep latency and sleep efficiency in insomnia patients in the maximum thermal transfer condition (13 + 7 minutes and 89 + 5%, respectively) did not differ from those of healthy age- and gender-matched sleepers (16 + 16 minutes and 89 + 7%, respectively).

Conclusion: FCTT improved sleep latency and sleep efficiency in insomnia patients in a dose-dependent manner. In the maximum condition, sleep values in insomnia patients did not differ from healthy controls. Replication in a large scale clinical trial is warranted to determine if FCTT should be considered as a treatment for insomnia.

Support (If Any): R43HL097537; Respironics Research Foundation; MH66227; MH061566; AG20677; MH24652; RR024153

0535

A PHASE I/IIA, DOSE FINDING, DOUBLE-BLIND, RANDOMIZED, PLACEBO CONTROLLED STUDY TO ASSESS THE SAFETY AND EFFICACY OF SUBLINGUAL FLUMAZENIL IN REVERSAL OF THE RESIDUAL EFFECTS OF HYPNOTIC DRUGS (ZOLPIDEM OR BROTIZOLAM)

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Introduction: Background: 30% of the insomnia patients suffer from residual morning drowsiness . Purpose: To study the safety and efficacy (dose finding) of sublingual Flumazenil (GABA-A antidote) in reversing the residual hypnotic effect of sleeping pills in healthy volunteers.

Methods: Methods: 20 healthy subjects slept for 1.5 hours following sleep induction (Zolpidem , n=10; Brotizolam n=10). Upon awakening, they underwent a physical examination and neurocognitive tests including immediate word recall test (iWRT), Digit Symbol Substitution Test (DSST), and mood/performance questionnaires including visual analogue scale (VAS) to assess subjective alertness. They were then treated by Flumazenil (0.4mg; n=10 and 1.6 mg; N=10) or placebo (n=20) and were re-evaluated after 20min and 60 minutes. A week later, the same procedures and evaluations were performed again.

Results: Results: All 20 volunteers (10 males, age 28.8 ± 5.7) completed the study without any adverse events. Flumazenil was superior to placebo by 59-93% (P<0.05-0.001) in improving performance in the various

neurocognitive tasks, and subjects reported a significant improvement in vigilance on a VAS with Flumazenil compared to placebo, both 20min following administration (3.0±0.6 vs 1.3±0.6, p<0.02) and 60min following administration of Flumazenil (4.7±0.6 vs 2.8±0.7, p<0.03). A parallel improvement was seen in the iWRT for Flumazenil vs placebo 20min following administration (4.2±0.8 vs 1.3±0.9words, p<0.005) and 60min following administration (5.4±1.1vs 1.2±1.2 words, p<0.02).

Conclusion: Conclusions: Sublingual administration of Flumazenil is safe and effective in reversing the hypnotic effects of both Zolpidem and Brotizolam, assessed both subjectively and objectively by performance tasks. There are numerous potential applications for this concept, particularly when the residual hypnotic effect is undesired. It may allow better treatment and improvement in sleep-wake rhythm in insomniac patients. However, further research is required.

Support (If Any): The study was supported by Coeruleus Ltd, Israel.

0536

THE DEVELOPMENT OF AN INSOMNIA SPECIFIC STAGE OF CHANGE QUESTIONNAIRE - HELPING CLINICIANS IDENTIFY PATIENT-SPECIFIC ADHERENCE

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Introduction: The behavioural components (Stimulus Control, Sleep Restriction) of Cognitive Behavioural Therapy (CBT) often seem paradoxical to individuals with insomnia. This might result in poor adherence to treatment. A number of patient reported-questionnaires based on the Transtheoretical Stage of Change (SOC) Model have been developed to identify adherence issues in other populations. However psychometric testing of these questionnaires crucially fails to include patient feedback. In this study we specifically investigated patient-perceived validity of a stage of change scale specific for insomnia (SOCSI)

Methods: Two versions of the SOCSI, adapted from published questionnaires were tested to establish patient preference: an algorithm using dichotomous responses versus a multiple-choice scale. Separate open questions on benefits/barriers and strategies for change were also included in the questionnaire. Individuals with insomnia undergoing CBT-I took part in cognitive interviews to establish individuals' thoughts process for each question/response formulation. Questions on layout and face/content validity were also included. The SCOSI was amended iteratively and interviews continued until no new problems emerged.

Results: Saturation was reached at 7 individuals (mean age=38, mean Insomnia Severity Index= 17). The algorithm was the preferred format (n=5/7). Some amendments to the SOCSI were recommended by participants including e.g. the use of the word 'action plan' to generically describe the behaviour change of interest, or the timeline used to distinguish between different stages. Interview responses indicated good face and content validity and no missing responses were indicated by individuals. Some participants (n=3) remarked that completing the questionnaire made them more aware of their motivation to use sleep strategies.

Conclusion: This study presents important patient-reported validity data. Results suggest that the SOCSI is valid and comprehensible to individuals. The brevity and easy of administering the SOCSI suggests it's potential for being an integral of the therapeutic process in daily clinical practice. Psychometric testing of the SOCSI is ongoing.

0537

EXPLORING THE LINK BETWEEN F.I.R.S.T. SCORES IN HIGH SCHOOL STUDENTS AND SUBSEQUENT INSOMNIA FOLLOWING THE TRANSITION INTO COLLEGE

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Introduction: The Ford Insomnia Response to Stress Test (F.I.R.S.T.) assesses predisposition to stress-induced sleep disturbance (Drake et al., SLEEP, 2004), as F.I.R.S.T. scores of adults are predictive of chronic insomnia at 12-month follow-up. The current study evaluated whether the F.I.R.S.T. is associated with insomnia in emerging adults in the context of a major life stress (Weeks 1-2 of college) and daily stressors (Weeks 7-8 of the first semester).

Methods: High school seniors completed a multi-dimensional survey that included the F.I.R.S.T. in May or August after college acceptance. Once enrolled at Brown University, they completed online daily sleep diaries for 82 days and biweekly surveys where they reported insomnia difficulty in the prior two weeks. Analyses included 96 students (ages 18-21 years, mean=18.1 years, 55 females) who reported no insomnia in high school. We calculated two insomnia scores for Weeks 1&2 and Weeks 7&8, assigning 1-point for each day with reported sleep onset latency (SOL) >=30 min or wake after sleep onset (WASO) >=20 min; these scores were doubled if participants endorsed insomnia complaints on a concurrent biweekly survey.

Results: A trend was found for the correlation (R=.19; P=.071) of the F.I.R.S.T. (mean=18.1) and insomnia scores (mean=4.05) at week 2. The F.I.R.S.T. was correlated (R=.22; P=.03) with insomnia scores (mean=4.17) at week 8. Insomnia score using only SOL was correlated with the F.I.R.S.T. at week 2 (R=.26; P=.01) and week 8 (R=.33; P=.001), but a WASO insomnia score was not correlated with F.I.R.S.T. at either assessment.

Conclusion: These results support an association between the F.I.R.S.T. and insomnia within the context of daily stressors (Weeks 7/8) and a trend within the context of life-changing stress (Weeks 1/2). Students with higher F.I.R.S.T. scores reported longer sleep latency in the context of both daily and life-changing stressors during their first semester of college.

0538

DETRIMENTAL EFFECTS OF DOUBLE OCCUPATION ON THE SLEEP OF STUDENTS

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Introduction: Proportion of working college students has reached nearly 60% at the beginning of the new millennium. Working and studying have been documented to impact on academic performance. However, little is known about how it impacts on sleep quality.

Methods: A total of 8,937 individuals aged 18 years or older, representative of the general population of Texas, New York and California states were interviewed by telephone using the Sleep-EVAL system; 1,095 of them were aged between 18 and 24 years. The questionnaire included the assessment of insomnia symptomatology, sleep/mental disorders according to DSM-IV classification.

Results: Working students represented 34% of the young adults; students only 20%; daytime workers 18.8%; shift workers 16.2% and young adults without occupation represented 11%. Insomnia and excessive daytime sleepiness were frequent complaints among the young adults: 17.4% of young adults complained of a nonrestorative sleep (NRS), 19.6% of a difficulty maintaining sleep (DMS) and 13.0% of difficulty initiating sleep (DIS) at least 3 nights per week. Moderate or severe daytime sleepiness (EDS) was reported by 32.3% of them. A sleep duration <6 hours was reported by 17.9% of the young adults. In multivariate models after adjusting for age, gender, health and mental disorders, being a working student was a significant predictor for NRS (OR:2.2); sleep duration < 6 hours per night (OR: 2.2) and excessive daytime sleepiness (OR:2.1).

Conclusion: A sizable number of working students are sleep deprived with a sleep duration about one hour shorter than the norms for this age group. As a result, they are twice more likely to be sleepy during the daytime. Furthermore the double occupation negatively affects their academic performance.

0539

NIGHTTIME COGNITIVE DISTRACTION AND INSOMNIA SEVERITY AMONG UNIVERSITY STUDENTS

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Introduction: Previous literature highlights the positive associations between arousing pre-sleep cognitions and insomnia severity. Studies have also shown that a style of cognitive distraction (strategies used to withdraw from unwanted or arousing thoughts and attempts to think about more pleasant content) has been negatively associated with sleep difficulties. This study evaluates whether this cognitive thought management style is predictive of insomnia after accounting for well established risk factors for insomnia (depression, anxiety, pain, and sleep hygiene). This study also focuses on whether this cognitive style interacts with other risk factors for insomnia to lessen the severity of sleep problems.

Methods: This cross-sectional investigation included 616 college students (mean age = 19, 59% female, and 70% European-American). Participants completed surveys for course credit and all measures were completed online. The Insomnia Severity Index was used to measure insomnia and the Thought Control Questionnaire Insomnia- Revised measured the extent of nighttime cognitive distraction in response to arousing or unwanted thoughts.

Results: A hierarchical multiple regression showed that after accounting for sleep hygiene, depression, anxiety, and pain, nighttime cognitive distraction was negatively associated with insomnia severity (β = -.16, p < .01). After accounting for all other factors, cognitive distraction moderated the relationship between sleep hygiene and insomnia severity (β = -.28, p < .01). Those with poor sleep hygiene and a high frequency of cognitive distraction reported better sleep as compared to those with poor sleep hygiene and lower frequencies of this thought management strategy.

Conclusion: Nighttime cognitive distraction may be an important predictor of insomnia severity over and above well-established determinants. Usage of this cognitive style is also associated with less risk of sleep problems while engaging in poor sleep hygiene. These findings underscore the importance of distraction from arousing thoughts in order to improve sleep.

0540

MONTHLY FLUCTUATIONS OF SLEEP AND INSOMNIA SYMPTOMS OVER THE COURSE OF A YEAR IN A POPULATION-BASED SAMPLE

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Introduction: The longitudinal course of insomnia is not well documented. Most studies examining temporal fluctuations of symptoms have used yearly assessment intervals. The objective of this study was to document the course of insomnia symptoms and sleep quality by examining their fluctuations over shorter (i.e., monthly) intervals for one year.
Methods: Participants were 100 adults (mean age = 49.9 years; 66% women) selected from a larger sample enrolled in a longitudinal study of insomnia. They completed 12 monthly telephone interviews assessing sleep and insomnia symptoms, use of sleep aids, stressful life events, and physical and mental health problems for the previous month. Of a potential 1200 interviews, 1121 (94.3%) were completed. Participants were classified in one of three groups based on data collected at each assessment: good sleepers (GS; n= 42 at baseline), insomnia symptoms (SYMP; n= 34 at baseline), and insomnia syndrome (SYND; n= 24 at baseline).
Results: There were significant fluctuations of sleep/insomnia symptoms over time, with 84% of the participants changing status at least once over the 12 assessments (GS, 78%, SYND, 75%, and SYMP, 97%). On average, the sleep status of an individual changed 2.75 times over the 12 monthly assessments. Individuals with SYMP changed status significantly more frequently (3.55) than GS (2.14), but not more than SYND (2.66). Moreover, 85% of individuals with SYMP reported improved sleep (i.e., became GS) at least once over the year, compared to 29% who reported sleep worsening (i.e., became SYND). Among GS, risks of developing insomnia symptoms and syndrome over the subsequent months were respectively 17.6% and 3.2%.
Conclusion: Repeated assessment of sleep and insomnia symptoms showed significant variability over monthly intervals. These findings highlight the importance of conducting assessment at shorter than the usual yearly interval in order to capture more reliably the course of insomnia over time.
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0541

DIFFERENTIAL PATHWAYS LEADING TO INCIDENT INSOMNIA: A GENERAL POPULATION, LONGITUDINAL STUDY

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Introduction: Previous population-based, longitudinal studies have shown that new onset insomnia may emerge either from poor sleep or normal sleep patterns. In this study we examined the pattern of risk factors involved in the development of insomnia from a premorbid status of normal sleep vs. poor sleep.
Methods: From a random, general population sample of 1741 adults of the Penn State Cohort, 1395 were followed-up after 7.5 years. In this study we included those with normal sleep at baseline and follow-up (n = 590) and those who were normal sleepers (n = 65) or poor sleepers (n = 68) at baseline and developed into chronic insomnia. Medical and sleep history, 8-hour PSG and MMPI-2 were obtained at baseline, and sleep history also at follow-up.

Results: Younger age, minority, obesity, caffeine consumption, allergy/asthma, kidney/bladder, migraine, thyroid, depression, and alcohol use disorder significantly increased the odds of developing insomnia from normal sleep at baseline. Female gender, younger age, caffeine and tobacco consumption, family history of sleep problems, anemia, migraine, ulcer, depression, and alcohol use disorder predicted the development of insomnia from poor sleep at baseline. Poor sleepers who developed insomnia also showed higher elevations in all personality scales, except hypomania, when compared to normal sleepers, while in normal sleepers who developed insomnia only depression was significantly higher.
Conclusion: These data suggest that there are two differential pathways leading to insomnia. Physical health appears to play a primary role in the development of insomnia in normal sleepers, whereas mental health and maladaptive personality characteristics appear to play a major role in the development of insomnia in poor sleepers. These data support the need to develop differential preventive strategies to reduce incident insomnia.

0542

POTENTIAL PROTECTIVE FACTORS IN INDIVIDUALS VULNERABLE TO STRESS-RELATED INSOMNIA

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Introduction: Previous studies have suggested individual differences in vulnerability to experience insomnia under stressful conditions. This vulnerability has been associated with maladaptive stress coping strategies and hyperarousal among good sleepers but not necessarily among individuals with insomnia. The present study examined potential factors that might differentiate individuals with and without insomnia among those with a high vulnerability to stress-related insomnia.
Methods: Participants were 847 adults (mean age = 47.3 years; 73.3% women) selected from a larger population-based sample enrolled in a longitudinal study of insomnia. They were selected for the present analysis on the basis of their high vulnerability to stress-related insomnia as assessed with the Ford Insomnia Response to Stress Test (score higher than 21). Among those, two groups were formed based on their sleep status: Good Sleepers (n = 509) and Insomnia Syndrome (n = 338). Dependent variables were trait anxiety, arousal predisposition, stress perception and coping strategies, and beliefs and attitudes about sleep.
Results: A MANCOVA controlling for age and a past episode of insomnia revealed that Good Sleepers with high vulnerability to stress-related insomnia were significantly less anxious ($\eta^2 = .22$), less predisposed to activation ($\eta^2 = .07$), appraised life's events as less stressful ($\eta^2 = .18$), and endorsed fewer dysfunctional beliefs about sleep ($\eta^2 = .15$) compared to individuals with an Insomnia Syndrome and a high vulnerability to stress-related insomnia. The Good Sleepers group also relied less on emotion-focused strategies ($\eta^2 = .06$), but more on task- ($\eta^2 = .04$) and avoidance-oriented strategies ($\eta^2 = .02$).
Conclusion: Lower levels of anxiety, perception of stress, and arousal predisposition, and less dysfunctional beliefs about sleep might be protective against chronic insomnia among individuals otherwise vulnerable to stress-related insomnia. A longitudinal design is needed to test more rigorously this hypothesis.
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0543

THE UTILITY OF POLYSOMNOGRAPHY IN PREDICTING PERSISTENT INSOMNIA: A GENERAL POPULATION, LONGITUDINAL STUDY

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Introduction: Chronic insomnia tends to be a persistent problem, with only few experiencing full remission. None of the available population-based, longitudinal studies have examined the role of polysomnographic (PSG) variables such as sleep apnea or sleep duration on the persistence of insomnia. We hypothesized that objective short sleep duration will be a strong predictor of persistent insomnia.

Methods: From a random, general population sample of 1741 adults of the Penn State Cohort, 1395 were followed-up after 7.5 years. In this study we included those with normal sleep at baseline and follow-up (n = 590) and those who were insomniacs at baseline (n = 149) and developed into persistent insomnia (n = 65), partially remitted insomnia (n = 47), or remitted insomnia (n = 37). Medical and sleep history and 8-hour PSG were obtained at baseline, and sleep history also at follow-up. Multinomial logistic regression models were adjusted for age, race, gender, obesity, sleep apnea, physical health problems, mental health problems, cigarettes, caffeine and alcohol consumption.

Results: Objective short sleep duration significantly increased the odds of persistent insomnia as compared to normal sleep (OR=3.46) and to remitted insomnia (OR=4.54) whereas sleep apnea did not predict either the persistence or the remission of insomnia.

Conclusion: Objective short sleep duration is a strong predictor of persistent insomnia. These data further support the validity and clinical utility of objective short sleep duration as a novel marker of the severity of insomnia.

0544

EEG SEGMENT DURATION CALCULATED BY ADAPTIVE SEGMENTATION AS A MEASURE OF SLEEP STATE STABILITY IN INSOMNIA

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Introduction: Automated scoring of sleep can enhance analysis of the EEG biological signal. This study utilizes adaptive segmentation to analyze frequency segments across time looking at microstructure of sleep and state analysis not restrained by 30 second epochs. Morpheus® uses a multi-dimensional mathematical model of adaptive segments so that it replicates what the human does in terms of looking at frequency and amplitude characteristics. This study assesses signal processing outcomes using adaptive segmentation at baseline comparing insomnia screen fails(ISF) with normals(NL) and randomized insomnia(IN) patients.

Methods: A post-hoc analysis of three groups of adults is examined based on automated analysis: 35 IN; 20 NL; and 38 ISF. HF mean segment duration is reported. This represents baseline PSG pre-treatment analysis. Advanced spectral parameters were analyzed in 2 hour time intervals for each group. Means, standard deviations, and t-tests are reported.

Results: Means and standard deviations are measured as % of TIB. Mean segment duration is: d(HF): hours 1-2: ISF=1.58 (0.38); IN=1.66 (0.37); NL=1.28 (0.16). Hours 3-4: ISF=1.28 (0.26); IN=1.23 (0.44); NL=1.08 (0.19). Hours 5-6 ISF=1.18 (0.22); IN=1.22 (0.25); NL=1.07 (0.19). Hours 7-8 ISF=1.27 (0.22); IN=1.28 (0.25); NL=1.14 (0.19). Results of t-tests of mean segment duration: d(HF) are significant p<

0.05 comparing NL to ISF/IN at each 2 hour segments and not significant with ISF to IN at any time point studied.

Conclusion: Adaptive segmentation demonstrated an increase in high frequency mean segment duration in insomnia and screen fail insomnia patients compared to normals across each 2 hour interval. This suggests in insomnia patients HF state is more persistent than in normals. These findings support the premise of hyperarousal in insomnia.

0545

SLEEP EEG POWER SPECTRA TRANSITIONS DURING SLOW WAVE SLEEP IN PRIMARY INSOMNIA

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Introduction: The pathophysiology of insomnia is not well understood. There is no specific physiologic marker for this condition. Individuals with insomnia are considered to be in a hyperaroused state during sleep. This study assesses signal processing outcomes using adaptive segmentation at baseline analyzing slow wave sleep (SWS) as a measure of sleep homeostasis. We compared SWS dynamics across the night in insomnia screen fails(ISF) with normals(NL) and randomized insomnia(IN) patients. Morpheus® is a system that performs automated analysis of sleep staging using a multidimensional mathematical analysis of EEG applying adaptive segmentation and fuzzy logic with Markov models enabling multiple spectral power EEG measurements.

Methods: A post-hoc analysis of spectral patterns of three groups of adults is examined based on automated analysis: 35 IN; 20 NL; and 38 ISF. This represents baseline night analysis. Advanced spectral parameters assessing slow wave sleep were analyzed for each group at 2 hour intervals during the night and assessed the probability of transitioning from slow wave sleep to a high frequency state.

Results: Means and standard deviations are measured as % of TIB. For LF% hours 1-2: ISF=2.53(2.38); IN=2.53(2.65); NL=3.26(1.66). Hours 3-4: ISF=3.78(2.52); IN=4.26(3.72); NL=2.97(2.18). Hours 5-6 ISF=2.09(1.62); IN=1.91(1.99); NL=1.23(1.39). Hours 7-8 ISF=0.92(0.94); IN=1.58(3.02); NL=0.49(0.65). T-tests of 2 hour intervals of LF% comparing groups were significant p<0.05 at 5-6 hours for LF% NL/ISF. Means and standard deviations for probability of transition from LF to HF as a % of TST were: hours 1-2: ISF=0.09 (0.09); IN=0.009 (0.01); NL=0.07 (0.05). Hours 3-4: ISF=0.07 (0.05); IN=0.03 (0.02); NL=0.07 (0.03). Hours 5-6 ISF=0.08 (0.07); IN=0.01 (0.01); NL=0.09 (0.06). Hours 7-8 ISF=0.09 (0.09); IN=0.009 (0.01); NL=0.09 (0.12). T-tests of 2 hour probability transition comparing groups were significant p<0.05 at 1-2/5-6 hours for NL/ISF; hours 3-4 NL/ISF; 5-6 hours NL/IN; hours 7-8 for ISF/IN.

Conclusion: If one interprets SWS as a function of homeostatic drive then insomnia patients tend to have more stability and less probability of transitioning into a HF state. The distribution of this finding is significant in the last half of the night probably suggesting and increase in homeostatic drive.

0546

RELATIONSHIP OF POLYSOMNOGRAPHIC DETERMINED SLEEP AND BODY MASS INDEX IN PATIENTS WITH INSOMNIA

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Introduction: Large number of studies has consistently demonstrated that habitual short sleep duration may relate to obesity. Self-reported data also indicate that obese individuals may have higher incidence of subjective sleep disturbances. Slow wave sleep (SWS) is thought to be the mostly restorative state and its reduction has been reported in insom-

nia. In this study, we assessed relationship of polysomnographic determined sleep, especially SWS amount, and body mass index (BMI) in patients with insomnia.

Methods: One hundred forty one insomnia sufferers and 55 health volunteers completed overnight polysomnographic recording, and data of height and body weight were also collected. The measures of total sleep time, sleep efficiency, sleep latency, percentage of N1, 2 and 3 (SWS), rapid eye movement sleep (REMS), and apnea/hypopnea index (AHI) were analyzed.

Results: No significant correlation was obtained between total sleep time and BMI among insomniacs and among volunteer individuals. Compared to volunteers, insomnia patients exhibited significant increases in sleep latency and N1 percentage, and decreases in total sleep time, SWS and REMS percentage, but no difference in BMI. Based on values of SWS percentage, we divided insomnia into three groups of short (7.2±3.2%), intermediate (14.7±1.8%) and long (26.6±5.9%) SWS groups, and each group had 47 subjects. We found that short SWS group had significantly greater BMI (23.3±3.0) than long SWS (21.4±2.4), no difference to intermediate SWS group (22.9±2.6). Further analysis with linear multiple regression showed that reduction of SWS was significantly related to increase of BMI in insomnia patients, not in volunteers after control confounders (e.g, age, sex and AHI).

Conclusion: The finding may suggest that poor quality of sleep in terms of reduction in SWS percentage may associate with higher BMI in insomnia patients.

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0547

SLEEP ARCHITECTURE PREDICTS THE MISMATCH BETWEEN SUBJECTIVE AND OBJECTIVE SLEEP DURATION

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Introduction: Patient self-report of sleep duration may not reflect objective measurement. Improved understanding of the relation between sleep architecture (stages, fragmentation, etc) and subjective-objective mismatch might yield important diagnostic and prognostic information. We hypothesized that the degree of mismatch among insomnia patients would correlate with metrics of sleep fragmentation.

Methods: We performed a retrospective analysis of ~1000 patients undergoing diagnostic polysomnography at our center. Patients completed a post-study estimate of sleep latency, total sleep time, and certainty regarding each answer. We excluded those with neurological or psychiatric diseases, or those taking any medication influencing sleep (final n=312). Insomnia category was defined by self-reported on intake questionnaire, yielding 3 groups: insomnia alone, sleep apnea alone (AHI >5), or both.

Results: While a mismatch between subjective report of sleep (latency and total sleep time) was evident in all groups, it was most pronounced in insomnia patients who more substantially underestimated their sleep. We found significant correlations between subjective-objective mismatch of total sleep time, and fragmentation indices (such as EEG arousals, brief awakenings, sleep efficiency, periodic leg movements, and respiratory events) (0.2 to 0.35, Spearman's R). The extent of sleep underestimation was inversely related to certainty, suggesting a tendency toward pessimism when guessing. However, errors in latency showed only small correlation with errors in total sleep, arguing against a general "exaggerator" phenotype. We also observed that subjective sleep duration (across a range of accuracy) correlated best with the duration of REM sleep and of N2. We present different weighting schemes applied to sleep stage metrics to use architecture to predict self-reported sleep duration.

Conclusion: Subjective-objective mismatch, which was common in patients reporting insomnia, correlated with several fragmentation metrics. Additionally, the prediction of self-reported sleep duration based on

sleep stages suggests possible mechanistic links between sleep architecture and subjective estimation of sleep duration.

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0548

THE FIRST REM SLEEP PERIOD: LATENCY AND DURATION AS INDICATORS OF FIRST NIGHT EFFECTS IN GOOD SLEEPERS AND OF REVERSE FIRST NIGHT EFFECTS IN INSOMNIA SUFFERERS

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Introduction: While first night effects (FNE) are often observed in good sleepers (GS), individuals with insomnia (INS) are more susceptible to reverse FNE (RFNE). Sleep efficacy, sleep onset latency and total REM time are habitually used to quantify these effects. The present study is aimed at evaluating if the first night spent in the sleep laboratory could affect REM onset latency (REML) and duration of the first REM sleep period (REMD). GS and INS will be compared on these measures and INS subdivided in paradoxical (IPA) and psychophysiological insomnia (IPS).

Methods: 33 IPS (Mean age=39.5), 21 IPA (Mean age=39.0) and 43 GS (Mean age=35.3) completed four consecutive PSG nights in the laboratory. The first three nights (N1, N2 and N3) were used in this study. REML was defined as the duration between the first epoch of Stage 2 and the first epoch of REM sleep. REMD was computed by subtracting the start time from the end time of this period.

Results: Repeated measures ANOVAs (3x3; Groups x Nights) were performed. A main effect of night was found for REML ($p \leq .001$), results showing a night to night decrease in REML. Mean and (SD) were respectively for IPS: [N1=112.4 (76.2), N2=95.7 (55.6), N3=78.0 (33.7)]; for IPA: [N1=97.7 (37.7), N2=92.4 (47.1), N3=71.5 (35.7)] and for GS: [N1=87.8 (36.2), N2=86.5 (46.4), N3=79.1 (35.7)]. No other significant main effects or interactions were found for REML or REMD.

Conclusion: Results showed that experience of sleeping in the laboratory had an effect on REML. However, nightly changes in latency of the first REM period may not be an adequate indicator of FNE and RFNE since status (being good sleepers or suffering from insomnia) was not related to observed changes. The clinical relevance of these changes remains to be investigated.

Support (If Any): Supported by the Canadian Institute of Health Research.

0549

THE ASSOCIATION BETWEEN PRE-SLEEP SUBJECTIVE AROUSAL AND PHYSIOLOGICAL MEASURES OF AROUSAL DURING SLEEP-ONSET PERIOD IN PATIENTS WITH PRIMARY INSOMNIA AND NORMAL SLEEPERS

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Introduction: Hyperarousal has been recognized to be a major factor for insomnia. However, the term "arousal" was measured differently for different studies. The present study is to explore the associations of subjective ratings of somatic and cognitive arousal with physiologically arousal as measured by EEG and heart rate variability (HRV) prior and after sleep onset.

Methods: 15 patients with primary insomnia (10F; mean age=36.6) and 15 normal sleepers (8F; mean age=34.2) underwent one night of PSG recording in a sleep laboratory. They completed the Pre-sleep Arousal

Scale (PSAS) before bedtime. HRV and EEG spectrum analyses were conducted for the EKG and EEG data collected during the 5 minutes prior to sleep onset and the 5 minutes after.

Results: Both cognitive and somatic subscales ratings were higher in insomnia group. Also, insomnia group showed higher alpha power both prior and after sleep onset, and higher beta power after fallen asleep (C3: F=4.78, p=.037). In terms of the correlations between PSAS score and EEG power, insomnia group showed significant negative correlation between somatic arousal and delta power (C3: r=-.56, p=.029; C4:r=-.53, p=.042), positive correlation between somatic arousal and alpha power (C3: r=.57, p=.027; C4:r=.56, p=.029), negative correlation between cognitive arousal and beta power (C3: r=-.55, p=.032; C4:r=-.53, p=.042) before sleep onset. After sleep onset, insomnia group showed positive correlation between somatic arousal and theta power (C3: r=.62, p=.015; C4:r=.54, p=.038). As regarding HRV, only correlation between somatic arousal and normalized high frequency (HF(nu)) in insomnia group after sleep onset (r=.52, p=.049) was significant. No significant correlations were obtained in normal sleepers.

Conclusion: The results indicate that subjective somatic arousal is associated with cortical arousal as measured by EEG and ANS arousal by HRV in insomnia group, but not in good sleepers. Subjective feelings of cognitive arousal may be less associated with either ANS or cortical arousal.

0550

PATIENTS' ATTRIBUTIONS ABOUT THE CAUSES OF INSOMNIA

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Introduction: This study investigated the possibility that the 'folk theories' or attributions a patient holds about their disorder may impact their treatment preference. This is important because treatment preference may influence engagement and compliance with treatment which, in turn, will impact outcome. Insomnia is the focus as it is prevalent and associated with significant impairment of quality of life. Moreover, there are various treatment options.

Methods: Participants were 69 patients with chronic insomnia. They completed the 'Causal Attributions of My Insomnia Questionnaire' (CAM-I), a questionnaire evaluating potential causal explanations/attributions about insomnia on Likert-type scales (1 = very likely; 7 = very unlikely). Several other assessment instruments were administered as part of a larger treatment study (e.g., Duke Interview for Sleep Disorders, SCID-I).

Results: Of 12 factors rated, emotions and thinking patterns were most commonly endorsed as 'contributing to insomnia' (60% and 58% of patients, respectively, endorsed these factors as 'very likely'). Patients were reasonably confident that targeting these factors in treatment would alleviate their insomnia (emotions M = 5.96; SD = 1.38; thinking patterns M = 6.00; SD = 1.25). Percentage of patients who rated that a psychological treatment could help varied from 30% for genetic factors to 59% for emotions. Patients who rated that a biological treatment could help varied from 19% for environmental factors to 40% for biochemical factors. Those who endorsed thinking patterns (t=6.57, p < .001), environment (t=4.50, p < .001), scheduling (t=4.29, p < .001) and emotions (t=5.76, p < .001) as likely contributors were more confident that a psychological than biological treatment would help. Surprisingly, no contributing factor assessed (hormones, arousal, genetics) were endorsed as more likely to be alleviated by a biological treatment.

Conclusion: Patient's attributions influenced treatment choice. Patients were more confident in psychological treatments over biological treatments.

0551

SLEEP VARIABLES RELATED TO SLEEP QUALITY RATING

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Introduction: Sleep researchers frequently use the term sleep quality, which lacks an established definition. The purpose of the present study is to determine which sleep variables are most closely associated with perceived sleep quality in people not having insomnia (PNI) and in people with insomnia (PWI).

Methods: Using random-digit dialing, we recruited 772 participants ranging in age from 20 to 80+, with approximately 50 men and 50 women in each decade. Participants completed 2 weeks of sleep diaries which included a daily sleep quality rating (SQR) on a scale from 1 (poor sleep) to 5 (excellent sleep). The present sample included PNI (n = 400) and PWI (n = 137). PNI satisfied ICSD insomnia diagnostic criteria. Excluded were individuals who were partial qualifiers for PNI and PWI.

Results: Stepwise multiple regression found that for PNI, sleep efficiency (SE) best predicted SQR, explaining 7.3% of variance in SQR. Number of awakenings (NWAK) explained an additional 1.8% of variance. Sleep onset latency (SOL), wake time after sleep onset (WASO), and total sleep time (TST) were excluded. For PWI, WASO was the best predictor of SQR, explaining 20.8% of the variance in SQR. Together, NWAK and TST explained an additional 9.9% of variance. SE and SOL were excluded.

Conclusion: NWAK was the only sleep variable that predicted a significant amount of variance for both PNI and PWI. SE was the best predictor of SQR for PNI, whereas WASO was the best predictor of SQR for PWI. 91% of variability in SQR among PNI remained unexplained after accounting for self-reported sleep patterns, and 70% of SQR was unexplained among PWI. Most of perceived sleep quality may be a function of sleep stages and factors unrelated to sleep pattern and architecture sometimes grouped under the umbrella of nonrestorative sleep.

0552

THE EFFECTS OF SLEEP DISTURBANCE ON PSYCHIATRIC AND COGNITIVE FUNCTIONING FOLLOWING TRAUMATIC BRAIN INJURY

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Introduction: Traumatic brain injury (TBI) is a leading cause of death and permanent disability in the US each year and is considered the hallmark injury of the wars in Iraq and Afghanistan. Insomnia following TBI is one of the most common and yet least studied of the post-TBI sequelae and may contribute to residual mood and cognitive difficulties in these patients. We evaluated these factors in a sample of Veterans with mild to moderate TBI (mTBI).

Methods: Retrospective chart reviews of Veterans' clinical sleep, psychiatric, and neuropsychological test data were conducted. Bivariate correlations were performed to assess the relationship between sleep and measures of cognitive and emotional functioning.

Results: 316 Veterans (mean age=32 yrs; mean education=13.5 yrs) were evaluated. 85% of patients reported sleep disturbance as measured by scores on Item #16 on the Beck Depression Inventory (BDI), with 71% of the total sample reporting getting less sleep. In a subset of patients (n=94) who were administered the Pittsburgh Sleep Quality Inventory (PSQI), 98% reported clinically significant sleep disturbance (PSQI

>5). Self-reported sleep latencies averaged 51 minutes, total sleep times averaged 5.4 hours, and sleep efficiencies averaged 77%. Total PSQI scores were positively correlated with BDI total score (.547, p<.001, n=93) and negatively correlated with neuropsychological measures of test-taking effort (Test of Memory Malingering: -.330, p=.002, n=87). PSQI subscale scores revealed a pattern of results suggesting a relationship between greater sleep complaints and poorer attention, higher number of intrusions, and greater level of disinhibition.

Conclusion: Poor sleep is a pervasive complaint in Veterans with mTBI, with levels of disturbance exceeding the general population prevalence. Sleep disturbance, such as insomnia, may play a significant role in frontal/subcortical cognitive deficits, depressive symptoms, and recovery of normal performance following mTBI. Further research is needed to determine the causal relationships between sleep, depression, and cognitive performance.

0553
ETHNIC EFFECTS ON WORKING MEMORY CAPACITY IN SLEEP DISORDERS

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Introduction: Previous literature has examined the neurocognitive deficits associated with sleep disorders. Studies suggest deficits in working memory amongst patients with OSAS, but equivocal results with other sleep disorders. There is little information about whether these deficits are related to ethnicity. The goal of the current study was to investigate the working memory capacity (WMC) of participants with insomnia and other suspected sleep disorders compared to normal sleepers, and determine if ethnicity contributed to differential effects.

Methods: 964 undergraduate college students (796 Caucasian-Americans (CA), 168 African-Americans(AA)) completed the Automated Operation Span task to measure WMC, the Global Sleep Assessment Questionnaire to determine the frequency of suspected sleep disorders, and the Insomnia Severity Index. Participants with suspected sleep disorders were identified as experiencing symptoms of a sleep disorder usually or always in the past four weeks. Participants also provided demographic information, and ICSD-II criteria to ascertain an insomnia diagnosis. Between-subjects t-tests and ANCOVA were conducted.

Results: In this sample 23.8% met ICSD-II criteria for insomnia, 1.5% for suspected sleep apnea, 6.5% for nightmares and/or parasomnias, 8.6% for RLS symptoms, and 7.7% for PLMD symptoms. Only participants with insomnia and those with suspected RLS had significantly lower WMC compared to normal sleepers. A two-way ANCOVA was conducted to explore the impact of ethnicity and these sleep disorders on WMC. There was a significant interaction, p = .022, indicating AA with insomnia have lower WMC, M=39.4, than CA with insomnia, M=45.4, controlling for health status, mental disorder diagnosis, age, gender, and body mass index.

Conclusion: The ability to engage in an attention-demanding memory task is more compromised in RLS, and in insomnia particularly in AA compared to CA. Treatment for AA with insomnia may need to emphasize improvement in cognitive symptoms.

0554
COGNITIVE-BEHAVIORAL TREATMENT OF CHRONIC INSOMNIA. RANDOMIZED STUDY IN A SAMPLE OF COLOMBIAN PATIENTS

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Introduction: The cognitive-behavioral treatment for insomnia CBTI indicated with high effectiveness in patients with chronic insomnia, have not been reported in Hispanic patients.

Methods: The study aimed to evaluate the effectiveness of CBTI in patients with primary conciliation and maintenance insomnia in Colombian subjects. A prospective, randomized, double-blind study in patients referred by several sleep centers between July 2008 and January 2009. Eighty-seven patients (43 men and 44 women, with an average of 46 years, the average of the symptoms is 9.7 years, ranging from 2 years to 15). Patients were compared in three groups of 29 participants each. The first group received multicomponent treatment (MCT) (sleep restriction, sleep hygiene education, lifestyle education, problem solving and cognitive restructuring). The second group received training in relaxation and sleep restriction (BT). The third group received training in problem solving (P). Monitoring is performed at 6 months and a year. Subjective measures were used as sleep diary and actigraphy, to assess sleep patterns and, sleep latency, total sleep time and sleep efficiency.

Results: MCT showed improvements that were maintained at 6 months, sleep efficiency, sleep latency and total sleep time, which were significantly different interventions only with BT or P (p = 0.01). The effectiveness of sleep in patients with MCT increased from 56% to 82% at six months and remained at 79%. Sleep latency decreased from 90 minutes to 30 minutes and remained at 35 minutes in the year and total sleep time step of three hours to six hours which is retained a year. The linear regression analysis is to describe that 76% of changes are explaining the procedures.

Conclusion: CBTl therapy showed significant differences in favor after the proposed follow-up periods, similar to previous studies reporting on the subject in English-speaking countries.

0555
NOCTURNAL INSOMNIA SYMPTOMS AND DAYTIME FUNCTIONING IMPAIRMENTS

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Introduction: The relationship between nocturnal insomnia symptoms and reported daytime consequences remains poorly understood. For example, greater fatigue and disturbed mood are not necessarily tributary of the insomnia symptoms' severity. This study examined whether the type and severity of diurnal symptoms varied according to the type of nocturnal insomnia complaint.

Methods: Participants were 514 adults (70% women), aged 18 years old and older (mean age = 49.6 years old), selected from a larger population-based sample taking part in a longitudinal study of insomnia. Responses to the Insomnia Severity Index (ISI) and Pittsburgh Sleep Quality Index (PSQI) were used to classify participants into one of five groups based on the nature of insomnia symptoms: (1) difficulty initiating sleep (early; N=75), (2) difficulty maintaining sleep (middle; N=55), (3) early morning awakenings (late; N=75), (4) mixed (N=206), or (5) non-restorative sleep (NRS; N=103). Participants completed measures of daytime fatigue and sleepiness, depression and anxiety symptoms, and quality-of-life. Group differences were tested using ANOVAS with multiple range tests for post-hoc comparisons.

Results: Individuals with middle and late insomnias did not differ significantly from each other on any of the daytime indicators. Few significant differences were observed between the NRS, mixed, and early insomnia subgroups, but these subgroups were generally more impaired during the day than individuals with middle or late insomnia. For example, they reported being more fatigued than the middle and late subgroups and reported more anxiety and depression symptoms than the middle subgroup. In general, individuals with NRS reported poorer quality of life (e.g., energy and mental health subscales) than other subgroups, which did not differ from each other. No group difference was observed with respect to sleepiness.

Conclusion: These findings indicate that the nature and severity of daytime impairments vary as a function of insomnia symptoms, with NRS and mixed insomnia complaints being associated with more severe impairments. Future research should examine whether treating different nocturnal symptoms produce different outcomes on daytime symptoms.

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0556

ACTIGRAPHIC CHARACTERIZATION OF INSOMNIA COMPLAINTS IN OPERATION ENDURING FREEDOM/ OPERATION IRAQI FREEDOM VETERANS

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Introduction: Insomnia is inherent in PTSD and sometimes follows mTBI; however, there is limited data about insomnia in Operation Enduring Freedom/Operation Iraqi Freedom veterans, where PTSD and mTBI often coexist. Our aim was to compare sleep characteristics of three groups of OEF/OIF veterans: (1) healthy sleepers (HS), (2) those with insomnia associated with post-traumatic stress disorder and mild traumatic brain injury (PTSD-mTBI), and (3) those with insomnia associated with PTSD alone.

Methods: Consecutive veterans with insomnia complaints (>1 month) were recruited from the Miami VA Post Deployment clinic between 6/2009-12/2009. Exclusion criteria were history of insomnia or TBI predating deployment, and current substance abuse or significant sleep disordered breathing (AHI>15). Participants completed the Duke Structured Interview for Sleep Disorders, detailed medical history, and questionnaires about insomnia, sleepiness, pain, fatigue, depression, and PTSD. Participants underwent polysomnography (PSG) followed by two weeks of actigraphy (ACT) with sleep logs. HS were subjects without sleep disorders on interviews and PSG. Clinical and ACT/sleep log variables median (interquartile ranges) were compared between PTSD, PTSD-mTBI, and HS groups. Kruskal-Wallis test and Fisher-Freeman-Halton Exact test were used to compare nonparametric continuous and categorical variables. Post-hoc analysis with pairwise comparisons was performed.

Results: Six HS, 9 with PTSD, and 15 with PTSD-mTBI were recruited. There were no significant demographic differences between the groups. There were no differences in insomnia, pain, fatigue, depression or PTSD severity between PTSD and PTSD-mTBI groups. Epworth Sleepiness score was significantly higher in PTSD-mTBI insomniacs [14(9)] compared to HS [5(5)] but not different than PTSD insomniacs [8(7)]. ACT total sleep time (TST) was significantly longer and wake after sleep onset (WASO) was significantly shorter in PTSD-mTBI insomniacs as compared to PTSD insomniacs.

Conclusion: PTSD-mTBI insomniacs commonly report hypersomnia, despite longer TST and decreased WASO as compared to PTSD insomniacs, suggestive of central hypersomnia components.

0557

SLEEP PERCEPTION AND MULTIPLE SLEEP LATENCY TEST IN PATIENTS WITH PRIMARY INSOMNIA

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Introduction: Hyperarousal during both diurnal and nocturnal periods may be the central pathophysiological changes for patients with primary insomnia (PI). Compared to health control, PI normally have significantly lower amount of subjective sleep with respect to objective evaluated sleep, and also exhibit greater score of multiple sleep latency test (MSLT). The former suggests nocturnal sleep state misperception and the latter may reflect diurnal physiological arousal. The relationship of diurnal physiological arousal and nocturnal sleep state misperception has not been studied in PI patients.

Methods: The data for overnight polysomnography, morning questionnaire, four naps MSLT and Epworth Sleep Scale (ESS) were collected in PI patients (n=122, age 39.3±10.9) and health control (n=48, age 38.5±12.7). Sleep perception (SP) was calculated with subjective sleep time/objective sleep time *100%.

Results: Compared to control, PI patients had significantly reductions in time spent in total sleep and slow wave sleep, in REM percentage and prolonged sleep latency, greater MSLT value and lower ESS score. The means of SP significantly differed (p<0.001) between PI patients (56.4±38.8%) and control (99.3±13.6%). Among individuals of PI, the values of SP was negatively correlated to MSLT score (r=-0.20, p<0.05) and positively associated to ESS score (r=0.28, p<0.01) and objective total sleep time (r=0.20, p<0.05). In PI patients, two-way ANOVA using age as a covariate revealed that MSLT score had significantly main effect on SP value, but objective sleep time did not. In control, both MSLT and objective sleep time did not have effect on SP value.

Conclusion: Sleep state misperception with lower estimated subjective sleep amount relative to objective sleep and hyperarousal reflected with greater MSLT score were found in PI patients compared to health control. Hyperarousal and sleep state misperception may have mutual effects for PI patients.

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0558

INSOMNIA SEVERITY LEVEL IMPACTS CEREBRAL ACTIVATION DURING WORKING MEMORY

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Introduction: Insomnia remains the most commonly reported sleep disorder, however, very little is understood concerning its neuropathophysiology, especially as it relates to cognitive performance. Similarly, little is known about how insomnia severity impacts cerebral function. Here, we utilized Functional Magnetic Resonance Imaging (fMRI) to examine cognitive performance during a working memory task across two different severity levels of Primary Insomnia (PI).

Methods: Nineteen subjects with PI completed a verbal n-back task during fMRI scanning. Using Insomnia Severity Index (ISI) scores from the previous night, subjects were classified as "Mild" (scores=8-14) vs. "Moderate" (scores=15-22) PI. Cerebral responses were compared between groups for both an easy (1-back) and difficult (3-back) version of the task.

Results: Insomnia severity did not affect task performance. On 1-back, only one small region (right precuneus) showed a group difference (Mild>Moderate) in activation. On 3-back, Mild PIs again showed

greater activation than Moderate PIs in right precuneus as well as in bilateral parahippocampal gyri. In contrast, Moderate PIs showed stronger cerebral responses in bilateral Inferior Frontal gryri, right Middle Frontal gyrus, bilateral Inferior Parietal lobes, and right Superior Parietal lobe (p≤.05).

Conclusion: While insomnia severity did not affect performance on either version of n-back, when the task became more difficult the groups showed different patterns of cerebral response in achieving the same performance. Mild PIs may show stronger parahippocampal activation because they relied more on an encoding strategy. Alternatively, some recent literature suggests increased insomnia severity as measured with ISI is associated with reduced hippocampal volumes, and this could underlie the reduced activation for Moderate PIs in the parahippocampus. Moderate PIs may have shown increased activation in working memory regions because they relied more than Mild PIs on keeping stimuli online during the task. Or alternatively, Moderate PIs needed to recruit additional working memory resources to compensate for more severe insomnia-related effects. Future studies should attempt to examine both volumetric and compensatory changes in PI as they relate to performance in this and other cognitive domains.

0559

ESTIMATED CREATININE CLEARANCE IS DECREASED IN SUBJECTS WITH CHRONIC PRIMARY INSOMNIA

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Introduction: Insomnia, through sustained arousal and increased neural influences from the sympathetic nervous system, has theoretically the potential to affect filtration capacity of the kidneys. In this study we assessed kidney function in healthy subjects with chronic insomnia and good sleepers.

Methods: We revised the charts of 25 normotensive insomnia subjects (15 F, age 51±9 years) and 16 good sleepers (10 F, age 49±9 years), who underwent one night of polysomnography and morning blood sampling. Subjects were free of any significant medical or psychiatric co-morbidity or other sleep disorders and were on no medications (except 2 insomniacs on benzodiazepines). Morning plasma creatinine was used to provide the estimate of creatinine clearance rate (eCcr), using the Cockroft-Gault formula. This measure is an accepted approximation of ultra-filtration capacity of the kidneys and is used clinically to provide an index of renal function. Between-group comparisons were performed by unpaired t-tests. Univariate and multivariate predictors of eCcr were also assessed by regression analyses using systolic blood pressure (SBP) and sleep variables as covariates.

Results: Insomnia subjects had a lower eCcr compared to controls (87 ± 18 ml/min versus 105 ± 27 ml/min, p<0.05). SBP was also higher in insomniacs than in controls (125 ±15 versus 114±13 mmHg, p<0.05). ECcr was positively associated with the % slow-wave sleep (r = 0.44, p<0.01) and negatively with % of stage 2 sleep (r = -.34, p<0.05). The % of slow-wave sleep and the diagnosis of insomnia accounted for 30% of the variance of estimated eCcr in the multivariate model (p<0.01).

Conclusion: Our data suggest that insomnia and poor sleep are associated with lower filtration capacity of the kidneys in otherwise healthy subjects. Insomnia, which is a highly frequent complaint in both early stage and end-stage chronic kidney disease, could contribute to the further deterioration of kidney function in patients with chronic kidney disease.

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0560

USE OF CARDIOPULMONARY COUPLING IN PRIMARY INSOMNIA

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Introduction: To investigate the association between electrocardiogram (ECG)-based cardiopulmonary coupling algorithm and polysomnography (PSG) in primary insomnia patients. New, less-invasive methods to assess sleep quality over time in the home environment have the potential to improve treatment monitoring in insomnia patients.

Methods: Individuals with primary insomnia (PI) (6F and 6M; age=39.4 ± 9.6 yrs) and normal controls (NC) (4F and 5M; age=35.7 ± 7.4 yrs) were recruited into the study. Overnight PSG was performed, including ECG. Cardiopulmonary coupling (CPC) is an automated algorithm that uses the ECG signal to objectively measure sleep quality. PSGs were scored according to 2007 AASM criteria. Comparisons were based on CPC measures of sleep quality generated in mean percent of the windows analyzed for high frequency coupling (HFC), low frequency coupling (LFC), very low frequency coupling (VLFC) and other frequencies.

Results: T-tests were performed to assess group differences on CPC measures. NC and PI differed on HFC (57.3% vs. 34.5%; p=.008) and LFC (30.7% vs. 45.4%; p=.024) and trended toward differences on VLFC (11.6% vs. 18.0%; p=.062) and other frequencies (0.46% vs. 2.1%; p=.067). Further, NC and PI differed on eLFC broad band (17.2% vs. 29.4%; p=.007) but not on eLFC narrow band (0.59% vs. 0.91%; p=.649).

Conclusion: These results suggest that CPC measures may provide relatively low-cost, clinically useful insight into the sleep quality of patients diagnosed with primary insomnia, and possibly into monitoring the effects of therapy.

0561

5-HTTLPR POLYMORPHISMS AND VULNERABILITY TO STRESS-RELATED SLEEP DISTURBANCES

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Introduction: The short (S) allele of the serotonin transporter gene promoter (5-HTTLPR) is associated with chronic insomnia; specifically with poor sleep quality in individuals exposed to chronic stress. The Ford Insomnia in Response to Stress Test (FIRST) measures trait-like vulnerability to stress-related sleep disturbance and predicts occurrence of chronic insomnia. We hypothesized that the S allele of 5-HTTLPR would be associated with vulnerability to stress-related sleep disturbance as measured by higher FIRST scores.

Methods: Sleep, mood, and other behaviors of 249 first-year college students (mean age 18.2 years (ages 17-21), 124 males) were assessed using an online survey, including the FIRST. DNA was obtained from buccal cells, and genotyping of the 5-HTTLPR and SNP rs25531 A/G polymorphisms was performed. The low-expressing S and LG alleles were designated S′ and the high-expressing LA allele was designated L′.

Results: Mean FIRST scores did not differ across genotype groups (S'/S', S'/L', L'L') (F2,246=0.5, p=0.6), nor did the genotype distribution or allelic frequencies differ between "high FIRST" vs. "low FIRST" groups (defined by median-split). Male carriers of 1-2 copies of L (long allele, LG and/or LA) had significantly higher FIRST scores than males with two copies of S (S/S: 17.0±6.0 vs. S/L&L/L: 19.2±5.4, t=2.1, df=122, p=0.04). We observed a similar trend using the L'S' model: (S'/S': 17.4±6.0 vs. S'/L'&L'/L': 18.4±5.6, t=1.9, df=122, p=0.05). Males with at least one L' allele were over-represented in the "high FIRST" group and carriers of two S' alleles were under-represented in the "low FIRST" group ($\chi2$=4.5, df=1, p=0.03).

Conclusion: These data show an association between higher expressing 5-HTTLPR allele and risk for stress-related sleep disturbance in male first-year students. These findings add evidence to the model of an association between the serotonin transporter expression level and the spectrum of stress-related disorders, the direction of the link being mediated by sex among other factors.

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0562
PATTERNS OF INSOMNIA IN OBSTRUCTIVE SLEEP APNEA PATIENTS WHO ARE ADHERENT TO CPAP

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Introduction: Insomnia frequently co-occurs with Obstructive Sleep Apnea (OSA) and there is evidence that insomnia persists despite effective treatment of OSA. In order to separate insomnia symptoms due to OSA from independent insomnia symptoms, we examined the patterns of insomnia in OSA patients adherent to CPAP.

Methods: We analyzed Insomnia Severity Index (ISI) item scores in 35 OSA patients who used CPAP therapy ≥ 4 hours per night during the first 30 days of treatment (Average use 384±78.6 minutes). The ISI was completed prior to initiation of CPAP and an average of 43±6.6 days post CPAP initiation. ISI items are scored on a 0-4 scale with scores of ≤ 1 representing none/mild symptoms and scores of ≥2 representing moderate to very severe symptoms. Patients were classified into one of two insomnia symptom patterns, which were defined as: RESPONDERS (≥ moderate pretreatment symptoms and none/mild follow-up symptoms) and PERSISTERS (≥ moderate symptoms at both time points).

Results: 51.4% (N=18) of patients were classified as responders and 48.6% (N=17) as persisters. Compared to the persisters, responders experienced greater reductions in insomnia symptoms following treatment (total insomnia score reductions of 4.2 vs. 1.9; t=2.7, p = .012). At follow-up, responders had significantly lower scores than persisters for falling asleep (0.33 vs. 1.41, t=-4.6, p < .001), staying asleep (0.56 vs. 1.82; t=-5.2, p < .001), waking too early (0.56 vs. 1.65; t=-4.3, p < .001), and the insomnia subscale (1.4 vs. 4.9; t=-6.6, p < .001).

Conclusion: 1) Treatment of OSA with CPAP is clearly associated with marked reduction of insomnia symptoms for over half of symptomatic patients. 2) These data confirm that a substantial proportion of OSA patients have persistent insomnia symptoms which may require further targeted treatment.

0563
INSOMNIA AMONG SLEEP APNEA PATIENTS AND CONTROLS

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Introduction: Insomnia and obstructive sleep apnea (OSA) often co-exist, but the nature of their relationship is unclear. The aim of this study was to compare the prevalence of initial and middle insomnia between OSA patients and controls with and without OSA symptoms.

Methods: Two groups were compared in this study, OSA patients (n=824) and a control group of individuals, 40 years and older from the general population in Iceland (n=724). The control group was subdivided into individuals without (n=630) and with (n=88) OSA symptoms (habitual snoring and witnessed apneas). The prevalence of insomnia was evaluated in these groups and the relationship between OSA and insomnia symptoms was examined. All subjects answered the same questionnaires on health and sleep and OSA patients underwent a sleep study. Altogether, 53% of controls were males compared to 80% of OSA patients. The mean age among controls was 54.4 and 56.3 among OSA patients.

Results: The majority of OSA patients (57.6%) reported difficulties maintaining sleep (DMS) compared to 32% of controls (p<0.001). Difficulties initiating sleep (DIS) was reported among 15% of OSA patients compared to 14% of controls. Symptoms of DMS were reported among 36.7% of controls with OSA symptoms compared to 29.9% of controls without OSA symptoms (p=0.194). Symptoms of DIS were reported among 17.8% of controls with OSA symptoms compared to 13.3% of controls without symptoms (p=0.251). Symptom of DIS and DMS were not related to OSA severity but the co-existence of OSA and insomnia had an additional negative affect on quality of life estimated by the Short Form 12.

Conclusion: DMS is almost twice as common among OSA patients compared to controls while the prevalence of DIS is similar between the groups. It is possible that DMS is rather a symptom of OSA than a primary insomnia symptom among these patients.

0564
TRENDS IN INSOMNIA DIAGNOSIS AND COMORBID DISORDERS IN AN EPIDEMIOLOGICALLY REPRESENTATIVE SAMPLE OF OVER 31 MILLION PATIENT VISITS FOR INSOMNIA (ICD9-CM CODE780.52) IN THE US FROM 1995 TO 2006

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Introduction: We examined the trends in insomnia diagnosis, and its comorbidity with all major diagnostic categories in the ICD9-CM,from an epidemiologically representative sample of an estimated 31 million patient visits with the diagnosis of Insomnia (ICD-CM code780.52) from 1995-2006. To our knowledge, there are no studies of insomnia from an epidemiologically representative sample in the US.

Methods: Data collected between 1995-2006 by the National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Care Survey (NHAMCS),which are nationally representative samples of health care visits in the USA, were studied. For each patient visit upto 3 medical diagnoses are documented by physicians using the ICD9-CM

codes. Visits where at least one of 3 possible diagnoses was Insomnia (ICD9-CM code 780.52) were studied.

Results: There were an estimated 31,038,892(±SE)(±2,004,876)patient visits(unweighted count=1512) with the diagnosis of Insomnia (ICD9-CM code 780.52): 63.4%(±2.1%)female and 36.6%(±2.1%)male; 82.3%(±2.4%)'white',10.7%(±1.8%)'black'; mean± age:42.48±0.20 years. The odds ratio(OR) for Insomnia diagnosis from 2001-2006 versus 1995-2000 was 1.34(95%CI 1.08-1.67), with the greatest increase among the <19 years age group(OR=2.99, 95%CI 1.29-6.94)followed by the 41-65 yrs age group (OR=1.44, 95%CI 1.11-1.87). The comorbidity of Insomnia with other ICD9-CM diagnostic groups was the highest for the following groups of disorders: Mental(OR=5.92, 95% CI 4.89-7.17), Musculoskeletal(OR=1.49, 95%CI 1.16-1.90),Endocrine (OR=1.48, 95%CI 1.14-1.94),and Circulatory(OR=1.33, 95%CI 1.004-1.77). The most common mental disorders associated with Insomnia diagnosis were: Depression Not Elsewhere Classified (ICD9-CM 311)(27.8%), Anxiety State Unspecified (ICD9-CM 300.00)(19.9%), Neurotic Depression (ICD9-CM 300.4)(15.0%), Attention Deficit Disorder with Hyperactivity (ICD9-CM 314.01)(4.7%),and Panic Disorder(ICD9-CM 300.01)(3.6%).

Conclusion: The diagnosis of insomnia has increased progressively from 1995 to 2006, with the greatest increase among the <19 years age group. Insomnia is most commonly comorbid with Mental Disorders, the most common comorbidities being the unspecified depressive (27.8%) and anxiety(19.9%) disorders. Insomnia patients should be routinely assessed for psychiatric comorbidity.

0565

BRAIN STRUCTURAL DAMAGE IN IDIOPATHIC REM SLEEP BEHAVIOR DISORDER

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Introduction: Idiopathic Rapid Eye Movement Sleep Behavior Disorder (iRBD) often precedes the onset of α-synucleinopathies, as Parkinson disease (PD) and Dementia with Lewy bodies (DLB). Aim of this study was to assess in vivo the presence of brain abnormalities in iRBD patients. We evaluated both grey matter (GM) and white matter (WM) by Magnetic Resonance Imaging (MRI) and Diffusion Tensor Imaging (DTI) and we made comparisons between iRBD and age-matched controls.

Methods: We studied 10 iRBD patients (9 males, 1 female, mean age= 68.6 years, mean age of RBD onset = 61.1 years) and 16 age- and gender-matched control subjects (10 males, 6 females, mean age= 64.8 years). Each patient underwent a complete neurological interview and examination to assess the presence of clinical features suggestive for RBD, and to exclude any other sleep disturbance. To confirm the iRBD diagnosis, all patients underwent full nocturnal polysomnographic (PSG) recording. We acquired high-resolution anatomical images of WM and GM and performed whole-brain comparisons between iRBD and control subjects. We used Voxel-Based Morphometry (VBM) to study the cortical volume and we analyzed DTI images using Tract-Based Spatial Statistic (TBSS) to evaluate WM microstructure. Probabilistic tractography was used to identify the WM tracts involved in the pathology.

Results: iRBD patients showed significant reduction of fractional anisotropy (FA) in the right parieto-temporal area, which is compatible with an involvement of the Superior Longitudinal Fasciculus (SLF). Using VBM, iRBD patients had a significant decrease of GM volume the right supramarginal gyrus (BA 40), a region anatomically close to the area with reduced FA. These results are consistent with published clinical data, reporting an impairment in visuo-spatial abilities in RBD patients, but also with the hypothesis of a link between iRBD and α-synucleinopathies given the observation of parieto-occipito-temporal damages both in non-demented PD and DLB patients.

Conclusion: iRBD patients showed changes in grey and white matter regions known to be involved in visuo-spatial abilities and that exhibit neurodegenerative pathology in early PD or DLB. Our results suggest that iRBD-related abnormalities can be detected in vivo with VBM and DTI, widely available MRI techniques.

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0566

MOTOR IMPROVEMENT DURING RBD IN MSA

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Introduction: Multiple system atrophy (MSA) is an atypical parkinsonism characterised by severe motor disabilities that are poorly levodoparesponsive. Most patients develop REM sleep behavior disorder (RBD). Because parkinsonism is absent during RBD in patients with Parkinson's disease, we studied the movements of patients with MSA during REM sleep.

Methods: Forty-nine non-demented patients with MSA and 49 patients with idiopathic Parkinson's disease were interviewed along with their 98 bed partners using a structured questionnaire. They rated the quality of movements, vocal and facial expressions during rapid eye movement sleep behavior disorder as better than, equal to, or worse than the same activities in an awake state. Sleep and movements were monitored using video-polysomnography in 22/49 patients with MSA and in 19/49 patients with Parkinson's disease. These recordings were analysed for the presence of parkinsonism and cerebellar syndrome during REM sleep movements.

Results: Clinical RBD was observed in 43/49 (88%) patients with MSA. Reports from the 31/43 bed partners who were able to evaluate movements during sleep indicate that 81% of the patients showed some form of improvement during RBD. These included improved movement (73% of patients; faster, 67%; stronger, 52%; and smoother, 26%), improved speech (59% of patients; louder, 55%; more intelligible, 17%; and better articulated, 36%), and normalised facial expression (50% of patients). The rate of improvement was higher in Parkinson's disease than in MSA, but no further difference was observed between the two forms of MSA(predominant parkinsonism vs. cerebellar syndrome). Video-monitored movements during REM sleep in patients with MSA revealed more expressive faces, and movements that were faster and more ample in comparison to facial expression and movements during wakefulness. These movements were still somewhat jerky but lacked any visible parkinsonism. Cerebellar signs were not assessable.

Conclusion: We conclude that parkinsonism also disappears during RBD in patients with MSA, but this improvement is not due to enhanced dopamine transmission because these patients are not levodopasensitive. These data suggest that these movements are not influenced by extrapyramidal regions; however, the influence of abnormal cerebellar control remains unclear. The transient disappearance of parkinsonism here is all the more surprising since no treatment (even dopaminergic) provides a real benefit in this disabling disease.

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0567

REM BEHAVIOR DISORDER IS ASSOCIATED WITH DEPRESSION IN PARKINSON'S DISEASE

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Introduction: REM Behavior Disorder (RBD) and depression are common and debilitating problems in Parkinson's disease (PD). To our knowledge, no study has evaluated the relationship between depression and objective measures of RBD in PD. We hypothesized that PD patients with RBD experience more depressive symptoms than PD patients without RBD.

Methods: 51 PD patients (Men=35; Age=68±9.7yrs) underwent PSG assessing RBD (REM without atonia; EMGscore=average of tonic and phasic REM activity) and completed the Beck Depression Inventory (BDI) and RBD Screening Questionnaire (RBDSQ). Patients were classified into diagnostic categories: yes-RBD (n=22; EMGscore≥10% plus RBDSQ≥5 or observed-RBD), no-RBD (n=16; EMGscore<10% plus RBDSQ<5), or probable-RBD (n=18; EMGscore≥10% or RBDSQ≥5). Mean BDI scores differences were assessed with ANOVA. Associations between RBD and BDI were tested using hierarchical linear regression adjusting for age and AHI.

Results: There was a significant differences in mean BDI scores between RBD classifications [$F(2,50)$=4.67; p=0.014]. Post-hoc analyses suggested that yes-RBD (M =12.27, SD=6.94) and probable-RBD (M=12.54, SD=7.33) groups endorsed more depressive symptoms compared those in the no-RBD group (M=6.5, SD=4.41). A restricted regression model including age and AHI explained significant propor-

tion of the variance in BDI [R2=0.12, F(2,48)=3.33, p=0.044] with age significantly predicting BDI (β=-0.251, t=-2.52, p=0.015). The addition of the categorical variable of RBD diagnosis significantly increase the variance explained in BDI [ΔR2=0.09, F(2,47)=5.63, p=0.021]. When the categorical data were replaced with continuous variables representing RBD severity (RBDSQ and EMGscores), the variance explained in BDI significantly increased (ΔR2=0.15, F2,46=4.86, p=0.012; RBDSQ (β=0.64, p=0.029; age β=-0.249, p=0.011; EMGscore and AHI not significant). This full model (AHI, age, RBDSQ and EMGscore) explained significant proportion of variance in BDI score [R2=0.28, F(4,46)=4.36, p=0.005].

Conclusion: Preliminary results suggest that PD patients with RBD have significantly more depressive symptoms than those without RBD. Furthermore, RBD symptoms are an independent predictor of depression in our PD population after controlling for AHI and age.

0568

USING POLYSOMNOGRAPHY AND CLINICAL HISTORY TO DIAGNOSE REM SLEEP BEHAVIOR DISORDER IN PARKINSON'S DISEASE: A PROPOSED CLASSIFICATION SYSTEM

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Introduction: Sleep Behavior Disorder (RBD) is a parasomnia that involves acting out violent dreams with loss of muscle atonia during REM sleep. There is a need for consistent and validated methodology for diagnosis and classification of RBD. We aimed to assess and validate existing cutoff scores for diagnostic measures of RBD in Parkinson's Disease (PD). We hypothesized that a combination of objective and subjective measures would increase diagnosis accuracy.

Methods: 51 PD patients (age=68.1±9.69yrs, 35-males) underwent an overnight PSG and clinical evaluation using the REM behavior screening questionnaire (RBDSQ). EMGscore was computed as the average percent tonic and phasic EMG muscle activity during REM sleep. Previously validated cutoff scores of RBDSQ≥5 and EMGscore≥10, observational data from the technician notes, and PSG-synchronized video recording were used to assess sensitivity and specificity of these diagnostic methods alone. Patients were then classified into 3 groups according to both the RBDSQ and the EMGscores (yes-RBD: EMGscore≥10% plus RBDSQ≥5; no-RBD: EMGscore<10% plus RBDSQ<5; probable-RBD: EMGscore≥10% or RBDSQ≥5) and sensitivity and specificity were calculated using video/technician observational data.

Results: The EMGscore≥10% as gold standard for RBD diagnosis showed that the RBDSQ≥5 results in a sensitivity of 58% and specificity of 90%. Using the RBDSQ as gold standard for RBD diagnosis, the EMGscore≥10% revealed sensitivity of 84% and specificity of 65%. Using video/technician observation as gold standard the EMGscore≥10% showed a sensitivity of 100% and a specificity of 53% and the RBDSQ≥5 yielded a sensitivity of 92% and a specificity of 66%. Finally, using the behavioral observations as a gold standard for diagnosis, the classification into the 3 groups based on both methods showed a sensitivity of 92.9% and a specificity of 78.9%.

Conclusion: These results suggest that subjective and objective measures for RBD diagnosis can be combined to improve sensitivity and specificty of RBD diagnosis in PD. Based on our data, an RBD classification is proposed: Those with confirmed observation of RBD during

PSG or with PSG findings and history should be considered as yes-RBD. Those with either a history but no PSG findings or PSG findings but no history should be considered probable-RBD.

0569

CLINICAL AND POLYSOMNOGRAPHIC CHARACTERISTICS OF PATIENTS WITH RAPID EYE MOVEMENT SLEEP BEHAVIOR DISORDER

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Introduction: Rapid eye movement sleep behavior disorder (RBD) is an age related chronic parasomnia and predominantly affects males. This illness has not received much attention in Chinese community. We investigate clinical characteristics and polysomnographic sleep between late-onset and early-onset RBD patients.

Methods: Twenty-eight consecutive patients fulfilling the criteria for RBD were studied. All patients were divided into two groups of early-onset (n=10, female 6) and late-onset (n=18, female 3), on the basis of the onset age with cutoffs at ≤ 50 and >50 years. Two patient groups had their respective sex- and age-matched healthy controls. All subjects were required to fill a 13-item self-reported RBD questionnaire (RBDQ-HK) and underwent an overnight polysomnographic assessment.

Results: Compared to early-onset group (60%), late-onset group (17%) had less percentage of female (p<0.01). RBDQ-HK revealed that late-onset patients had significantly more motor behaviors in responses to dream (39.59±9.95 vs.29.00±7.32, p<0.001), including limb movements (7.33±2.38 vs. 4.40±2.46, p<0.01) and falling out of bed (3.89±1.75 vs. 2.00±2.67, p<0.05), relative to those of early-onset patients. Compared to controls, both early-and late-onset groups had significantly more dream related behaviors (e.g., talking, shouting, punching, kicking and sleep related injuries). For polysomnographic data, both late-onset (41.81±29.27 vs. 73.27±26.31 min, p<0.01) and early-onset (42.50±26.71 vs. 67.55±25.82 min, p=0.08) patients had less duration and percentage of slow wave sleep, compared to their respective controls. No differences were obtained in other measures of sleep relative to controls, and did not differ between late- and early-onset groups in sleep measures.

Conclusion: The current investigation suggests that 1) female RBD is not rarely seen, 2) late-onset patients have more severe dream enacting behaviors than early-onset patients do, 3) both late- and early-onset patients have less amount of slow wave sleep. In contrast to the literature, the later finding provides novel data suggesting that RBD patients appear to have low quality of sleep reflected with reduced slow wave sleep.

0570

DEVELOPMENT OF REM SLEEP BEHAVIOR DISORDER SEVERITY INDEX AS A TOOL FOR EVALUATING TREATMENT EFFICACY

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Introduction: REM sleep behavior disorder (RBD) patients are not always aware of nocturnal behaviors, and response to treatment is usually dependent on observation by a bed partner or family members. In Japan where most of the elderly couples sleep in a separated bedroom, it is often difficult to estimate alteration in nocturnal behaviors. Patients seem to report less vivid dreams with neutral emotions when violent

behaviors and/or vigorous sleep talk were under control, however, this tendency has not been well investigated. We developed a questionnaire for evaluating dream frequency and intensity by RBD patients and their behaviors by family members to see whether it could be used as a tool for evaluating treatment efficacy even in a patient who lives alone.

Methods: Consecutive 28 patients (man 24/ woman 4, age:67.2±7.1 years) with idiopathic RBD (iRBD) who came to our clinic from October 2005 to December 2009 were studied. RBD severity index (RBDSI), which is composed of four questions about frequency and intensity of the dreams for patients (RBDSI-A) and six questions about observed behaviors for his/her bed partner or family members (RBDSI-B), were performed twice or more, mostly before and after treatment by clonazepam. Seven patients were excluded from the analysis who responded the questionnaire only once.

Results: RBDSI-A decreased from 10.9±3.1 (range 4-16) to 7.3±2.8 (range 3-15) and RBDSI-B decreased from 14.2±4.1 (range 7-21) to 7.9±4.9 (range 0-18), and RBDSI-A and B scores are significantly correlated. Clonazepam was effective, which was clearly shown by decrease in RBDSI-A and RBDSI-B. There were five patients with no medication in whom both RBDSI-A and RBDSI-B decreased as time went by.

Conclusion: RBDSI could be used to assess the efficacy of drug treatment in most of the patients, and it could also be applicable for evaluating the natural course. RBDSI-A seems to reflect severity of iRBD to some extent, therefore, it could be a workable tool to evaluate nocturnal behaviors of iRBD patients who have no observer.

0571

SLEEP-RELATED EATING DISORDER AND OBSTRUCTIVE SLEEP APNEA

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Introduction: Sleep-related eating disorder (SRED), consisting of recurrent episodes of eating following arousal from nighttime sleep, is frequently associated with other sleep disorders in particular parasomnias. A strong association with obstructive sleep apnea (OSA) has not been reported in patients with SRED and it is unclear whether OSA is a cause or consequence of SRED. We present a retrospective review of 39 cases of SRED with specific attention towards the prevalence of OSA.

Methods: Retrospective review of records of patients, diagnosed with SRED at Winthrop University Hospital from April 2005 to December 2010, detailing demographic, clinical and polysomnographic characteristics.

Results: 39 patients(54% females / 46% males) with age ranging 21-75 years(mean: 48.1+/-15.0) with BMI 21.5-50.8(mean31.1+/-6.4) diagnosed with SRED, described variable symptoms including nocturnal eating(100%), snoring(77%), EDS(74.36%), sleepwalking(46.15%), sleep talking(25.64%), insomnia(81.6%). All patients with insomnia(100%) reported difficulty in maintenance of sleep(95% CI 89-100). Nocturnal eating episodes were described as occurring 2-3 times/week with 70.97% endorsing eating "high calorie/high carb" foods. 2 patients acknowledged eating raw bacon/frozen food and one described history of almost causing a fire while trying to cook at night. 37.14% of patients reported full recall, 11.43% no recall, and 51.43% variable recall. Morning anorexia was reported in 15.79% of patients. Mood disorders were noted in 47.37% of patients (72.2% depression, 38.8% anxiety disorder and 22.2% bipolar disorder). Salient polysomnographic features included median sleep latency of 23.0 minutes, sleep efficiency of 32-96 %(mean: 76.8+/- 14.0), % REM sleep 1.2- 25 %(mean: 14).OSAS was noted in 73.53% (95% CI 56.9%-85.4%), with Apnea Hypopnea Index (AHI) ranging from 0.3-96.6 (median: 10.1).

Conclusion: There is a high prevalence of OSA in patients with SRED. Treatment of OSAS may reduce the number of arousals triggering nocturnal eating episodes and improve SRED. Further studies are needed to confirm this hypothesis.

0572

REM SLEEP BEHAVIOR DISORDER SCREENING QUESTIONNAIRE IN PARKINSONIAN SYNDROMES: VIDEOPOLYSOMNOGRAPHIC CHECK

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Introduction: Videopolysomnography (VPSG) is required by the International Classification of Sleep Disorders to establish a diagnosis of REM sleep behaviour disorder (RBD). VPSG is time and resource consuming in routine clinical practice. In 2004, we developed an RBD screening questionnaire, structured in three sections to evaluate nocturnal sleep quality, RBD and other movement disorders during sleep. The questionnaire explores details of RBD semeiology (vocalisations, motor behaviour, consciousness and dreaming, dream contents upon awakening) and episode frequency. The aim of this study was to verify the reliability of the questionnaire by means of VPSG in patients with a parkinsonian syndrome at onset (≤3 year history).

Methods: We recruited 24 consecutive patients (13 men; 11 women; mean age 59±12 years; disease duration: 19±10 months). The screening questionnaire was administered to patients and, when possible, to their bed partner. All patients underwent VPSG, including EEG, EOG, chin and limb EMG muscles. Sleep stages and the tonic and phasic components of REM sleep were scored according to the American Academy of Sleep Medicine (AASM) criteria.

Results: The questionnaire was positive in four patients, and at least one of RBD episode was recorded during VPSG. VPSG in one patient, who reported only one episode of RBD during his life, disclosed excessive amounts of sustained or intermittent elevation of submental EMG tone and excessive phasic submental or limb EMG twitching during REM sleep, but no RBD episodes were recorded. No RBD episode was recorded in the 19 patients with negative questionnaire.

Conclusion: Although our cohort was small, this study suggests that our RBD questionnaire is reliable in the diagnosis of RBD in parkinsonian syndrome at onset. The use of a semistructured questionnaire does not replace VPSG, but may help sleep specialists suspect RBD.

0573

NOCTURNAL PERIODIC AND NON-PERIODIC LIMB MOVEMENTS IN CHILDREN WITH PARASOMNIAS

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Introduction: Sleep terrors and sleepwalking are two common childhood parasomnias, which occur in deep non-rapid eye movement sleep. Despite widespread prevalence of these disorders, and the recognition that they may arise from incomplete arousal, their pathophysiology is not well understood. We studied the occurrence of obstructive sleep apnea (OSA), periodic Leg movement (PLM), and non-periodic leg movement in patients with parasomnias. Our hypothesis is that nocturnal limb movements can trigger abrupt and incomplete EEG arousals and parasomnias.

Methods: A retrospective review of 1507 consecutive polysomnograms, performed in Children's Mercy Hospital Sleep Diagnostic Unit from October 2007 to November 2010.

Results: One hundred and one patients with parasomnia identified by history underwent polysomnography. The mean age for this group of patients with parasomnias was 6.02 years ± 3.71 (ranged 10 months to 17 years). Of these 101 patients, 34 patients (33.6%) had OSA, and 15 patients (14.8%) had PLM disorder (PLM index>5). Twelve of these 14 patients had one or more episodes of confusional arousals documented on the night of sleep study. In 9 (8.9%) of 14, the confusional arousal was preceded by leg movements.

Conclusion: Both periodic and non-periodic leg movements may be the potential triggers for confusional arousals in children with history of parasomnias.

0574

FEAR OF SLEEP IN TRAUMA-EXPOSED ADULTS WITH CHRONIC NIGHTMARES

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Introduction: Posttraumatic stress symptoms, including nightmares and insomnia, are commonly experienced subsequent to traumatic events. It has been hypothesized that fear of sleep plays a role in these symptoms. Limited research has examined the relationships between trauma exposure, fear of sleep, and posttraumatic stress symptoms.

Methods: Forty-one trauma-exposed adults seeking treatment for chronic nightmares completed measures assessing fear of sleep, PTSD, nightmares, insomnia, and sleep hygiene. Fifty-four percent met criteria for PTSD ($n = 22$).

Results: Pearson product-moment correlations revealed significant relationships between fear of sleep and nightmare frequency ($r = .50$, $p = 0.001$), nightmare severity ($r = .47$, $p < 0.05$), PTSD severity (with nightmare and sleep items removed; $r = .66$, $p < 0.001$), insomnia severity ($r = .46$, $p < 0.05$), and poor sleep hygiene ($r = .34$, $p < 0.05$). Hierarchical regression examined if nightmares predict fear of sleep after controlling for PTSD. The total PTSD score (with nightmare and sleep items removed) was entered at Step 1, explaining 41.0% of the variance in fear of sleep. After entry of nightmare frequency and severity at Step 2, the total variance explained was 46.8 %, $F (3, 37) = 9.98$, $p < .001$. Nightmares explained an additional 6.1% of the variance in fear of sleep after controlling for PTSD, R square change = .06, F change $(2, 34) = 1.94$, $p = .16$. In the final model, only PTSD severity was a statistically significant predictor of fear of sleep.

Conclusion: In a sample of chronic nightmare sufferers with and without PTSD, nightmares did not explain a significant amount of variance in fear of sleep after controlling for PTSD symptoms. This suggests fear of sleep is associated with a broader reaction to trauma than nightmares alone. Data collection is in progress and analyses with full data will be presented.

0575

ACTIGRAPHY FOR ASSESSMENT OF REM SLEEP BEHAVIOR DISORDER IN PARKINSON'S DISEASE

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Introduction: REM sleep behavior disorder (RBD) is a common cause of sleep disruption in Parkinson's disease (PD). A small study recently evaluated actigraphy as a tool to assess RBD symptoms in PD patients and reported that having RBD, defined by RBD Screening Questionnaire (RBDSQ) score, was associated with increased number of actigraphically recorded wake bouts. Our goal was to further investigate this association in a larger sample using both objective and subjective measures to assess RBD.

Methods: 41 PD patients (27 men; mean 67.3 years) underwent simultaneous objective and subjective assessment for RBD by overnight PSG (REM without atonia; EMGscore=average tonic and phasic REM activity) and RBDSQ. Patients wore an actigraph (MiniMitter/Respironics Inc). Sleep/wake variables were calculated (Actiware 5.0) at three sensitivity thresholds (20, 40, and 80 activity counts/epoch). Patients were classified either yes-RBD (n=18; PSGscore≥10% plus RBDSQ≥5 or observed RBD), no-RBD (n=13; EMGscore<10% plus RBDSQ<5), or probable-RBD (n=10; EMGscore≥10% or RBDSQ≥5). Differences in mean number and duration of wake bouts between groups were assessed with ANOVA. Differences in mean number and duration of wake bouts based on standard cutoff RBDSQ score alone (RBD+ = RBDSQ≥5; RBD- = RBDSQ < 5) were assessed using T-tests.

Results: There were no significant differences between the yes-RBD, no-RBD, and probable-RBD groups for mean number (36.5 ±21.8, 27.6 ±10.74, and 39.3 ±27.34) or average duration of wake bouts (1.73 ±0.99, 1.68 ±0.8, and 1.89 ±1.84 min) regardless of threshold. Additionally, there were no significant differences between RBD+ and RBD- groups in mean number (34.9 ±21.24 vs. 33.8 ±20.6) or duration (1.97 ±1.46 vs. 1.52 ±0.73 min) of wake bouts regardless of threshold. There were no group differences in total sleep time or sleep efficiency as measured by PSG.

Conclusion: RBD, whether defined by a combination of subjective and objective criteria or by RBDSQ alone, was not associated with increased number or duration of wake bouts in this small group of PD patients. Additional studies including larger groups of patients may be required to determine if actigraphy has a role in evaluation of RBD.

0576

SUSTAINED RELEASE AND STANDARD PREPARATION MELATONIN FOR THE TREATMENT OF REM SLEEP BEHAVIOUR DISORDER

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Introduction: The aim of this study was to assess the efficacy and safety of melatonin in treating patients with REM sleep behaviour disorder (RBD). We looked at the efficacy of both standard preparation and sustained release melatonin (Circadin®).

Methods: A retrospective study was performed on all patients who were diagnosed with RBD and treated with melatonin from 2005-2010. The department's database and electronic patient records were used to compile the data set. RBD was defined according to ICSD2 criteria.

Results: A total of 42 patients started melatonin for RBD. The mean age was 58.7 years, with 39 males and 3 females. Mean duration of treatment with melatonin was 11.3 months. Patients were divided into 3 groups; idiopathic RBD (n=23), drug induced RBD (n=14) and secondary RBD (n=5). Patients with drug induced RBD were taking a medication known to cause RBD, but which could not be stopped. Secondary RBD included patients with Parkinson's disease and narcolepsy. Of the 42 patients, 27 took sustained release melatonin (mean dose 2.3 mg) and 14 took standard release melatonin (mean dose 3.6mg). Four changed from standard to sustained release melatonin. Two changed from sustained release to standard melatonin. Of the 42 patients, 13 (31%) of patients showed a complete response, 14 (33%) a partial response, 3 (7%) an initial response and 12 (29 %) no response. Of those showing a complete response 75% were taking sustained release melatonin. Of non responders 67% were taking standard preparation melatonin. Side effects were seen in 17% an included rash, abdominal pain, daytime drowsiness or insomnia.

Conclusion: Melatonin appears to be a safe and effective treatment for RBD. Sustained release melatonin appears to be more effective than standard preparation melatonin. Melatonin also appears to be effective in the treatment of drug induced RBD.

0577

VARIATION IN CARDIAC FREQUENCY PRIOR TO THE ONSET OF SLEEPWALKING EPISODES

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Introduction: Some pilot data suggest that cardiac activation may precede the onset of sleepwalking episodes, but findings were limited by a small sample size and methodological considerations. The present study investigated cardiac autonomic modulation in the minutes and seconds preceding sleepwalking episodes in a larger sample and with more advanced techniques.

Methods: Participants were 17 subjects (8 women, 9 men, aged 29 ± 8 years) who met ICSD diagnostic criteria for sleepwalking. Each experienced a somnambulistic episode in the sleep laboratory following 25 hours of sleep deprivation. Electrocardiographic recordings preceding each episode were investigated. Heart rate variability in both time and frequency domains was used to compare cardiac autonomic modulation from min 3 to episode onset (segA) and from min 6 to 3 (segB). Time domain analyses included mean R-R interval (RR) and standard deviation of RR (sdRR). Frequency domain analyses included power in the low and high frequency band of RR variability (LF and HF) in both absolute and normalized units and LF/HF ratio. Changes in RR were also assessed over the 5 seconds preceding episode onset compared to the average RR from the 2 preceding minutes.

Results: There was a significant reduction in sdRR (from 44 ± 18 ms to 37 ± 14 ms, $p < 0.001$) and total power (from 2132 ± 1965 ms2 to 1617 ± 1298 ms2, $p < 0.001$) from segB to segA. LF and HF in absolute value also decreased with no change in the normalized units and LF/HF ratio. RR also slightly decreased in the five RR intervals preceding the sleepwalking episodes ($p < 0.05$.

Conclusion: These findings indicate that a significant change in the cardiac modulation of RR occurs during the 3 minutes prior to sleepwalking onset, and that both branches of the autonomic nervous system are affected. A further activation occurs in the seconds immediately preceding episode onset.

0578

FREQUENCY OF PARASOMNIAS IN PATIENTS WITH NON-EPILEPTIC SEIZURES

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Introduction: PNES have been associated with a history of psychosocial stresssors, an association that has also been suggested for certain types of parasomnias. There is little data on frequency of parasomnias in patients with PNES.

Methods: We selected a cohort of patients (n=9) with video-EEG (vEEG) confirmed PNES from our Epilepsy Monitoring Unit database and administered sleep questionnaires (Epworth Sleepiness Scale, Munich Parasomnia Scale) on follow-up visits and phone interviews. An age-matched group of patients with vEEG-confirmed epilepsy (n=9) were interviewed for comparison. Participants were scored based on frequency of responses to questions relating to twenty- one distinct parasomnias. Results were converted to categorical data and responses

of PNES patients were compared to epilepsy patients using Chi square analysis (SPSS v16).

Results: PNES patients reported a higher frequency of NREM parasomnias when compared to epilepsy patients, notably hypnic jerks (77.8% vs. 11.1%, p=0.004), rhythmic foot movements (55.6% vs. 0%, p=0.023), exploding head syndrome (44.4% vs. 0% p=0.023), and bruxism (66.7% vs. 0%, p=0.003). No patients in either group reported symptoms of REM Behavior Disorder. There was no significant difference in subjective sleepiness as determined by Epworth scores.

Conclusion: Patients with PNES in our study population had a higher reporting frequency of NREM parasomnias when compared to epilepsy patients, and a much higher frequency when compared to general population prevalence estimates. This may be due to a higher prevalence of psychosocial stressors in this population. Parasomnias should always be considered in the differential of paroxysmal nocturnal events in these patients.

0579

ELEVATED C-REACTIVE PROTEIN (CRP), BUT NOT INTERLEUKIN-6 (IL-6) OR TUMOR NECROSIS FACTOR ALPHA (TNF-A), IS ASSOCIATED WITH PERIODIC LIMB MOVEMENTS (PLMS)

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Introduction: The inflammatory markers CRP, IL-6, and TNF-a are associated with cardiovascular disease risk and with some conditions of disordered sleep, including obstructive sleep apnea. While restless legs syndrome is known to be associated with cardiovascular disease, the mechanism for this relationship is unknown. We evaluated the association between PLMS and inflammation as a possible mechanism for this relationship.

Methods: A convenience sample was assembled of 167 RLS and/or PLMS patients evaluated at the Emory Sleep Center for whom leg actigraphy (PAM-RL, Philips Respironics) results were available while the patients were not taking dopaminergic, opiate, or gabapentin medications. Banked plasma was assayed for hsCRP by nephelometry (Dade-Behring) and for IL-6 and TNF-a by fluorokine multianalyte profiling (R&D Systems). CRP was categorized as low-normal (<3 mg/L) or high (3-10 mg/L); values > 10 were excluded as likely reflecting acute inflammation. IL-6 and TNF-a were divided into quartiles and lowest versus highest quartiles compared. Information about subjects' demographic and clinical features was collected from research and clinical databases.

Results: Mean PLMI was significantly higher among those with elevated CRP levels (40.2/hr vs 26.1/hr, t = -2.10, p = 0.04), but did not differ between those with high versus low IL-6 or high versus low TNF-a. In an unadjusted logistic regression model, the OR for each PLM/hr was 1.015 (95% CI 1.003, 1.03). After adjustment for age, race, gender, diabetes, hypertension, hyperlipidemia, CRP-lowering medications, and clinically-suspected sleep apnea, the OR for each incremental PLM/hr was 1.016 (1.001, 1.03).

Conclusion: PLMS are associated with increased CRP, with a single PLM per hour corresponding to a 1.5% increased risk for elevated CRP. After controlling for relevant confounders, the relationship between PLMS and CRP remains apparent. Further investigation into the relationship between PLMS and inflammation is warranted.

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0580

THE MU OPIATE RECEPTOR KNOCK-OUT MOUSE SHOWS INCREASED SENSITIVITY TO PAIN, INCREASED MOTOR ACTIVITY DURING THE SLEEP PERIOD AND DECREASED SERUM IRON PARALLEL TO HUMAN RESTLESS LEGS SYNDROME

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Introduction: Opioids are a well accepted second line therapeutic agent for Restless Legs Syndrome(RLS). The opioid effect is opiate receptor specific based upon receptor blocking studies. We have previously shown in an autopsy study and in an in-vitro animal model that hypofunction of the endogenous opioid system seems to play a role in RLS. Our data and the data of others, in combination, suggest that RLS is characterized by relative deficiencies in the endogenous opioid, dopamine and iron systems.

Methods: In the current in-vivo study we utilized mu opiate receptor Oprm1 knock-out mice and control (wild type) mice. We studied serum iron and the circadian pattern of motor activity as measured by wheel running.

Results: The Oprm1 knock out mouse is characterized by an increased sensitivity to pain as has been demonstrated in human RLS in 2 different studies. In mice the sleeping period is during the day. In the Oprm 1 knock out mouse there is increased motor activity during the normal sleeping period compared to controls as in human RLS (P <.05). Serum iron is decreased in the Oprm1 knock out mouse compared to controls as is comparable to the decrease in serum of the iron binding protein ferritin in human RLS(p <.001).

Conclusion: Opiate receptor knock out mice demonstrate 3 features to date characteristic of human RLS: (a) increased sensitivity to pain; (b) increased motor activity during the normal sleep period; and (c) decreased serum iron related levels. The next step is to measure Periodic Limb Movements in Sleep (PLMS) in the mice and to determine if the brains of the mu opiate receptor deficient mice show iron deficiency, down regulation of Dopamine D2 receptors and up regulation of the rate limiting step for dopamine synthesis, Tyrosine Hydroxylase, as in human RLS.

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0581

WHICH RECEPTOR SUBTYPE IS THE TARGET OF DOPAMINE-AGONISTS IN RESTLESS LEGS SYNDROME?

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Introduction: Dopamine-agonists are the first line treatment in restless legs syndrome and periodic leg movements. However, we still ignore which dopamine receptor subtype is targeted by these compounds. The aim of this study was to compare the efficacy of equivalent low dosages of the most selective D3 receptor subtype dopamine-agonist available pramipexole and that of the most selective D2 receptor subtype bromocriptine on restless legs syndrome.

Methods: A placebo-controlled prospective investigation was carried out on 45 drug naïve patients with idiopathic restless legs syndrome. Each patient underwent two consecutive full night polysomnographic studies, the first recording was performed without pre-medication, before the second recording one group received a single oral dose of 0.25 mg pramipexole and a second group a single oral dose of 2.5 mg bromocriptine, the remaining patients received placebo. Subjective evaluation of the severity of symptoms was also assessed the morning after each polysomnography.

Results: Subjective symptoms were improved by both compounds, with pramipexole inducing the most important improvement. Side effects were preponderant after bromocriptine. Pramipexole was more effective than bromocriptine in reducing periodic leg movements in patients with a high level of PLM index at baseline. Typical periodic movements (inter-leg movements intervals 10-40) disappeared completely after pramipexole treatment but persisted, even if reduced, after bromocriptine.

Conclusion: This study shows the superior efficacy of a drug targeting D3 receptor subtypes than a drug targeting preferentially D2 subtypes in restless legs syndrome; establishing the specific target of dopamine-agonists in restless legs syndrome has scientific relevance and important clinical implications.

0582

RELATIONSHIP BETWEEN CLINICALLY SIGNIFICANT AUGMENTATION OF RESTLESS LEGS SYNDROME (RLS) AND DOSAGE OF ROTIGOTINE TRANSDERMAL SYSTEM: POST HOC ANALYSIS OF A 5-YEAR PROSPECTIVE, MULTINATIONAL, OPEN-LABEL STUDY

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Introduction: Previous data have shown improvement in RLS symptoms with rotigotine transdermal system across the EU-approved dose range (1-3 mg/24h). Augmentation is the main complication of long-term dopaminergic treatment in RLS. This analysis evaluates the relationship between rotigotine dose and clinically significant augmentation over a 5-year period, to provide additional information on dosing for optimal long-term RLS management.
Methods: SP710 (NCT00498186) was a 5-year, prospective, open-label follow-up of a placebo-controlled phase II trial with rotigotine. Patients were titrated to optimal dose of rotigotine (0.5-4.0 mg/24h) and periodically evaluated for safety and efficacy. A computerized algorithm pre-selected patients who either met the Max Planck Institute (MPI) diagnostic criteria for augmentation (García-Borreguero et al. Sleep Med. 2007;8:520-30) or had discontinued the study following loss of efficacy. These cases were examined by an international expert panel for definite confirmation and evaluation of clinical significance.
Results: Of 295 patients enrolled, 290 entered open-label maintenance and 126 (43%) completed the 5-year follow-up. In 44% of patients the modal (most frequently applied) dose during open-label maintenance was 4 mg/24 h. In 39 (39/295 [13.2%]) patients augmentation was confirmed as clinically significant; 15 (15/295 [5.1%]) were taking EU-approved doses (1-3 mg/24h). The first clinically significant episode occurred more frequently when patients were taking higher doses (4 mg/24h [24 cases], 3 mg/24h [7 cases], 2 mg/24h [8 cases]). The majority of patients who withdrew due to clinically significant augmentation, as assessed by the expert panel, did so while on 4 mg/24h (8 patients; 3 mg/24h [3 patients], 2 mg/24h [1 patient]).
Conclusion: These data represent the first long-term assessment of augmentation outcomes by dose of any RLS treatment. Long-term risk of clinically significant augmentation for patients treated with rotigotine transdermal system increased when dose was titrated above 1 mg/24h, with no further increase observed until dose reached 4 mg/24h. These data suggest augmentation rates are low for the EU-approved dose level (1-3 mg/24h) of rotigotine and, in addition, the risk of augmentation can be mitigated by maintaining RLS patients at their lowest effective rotigotine dose.
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0583

OBSERVATIONAL STUDY OF RESTLESS LEGS SYNDROME (RLS) AND SUBSEQUENT CARDIOVASCULAR (CV) RISK USING US CLAIMS DATA

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Introduction: RLS is a circadian disorder with peak symptoms at night that has a significant motor counterpart in the form of periodic limb movements (PLMs) in sleep. Published data suggest an association between RLS and CV risk. We investigated this association further through analysis of a US observational administrative claims database (IMS Pharmetrics®) investigating risk of major CV events amongst RLS patients.
Methods: A two-year matched retrospective cohort study was performed on a dataset containing longitudinal records on demographics, diagnoses, procedures, providers, prescriptions and claims. Patients with clinical diagnoses of RLS ≥2 visits before December 2005 were continuously enrolled between January 2006 and December 2007. RLS patients were matched 1:1 by age, gender and comorbidities (including hypertension) to healthy controls. CV diagnoses were recorded for the two-year observation period. Relative risks (RR, 95% CI) for specific outcomes by study group were computed.
Results: In total, 3485 RLS patients were matched to 3485 healthy controls. Mean age was 55 years; female/male ratio was 2.34. 33% of the patients with RLS received ≥1 dopamine agonist. Overall, the most frequently observed CV diagnoses during follow-up were hypertension (48%), cardiac dysrhythmias (9.3%), chronic ischemic heart diseases (8.5%), occlusion and stenosis of cerebral arteries (2.81%), cardiomegaly (2.50%), and hypertensive heart disease (2.43%). There was a 12% increase in RR versus healthy controls for developing any CV event during follow-up (p<0.01). RR (95% CI) for CV events by category were, in decreasing order: other forms (non-ischemic) of cardiovascular diseases, 1.33 (1.20; 1.47); cerebrovascular diseases, 1.31 (1.12; 1.53); disease of the pulmonary circulation, 1.28 (0.86; 1.92); ischemic heart diseases, 1.20 (1.06; 1.35); diseases of the arteries, 1.19 (1.01; 1.43); and hypertension, 0.99 (0.84; 1.03).
Conclusion: These data suggest that there is a significant association between a diagnosis of RLS and subsequent records of major CV conditions. Moreover, this study provides a basis to consider RLS as a distinct risk factor in addition to hypertensive disease, and confirms the need for early diagnosis of RLS, to facilitate monitoring of patients for subsequent development of serious CV events.
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0584

ASSOCIATION OF INCIDENT CARDIOVASCULAR DISEASE WITH PERIODIC LIMB MOVEMENTS DURING SLEEP IN ELDERLY MEN: OUTCOMES OF SLEEP DISORDERS IN OLDER MEN (MROS) STUDY

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Introduction: Restless legs syndrome (RLS) is associated with prevalent cardiovascular disease through an unknown mechanism. Periodic limb movements during sleep (PLMS) occur commonly in persons with RLS, causing repetitive sympathetic activation. We hypothesized that PLMS frequency (PLMI) and PLMS arousal frequency (PLMAI) are predictive of incident cardiovascular disease, including coronary heart

disease (CHD), peripheral arterial disease (PAD) and cerebrovascular disease (CBD) in an elderly male cohort.

Methods: 2,911 men (mean age 76 years) in the observational MrOS sleep study cohort underwent in-home polysomnography with measurement of PLMS and were followed four years for the outcomes CHD, CBD, PAD and all-cause cardiovascular disease (cCVD): CHD, CBD or PAD. Cox proportional hazards regression assessed association between PLMI, PLMAI and these outcomes. Models were minimally adjusted for age, clinic and BMI, then fully adjusted for conventional cardiovascular risk factors. Secondary analyses examined the association between incident hypertension and the potential interaction of PLMS with prevalent hypertension.

Results: During the follow-up period, 500 men experienced cCVD: 345 CHD, 117 CBD and 98 PAD events. In fully adjusted models, men with PLMAI>5 compared to the referent PLMA<1 group had 1.26-fold increased relative hazard (RH) for cCVD. Similar findings were observed between increasing PLMI category and cCVD. For PAD, men with PLMI≥30 compared to the referent PLMI<5 group had a 2-fold increased RH (1.14-3.49, p=0.025). Compared to the referent group, men with PLMI ≥30 had an increased risk of CHD (RH=1.31, 1.01-1.70; p=0.045) after minimal adjustment, but this association attenuated after further adjustments. After stratification, the risk of incident cCVD among the high PLMI and PLMAI groups was significantly elevated only for men without prevalent hypertension (p interactions <0.10). There was no association seen between PLMS with CBD or incident hypertension.

Conclusion: These findings provide evidence that PLMS frequency is associated with incident cardiovascular disease in community dwelling elderly men.

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0585

PROSPECTIVE STUDY OF RESTLESS LEGS SYNDROME AND RISK OF ERECTILE DYSFUNCTION

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Introduction: We previously reported that restless legs syndrome (RLS) was cross-sectionally associated with erectile dysfunction (ED). However, to date, the associations have not been examined in prospective studies.

Methods: We prospectively examined whether RLS was associated with a higher risk of developing ED during 6 years of follow-up among 11,113 men (mean age 64 years) free of ED, diabetes and arthritis in 2002 in the Health Professionals Follow-up Study. RLS were assessed using a set of standardized questions in 2002. Men were considered to have RLS if they met four RLS diagnostic criteria recommended by the International RLS Study Group and had restless legs symptoms ≥5 times/month. Erectile dysfunction was assessed by questionnaires in 2000, 2004 and 2008.

Results: We identified 1,979 incident ED cases. Men with RLS were more likely to develop ED (Relative Risk (RR)=1.48; 95% confidence interval (CI): 1.14-1.92, P=0.003) relative to those without the syndrome, after adjusting for age, smoking, body mass index, use of antidepressants, history of several chronic diseases, and other covariates. A higher frequency of symptoms was also associated with an increased risk of ED; the adjusted RRs were 1.38 (95% CI: 1.0-1.9) and 1.66 (95% CI: 1.1, 2.5; P trend = 0.002) for men with RLS symp¬toms 5-14 times/mo, and 15+ times/mo, respectively, relative to those without RLS. Fur-

ther adjusting for the variable indicating sleep disorder attenuated the relative risk of ED slightly (RR=1.41; 95%CI: 1.07-1.86). In the joint analysis, men with RLS and sleep disorder were 1.68 times (95%CI: 1.1-2.6) more likely to develop ED, compared to men with neither RLS nor sleep disorder.

Conclusion: Men with RLS had a higher risk of ED and the magnitude of the risk was increased with a higher frequency of the RLS symptoms. Combination of sleep disorder with RLS further increased the risk of ED.

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0586

PATIENTS WITH RESTLESS LEGS SYNDROME DO NOT HAVE INCREASED COMMON RISK FACTORS FOR CARDIOVASCULAR DISEASE

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Introduction: Restless legs syndrome might represent a condition at risk for cardiovascular disease; the role of sleep periodic leg movements, sleep deprivation, and presence of common risk factors for heart disease in these patients remains to be determined. The aim of this study was to evaluate the eventual presence of risk factors for cardiovascular disease in restless legs syndrome.

Methods: Eighty-seven consecutive patients affected by idiopathic restless legs syndrome were included in this study together with 81 controls. Complete blood count, chemistry, and kidney function test were obtained. We also detected subjects suffering from diabetes mellitus, kidney diseases, heart diseases, disc herniation, neuropathy, blood diseases, liver diseases, artery diseases, dyslipidemia or hypertension. Polysomnography was recorded in 66 and cerebral neuroimaging was obtained in 59 patients with restless legs syndrome.

Results: None of the differences in blood test parameters was statistically significant; however, hypertension was found to be more frequent in controls and dyslipidemia was more frequent in restless legs syndrome patients, but this was explained by its higher frequency in patients also affected by obstructive sleep apnea. A diagnosis of cerebrovascular disease was posed for 14 restless legs syndrome patients (16.1%) but no predictive factor for its presence was found at the binomial logistic regression.

Conclusion: Our findings argue against the presence of an altered lipid metabolism as a risk factor for the development of cerebrovascular disease in restless legs syndrome patients, even if they do support the idea that cerebrovascular disease might be frequent in this condition.

0587

RELATIONSHIP BETWEEN SLEEP BRUXISM FREQUENCY AND UPTAKE ABILITY OF HUMAN PERIPHERAL SEROTONIN TRANSPORTER

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Introduction: Sleep bruxism (SB) would be recognized to relate to serotonin nerve system according to the previous case reports; however this pathogenesis still remained unclear. The aim of this study was to compare the uptake ability of serotonin transporter (SERT) from peripheral platelets between severe and mild bruxism human subjects.

Methods: Subjects were recruited from the trainees of Okayama University Hospital who were recognized to present severe or mild bruxism by initial subjective screening assessment. Individual SB frequency was objectively assessed for 3-consecutive nights by self-contained EMG detector/analyzer system in their home environment. Since this system indicated individual SB level in 4-grades (scores 0, 1, 2 and 3), the whole scores of the 3-night assessments were used as diagnostic criteria to classify mild bruxism subjects (score 0 or 1) and severe bruxism subjects (score 2 or 3). Fasting peripheral venous blood samples were collected in the next morning of the final SB assessment. The amount of SERTs collected from peripheral platelets was quantified by ELISA assay (Uscn Life Science Inc.), and SERT uptake ability was assessed by the [3H+] serotonin uptake assay, immediately after sample collection.

Results: Of which 39 applicants (28.0+/-4.02 yrs, male/female: 12/27), 13 severe bruxism subjects (28.0+/-4.68, male/female: 5/8) and 7 mild bruxism subjects (30.2+/-5.61, male/female: 3/4) were treated as eligible subjects. Gender distribution, mean age and total amount of SERTs showed no significant difference between these groups (p=0.85: Chi-square test, 0.64, 0.46: t-test). However, the [3H+] serotonin uptake was significantly higher in subjects with mild-bruxism than severe bruxism subjects group (12.79+/-1.97, 8.27+/-1.91 fmol/ 105 platelets/ min, p<0.001, t-test).

Conclusion: These results suggested that the SERT ability would be related to sleep bruxism frequency. Further research should be necessary to verify the mechanisms underlying the difference in SERT uptake ability between severe and mild bruxism human subjects.

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0588

LONG-TERM USE OF PRAMIPEXOLE IN THE MANAGEMENT OF RESTLESS LEGS SYNDROME

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Introduction: Few studies have examined the long-term use of dopamine agonists for restless legs syndrome (RLS). We report a cohort study of 50 patients initially prescribed pramipexole in 1998-2002. The objective was to determine duration of treatment, long-term efficacy, and development of side effects and augmentation over an extended period.

Methods: We performed a long-term analysis on a previously reported group of patients initially followed for a mean of 27.2 months (Silber et al Sleep 2003). Data was collected using retrospective chart reviews, written surveys, and systematic telephone interviews.

Results: Pramipexole was used for a mean of 8 years (range 0.6 - 12 years). Nine (18%) discontinued pramipexole because of poor efficacy (4), impulse control disorders (ICD) (2), augmentation (1), and resolved symptoms (2). At the date of last contact, pramipexole was reported completely effective in 40%, partially effective in 58%, and ineffective in 2%, compared to 67% completely effective and 27% partially effective at the end of the initial study. The median daily dose increased from 0.38 mg after initial stabilization to 1.0 mg at the end of the study. 64% of patients experienced side effects. 56% reported daytime sleepiness including 10% reporting sleep attacks while driving. This compared to 5% with sleepiness at the end of the initial study. ICD developed in 10%, including hypersexuality, excessive spending, excessive nighttime eating and pathologic gambling. Augmentation developed in 38% of patients, after a mean of 15 months of treatment (compared to 33% in the initial study).

Conclusion: Although efficacy dropped and dose increased with time, the majority of patients remained on pramipexole. Most cases of augmentation developed within the first 2 years of commencing therapy (overall rate 38%). Sleepiness increased with time and 10% developed ICD. The study highlights the need for further research into alternative non-dopaminergic treatments for RLS.

0589

EFFECTS OF ROTIGOTINE TRANSDERMAL SYSTEM ON SLEEP ARCHITECTURE IN PATIENTS WITH IDIOPATHIC RESTLESS LEGS SYNDROME (RLS): A POST-HOC ANALYSIS OF DATA FROM A RANDOMIZED PLACEBO-CONTROLLED POLYSOMNOGRAPHIC STUDY

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Introduction: In a placebo-controlled study (SP794: NCT00275236), rotigotine transdermal system significantly reduced Periodic Limb Movement (PLM) Index (primary endpoint) in patients with RLS and PLMs in sleep. As PLMs occur predominantly during non-REM (NREM) sleep, their reduction may increase duration of NREM sleep and alter other sleep parameters. Study data were analysed to evaluate the effect of rotigotine on sleep architecture.

Methods: 67 patients were randomized (rotigotine/placebo), titrated to optimal dose (1-3 mg/24h) over 3 weeks and maintained for 4 weeks. Polysomnographic data were recorded on 2 consecutive nights before baseline and before end of maintenance (EoM) and read centrally. This post-hoc analysis was conducted on a subset of patients (rotigotine [31]; placebo [13]) for whom a separate analysis was being conducted, which also generated sleep architecture results.

Results: Baseline to EoM changes were numerically greater with rotigotine versus placebo for total sleep time (LS Mean±SE; 11.2±17.3 mins), wake after sleep onset (-11.1±14.4 mins) and sleep efficiency (2.8±3.4%). Duration of NREM 1 sleep increased from baseline to EoM with rotigotine by 3.8±2.1 mins but decreased with placebo (-3.7±3.3 mins; between-treatment difference, 7.4±3.9 mins). NREM 2 duration increased from baseline to EoM in both groups, but to a numerically greater extent with rotigotine (24.6±8.2 mins) versus placebo (1.3±12.6 mins; between-treatment difference, 23.3±15.0 mins). In contrast, duration of NREM 3 was reduced from baseline to EoM in both groups (rotigotine, -12.3±3.9 mins; placebo, -1.5±6.1 mins; between-treatment difference, -10.8±7.3 mins). REM latency decreased in both groups, but to a numerically lesser extent with rotigotine (-9.8±11.8 mins) versus placebo (-36.3±18.3 mins; between-treatment difference, 26.5±21.8 mins). P>0.05 for all comparisons (ANCOVA).

Conclusion: Primary efficacy data showed a therapeutic effect of rotigotine in reduction of PLM Index in RLS patients. In this post-hoc analysis, a trend towards improved sleep architecture was observed with rotigotine. Improvements did not reach statistical significance, which may be explained by small sample size and short observation time.

Support (If Any): UCB Pharma Inc, delegated by Schwarz Pharma Ltd, Ireland

0590

GABAPENTIN ENACARBIL IN SUBJECTS WITH PRIMARY RESTLESS LEGS SYNDROME WITH AND WITHOUT SEVERE SLEEP DISTURBANCE: SECONDARY ANALYSES OF NOVEL SLEEP ENDPOINTS FROM TWO STUDIES

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Introduction: Novel sleep endpoints were evaluated in gabapentin enacarbil (GEn)-treated subjects with primary Restless Legs Syndrome (RLS).

Methods: Data from two 12-week, multicenter, double-blind, randomized, placebo-controlled studies (XP052 and XP053) of subjects with moderate-to-severe primary RLS were retrospectively pooled for analyses of novel sleep endpoints (comparing GEn 1200mg and placebo groups). Subjects were divided into subgroups based on response to item 4 on the International Restless Legs Scale at baseline: severe/very severe or moderate-to-no sleep disturbance. Two novel sleep endpoints were derived using the sponsor-developed 24-Hour Patient RLS Record: sleep time (ST) and time awake during the night (TAN); these endpoints were compared with similar endpoints derived using the Pittsburgh Sleep Diary (PghSD): total sleep time (TST) and wake time after sleep onset (WASO).

Results: The integrated, modified intent-to-treat population comprised 427 subjects (GEn 1200mg=223; placebo=204). At baseline, 43.8% and 56.2% of subjects reported severe/very severe and moderate-to-no sleep disturbance, respectively. In the severe/very severe sleep disturbance subgroup, GEn 1200mg decreased TAN compared with placebo at Week 12/early termination (ET) (unadjusted mean [SD] change from baseline: -17.2 [175.36] minutes for placebo, -83.1 [177.11] minutes for GEn 1200 mg; chi-squared value for adjusted mean treatment difference [AMTD] using nonparametric analysis of covariance [ANCOVA]: 10.9; P=0.0010); no significant treatment difference was seen for TAN in the moderate-to-no sleep disturbance subgroup (P=0.8047), or in either subgroup for ST at Week 12/ET. GEn 1200mg decreased WASO compared with placebo at Week 12/ET in both subgroups (parametric ANCOVA): severe/very severe sleep disturbance AMTD: -12.7; 95% CI: -20.35, -5.15; P=0.0011; moderate-to-no sleep disturbance AMTD: -4.8; 95% CI: -8.36, -1.15; P=0.0100); no significant treatment difference was seen in either subgroup for TST at Week 12/ET.

Conclusion: Evaluation of sleep endpoints derived using the 24-Hour Patient RLS Record and the PghSD yielded similar results.

Support (If Any): XenoPort, Inc., Santa Clara, CA and GlaxoSmithKline, Research Triangle Park, NC

0591

GABAPENTIN ENACARBIL FOR RESTLESS LEGS SYNDROME: RESULTS FROM INTEGRATED SAFETY DATA

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Introduction: Gabapentin enacarbil (GEn) is a non-dopaminergic treatment under investigation for moderate-to-severe primary Restless Legs Syndrome (RLS). Subject data were integrated to evaluate the long-term safety of GEn in adults with RLS.

Methods: Data from the 52-week open-label extension study XP055 and relevant parent studies were integrated to provide long-term safety information on GEn treatment in RLS. Completers of one of four double-blind placebo-controlled parent studies (XP052, XP053, XP081 [12-week studies], or XP083 [2-week study]) had the option of participating in XP055. This summary includes safety data from all subjects who received GEn in a parent study and all subjects who received GEn in XP055. GEn was dosed once daily at 5PM with food; this grouping included 600mg, 1200mg, 1800mg, and 2400mg.

Results: A total of 777 subjects received at least one dose of GEn; mean (SD) age was 49.3 (12.51) years and 60% were female. Roughly half of subjects (371/777 [48%]) received GEn for ≥12 months and 74% (577/777) received GEn for ≥3 months. Total duration of exposure was highest in the 1200mg group (307.24 subject-years). Somnolence (30%) and dizziness (22%) were the most frequently reported adverse events (AEs) in GEn-treated subjects; each led to withdrawal in 2% (18/777) of subjects. Any AE led to withdrawal of 14% (108/777) of subjects. Serious AEs were reported by 3% (20/777); none were reported more than once. Most subjects reported no RLS symptoms or a delay in time to onset of symptoms based on the 24-hour RLS Symptom Diary at each assessment (Week 12 [78% (303/390)] - Week 64/65 [87% (151/173)]).

Conclusion: The most common AEs were somnolence and dizziness; generally these AEs were not treatment limiting. There was no pattern of earlier RLS symptom onset observed that would suggest augmentation associated with up to 64 weeks of GEn treatment.

Support (If Any): XenoPort, Inc., Santa Clara, CA and GlaxoSmithKline, Research Triangle Park, NC

0592

AN INTEGRATED ANALYSIS OF 600MG AND 1200MG DOSES OF GABAPENTIN ENACARBIL VERSUS PLACEBO IN SUBJECTS WITH MODERATE-TO-SEVERE RESTLESS LEGS SYNDROME (RLS) PARTICIPATING IN THREE 12-WEEK TRIALS

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Introduction: Gabapentin enacarbil (GEn), an investigational non-dopaminergic treatment that provides dose-proportional, sustained exposure to gabapentin, has demonstrated efficacy in reducing RLS symptoms. Data from subjects with RLS who participated in three 12-week trials were retrospectively integrated to evaluate the efficacy and tolerability of GEn.

Methods: Data from three 12-week, multicenter, double-blind, randomized, placebo-controlled studies were integrated for the GEn 600mg, GEn 1200mg, and placebo groups to provide efficacy and tolerability data on GEn treatment in RLS. Analyses evaluated change from baseline in the International Restless Legs Scale (IRLS) total score and proportion of responders on the investigator-rated Clinical Global Impression-Improvement (CGI-I) scale at Week 12 last observation carried forward (LOCF). Safety assessments included treatment-emergent adverse events (TEAEs).

Results: The integrated modified intent-to-treat population comprised 671 subjects (GEn 600mg = 161; GEn 1200mg = 266; placebo = 244). GEn 600mg improved mean [SD] IRLS total score versus placebo from baseline to Week 12 LOCF (−13.8 [8.49] versus −9.3 [8.17]; adjusted mean treatment difference [AMTD]: −4.3; 95% confidence interval [CI]: −6.01, −2.52; P<0.0001). GEn 1200mg improved mean [SD] IRLS total score versus placebo from baseline to Week 12 LOCF (−13.3 [9.25] versus −9.3 [8.17]; AMTD: −3.9; 95% CI: −5.30, −2.46; P<0.0001). More subjects receiving GEn 600mg were CGI-I responders versus placebo (70% versus 42%; adjusted odds ratio [AOR]: 3.1; 95% CI: 1.96, 4.89; P<0.0001). Similarly, more subjects receiving GEn 1200mg were CGI-I responders versus placebo (75% versus 42%; AOR: 4.2; 95% CI: 2.87, 6.14; P<0.0001). The safety population comprised 677 subjects (GEn 600mg = 163; GEn 1200mg = 269; placebo = 245). The two most commonly reported TEAEs (GEn 600mg, GEn 1200mg, placebo) were somnolence (20%, 23%, 5%) and dizziness (13%, 22%, 4%).

Conclusion: GEn 600mg and 1200mg significantly improved RLS symptoms compared with placebo. No new tolerability issues were identified.

Support (If Any): XenoPort, Inc., Santa Clara, CA and GlaxoSmithKline, Research Triangle Park, NC

0593

CLINICAL CONTEXT FOR THE INTERNATIONAL RLS STUDY GROUP RATING SCALE (IRLS): AN ASSOCIATION ANALYSIS BETWEEN THE IRLS AND RLS-6

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Introduction: The IRLS is a validated instrument for measuring restless legs syndrome (RLS) severity. While IRLS is the gold standard for assessing outcome in clinical trials, its clinical context may be underappreciated in routine practice. An association analysis was conducted between the IRLS and RLS-6 (another validated scale for assessing RLS severity, and impact on sleep/daytime sleepiness), to provide clinical context for the IRLS.

Methods: This was a post hoc analysis of a Phase III, double-blind trial (SP790 [NCT00136045]) of patients with moderate-to-severe idiopathic RLS randomized to rotigotine transdermal system (3-week titration to fixed dose [1-3 mg/24 h], then 6-month maintenance) or placebo. IRLS and RLS-6 scale associations were analysed using the safety set (rotigotine and placebo groups combined; n=458), and correlation coefficients were calculated.

Results: For all six RLS-6 items, categorical and continuous variable analyses showed a trend of increasing RLS-6 score with increasing IRLS disease severity categories/scores. Of the four RLS-6 items designed to assess RLS severity, Items 2 (symptom severity when falling asleep), 3 (symptom severity during the night) and 4 (symptom severity at rest) showed strong correlations with IRLS scores at baseline (r=0.56, 0.67 and 0.55, respectively), EoM (r=0.77, 0.84 and 0.77, respectively), and change from baseline to EoM (r=0.63, 0.72 and 0.59, respectively); Item 5 (symptom severity during activity), showed a moderate to strong correlation with IRLS score (baseline, 0.35; EoM, 0.57; change from baseline to EoM, 0.36). IRLS score was also strongly correlated with RLS-6 Items 1 (satisfaction with sleep [baseline, 0.66; EoM, 0.73; change from baseline to EoM, 0.66]) and 6 (daytime sleepiness/tiredness [baseline, 0.63; EoM, 0.64; change from baseline to EoM, 0.51]).

Conclusion: This rotigotine Phase III trial post hoc analysis against the RLS-6 supports the IRLS as a clinically meaningful disease severity scale, and suggests that the IRLS is sensitive to detection of a range of RLS symptoms.

Support (If Any): UCB Pharma Inc, delegated by Schwarz Pharma Ltd, Ireland

0594

LOWER MOLECULAR WEIGHT INTRAVENOUS IRON DEXTRAN FOR RESTLESS LEGS SYNDROME

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Introduction: IV iron holds promise of providing a lasting treatment correcting a basic pathology of restless legs syndrome (RLS), but studies have shown inconsistent results. This prospective study evaluates IV iron dextran treatment of RLS.

Methods: Twenty-one idiopathic RLS patients mean age ±standard deviation 55.52±9.60, 15 (71.4%) female received four weekly intravenous doses of 250mg iron dextran. Subjects on RLS medication were tapered off starting one week after the last IV dose. Blood and CSF were obtained before and 3 weeks after treatment.

Results: After treatment, 16 of the 21 subjects (76%) showed much or complete improvement of RLS symptoms; 10 (48%) showed complete improvement 2 months after treatment and stopped all RLS medications; 5 (24%) showed much improvement with reduced doses of RLS medications; One showed improvement but did not change RLS medication. Eight patients (38%) were remitters (IRLS score ≤ 10). Five (24%) showed no improvement. Changes in IRLS did not significantly correlate with changes in CSF ferritin. The response to IV iron could not be predicted by patients' demographics, nor by either blood or CSF iron baseline characteristics. Means ± SDs for Baseline vs 3 weeks after treatment were CSF ferritin 7.05±2.45 vs 8.58±2.37, Serum ferritin 40.37±38.70 vs 273.51±149.45 (p=0.000), IRLSS 23.57±6.80 vs 16.14±9.56 (p=0.001). RLS symptom improvement started between one and 6 weeks after treatment. Treatment benefits lasted from three months to at least a year with effectiveness continuing for some at the last follow up.

Conclusion: Intravenous iron dextran showed significant improvement of RLS symptoms in 76% of the subjects without any significant adverse effects. CSF ferritin increased after IV iron but had only a weak non-significant relation to treatment effects. Intravenous iron dextran can be used effectively and safely in the treatment of RLS.

0595

PREVALENCE OF RESTLESS LEG SYNDROME IN A VETERAN POPULATION WITH SPINAL CORD INJURIES AND DISORDERS

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Introduction: Sleep disturbances are common among patients with Spinal Cord Injuries and Disorders (SCI/D). Purpose: Determine prevalence of Restless Legs Syndrome (RLS) in a veteran population with SCI/D.

Methods: Using the VA national database, 666 people with SCI/D were identified. Of the 199 meeting inclusion criteria, 162 participated and were screened by mailed questionnaire using diagnostic criteria for RLS. Forty-two interviewed by phone with board certified sleep specialists for confirmation of RLS. Demographic and diagnostic information was collected. Etiology of SCI/D was categorized [trauma, multiple sclerosis (MS), vascular, other/unknown]. Magnetic resonance imaging (MRI) determined location and completeness of spinal cord lesions.

Results: Of the 162 who participated, 101 screened negative and 61 screened positive for RLS. Of the 61 screening positive, 31(51%) confirmed positive RLS by sleep specialists and 11(18%) confirmed negative RLS, and 19(31%) could not be reached. Prevalence of confirmed RLS was 22% (31/143). MS 55% (17/31) and trauma 36% (11/31) were the most common etiologies among RLS patients. Seventy-one percent of patients with RLS received RLS medications, compared to 46% without RLS (P=0.015). Of those with RLS, 89% developed symptoms after SCI/D (P=0.035) and reported greater burden. There was no statistically significant difference in prevalence of RLS between spinal cord levels, or by cross-sectional location or completeness of spinal cord lesions. There was a higher prevalence of RLS in patients with both cervical and thoracic lesions (18% +RLS verses 5% -RLS).

Conclusion: Prevalence of symptomatic RLS in these veterans with SCI/D was triple to the general population (22% compared to 7.3%). Majority developed RLS after SCI/D requiring RLS pharmacotherapies due to greater levels of burden. Higher prevalence of RLS was in patients with both cervical and thoracic lesions. Larger sample studies may suggest relationships between prevalence of RLS with level of injury and location of cord lesions.

0596

ONSET OF ACTION OF ROTIGOTINE TRANSDERMAL SYSTEM IN THE TREATMENT OF RESTLESS LEGS SYNDROME (RLS): A POST-HOC ANALYSIS OF DATA FROM A 1-WEEK PILOT STUDY

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Introduction: Placebo-controlled trials have demonstrated the efficacy of rotigotine transdermal system in the treatment of moderate-to-severe idiopathic RLS; however, rotigotine onset of action has not previously been investigated. SP666 was a double-blind pilot study with rotigotine in patients with RLS. In this post-hoc analysis, onset of action was assessed using RLS symptom severity ratings following first patch application.
Methods: Patients received rotigotine (0.5, 1.0 or 2.0 mg/24h) or placebo (n=17/13/19/14 respectively) for 1 week without titration, and recorded their ratings of RLS symptom severity (0=no symptoms; 10=maximum symptoms), sleep satisfaction (-3=very dissatisfied; 3=very satisfied) and daytime sleepiness/tiredness (0=none to 10=maximum) in daily diaries. The first post-treatment assessment (T1) was from diary entries completed the morning after first dose of trial medication, ie ~12 hours after first patch application.
Results: Baseline to T1 improvements were observed with rotigotine versus placebo in severity of symptoms while falling asleep (mean±standard deviation [SD] change from baseline: rotigotine, -1.17±2.75, -1.15±2.72 and -1.92±3.39 points with 0.5, 1, and 2 mg/24 h respectively; 0.27±1.31 points with placebo), symptom severity during the night (rotigotine, -1.37±3.83, -1.69±2.29 and -2.46±3.44 points; placebo, -0.06±1.38 points), daytime symptom severity while resting (rotigotine, -0.42±2.31, -0.36±1.52, and -1.4±2.59 points; placebo, 0.04±1.30 points), sleep satisfaction (0.84±2.51, 0.91±1.86 and 0.37±2.13 points; placebo, 0.28±1.03 points), and daytime sleepiness/tiredness (rotigotine, 0.71±2.09, 0.28±1.39 and 0.98±1.93 points; placebo, -0.38±1.20 points). As the first patch was applied in the evening and T1 took place the following morning, no change in daytime symptom severity can be expected.
Conclusion: Rotigotine showed a descriptive benefit versus placebo in alleviating RLS symptoms at the first post-treatment timepoint assessed. In this post-hoc assessment, statistical analysis was descriptive only, due to low patient numbers; however, these results suggest an onset of action of rotigotine within 1 day, and possibly within the first 12 hours after initial patch application.
Support (If Any): UCB Pharma Inc, delegated by Schwarz Pharma Ltd, Ireland

0597

EVALUATION OF THE ASSOCIATION BETWEEN THE INTERNATIONAL RLS STUDY GROUP RATING SCALE (IRLS) AND THE RESTLESS LEGS SYNDROME QUALITY OF LIFE QUESTIONNAIRE (RLS QOL): A POST HOC ANALYSIS OF A PHASE III ROTIGOTINE CLINICAL TRIAL

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Introduction: The IRLS and RLS QoL are both validated, disease-specific instruments for assessing disease severity and quality of life, respectively, in patients with restless legs syndrome (RLS). To understand how IRLS scores relate to meaningful benefits from the patient perspective, we carried out a scale association analysis between the IRLS and the 12-item RLS QoL (developed by R Kohnen).
Methods: In a Phase III, double-blind trial (SP790 [NCT00136045]), patients with moderate-to-severe idiopathic RLS (IRLS ≥15) were randomized to rotigotine transdermal system (1-3 mg/24h titrated to fixed dose over 3 weeks, maintained at that dose for 6 months) or placebo. Rotigotine-treated patients achieved significantly greater improvements in IRLS score from baseline to end of maintenance (EoM), and quality of life (as measured by mean changes in RLS QoL total score) improved in a dose-dependent manner. Scale associations were analysed categorically for IRLS and RLS QoL total scores, and as continuous variables, using the safety set of rotigotine- and placebo-treated patients combined (n=458).
Results: At baseline and EoM, categorical analysis showed a trend towards higher RLS QoL scores (ie, worsening quality of life) with increasing disease severity category on the IRLS. Mean baseline RLS QoL scores were 19.71, 29.14 and 40.81 in IRLS categories 11-20, 21-30 and 31-40, respectively. Mean EoM RLS QoL scores were 7.66, 19.21, 29.91 and 43.92 in IRLS categories 0-10, 11-20, 21-30 and 31-40, respectively. Pearson correlation coefficients at baseline (0.69; p<0.0001), EoM (0.82; p<0.0001) and change from baseline to EoM (0.73; p<0.0001) all indicated a strong correlation between the IRLS and RLS QoL; similar results were seen with Spearman rank-order correlation coefficients (0.67, 0.82 and 0.75, respectively; p<0.0001 for all three).
Conclusion: In this post hoc analysis of a rotigotine Phase III trial, the strong correlation between IRLS and RLS QoL demonstrates that changes in IRLS scores reflect quality of life changes that are meaningful to patients.
Support (If Any): UCB Pharma Inc, delegated by Schwarz Pharma Ltd, Ireland.

0598

ASSOCIATION ANALYSIS BETWEEN THE INTERNATIONAL RLS STUDY GROUP RATING SCALE (IRLS) AND THE CLINICAL GLOBAL IMPRESSION ITEM I (CGI-1): PROVIDING CLINICAL CONTEXT FOR THE IRLS

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Introduction: The IRLS is a validated, disease-specific instrument for assessing restless legs syndrome (RLS) severity. However, its clinical relevance may be under-recognized in routine practice compared with instruments such as the Clinical Global Impression (CGI) scale. To provide clinical context for absolute scores or change scores on the IRLS, we conducted a scale association analysis between the IRLS and CGI-1.
Methods: Data from a Phase III, double-blind, randomized, placebo-controlled trial (SP790 [NCT00136045]) were used in this post hoc analysis. Patients with moderate-to-severe idiopathic RLS treated with rotigotine transdermal system (1, 2 or 3 mg/24 h titrated to fixed dose over 3 weeks and maintained at that dose for 6 months) achieved significantly greater improvements in IRLS and CGI-1 scores from baseline versus placebo. Scale associations were analysed categorically for IRLS and CGI-1 total scores, and as continuous variables, using the safety set of rotigotine- and placebo-treated patients combined (n=458).
Results: At baseline, all patients had IRLS scores ≥ 15 and CGI-1 scores ≥ 4; at end of maintenance (EoM), patients were distributed across all IRLS and CGI-1 categories. At baseline and EoM, categorical analysis showed a trend towards greater RLS severity on the IRLS with increasing disease severity category on the CGI-1. Mean CGI-1 scores increased with increasing disease severity category on the IRLS: mean CGI-1 scores were 1.64, 3.13, 4.40 and 5.20 in IRLS categories 0-10, 11-20, 21-30 and 31-40, respectively, at EoM. Pearson correlation coefficients at baseline (0.62; p<0.0001), EoM (0.84; p<0.0001) and for change from baseline to EoM (0.79; p<0.0001) all indicated strong correlation between the IRLS and CGI-1 scale, in line with the published validation analysis of the IRLS.
Conclusion: In this post hoc analysis of a rotigotine Phase III trial, the strong correlation of IRLS with CGI-1 - an investigator-completed scale documented to be clinically meaningful - demonstrates that reductions in IRLS represent clinically meaningful benefit to patients with idiopathic RLS.
Support (If Any): UCB Pharma Inc, delegated by Schwarz Pharma Ltd, Ireland

0599

SLEEP IMPROVEMENT WITH ROTIGOTINE TRANSDERMAL SYSTEM IN PATIENTS WITH MODERATE-TO-SEVERE IDIOPATHIC RESTLESS LEGS SYNDROME (RLS): RESULTS FROM TWO 6-MONTH PLACEBO-CONTROLLED TRIALS

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Introduction: Two placebo-controlled trials (SP790: NCT00136045; SP792: NCT00135993) in RLS patients showed rotigotine to be an efficacious monotherapy based on IRLS and CGI-1. Significant improvements in sleep quality were demonstrated at all rotigotine doses tested versus placebo, as measured by the Medical Outcomes Study (MOS) sleep scale (Trenkwalder et al. Lancet Neurol 2008; Hening et al. Mov Disord 2010). Data were evaluated to analyse temporal aspects of sleep improvement and determine whether optimal sleep was achieved.
Methods: Following titration (SP790: 3 weeks, SP792: 4 weeks), patients (SP790 [n=447]; SP792 [n=494]) received rotigotine (0.5 [SP792 only], 1.0, 2.0 or 3.0 mg/24h) or placebo for up to 6 months. Patients completed the MOS questionnaire at baseline and monthly maintenance visits.
Results: In both trials, mean change from baseline scores in MOS parameters most relevant to RLS symptoms showed improvement with rotigotine versus placebo following dose titration (sleep disturbance [items 1, 3, 7, 8] [SP790/SP792: -22.3/-24.5 vs -10.7/-20.3 for placebo]; sleep adequacy [items 4, 12] [20.6/16.1 vs 8.0/12.4]; sleep problems Index II [items 1, 3-9, 12] [-18.0/-18.0 vs -9.2/-14.2]) and were maintained over the 6-month maintenance period. Sleep quantity (item 2) increased following dose titration with rotigotine versus placebo in SP790 (by 0.82 vs 0.41 hours per night) and was maintained thereafter, but remained similar between SP792 treatment groups. There was little difference between rotigotine and placebo treatment groups for scores in other MOS categories. The proportion of rotigotine- and placebo-randomized patients achieving optimal sleep (as defined in MOS) in SP790 increased from baseline to end of maintenance (EOM) (rotigotine, 18.9% [59/312] baseline vs 34.4% [101/294] EOM; placebo, 19.6% [21/107] vs 28.3% [28/99]). Similar results were observed in SP792 (rotigotine, 32.1% [124/386] vs 49.8% [157/315]; placebo, 23.5% [23/98] vs 38.6% [32/83]). Results presented are descriptive.
Conclusion: Rotigotine was associated with more patients achieving optimal sleep versus placebo. For parameters of MOS most relevant to RLS symptoms, benefits of rotigotine versus placebo were observed by the end of dose titration and were maintained consistently over 6 months.
Support (If Any): UCB Pharma Inc, delegated by Schwarz Pharma Ltd, Ireland

0600

SYMPATHETIC SKIN RESPONSE (SSR) IN RESTLESS LEGS SYNDROME

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Introduction: The sympathetic skin response (SSR) is a slow wave resulting from activation of the sudomotor sympathetic efferent fibers. SSR is well correlated with other autonomic function tests and its abnormality is documented in a variety of neurologic disorders such as diabetic neuropathy, cerebrovascular disease, Parkinson's disease, Multiple Sclerosis that are frequently associated with Restless Legs Syndrome (RLS). The evaluation of the sympathetic nervous system condition

could be helpful to improve the understanding of physiopathology and diagnoses of RLS.

Methods: Twelve patients meeting the four diagnostic criteria of the International Classification of Sleep Disorders, 2005, for RSL were examined. Each subject completed the Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS). All subjects signed an informed consent and the study was approved by Ethics Committee. Records were obtained with surface electrodes on foot after an electrical stimulation at Posterior Tibial nerve. We also obtained a correlation of the abnormal SSR with others neurophysiologic abnormal findings.

Results: The relationships between SSR abnormalities and RLS were analyzed. SSR was present in 9 patients (75%) and it was abnormal in 3 patients (25%), including abnormal foot latency with normal hand latency in 1 (33%), and no response in 2 (66%). We found no significant changes in SSR that could be associated with RLS.

Conclusion: SSR is a simple and effective means of assessing the function of Autonomic nervous system. Abnormalities in SSR are associates with cardiovascular diseases. Although, RLS has higher risk of cardiovascular diseases, there is no correlation of RLS and impairment of the sympathetic nervous system.

0601

HIGH PREVALENCE OF RESTLESS LEGS SYNDROME IN ASSOCIATION WITH RADICULOPATHY

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Introduction: The pathophysiological mechanisms of Restless legs syndrome (RLS) is still unknown. Radiculopathy has been clinically reported to be associated with RLS and it is describe as a risk factor for development of RLS symptoms. The aim of this study was to determine the neurophysiological changes in RLS using electromyography exam.

Methods: We evaluated 35 patients with clinical diagnostic of RLS that have full criteria for RLS by International Classification of Sleep Disorders, 2005, submitted to a clinical interview and neurological examination. Each subject completed the Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS). Informed consent of all study members was obtained after a full explanation of the survey. All patients were investigated with electromyography exam.

Results: The results were analyzed by statistical methods. The mean age was 60,4 years. 11 (31%) patients were observed with RLS with Radiculopathy. 5 (14%) had RLS and Polyneuropathy. 19 (54%) has a RLS without signs of impairment of peripheral nervous system. The most frequent abnormality in electromyography exam was axonal degeneration of muscular fibers in L5 nerve root, which was evidenced in 10 (90)% of the cases of Radiculopathy in association with RLS.

Conclusion: We found a significantly higher prevalence of Radiculopathy in electromyography findings in patients with RLS. These findings could be useful for a better comprehension of the physiopathology in Restless Legs Syndrome.

0602

STIMULANT USE IN NARCOLEPTICS WITH CARDIAC ARRHYTHMIA

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Introduction: Stimulants are a mainstay of therapy in treating hypersomnolence of narcolepsy. There is a paucity of data on the long term cardiovascular safety for the use of stimulants in this setting. The results of continuing stimulants once cardiovascular morbidities have been diagnosed has not yet been reported.

Methods: A retrospective chart review was performed using the electronic medical record that queried narcoleptic patients, age 18 or above, with a history of stimulant use for hypersomnolence with documented concern for palpitations or arrhythmia. The primary cardiac condition, type of arrhythmia, type of device if implanted, length and type of stimulant therapy, mortality, and stimulant therapy changes after cardiovascular diagnosis were noted.

Results: Ten narcoleptic patients were identified (age range 32-89, mean 67.1, SD 16.1) of the approximately 350 age-matched narcoleptic patients in the narcolepsy Mayo Clinic database. Nine of the ten continued to use stimulants after cardiovascular disease was first diagnosed, with average length on stimulants prior to cardiovascular diagnosis of 16.6 (SD 8.95) years. Average time from stimulant initiation to implantable cardiac device (n = 4) was 23.4 (SD 8.14) years. For those who did not receive an implantable cardiac device (n = 6), stimulant therapy was continued for average of 3.76 years (SD 1.67) after arrhythmia was identified. During this follow up period, none of the 6 subjects required any cardiac intervention. Methylphenidate was the most commonly used stimulant (6 of the 10 subjects).

Conclusion: Continued stimulant therapy in narcoleptic patients whose physicians noted concern for palpitations and arrhythmia was well tolerated, even in those not receiving implantable cardiac devices. Close follow up of these patients, however, is recommended.

0603

BENEFIT AND RISK OF MODAFINIL IN IDIOPATHIC HYPERSOMNIA VS. NARCOLEPSY WITH CATAPLEXY

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Introduction: The benefit/risk ratio of modafinil was recently re-evaluated by the European Medicines Agency and was shown to be negative for idiopathic hypersomnia because of insufficient data. We compared the effects of modafinil in a large cohort of patients with idiopathic hypersomnia (with and without long sleep time) vs. narcolepsy/cataplexy.

Methods: The benefit (Epworth sleepiness score, ESS; visual analog scale, patient and clinician opinions) and risks (habituation, adverse effects) of modafinil were studied in a consecutive clinical cohort of 104 patients with idiopathic hypersomnia (59 with long sleep time) and 126 patients with narcolepsy/cataplexy.

Results: Modafinil was the first line treatment in 96-99% of patients. It produced a similar ESS change in hypersomniacs and in narcoleptics (-2.6±5.1 vs. -3±5.1), and a similar benefit as estimated by the patients (6.9±2.7 vs. 6.5±2.5 on a visual analog scale) and clinicians. The ESS change was lower in hypersomniacs with long sleep time than in those without. Sudden loss of efficacy and habituation were rare in both groups. Hypersomniacs reported similar but more frequent adverse effects with modafinil than narcoleptics: nervousness (14%), palpitations (13%), headache (11%).

Conclusion: Modafinil has an excellent benefit/risk ratio in idiopathic hypersomnia, more marked without than with long sleep time, similar to its effect on narcolepsy/cataplexy.

0604

EFFECT OF GAMMAHYDROXYBUTYRATE ON CYCLIC ALTERNATING PATTERN (CAP) IN PATIENTS WITH NARCOLEPSY WITH CATAPLEXY

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Introduction: Gammahydroxybutyrate(GHB) treatment in narcoleptic patients had been shown to alleviate symptoms of narcolepsy-cataplexy. However GHB effect on cyclic alternating pattern(CAP) had not been studied. This study will show changes of CAP parameters after initiation of GHB.

Methods: Polysomnography and CAP of 10 narcolepsy with cataplexy patients initiated on GHB were retrospectively analyzed blindedly to compare during baseline and follow-up.

Results: Compared to baseline, follow-up polysomnography after initiation of GHB[mean duration(sd)8.14 ±4.1 week; mean dose(sd)6.8±2.0g] revealed similar results in mean total sleep time(409.5±42.1vs411.4±33.8minutes) and sleep efficiency(85.5±8.3vs85.9±8.0%).There were decrease in REM sleep(21.2±5.9vs15.8±8.2%,p=0.04)and increase in NREM sleep(78.8±5.9vs84.2±8.2%,p=0.04) with significant increase in slow wave sleep(27.9±12.7vs39.7±16.21%, p=0.03), while N1 and N2 sleeps remained unchanged. Despite similar CAP rate(63.6 ±15.3vs67.2±13.7%), ratio of A1 subtype(60.4 ±6.3vs77.5±7.4%,p=0.005) increased with reciprocal decreases in A2(21.6±16.9vs 13.8±3.5%,p=0.028)and A3 subtypes(18.1±7.2vs8.7±4.3%,p=0.007). These effects of GHB on CAP subtypes were most prominent in N2 sleep in which significant increase in A1 index(37.2± 13.0vs53.3 ±16.5cycle/hour,p=0.005) and decrease in A3 index(19.2± 8.0vs10.6 ±5.7 cycle/hour, p=0.01) occurred in this stage. While in other NREM stages, A1, A2 and A3 indices remained constant. However structure of CAP remained unchanged as evident by similar CAP sequence duration, phase A and phase B durations. Arousal index also decreased after GHB administration, both in NREM (20.03±8.18vs12.35±4.18 per hour, p=0.005) and REM sleeps(16.36±5.54vs9.28±7.82 per hour, p=0.047).

Conclusion: GHB treatment in narcoleptic patients resulted in decrease in REM sleep and increase in slow wave sleep. GHB affected both NREM and REM sleeps. In NREM sleep GHB altered CAP subtypes but had no effect on CAP structure. Alteration of CAP subtypes consisted of increase A1 subtype and decreases in A2 and A3 subtypes. These changes were most prominent in stage N2 sleep, thus promoting sleep oscillation towards greater NREM stability. REM sleep was also altered by GHB with reduction of arousal index.

0605

EXAMINING THE FREQUENCY OF STIMULANT MISUSE AMONG PATIENTS WITH PRIMARY DISORDERS OF HYPERSOMNOLENCE: A RETROSPECTIVE COHORT STUDY

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Introduction: Narcolepsy and idiopathic hypersomnia are commonly treated by sleep specialists and encountered by other medical providers. Although pharmacotherapy with modafinil and the traditional stimulants is considered the mainstay of treatment, physicians are often uncomfortable with their long-term prescription because of concerns regarding patient misuse. The goal of this study was to assess the frequency of stimulant misuse in this population while under treatment at the Mayo Center for Sleep Medicine.

Methods: A retrospective cohort study was performed evaluating patients 18 years and older diagnosed with narcolepsy with and without cataplexy and idiopathic hypersomnia with and without long sleep between 1997 and 2007. Patients were included if they obtained stimulant prescriptions from and had at least one follow-up visit subsequent to initial diagnosis at our center. Stimulant misuse was defined by "drug-seeking behavior" (e.g., multiple drug sources or alleged lost prescriptions) which is systematically entered into the record by nursing staff, who, under the guidance of sleep specialists, determine eligibility of all patients for prescription refills.

Results: A total of 105 patients met inclusion criteria for the study, 45 (42%) were male. Mean age at multiple sleep latency test was 42 (+/- 16). Twelve (11%) patients had a past history of illicit substance misuse and one (1%) patient had previous stimulant misuse. 57 (54%) patients had a psychiatric diagnosis, including 50 (88%) with depression. Median duration of monitored stimulant therapy was 26 months (range 1-250). During this time, none of the 105 patients were found to have evidence of stimulant misuse.

Conclusion: This study suggests that the frequency of stimulant misuse in patients with narcolepsy and idiopathic hypersomnia is extremely low. The risk of drug misuse should not influence decisions to provide long term therapy.

0606

IS BIRTH ORDER ASSOCIATED WITH NARCOLEPSY RISK AMONG GENETICALLY SUSCEPTIBLE INDIVIDUALS?

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Introduction: Birth order may play a role in autoimmune diseases and in early childhood infections, both factors implicated in the etiology of narcolepsy. Narcolepsy is considered an autoimmune disease that has associations with HLA haplotypes, season of birth, anti-trib2 antibodies, and T-cell receptor alpha locus polymorphisms. Streptococcal infections are reported to be associated with narcolepsy. We sought to investigate the association between birth order and narcolepsy risk in a population-based case-control study, in which all study subjects were HLA-DQB1*0602 positive.

Methods: Between 2001-2005, 67 prevalent narcolepsy cases were enrolled, and 95 controls were recruited through random-digit dialing with frequency matching on age and sex. All subjects were between ages 18-50 years old, residents of King County, Washington, and positive for HLA-DQB1*0602. Genotyping was performed on DNA from buccal scrapings. Birth order was ascertained by asking, "What was your or-

der among your siblings?" We used logistic regression to generate odds ratios adjusted for income and African American race because these factors differed between cases and controls.

Results: Analyses included 67 cases (mean age 34.3 [SD=9.1], 70.2% female) and 95 controls (mean age 35.1 [SD=8.8], 75.8% female). Associations for birth order were as follows: First born (cases 44.1% vs. controls 50.2%, OR=1.0; Reference), second born (Cases 32.3% vs. Controls 32.9%, OR=1.6; 95% CI 0.7, 3.7), third born or higher (Cases 23.6% vs. Controls 16.8%, OR=2.5; 95% CI 1.0, 6.0). A linear trend was significant (p=0.039). Sibling gender did not differ between narcolepsy cases and controls (Brothers: Cases 55.2% vs. Controls 52.8%, OR=1.0; 95% CI 0.5, 2.0; Sisters: Cases 59.7% vs. Controls 59.2%, OR=1.5; 95% CI 0.7, 3.2).

Conclusion: Narcolepsy risk was significantly associated with higher birth order in a population-based study of genetically susceptible individuals. This finding supports an environmental influence on narcolepsy risk through an autoimmune mechanism, early childhood infections, or both.

0607

SEX DIFFERENCES IN NARCOLEPSY

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Introduction: Notable sex differences in disease prevalence, manifestation, and health consequencesare are well described in many common sleep disorders such as sleep disordered breathing, insomnia, and restless leg syndrome. However, sex differences in narcolepsy remain understudied, and there is little scientific information regarding the clinical significance and consequences of narcolepsy in women.

Methods: We performed a cross-sectional analysis on 109 consecutive patients with narcolepsy from a single academic adult sleep center from 2005-2010. Patients were administered a questionnaire evaluating symptoms, sleep habits, lifestyle parameters, and medical history at the time of their narcolepsy diagnosis. Responses were compared in men and women with narcolepsy with and without cataplexy. Polysomnographic data from the time of their diagnosis were also compared.

Results: Of the 109 narcoleptic subjects, 41 (38%) were men and 68 (62%) were women. Mean age at diagnosis and age of onset of symptoms did not differ between sexes(29 and 15 yrs respectively in men, vs 31 and 17 yrs respectively in women). Men and women were equally overweight (BMI 26 ±4 vs 27 ±6, respectively). Cataplexy was more common in women (56% vs 37%, p=0.05), but there were no sex differences in other narcolepsy-related symptoms (e.g. Epworth Sleepiness Score, sleep paralysis and hallucinations), and no sex differences in polysomnographic data. Occurrence of obstructive sleep apnea was high in this relatively young population, and expected sex differences were not observed (24.4% vs 17.6%, men and women, respectively, p=0.40). ADHD was more commonly diagnosed in men (19.5% vs 2.9%, p=0.006). Women and men were equally likely to complain of headaches, insomnia, depressed mood, anxiety, or chronic pain. Women were more likely to consume daily caffeine (82.4% vs 63.4%, p=0.03), but there were no differences in use of homeopathic wake-promoting therapies, tobacco, or illicit drugs. Finally, women more commonly reported that their sleep problems negatively impacted their sex life (55% vs 29%, p=0.01). Women and men reported similarly high occurrences of poor work/school performance (>90%), social dissatisfaction (>35%), and driving problems (>40%) related to sleepiness.

Conclusion: Women and men with narcolepsy were remarkably similar in narcolepsy related symptoms, demographics, and sleep study data. Despite this, important sex differences in medical and lifestyle consequences were appreciated.

0608

DRIVING AND SLEEP DISORDERS: DOES MSLT OR MWT BETTER PREDICT DRIVING PERFORMANCE?

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Introduction: The maintenance of wakefulness test (MWT) predicts simulated and real driving performance in non treated Obstructive Sleep Apnea Syndrome (OSAS) patients. Recently, epidemiological studies reported higher risk of road accidents for narcolepsy and hypersomnia comparing to OSAS. The aim of our study is to determine the ability of objective sleepiness measures (MWT or MSLT) to predict driving performance in patients suffering from OSAS and hypersomnia compared to healthy controls.

Methods: 148 subjects (38 healthy controls, 42 narcolepsy-hypersomnia and 70 OSAS patients) performed a total of 96 MWT (4X40-minute trials) and 77 MSLT (5x20-minute trials). For each test, a 40 min driving session on real car driving simulator with monotonous driving scenario was performed. Participants were divided into 3 groups defined by their scores at MWT or MSLT (pathological (0-19 min for MWT and 0-8 min for MSLT), intermediate (20-33 min for MWT and 9-11 min for MSLT), and alert (34-40 min for MWT and 12-20 min for MSLT).

Results: The results showed that only sleep latencies at MWT were correlated with number of inappropriate line crossings (r =- 0.31, p <0.002) for both patients and controls. In addition, the MWT pathological group had significantly more inappropriate line crossings than intermediate and alert groups (F (2.93) = 3.25, p <0.05). MSLT scores did not predict driving performances.

Conclusion: Our results show that pathological sleep latencies in MWT predict a driving impairment independently of the sleep pathology. In contrast, no relationship between sleep latencies on MSLT and driving performance was observed. We suggest that MWT could be useful to estimate driving performance in pathologically sleepy patients.

0609

A RELIABLE AND VALID INSTRUMENT FOR MEASURING WAKE INABILITY AND FATIGUE: THE SANGAL WAKE INABILITY AND FATIGUE TEST

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Introduction: Sleep disorders can cause sleepiness, usually measured by ability to fall asleep in soporific situations, subjectively using ESS or objectively using MSLT. Sleep disorders also cause wake inability (difficulty staying awake when desired) and fatigue (tiredness, lack of energy), which are not usually measured. This is an expanded report on an instrument to measure wake inability and fatigue, the SWIFT (Sangal Wake Inability and Fatigue Test).

Methods: A 12-item self-administered instrument with questions on wake inability and fatigue in different situations was developed and administered (along with ESS) to 223 adults ages 18-64 years (after excluding CNS disorders, untreated depression, history of apneic episodes in sleep, or on CNS-active medicines). 37 retook the tests a month later. SWIFT and ESS were then administered to 160 consecutive patients ages 18-64 tested with polysomnography (PSG) for obstructive sleep apnea (OSA, 135) or PSG and Multiple Sleep Latency Test (MSLT) for narcolepsy (25). The tests were re-administered to 26 OSA patients after CPAP for 1-3 months.

Results: Cronbach's alpha using data from normal subjects was 0.81 and test-retest intraclass coefficient was 0.83 (p<0.001). Factor analysis with varimax rotation revealed Factor 1 (36% of variance) including 8 items apparently related to general wake inability and fatigue (GWIF), and Factor 2 (21% of variance) including 4 items apparently related to driving wake inability and fatigue (DWIF). Normal subjects differed from sleep disorder patients in ESS, GWIF and DWIF, all p<0.001. ROC Curves showed area under the curve of 0.70 for ESS and DWIF and 0.76 for GWIF. ESS, GWIF and DWIF all improved with CPAP (p<0.01), with effect size of 1.0 for ESS, 1.3 for GWIF and 0.8 for DWIF. Of 10 patients greater than 1 SD from normal mean on ESS (≥10), 3 dropped below normal mean (≤5). Of 10 patients >1 SD from normal mean on GWIF (≥11), 5 dropped below normal mean (≤6). ESS (r= -0.62) but not GWIF or DWIF (both r= -0.16) was significantly correlated with MSLT.

Conclusion: SWIFT is a reliable instrument with excellent internal consistency and test-retest reliability. Both its factors (GWIF and DWIF) show discriminant validity between normal subjects and patients with OSA or narcolepsy symptoms, GWIF somewhat better than ESS. Both improve with CPAP treatment of OSA, GWIF somewhat better than ESS. The lack of correlation of GWIF or DWIF with MSLT (ESS being correlated) suggests SWIFT measures a different disability than ESS.

0610

FALSE-POSITIVE CASES IN MSLT BY ACCUMULATED SLEEP DEFICIENCY

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Introduction: MSLT is usually performed as objective assessment of sleepiness. It is performed on the following day after PSG. In most clinics and hospitals, patients are required to stay for a couple of days. However, if patients have chronic insufficient sleep, the accumulation of their sleep insufficiencies may affect MSLT results. Even if they get enough nocturnal sleep during the PSG, their sleep insufficiencies would not be fully recovered (Janjua T. 2003). In the present study, we compared each sleep latency by examining it with MSLT twice. First session is one hospitalized night with the following MSLT, and second session is three or more hospitalized nights with the following MSLT.

Methods: Ten males and one female (31.8+/-14.2 yrs) who performed MSLT twice were enrolled in our study. They complained about sleep-wake disorders in our hospital from 2004 to 2010. First, we examined these cases using standard PSG and MSLT procedure, however, their results were doubtful compared with sleep logs and other symptoms. Therefore, we examined these doubtful cases for the second time with two or more previous hospitalized nights and following PSG and MSLT procedure (total three or more hospitalized nights).

Results: Mean sleep latency was 6.4 min in 'one night' group and 14.8 min in 'three or more nights' group. There was a significant difference between these two groups (p<0.001).

Conclusion: Sleep latencies of 'one night' group were shorter than those of 'three or more nights' group. This may produce false-positive results at diagnosis when patients were examined by standard PSG and MSLT procedures. It is thought that the effects of insufficient sleep affect these procedures, consequently, shorten sleep latencies. Therefore, we need to consider the hospitalized durations before PSG and MSLT procedures. Reference: Janjua T. et al. Clinical caveat: prior sleep deprivation can affect the MSLT for days. Sleep Med. 2003; 4(1): 69-72.

0611

DIFFICULTY INITIATING NIGHTTIME SLEEP IN NARCOLEPSY

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Introduction: Narcolepsy is a sleep disorder causing severe, excessive daytime sleepiness in more than 90% of patients. Disrupted nighttime sleep can often be seen as well. Despite the overwhelming sleepiness during the day, some patients also report difficultly initiating sleep at nighttime. The aim of this study is to determine the prevalence of dif-

ficulty initiating nighttime sleep in patients meeting MSLT criteria for narcolepsy in an academic center.

Methods: All patients who met diagnostic criteria on their MSLT for narcolepsy from March, 2006 until November, 2010 were included. The diagnostic criteria used were based on the ICSD-R with MSLT results showing a mean latency of <8 minutes and two REM onset naps.

Results: Of the 26 patients meeting diagnostic criteria for narcolepsy by the MSLT, the average of the mean latency on the MSLT was 3.6 minutes, the median was 3.25. The overnight polysomnography showed a range of latency to sleep onset of 0-108 minutes. The overnight sleep onset latency median was 6 minutes and the mean was 20 minutes. Five of the 26 (19%) had a latency to sleep onset on the overnight study of >40 minutes.

Conclusion: A significant number of patients meeting MSLT criteria for narcolepsy have objective evidence on overnight polysomnography for difficulty initiating nighttime sleep despite severe, objective daytime sleepiness. Difficulty initiating sleep can be disturbing to the patient and worsen daytime sleepiness. Further investigation is necessary to determine the contributing factors to this difficulty initiating sleep in this population suffering from severe, daytime sleepiness. Possible factors include depression, medication effect, anxiety, co-morbid sleep disorders or first night effect in the lab.

0612

CLINICAL CHARACTERISTICS OF NOCTURNAL SLEEP AND CONCOMITANT SYMPTOMS IN HYPERSOMNIAS OF CENTRAL ORIGIN; ANALYSIS ON SELF-COMPLETED QUESTIONNAIRE

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Introduction: Symptoms other than excessive daytime sleepiness are not always evaluated well in patients with hypersomnia of central origin. In order to elucidate the clinical characteristics of hypersomnias, we performed questionnaire based study to check the nocturnal sleep problems and concomitant autonomic nerve system (ANS) symptoms.

Methods: Subjects are 327 hypersomnia patients (204 narcolepsy with cataplexy:NA, 29 idiopathic hypersomnia with long sleep time:IHS, 94 essential hypersomnia:EHS) recruited in Japan Somnology Center and 286 healthy controls. Self-completed questionnaire asking the frequency of nocturnal sleep problems and concomitant ANS symptoms were conducted and data were analyzed with SPSS software. All the participants provided written informed consent before the survey.

Results: Overall sleep latency was not different. Percentage of short sleep latency (less than 5 min) was high in NA (48.5% vs 33.8% in controls), while the percentage of sleep initiating problems (more than 30 min) were equally observed (5.8% in NA vs 5.6% in controls). Nocturnal awakening were significantly more in NA(70.7% vs 22.3% in controls) and less in IHS (10.3%). Times required for full awakening in the morning extended in IHS (33.9min vs 10.5min in controls, 11.5min in NA). Subjective difficulty of awakening was high in IHS (79.3%) and low in NA (5.8%) compared to controls (7.9%), indicating the difference in waking up process. Nocturnal talking was more in NA(30.6%) but also observed in IHS(17.4%) vs controls(4.5%). ANS symptoms were more frequent in IHS (dizziness 31.0%, orthostatic hypotention 42.9%, headache 44.8%). IHS showed more Raynaud phenomena (24.1% vs 1.8% in controls, 6.1% in NA) while NA showed more excessive sweating (53.7% vs 12.0% in controls, 29.3% in IHS). Majority of IHS patients (65.5%) suffered from fatigue.

Conclusion: Hypersomina of central origin show characteristic symptoms, especially in the process of waking up in the morning and body temperature regulation. These data will contribute to the better understanding of hypersomnia pathophysiology.

0613

IMPACT OF SODIUM OXYBATE ON HEALTH STATUS MEASURES IN NARCOLEPSY USING THE CLEVELAND CLINIC KNOWLEDGE PROJECT

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Introduction: Narcolepsy is often resistant to pharmacological interventions, many lacking head-to-head testing for superiority against sleepiness and other health measures. We investigated the self-reported impact of sodium oxybate on the Epworth Sleepiness Scale (ESS), Fatigue Severity Scale (FSS), Functional Outcomes of Sleep Questionnaire (FOSQ), and Patient Health Questionnaire-9 (PHQ-9), and self-reported total sleep time (TST).

Methods: Retrospective Cleveland Clinic Knowledge Project (KP) chart review compared patients pre- and post-sodium oxybate therapy at 3 and 6 months on ESS, FSS, FOSQ, and PHQ-9, to look for changes in sleepiness, fatigue, functional status, and depression respectively. No previous studies assessed FSS and PHQ-9 in relation to sodium oxybate; only one included FOSQ.

Results: Twenty patients (19 Females, age 42±13yrs, 8 with cataplexy, 85% on stimulants) had mean sodium oxybate dose of 5.7±1.4 g/day at 3 months and 6.6±1.1g/day at 6 months. ESS ratings at baseline (16.0±4.5) improved significantly at 3 (12.3±4.7; p=0.004) and 6 months (11.13±4.7; p=0.0008). FSS ratings at baseline (49.0±12.6) showed trend improvement at 3 (43.3±15.5; p=0.22) and 6 months (41.1±15.2; p=0.10). FOSQ ratings at baseline (20.1±18.9) did not improve at 3 months (19.2±13.1) but did at 6 months (25.8±20.9; p=0.01). PHQ-9 ratings (9.9±5.6 at baseline) improved significantly at 3 months (5.5±4.8; p=0.007) but not at 6 months (4.4±4.4; p=0.2). TST (baseline (8.2±1.7 hrs) decreased (7.4±1.0; p=0.015) at 3 months, but not significantly at 6 months (7.8±1.2; p=0.86).

Conclusion: In addition to improving sleepiness, sodium oxybate therapy for narcolepsy appears therapeutic across several self-reported measures. The relative benefit of this against other interventions for narcolepsy with cataplexy will require assessments across a variety of functional health domains.

0614

METABOLIC ALTERATIONS IN NARCOLEPSY WITH CATAPLEXY AND OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Several studies have shown an elevated body weight and altered metabolic parameters in patients with narcolepsy with cataplexy (NC). Moreover, there is an increased co-morbidity between NC and Obstructive Sleep Apnea (OSA). We explored metabolic alterations in hypocretin-1 deficient NC adult subjects, with and without OSA, compared with subjects complaining excessive daytime sleepiness (EDS), and with patients with Obstructive Sleep Apnea Syndrome (OSAS). A second aim was to confirm an increased prevalence of metabolic syndrome (MS) in NC.

Methods: According to the International Classification of Sleep Disorders (ICSD2), 30 NC patients, 11 patients with NC and co-morbid OSA, 21 with EDS, and 11 with OSAS, were consecutively enrolled. In all patients BMI, waist circumference, plasmatic glucose and lipid profiles were measured. Family history for metabolic/endocrine diseases was collected. Hypocretin-1 and HLA DQB1*0602 haplotype were investigated when possible.

Results: Compared to subjects with EDS, NC patients presented a homogenous BMI, significantly higher waist circumference (p=0.002), waist to hip ratio (p=0.012), fasting insulin (p=0.034) and a lower HDL cholesterol (p=0.019). NC also presented an higher prevalence of MS (p=0.002). Compared to OSAS subjects, NC patients with OSA presented a homogeneous BMI, a significantly lower HDL (p=0.02) and higher fasting insulin (p=0.03). There was no difference in MS prevalence. Family history did not play a role in any comparisons.

Conclusion: Compared to subjects without any sleep disorder, NC shows a significantly altered glucose and lipid profile and an increased presence of MS. When co-morbidity with OSA is included, NC patients still show more altered metabolic profile than OSAS patients, though MS presence is comparable.

0615

PERSISTENT HYPOTONIA WITH COMPLEX MOVEMENT DISORDER IN CHILDHOOD NARCOLEPSY-CATAPLEXY AT DISEASE ONSET

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Introduction: Narcolepsy with cataplexy (NC) is characterized by daytime sleepiness, cataplexy, sleep paralysis, hypnagogic hallucinations and disturbed nocturnal sleep. NC is associated to the loss of hypothalamic hypocretin-1 producing neurons and to the HLA-DQB1*0602 haplotype with evidence of autoimmune etiology.

Methods: In 31 children with NC (17 males, mean age of 12±3.4 years), motor phenomena were documented by means of video recordings at baseline and during emotional stimuli (cartoons watching). The occurrence of "negative" (paroxysmal head drops and falls, persistent eyelid narrowing and tongue protrusion, persistent facial hypotonia, persistent generalized hypotonia) and of "active" (raising of the eyebrows, perioral and tongue movements, facial grimaces, swaying of the head and/or trunk, stereotyped motor behaviors, dyskinetic or dystonic movements) motor features were assessed with a semi-quantitative approach. The "negative" and "active" composite score was related with age at NC onset, disease duration, MSLT features, cerebrospinal hcrt-1 and anti-streptolysin-O (ASO) titres (Pearson's correlations).

Results: Our patients showed frequently occurring "negative" and "active" motor phenomena, associated with evidence of hypotonic features at neurological examination, and significantly enhanced by emotional stimuli (p<0.005). Both "negative" and "active" motor phenomena during emotional stimuli were inversely correlated with NC duration (r= -0.55 and r= -0.45, respectively), whereas "active" motor phenomena were positively correlated with cerebrospinal hypocretin-1 concentration (r= +0.42 at baseline) and ASO titer (r= +0.46 and r= +0.38 at baseline and during emotional stimuli, respectively).

Conclusion: In childhood NC a complex movement disorder characterized by persistent hypotonia and a complex range of active movements occur close to disease onset. This movement disorder may share a common autoimmune etiology with NC, or may represent the heralding feature of cataplexy reflecting the acute hypocretinergic failure.

0616

UTILITY OF 24-HOUR CONTINUOUS POLYGRAPHIC RECORDING IN THE DIFFERENTIAL DIAGNOSIS OF HYPERSOMNIAS OF CENTRAL ORIGIN

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Introduction: The differential diagnosis of hypersomnias of central origin (CNS hypersomnias) is currently based on MSLT findings, namely mean sleep latency (SL) and sleep onset REM periods (SOREMPs), performed after an overnight complete polysomnographic (PSG) recording ruling out other causes of excessive daytime sleepiness (EDS).

Methods: We included in the study 100 consecutive patients complaining sleepiness in the absence of other sleep disturbances causing EDS, thus suggesting CNS hypersomnia. Each patient underwent 24-h continuous PSG recording (after an adaptation day), MSLT and the additional diagnostic procedures required for the diagnosis of CNS hypersomnia. Daytime PSG (number and duration of spontaneous naps, SOREMPs count) and MSLT findings were compared by means of Pearson's correlation and receiver operating characteristic (ROC) curves analyses.

Results: The diagnostic workup disclosed narcolepsy with cataplexy in 39 patients (age=32±15 yo, 20 males), narcolepsy without cataplexy in 7 (age=26±7 yo, 6 males), idiopathic hypersomnia in 21 (age=42±15 yo, 12 males), and subjective sleepiness in 33 subjects (age=38±12 yo, 19 males). Mean MSLT SL was inversely correlated with the number of spontaneous naps (r= -0.36, p=0.0002) and with daytime total sleep time (r= -0.26, p=0.009). The number of SOREMPs at MSLT and at daytime PSG were positively correlated (r= 0.78, p<0.0001). ROC curves showed a significant predictive value of daytime naps number and total sleep time (area under the curve=0.678 with p=0.003, and area=0.631 with p=0.028, respectively) versus a mean MSLT-SL ≤ 8', and of the number of daytime SOREMPs (area=0.931 with p<0.0001) versus MSLT-SOREMPs ≥ 2.

Conclusion: Daytime continuous PSG recording is able to predict MSLT results, providing useful diagnostic informations in the differential diagnosis of CNS hypersomnias.

0617

SLEEP-RELATED EATING DISORDER IS COMMON IN NARCOLEPSY: A CASE-CONTROL STUDY

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Introduction: To assess the prevalence of sleep-related-eating disorder (SRED) in patients with narcolepsy with cataplexy (NC) versus age-, sex-, and geographical origin- matched controls by means of a case-control study.

Methods: Thirty-eight NC patients (22 men; mean age of 42±18 years) and 38 matched controls were consecutively recruited. Self-administered questionnaires were used to investigate the presence of SRED, restless legs syndrome (RLS), nocturnal smoking (NS), psychopathological traits (using Eating Disorder Inventory-2, EDI-2; Maudsley Obsessive-Compulsive Inventory, MOCI; Beck Depression Inventory, BDI), and nocturnal sleep quality. Patients and controls were compared using non-parametric statistical tests (Mann-Whitney or Chi-Square for continuous or categorical data).

Results: NC patients showed an higher prevalence of SRED (37% vs 0%, p<0.0005), RLS (24% vs 3%, p=0.014), and NS (24% vs 0%, p=0.002), than controls. Moreover, NC patients showed more frequently an EDI-2 psychopathological profile (84% vs 37%, p<0.0005), and an higher BDI score (9±8 vs 5±5, p=0.009). When compared to the other patients, NC patients with SRED were more frequently women (71% vs 25%, p=0.005), with insomnia complaint (50% vs 4%, p <0.002). Moreover, SRED patients show an higher prevalence of bulimic trait at EDI-2 (21% vs 0%, p=0.043), higher scores at MOCI (13±6 vs 9±5, p=0.037) and at BDI (11±8 vs 7±8, p=0.05).

Conclusion: Our study showed a robust association of NC with SRED, RLS, and NS. Noteworthy, SRED is independent from RLS in NC patients. Our SRED patients are generally women with a bulimic profile, a tendency to compulsion and depression. SRED, together with RLS and NS, may concur in worsening sleep disruption in NC female patients with psychopathological traits. Further biochemical, polysomnographic and genetic studies are needed to investigate whether a common dysfunction underlie these sleep-related disorders, and whether the latter play a role to determine the NC-linked metabolic syndrome.

0618

NMDA RECEPTOR ANTIBODIES AND PSYCHIATRIC MANIFESTATIONS IN HYPOCRETIN DEFICIENT NARCOLEPSY

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Introduction: We have been reported that the patients with hypocretin/orexin deficient narcolepsy and severe psychosis had NMDA receptor (NMDAR) antibodies (APSS2009). NMDAR antibody is produced against tumor and migrated to brain, and then present psychiatric symptoms. This paraneoplastic brain syndrome usually develops in young women with ovarian teratoma, but some cases are in elder men. In this study, we measured NMDAR antibody in narcoleptic patients with and without psychiatric symptoms.

Methods: The study was extended total 5 cases with hypocretin deficient narcolepsy having psychosis and 10 cases with hypocretin deficient narcolepsy having no psychosis. Testing for NMDAR antibodies was performed in Kanazawa Medical University as following the method of Dr. Dalmau.

Results: We found that three narcolepsy patients, who had severe psychotic symptoms occurring 3 to 30 years after the narcolepsy onset (among 5 examined), were positive for the antibody (25/f, 37/f, 61/m). These cases were hypocretin deficient, but no significant neurological signs were noted. They were under stimulant medications, and their hallucinations and delusions were unchanged when the stimulants were withdrawn. Antipsychotics (3/3 cases) and modified electro-convulsion treatment (mECT, one case) were required to manage the psychotic symptoms. We were unable to identify any tumors in these three patients. On the other hand, the two out of 10 hypocretin deficient narcolepsy without psychosis have were positive for the antibody (15/f, 22/f).

Conclusion: The NMDA antibodies are positive for 3 among 5 cases with narcolepsy with severe psychosis (60%), and 2 among 10 cases with narcolepsy without severe psychosis (20%). Recently, several antibodies were reported to be positive in the patients with narcolepsy (ASO,Trib2). Since the NMDAR antibody is pathogenic for hypothalamic lesions, this antibody might be related to be hypocertin cell death. It was also reported that some cases of encephalitis lethargica (EL) are NMDAR antibodies positive. EL was first described by von Economo in 1920' and the prominent lesions were located in the hypothalamus.

Further studies are needed to the NMDAR antibodies in the cases with hypocretin deficient narcolepsy.

0619

DEREALIZATION IN KLEINE-LEVIN SYNDROME: AN HYPOPERFUSION IN THE ANGULAR GYRUS?

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Introduction: Kleine-Levin syndrome is a rare neuropsychiatric disorder primarily striking teenagers. It is characterized by recurrent and unusually long episodes of hypersomnia, associated with cognitive (confusion, apathy, derealization) behavioral (withdrawn attitude, and eating or sexual desinhibition) and psychological (altered mood, hallucination) disturbances. These serious episodes alternate with periods without any symptom, normal sleep and behavior typically lasting months to years. Derealization is the experience of the external world as strange or unreal. Objective: To localize cerebral perfusion abnormalities during episodes and correlate them with specific symptoms.

Methods: Seven patients (5 males, 2 females, 16-30 y old) with Kleine-Levin syndrome for 0.5-11 years underwent two brain Single Photon Emission Computed Tomographies, during symptomatic and asymptomatic periods. To localize brain regions with perfusion changes during symptomatic periods, asymptomatic imaging was subtracted from symptomatic imaging, after spatial normalization into a standard template. The subtracted images were analyzed for significant clusters with Statistical Parametric Mapping 5 and repositioned onto a standard brain magnetic resonance imaging.

Results: During these episodes, the patients experienced derealization (n=7), apathy (n=7) and major asthenia with a desire to sleep (n=7), bradyphrenia (n=4), anxiety (n=5), withdrawn attitude (n=6), temporal or spatial disorientation (n=5), agitation (n=2), amnesia (n=5), hypersexuality (n=3) and megaphagia (n=1). As an example of derealization, a patient described that he felt strange under the shower: he saw the water running on his body but did did not feel it at the same time. As a mean for the group, there was a significant hypoperfusion of the right and left medial orbitofrontal cortex, and in the right angular gyrus. In contrast, the left caudate nucleus, left putamen and ventrolateral nucleus of right thalamus were hyperperfused during the symptomatic periods.

Conclusion: The hypoperfusion in the medial orbito-frontal cortex (which is part of the reward and decision making system), could explain the apathy of the patients.The hypoperfusion in the right angular gyrus (which is known to integrate visual, tactile and proprioceptive information) could be the substrate of the derealization feeling in patients.

0620

SLEEP ONSET REM PERIOD(SOREMP) FREQUENCIES DURING MULTIPLE SLEEP LATENCY TEST(MSLT) : A PREDICTIVE FACTOR OF SYMPTOM SEVERITY OF NARCOLEPSY

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Introduction: The aim of this study is to determine the correlations between the number of sleep onset REM period (SOREMP) on multiple sleep latency test (MSLT) and Clinical features of narcolepsy, frequency of HLA DQB1*0602.

Methods: The subjects were 126 narcoleptic patients who suffered excessive daytime sleepiness. Patients who co-morbid with other sleep disorder such as sleep apnea were excluded. All subjects were tested by polysomnography and MSLT, have done HLA typing. We divided our subjects into three groups according to the number of SOREMP on MSLT and compared to clinical features, sleep pattern and frequency of HLA-DQB1*0602.

Results: we identified that a larger number of SOREMP was related with increase in incidence of clinical symptoms such as cataplexy, hypnagogic hallucination, and sleep paralysis. In polysomnography tests, Stage II sleep and REM sleep latency were decreased, as the number of SOREMP was increased . In MSLT, mean sleep latency and mean REM latency was also decreased with increasing the number of SOREMP. And Significant difference in the relation with the number of SOREMP and frequency of HLA-DQB1*0602 was found.

Conclusion: In this study, we found that the number of SOREMP on MSLT was correlated with clinical symptoms of narcolepsy , night sleep architecture of narcoleptics , and frequency of HLA-DQB1*0602. We may need more comprehensive and in-depth studies to find the pathogenesis of narcolepsy associated with the number of SOREMP.

0621

POOR SLEEP QUALITY IS ASSOCIATED WITH REDUCED PARTICIPATION IN PEOPLE WITH MULTIPLE SCLEROSIS

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Introduction: Sleep complaints are common in people with multiple sclerosis (MS). Poor sleep quality impairs performance and participation in the general population but the relationships between sleep quality and disability and participation in MS are not well characterized.
Methods: This study is a secondary analysis of data from a double blind placebo controlled clinical trial of ginkgo biloba for cognitive impairment in MS. The participants were 158 people with MS of any subtype, aged 18 to 65 years, with cognitive impairment ($\geq$ 1 s. d. < mean on the Stroop, paced auditory serial addition test, controlled oral word association test, or California verbal learning test) and without depression (Beck Depression Inventory II < 28). Sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI), disability was assessed with the Expanded Disability Status Scale (EDSS) and participation was assessed with the Community Integration Questionnaire (CIQ). Relationships between baseline PSQI, CIQ, and EDSS were examined with pairwise Pearson's correlations. P-values were adjusted for multiple tests with a false discovery rate (FDR) adjustment.
Results: There were statistically significant correlations between PSQI-total and CIQ-total scores (r -0.26, p <0.01) and CIQ social integration subscores (r -0.31, p 0.03). There were statistically significant correlations between PSQI subjective sleep quality (r -0.21, p 0.02), sleep disturbances (r -0.21, p 0.02) and daytime dysfunction (-0.20, p 0.03) subscores and CIQ-total scores. Furthermore, there were statistically significant correlations between PSQI subjective sleep quality (r -0.26, p 0.04) and daytime dysfunction (r -0.28, p 0.04) subscores and the CIQ social integration subscore. Other correlations were not statistically significant at the p<0.05 level.
Conclusion: Poor sleep quality is associated with decreased community integration, particularly decreased social integration, in people with MS and cognitive impairment at all levels of disability. Sleep evaluation and intervention may improve social integration in people with MS.
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0622

CARDIORESPIRATORY COMPLICATIONS OF FOCAL SEIZURES: A PILOT STUDY EXPLORING THE ROLE OF CARDIORESPIRATORY DYSFUNCTION AS A MECHANISM OF SUDDEN UNEXPLAINED DEATH IN EPILEPSY (SUDEP)

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Introduction: Prolonged hypercapnia and hypoxemia may be modifiable causes of death in SUDEP, the most common cause of death in epilepsy. Previous studies have used only limited EEG and respiratory channels. Our study goals were to investigate the feasibility of using closely spaced electrodes in the Epilepsy Monitoring Unit (EMU) and to characterize the respiratory impact of seizures. We aim to identify the associations between locations and characteristics of ictal discharges versus time-linked cardiorespiratory disturbances.
Methods: Addressing the first goal, we have placed closely-spaced scalp and intracranial EEG to define ictal onset and propagation pattern, and utilized CleveMed's Sapphire wireless PSG monitor (for nasal pressure, airflow, effort, SpO2, snore, plethysmography, heart rate) and Nonin's LifeSense (for EtCO2) and SenTec (for TcCO2) in our EMU in one patient. We plan to fully characterize 20 adults with focal epilepsy. Exclusions include obstructive sleep apnea, cardiac and pulmonary diseases, home oxygen supplementation, and prior brain surgery.
Results: At the time of this abstract submission, the technical challenges posed by monitoring in this setting have included 60-Hz interference in EEG and synchronization of data between the Sapphire PSG system and the Nihon Kohden EEG system.. A new interface device to enable the synchronization of the data between the Sapphire PSG system and the Nihon Kohden EEG system was developed and provides the capability for simultaneous cardiorespiratory and video-EEG monitoring. For the second goal, we have recorded one patient with focal epilepsy in the EMU after overcoming technical challenges. He tolerated the procedure well. No seizures were recorded during the 3 days of monitoring.
Conclusion: Respiratory interventions during seizures may be life-saving, but technical means are needed to determine their relative benefit. This is the first study to utilize a practical wireless portable sleep monitor to explore the relationship that respiratory disturbances may play in the mechanism of death in SUDEP.

0623

DAYTIME SLEEPINESS AND FATIGUE AFTER TRAUMATIC BRAIN INJURY: DRIVING SIMULATOR AND MAINTENANCE OF WAKEFULNESS TEST ASSESSMENT

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Introduction: Fatigue, daytime sleepiness, and attention difficulties are common following traumatic brain injury (TBI). The use of a driving simulator test could be a promising and ecologically valid tool to assess these daytime impairments. The aims of this study were to measure performance on a driving simulator task and examine its relationship with fatigue and sleepiness in individuals with TBI and healthy controls.
Methods: Participants were 16 adults (mean age = 38.7, 25% women) with moderate/severe TBI (mean time since injury = 60 months) and matched healthy controls (CTL; mean age = 38.3, 25% women). All participants underwent a 30-minute driving simulator task (including a divided attention task) in early afternoon, 4 Maintenance of Wakefulness Tests (MWT), and completed 9 hourly visual analogue scales of sleepiness and fatigue. T tests were computed to compare performance of TBI and CTL groups on driving simulator task. Pearson's correlations were

computed to explore the associations between sleepiness, fatigue, and driving performance for each group separately.

Results: TBI participants had more off-road accidents (4.25 vs. 2.75, p = .017) and a higher variability in their lateral roadway position (0.41 vs. 0.36, p = .048) compared to CTLs. Within the TBI group, mean sleep onset latency on the MWT was correlated with the number of centerline crossings (r =-0.52, p = .019) and the number of speeding events (r = -0.45, p = .039). Within the CTL group, reaction time on the divided attention task was associated with subjective ratings of fatigue (r = 0.54, p = .036) and sleepiness (r = 0.53, p = .038).

Conclusion: These results suggest that a driving simulator provide a useful and sensitive assessment technology to detect differences between individuals with TBI and healthy controls. Driving performance was associated with different sleep/fatigue indicators as a function of clinical status; objective sleepiness was associated with driving impairments in the TBI group whereas subjective sleepiness and fatigue were correlated with driving performance in the health controls.

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0624

HEALTH-RELATED QUALITY OF LIFE ASSOCIATIONS VARY BY TYPE OF SLEEP DISTURBANCES IN PARKINSON'S DISEASE

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Introduction: Non-motor manifestations including sleep disturbances are posited as significant determinants of health outcomes in Parkinson's disease (PD). Data are lacking about the association of different types of sleep complaints on health-related quality of life (HRQOL) of PD patients.

Methods: We analyzed data from 147 PD patients enrolled in an observational study of PD progression. We compared generic HRQOL (SF-36 health survey) and self-reported sleep disturbance (Medical Outcomes Study Sleep Scale: sleep initiation, sleep maintenance, snoring, awakening short of breath or with headache, sleep inadequacy, and daytime somnolence) of the PD patients with age- and gender-adjusted general population norms. In addition, we estimated the associations of the six sleep scales disturbance symptoms (independent variables) with HRQOL and with depression (measured by PHQ-9 and GDS-15), adjusting for PD disease stage (Hoehn & Yahr; H&Y). We regressed the 8 SF-36 scales, the SF-36 physical and mental health summary scores (PCS and MCS), the PHQ-9, and the GDS-15 onto the different sleep scales and the H&Y score.

Results: Mean age=72 years; 41% were female; mean PD duration=4.8 years; 7.2% were H&Y Stage 4 or 5. Compared with norms, study subjects had significantly worse severity of sleep maintenance, snoring, sleep inadequacy, and daytime somnolence and reported significantly worse HRQOL on all but the pain scale (all p<=0.0004). Across the multivariable models, awakening short of breath or with headache was most strongly associated with HRQOL and with depression, significantly associated with 6 of 8 SF-36 scales, both composite scores, and both depression measures (p<=0.05). Daytime somnolence and disturbances in sleep initiation were also strongly associated with HRQOL and with depression (5 of 8 SF-36 scales and 1 of 2 composite scores each; p<=0.05); sleep initiation disturbance was associated with GDS-15 (p<=0.001), and daytime somnolance was associated with both depression measures (p<=0.001). Snoring and sleep inadequacy were not associated with HRQOL or with depression, with the exception of sleep inadequacy with the SF-36 energy scale (p<0.001).

Conclusion: These findings suggest that exploration of non-motor symptoms of sleep initiation difficulties, shortness of breath or headache on awakening, and daytime somnolence should be part of the ongoing assessments of patients with PD.

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0625

OBSTRUCTIVE SLEEP APNEA IN ADULT AND PEDIATRIC PATIENTS WITH IMPLANTED VAGAL NERVE STIMULATORS

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Introduction: Vagal nerve stimulation (VNS) is an approved therapy for refractory epilepsy. VNS is believed to modulate vagal input to the nucleus of the solitary tract. Adverse effects of VNS include respiratory symptoms such as dyspnea and voice alteration. Recent awareness has heightened as a result of its likely association with obstructive sleep apnea (OSA). We have performed a review of pediatric and adult cases with an implanted VNS to evaluate the presence of OSA.

Methods: We reviewed the nocturnal polysomnograms on patients with an implanted VNS. We defined pediatric patients as patients below 16 years. We collected demographic and baseline polysomnographic data. The presence of obstructive sleep apnea (OSA) was compared between the two groups. We defined OSA as an apnea hypopnea index (AHI) of >1.5 events/hour in children and >5 events/hour in the adult subjects.

Results: We collected 16 cases. 5 were pediatric patients with a mean age 10.8 years (range 7-14 years) and 11 patients were adults with a mean age 27.8 years (range 16-62 years). There was an equal distribution of gender (8 males and 8 females).The mean BMI was 15.7 kg/m2 (SD +/-8) in the pediatric group and 26.9 kg/m2 (SD +/-8.9) in the adult group. 71% reported an abnormal Epworth Sleepiness score of >10. All 16 cases reported snoring. The mean sleep time was 6.3 hours (SD +/-1.5hours). The mean sleep efficiency was 86% and the sleep architecture was grossly intact (N1 5.6%, N2 65%, N3 17.7% and REM sleep 11.7%). 54.5% of the adult patients (AHI 12.5 SD +/- 6.6) and 60% of the pediatric patients (mean AHI 8 SD +/- 6) were diagnosed with OSA. All the adults and 2/3 of the pediatric cases diagnosed with OSA were of male gender. All the pediatric patients had cerebral palsy as the etiology of their seizure disorder. Neither group had significant central apneas (CAI >5). Clinical seizure activity was observed during the PSG in 40% pediatric and in 18% of the adult patients.

Conclusion: In our review, we confirm the presence of obstructive sleep apnea in our patients with a VNS implanted for refractory epilepsy. It appears from our observation that pediatric and adult patients are at equal risk for OSA with male gender being a significant risk factor. Thus, patients with an implanted VNS presenting with snoring and symptoms suggestive of sleep disordered breathing would benefit from a diagnostic PSG to rule out sleep apnea, especially if they are of male gender. Future studies to evaluate VNS parameters is also suggested

0626

DIFFERENTIAL EFFECTS OF MORNING LIGHT TREATMENT COMBINED WITH SLEEP HYGIENE THERAPY ON MEMORY-IMPAIRED INDIVIDUALS AND THEIR CAREGIVERS

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Introduction: Sleep problems are highly prevalent in older adults and are exacerbated in individuals with pathological memory decline. Because of issues of polypharmacy, non-pharmacological treatments have been examined, among them bright light administration. We tested the ability of bright light to improve sleep in dementia and MCI patients (age 77.9±8.1 yrs; MMSE 22.1±4.7) and their caregivers (age 68.8±12.7 yrs; MMSE 29.2±1.1).

Methods: Participants were randomized to receive either 30 minutes of bright (treatment, 4360±1760 lux) or dim (control, 76.2±90.1 lux) light within 30 minutes of arising. Sleep diaries and actigraphy were collected for a baseline week and the second of two weeks of light treatment. All 54 patient/caregiver dyads received sleep hygiene. We compared changes in the sleep of caregivers and patients between bright- and dim-light conditions using repeated measure ANOVA with post hoc t-tests, and used linear regression to identify predictors of changes in particular sleep parameters.

Results: Wake after sleep onset (WASO) and sleep efficiency (SE) declined in all caregivers, irrespective of treatment group (p<0.05), while time in bed (TIB) and total sleep time (TST) did not change. Patients exposed to dim light experienced no changes in sleep measures. Patients exposed to bright light experienced a decrease in both TIB and TST (p<0.05). The decreased TIB was associated with an earlier out-of-bed time (r^2=0.79, p<0.001). The decreased TST was associated with decreased SE (r^2=0.62, p<0.001) and increased WASO (r^2=0.44, p<0.001).

Conclusion: Caregivers had mixed results, with a decrease in WASO but a concomitant decline in SE. These results were not attributable to the light per se and were likely secondary to the sleep hygiene treatment or a participation effect. Bright light had notably negative effects in patients as it decreased TST. Longer or differently timed treatment may be necessary to evoke positive effects on sleep in both groups.

0627

QUALITY OF SLEEP AND THE RELATED FACTORS IN THE KOREAN PATIENTS WITH NON-VERTIGINOUS DIZZINESS

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Introduction: Poor sleep quality causes various daytime function impairments like fatigue and daytime sleepiness. Dizziness is a common presenting complaint and may be attributed broadly to a number of underlying disorders. However, studies on the sleep quality in patient with dizziness still remain. We hypothesized the patients with dizziness may have poor quality of sleep. The objective of this study was to investigate the quality of sleep and the related factors between the Korean patients with non-vertiginous dizziness (NVD) and the controls.

Methods: We investigated 112 patients who had presented NVD in neurology department and no major medical, psychiatric, and neurological disorders so that they completed the following questionnaires: the Pitts-burgh Sleep Quality Index (PSQI), the Fatigue Severity Index (FSS), the Epworth Sleepiness Scale (ESS), Beck Depression Inventory (BDI), Sleep Apnea scale of the Sleep Disorders Questionnaire (SA-SDQ). 117 dizziness-free controls were recruited via Health Screening Center. We used multiple linear regression analysis to estimate the differences in FSS, ESS and PSQI among the patients with NVD and the controls. Statistical models were progressively adjusted for age, sex, body mass index (BMI), SA-SDQ, and BDI.

Results: Patient with NVD had significantly higher PSQI score compared with the controls (7.6±4.3 vs. 5.4±2.6, p<0.01) and did not different from controls in FSS and ESS score. By multiple linear regression analysis, patients with NVD had significantly higher PSQI score (beta=2.20, 95% CI 1.27-3.13) without adjustment. It had also significantly higher compared with the controls after controlling age, sex, BMI, SA-SDQ. However, it was not significantly associated with the patients with NVD after additional adjustment for BDI.

Conclusion: Fatigue and daytime sleepiness are not different between two groups. The decreased quality of sleep in patients with NVD is not suggested by dizziness itself but can be explained by depression as the related factor.

0628

PARKINSON'S DISEASE (PD) AND PROGRESSIVE SUPRANUCLEAR PALSY (PSP) WITH LOW OREXIN LEVELS

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Introduction: Although excessive daytime sleepiness (EDS) commonly appears in Parkinson's disease (PD) and its related disorders, the mechanism underlying the generation of this symptom remains unclear. Recently, the levels of CSF orexin and its relation to EDS in PD were examined, but the results have been inconclusive. In this study, CSF orexin was measured in 150 patients with PD or progressive supranuclear palsy (PSP). The majority of these cases showed normal levels of orexin (200pg/ml-400pg/ml). Aside from these, however, we experienced 4 cases with PD or PSP which showed low orexin levels under 110 pg/ml.

Methods: case reports

Results: Case1: PD, A 58-year-old man: He suffered from EDS from high school days. At age 45, he was diagnosed with PD. He experienced frequent hypnagogic hallucinations with abnormal limb movements. MSLT showed short sleep latencies (SL) and SOREMPs. Case2: PD, A 57-year-old man: He became affected by EDS daily at age 57. Two years later, he had difficulty in moving his limbs and got diagnosis as PD. On MSLT, SL was short and SOREMPs were four times. Case3: PSP, A 74 year-old woman: She developed difficulty in walking and EDS from two years ago. She was diagnosed as probable PSP. Her EDS mimicked narcolepsy without cataplexy, because MSLT showed short SL (less than 2-min without SOREMPs). Case4: PSP, A 74 year-old man: He had had narcoleptic symptoms since age 20, but by age 40 his symptoms almost diminished. At age 69, he had narcoleptic symptoms again and got diagnosis as probable PSP. MSLT showed short mean SL less than 2.9 min and SOREMPs.

Conclusion: PD of Case1 and PSP of Case4 occurred 10 to 20 years after narcolepsy onset. PD of Case2 and PSP of Case3 occurred simultaneously with narcoleptic symptoms. We think the former cases of narcolepsy coexisted with PD or PSP. The latter cases of narcoleptic symptoms were secondary to PD or PSP. It means that these neuro-pathological changes may have caused the decrease of orexin neurons. Interestingly, these cases showed sleep architecture changes in PSGs. In Case1 and Case4, percentages of REM stages increased. Especially, the percentage of REM without atonia of Case1 increased up to 62%. Case2

and Case3 showed prolonged percentages of stage 3-4 sleep. Some neuropatological changes might be related to these sleep changes.

0629

SLEEP DISORDERED BREATHING AND OTHER SLEEP DYSFUNCTION IN MYOTONIC DYSTROPHY TYPE 2

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Introduction: Myotonic dystrophy type 2 (DM2) is a recently described hereditary myotonic dystrophy which is differentiated from myotonic dystrophy type 1 (DM1) by different genetic mutations. Sleep disordered breathing (SDB) has not been described in DM2 but is known to occur in DM1.
Methods: We are presenting six patients (four women and two men ages 51-63 years) with symmetric muscle weakness involving proximal more than distal muscles and thenar eminence percussion myotonia. Major sleep complaints included chronic insomnia, snoring, excessive daytime sleepiness and dream-enacting behavior (DEB) in one woman.
Results: Genetic testing was consistent with a diagnosis of DM2. Electromyography showed myopathic findings and myotonia. Overnight polysomnography (PSG) disclosed obstructive sleep apnea in four patients and REM behavior disorder (RBD) in one woman (REM without atonia and excessive phasic muscle bursts associated with dream enacting behavior). Other PSG findings included absent REM sleep in one and alpha-REM-spindle mixture in another who also had paradoxical movements in the respiratory effort channels suggesting increased upper airway resistance.
Conclusion: These sleep abnormalities (RBD in one and sleep disordered breathing in five patients) with DM2 are novel observations.

0630

AN INVESTIGATION OF SPONTANEOUS CORTICAL SLOW OSCILLATIONS DURING NREM SLEEP USING 256-CHANNEL EEG IN NON-EPILEPTIC AND EPILEPTIC SUBJECTS

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Introduction: Cortical slow oscillations (CSO) (<1Hz) are generated by the neocortex during Non-REM sleep. The surface negativity of CSO corresponds to the "down state" (DS) or hyperpolarization of cortical neurons intracellularly and a suppression of extracellular spiking activity. The "up state" (US) reflects a depolarization or heightened activity in the neocortical cells. Longer DS have been shown to be associated with larger CSO and more suppression of spiking activity. Therefore, the size of the CSO should indicate the amount of suppression of spiking activity in the cortical cells. Spike-Wave nocturnal seizures have been shown to emerge from CSO. The disruption of sleep homeostasis by epilepsy may lead to disruption of CSO generation. Using dense-array EEG, we attempt to investigate a comparison between Epileptic and Non-Epileptic spontaneously generated CSO during slow-wave sleep (SWS).
Methods: We acquired sleep EEG from 12 participants using a 256-channel sensor array (6 non-epileptic and 6 epileptic). Sleep stages were identified and CSO were scored during SWS from the first sleep cycle. CSO were evaluated in source space using a 4-shell spherical model that represents the scalp, skull, cerebrospinal fluid, and the cortex with low-resolution brain electromagnetic tomography method (LORETA). Statistical analyses were performed on the CSO source waveforms.
Results: We found a statistically significant difference in the strength of current between the Epileptic CSO grand average (GA) Regions of Interest (ROI) and the Epileptic CSO GA ROI. The Non-Epileptic CSO

GA ROI (M = .2871) had a significantly stronger current then the Epileptic CSO GA ROI (M = .1054), F (1,23)=47.597, p < .01.
Conclusion: We conclude that Non-Epileptic CSO is weaker then the Epileptic CSO in source space and that the Epileptic CSO suppresses less spiking activity during the DS. This could be an important clue towards the modulation of neural excitability related to nocturnal seizure pathology.

0631

CLINICAL AND POLYSOMNOGRAPHIC FINDINGS IN SUBJECTS WITH MULTIPLE SCLEROSIS

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Introduction: There is a dearth of information about the relationship between multiple sclerosis (MS) and sleep disordered breathing. The objectives of this retrospective study were to explore differences between apnea-hypopnea and central apnea indices in sleep-laboratory-referred patients with and without MS, and explore potential radiographic and clinical features that may predispose MS subjects to increased SDB prevalence or severity.
Methods: This was a retrospective study using existing standard nocturnal polysomnography (PSG) data from MS cases and controls referred to the University of Michigan Sleep Lab. Demographic data (age, gender, BMI) and PSG data including apnea-hypopnea index (AHI) and central apnea index (CAI) were collected on the following: 48 subjects with clinically definite MS; 84 control subjects matched by BMI, age and gender; and 48 randomly selected control subjects. Mean AHI and CAI were compared among MS cases and matched controls using paired T-tests. Multiple linear regression, adjusting for age, gender and BMI, was used to analyze differences between mean AHI and CAI among MS cases and randomly selected controls.
Results: Mean AHI was greater among MS cases (18.73±22.1) than matched controls (9.38±8.9, p=0.0114) or randomly selected controls (9.95±9.81, p=0.0050). Mean CAI was also greater among MS cases (3.47± 8.1) than matched controls (0.37±1.1, p=0.0178) or randomly selected controls (0.42±1.23, p=0.0173). Among MS cases, n=37 subjects had available clinical and/or MRI data to be stratified by the presence or absence of radiographic and/or clinical brainstem involvement. Of the n=22 MS subjects with evidence of brainstem involvement, differences with controls in AHI and CAI became more robust, while among n=15 MS subjects without brainstem involvement, these differences diminished and became non-significant.
Conclusion: These data suggest a predisposition for obstructive sleep apnea and accompanying central apneas among MS patients, particularly those with brainstem involvement.

0632

HEADACHE, SLEEP DISORDERS AND CERVICAL RADICULOPATHY ARE RELATED

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Introduction: The objective of this study was to document a perceived association between headache and sleep disorders in a neurologic clinic population. If such an association were found, one cause might be sleep in the lateral position. Another possible cause might be cervical radiculopathy, since this disorder has been shown to be prevalent in patients with sleep disorders. Previous studies have suggested a relationship between headache and sleep disturbances, while other studies suggest a relationship between cervical radiculopathy and headache.
Methods: In a retrospective review, the records of all new patients consecutively seen in a general neurology clinic with a primary diagnosis of

headache over one year's time were analyzed. As a part of their evaluation, those patients were queried regarding their sleep, and, if appropriate, were studied with polysomnography in an accredited sleep disorders center. Patients with changes on the neurologic exam suggestive of cervical radiculopathy were examined with EMG-NCV testing.

Results: Of the 700 patients who had a diagnosis of headache on initial evaluation, 491 (70%) also had sleep diagnoses. Of these patients with sleep diagnoses, 277 (56%) completed polysomnography examinations. 76% of the polysomnography group had upper airway resistance syndrome (UARS) or obstructive sleep apnea (OSA). Striking in the polysomnography group patients was the presence of concomitant cervical radiculopathy (73 %). Of the patients with cervical radiculopathy, 50% or more of total sleep time was spent in non-supine sleep, despite request by the technologist to sleep supine.

Conclusion: 1. Headache is strongly associated with sleep disordered breathing. 2. Cervical radiculopathy is strongly associated with sleep disordered breathing, confirming a previous study. 3. Non-supine sleep provoked by sleep disordered breathing may play a previously unrecognized role in headache and cervical radiculopathy.

0633

SEIZURE REDUCTION FOLLOWING NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE THERAPY FOR CO-MORBID OBSTRUCTIVE SLEEP APNEA IN EPILEPSY

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Introduction: Co-morbid OSA is frequent in epilepsy, and treatment with nCPAP may reduce seizure frequency but the degree of impact on seizure outcomes remains unclear. We hypothesized that seizure frequency would be reduced by nasal continuous positive airway pressure (nCPAP) therapy in epilepsy patients with co-morbid obstructive sleep apnea (OSA). We aimed to analyze the impact of nCPAP therapy on seizure frequency.

Methods: We retrospectively analyzed 184 epilepsy patients who underwent polysomnography between 1/1/00-5/30/09. Demographic, seizure frequency, antiepileptic drug load, and PSG variables were recorded. Seizure frequency was compared between epilepsy patients with OSA (apnea-hypopnea index (AHI)>5/hour) who were compliant with nCPAP and those who either deferred nCPAP or were non-compliant. Group comparisons were analyzed with 2-tailed T-tests or Wilcoxon signed rank tests in JMP or SAS (Chicago, IL).

Results: 110 (60%) epilepsy patients had OSA. Average AHI was 22.4 ± 20.8. Forty-three patients received nCPAP. Of 33 patients having pre- and post-nCPAP data, seizure frequency decreased significantly (t=2.138, p=0.04). 79% reported seizure reduction and 61% were responders (having a 50% or greater seizure reduction), and this effect held when antiepileptic drugs were unchanged or reduced (n=18, p=0.01). In patients who did not receive or comply with nCPAP therapy, there was no significant difference in seizure frequency (n=28, t=-1.411, p=0.17).

Conclusion: nCPAP treatment significantly reduces seizure frequency, and the degree of seizure improvement appears comparable to the effect of adjunctive antiepileptic drug therapy. Further prospective studies of the impact of co-morbid OSA in epilepsy patients on seizure burden and interictal state factors crucial to quality of life (i.e., mood state, vulnerability to antiepileptic drug adverse effects, and sleepiness/vigilance) are warranted.

0634

VAGUS NERVE STIMULATION THERAPY ENHANCES OBSTRUCTIVE RESPIRATIONS DURING SLEEP

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Introduction: Vagus Nerve Stimulator (VNS) therapy has been used in medication resistant Epilepsy with improved outcomes and utilization has increased over the past decade. In our center we have OSA patients with epilepsy that have VNS devices and have recognized many of these patients have periodic obstructive breathing patterns that correspond to their VNS stimulation settings. We sought to confirm this association and to also determine optimal methods of treating both the patients seizures and OSA rather than one at the detriment of the other.

Methods: The study was done in two parts. First, we reviewed all of our patients who have both VNS devices for the treatment of their epilepsy and who underwent NPSG testing. Next, assessment was done to identify if there was an association between the VNS stimulation pattern and the occurrence of OSA. In one patient modifications were made in the VNS settings during NPSG testing to clearly confirm the association between VNS stimulation and OSA occurrence and then modifications were made on the VNS stimulation settings to identify parameters that stopped producing OSA.

Results: Eight patients met our criteria of which six demonstrated OSA. All six demonstrated OSA in a pattern that correlated to the VNS stimulation rate. PAP titration was performed and initially prevented OSA from occurring during sleep. In three patients over time OSA worsened. Repeat titrations were performed and a clear pattern of periodic OSA was identified that was not adequately treated by prior CPAP pressures. To address the above observation one patient thus far was further evaluated by a repeat PAP titration. During the study, clear periodic obstructive apneas again occurred in accordance with her VNS settings. Stimulator parameters were modified to identify parameters that would not precipitate OSA. Lowering the stimulation rate from 25Hz down to 10 Hz resolved the precipitation of OSA during the study.

Conclusion: We claim that OSA is a potential complication of VNS therapy. This can be managed adequately but must be recognized when present. VNS stimulation parameters may require modification to optimize OSA treatment. We will present the clinical significance of these findings in relation to treating both OSA and Epilepsy. Further study is clearly needed on this topic since VNS is a useful treatment in Epilepsy patients.

0635

NOCTURNAL SEIZURES AND DYSREGULATION IN THE AUTONOMIC NERVOUS SYSTEM

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Introduction: There are several reports that nocturnal seizures and sudden unexpected death in epileptic patients (SUDEP) is related. Correlation of autonomic nervous system (ANS) dysregulation and SUDEP has been recognized. Heart rate variability (HRV) has been utilized to evaluate ANS. High frequency (HF) component (0.15-0.4 Hz) of HRV is known to represent parasympathetic modulation. HF tends to appear steadily in normal NREM sleep. Temporal correlation between ANS and nocturnal seizure is not known well. Complex demodulation analysis of HRV allows us to detect dynamic changes in HF with temporal resolution of 6.25 seconds, whereas other analyses (i.e. fast Fourier transform) have that of 1-2 minutes.

Methods: All of the nocturnal seizures captured in our epilepsy monitoring unit from January 2008 to September 2010 were reviewed retrospectively. Electrocardiogram data were analyzed with complex

demodulation analysis with dense spectrum array display. We studied the correlation of HRV with parameters of seizures 15 minutes before and after the onset.

Results: 30 nocturnal seizures were found in 18 patients. Average age was 37.8. 9 patients were men and 9 were women. 20 seizures were temporal onset, 4 were frontal, 2 were central and 4 were undetermined. 21 seizures occurred during N2 sleep and 9 occurred during N1 stage. None occurred either N3 or REM sleep. 21 out of 30 seizures had HF component before the onset. Among 21 seizures with HF, 9 seizures showed early disappearance of HF before the electrographic seizure onset. Out of 9 seizures, 7 were right hemispheric onset, 1 was left and 1 was unknown laterality. Right hemspheric onset seizures showed earlier HF disappearance than left (p=0.046) with Mantel-Haenstzel test. After 1 seizure, normal sleep pattern was regained within 15 minutes.

Conclusion: Right hemspheric onset in nocturnal seizures seemed to involve ANS earlier than left.

0636

USE OF THE BERLIN QUESTIONNAIRE IN IDENTIFYING STROKE PATIENTS AT RISK OF SLEEP APNEA

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Introduction: The Berlin Questionnaire is a validated tool used to identify patients at high or low risk of sleep apnea. The sensitivity, specificity, positive predictive value and likelihood ratio of the Berlin Questionnaire have previously been reported as 0.86, 0.77, 0.89 and 3.79, respectively. Sleep apnea is common among patients with stroke and transient ischemic attack (TIA). The Berlin Questionnaire has not been validated among patients with cerebrovascular disease.

Methods: We sought to evaluate the test characteristics of the Berlin Questionnaire in identifying sleep apnea among patients with an ischemic stroke or TIA. We used data from a multi-site randomized, controlled strategy trial that included ischemic stroke and TIA patients at two VA hospitals. All patients received polysomnography and completed a Berlin Questionnaire. Sleep apnea was defined as present if the apnea-hypopnea index (AHI) was ≥5 on the basis of the polysomnography.

Results: Among 92 veterans with polysomnography and Berlin Questionnaire data, 62% had sleep apnea. The sensitivity, specificity, positive-, negative- predictive value and likelihood ratio of the Berlin Questionnaire was 0.65, 0.34, 0.62, 0.37 and 0.99, respectively.

Conclusion: The Berlin Questionnaire does not appear to be a useful tool for identifying sleep apnea risk among patients with stroke or TIA, perhaps due to the high prevalence of sleep apnea in this population. In the absence of an effective sleep apnea screening tool, post-stroke and TIA patients may benefit from formal polysomnography.

0637

PREDICTORS OF CO-MORBID OBSTRUCTIVE SLEEP APNEA IN EPILEPSY

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Introduction: Co-morbid obstructive sleep apnea (OSA) is frequent in epilepsy. However, predictive features for OSA in this patient population remain unclear. We aimed to describe clinical predictors for co-morbid OSA in epilepsy.

Methods: We retrospectively analyzed 184 epilepsy patients who underwent PSG, including those with OSA (n=110, apnea-hypopnea index (AHI)>5/hour) and without OSA (n=74) between 1/1/00-5/30/09. Demographic, epilepsy syndrome, antiepileptic drug (AED) load, and PSG variables were recorded. Pearson correlation statistics were utilized to identify associations between clinical variables and OSA. Significantly associated clinical variables were then fit into multiple linear regression (treating natural log transformation of the AHI as a continuous outcome variable) and logistic regression (treating AHI as a binary outcome variable) models to identify clinical predictors for OSA utilizing SAS (Chicago, IL).

Results: PSG yielded OSA diagnosis in 111 (60%) patients, with average AHI of 22.4 ± 20.8. Clinical variables associated with OSA were age (p=0.0002), neck circumference (p=0.0001), and witnessed apneas (p=0.018). Hypersomnia complaint (p=0.11), snoring (p=0.89), gasping (p=0.10), epilepsy syndrome (p=0.92), AED drug load (p=0.50), AED mono- or polytherapy (p=0.98), and BMI (p=0.11) were not associated with OSA. Multiple linear (ML) and logistic regression (LR) both identified age (ML p=0.0001, LR p=0.001) and neck circumference (ML p=0.0002, LR p=0.017) as independent predictors for OSA. With neck circumference removed from the model, male gender also became a significant predictor (ML p=0.0004, LR p=0.002).

Conclusion: Co-morbid OSA in epilepsy patients is predicted by older age and enlarged neck circumference. The association of male gender with OSA in epilepsy may also be mediated by a larger neck circumference. Epilepsy-related factors (epilepsy type, AED load) and overweight body habitus were not significant predictors. Routine measurement of neck circumference may assist in selecting patients with possible co-morbid OSA for diagnostic polysomnography in patients with epilepsy.

0638

LEVO-DOPA (L-DOPA) AND DOPAMINE AGONIST (DA)-NAIVE IDIOPATHIC PARKINSON'S DISEASE (PD) PATIENTS DEMONSTRATE MAINTENANCE OF WAKEFULNESS TEST (MWT)-DEFINED ALERTNESS

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Introduction: Animal models of PD suggest deficits in daytime alertness but characterization of the daytime alertness continuum in human disease is typically contaminated by medication use. We report MWT comparisons of treated and untreated PD patients matched for disease stage and motor impairment.

Methods: Idiopathic PD pts (n = 48) (X age = 63.9; 31 M, 17 F) underwent a 48 hr sleep lab protocol of 2 PSG nts followed by 2 days of 4-nap MWT. MWT duration was held constant at 40 mins; we scored sleep latency to 3 consecutive sleep epochs (SLAT3) and obtained means for

each pt across naps. Eight had never received any exposure to L-dopa or DA; 40 received either or both of these drug classes. All underwent UPDRS; for those receiving L-dopa/DA, ratings were made in "on" condition. Mean (SD) UPDRS Motor Score = 18.2 (8.1); mean (SD) yrs diagnosed = 5.8 (3.5).

Results: Groups did not differ in age, sex, or UPDRS, but differed in yrs since diagnosis (2.1 for never treated vs 6.5 for L-dopa/DA treated, t = 6.9, p. < .0001). Pts receiving L-dopa/DA fell asleep more quickly when compared to pts not receiving either medication (20.4 [12.5] mins vs 31.9 [9.5] mins, t = 2.28, p < .03; effect size d = .98). We then truncated the former (n = 13) to include only pts with disease duration of 4 yrs or less (maximum duration for L-dopa/DA naive group). UPDRS scores were equivalent (16.1 vs 16.8, NS), but MWT comparison was highly statistically significant (p < .005; effect size d = 1.44), suggesting a highly robust effect, despite smaller sample.

Conclusion: These data suggest that although the degenerative processes associated with PD may be associated with deficits in alertness, L-dopa and/or DA contribute to that effect.

Support (If Any): R01 NS-050595; KL RR-025009 (ACTSI)

0639

DIFFERENTIAL ASSOCIATIONS BETWEEN LEVODOPA (L-DOPA) VS DOPAMINE AGONIST (DA) DOSE AND MAINTENANCE OF WAKEFULNESS TEST (MWT) MEASURES OF ALERTNESS IN IDIOPATHIC PARKINSON'S DISEASE (PD)

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Introduction: Medications influencing the dopaminergic system are suspected to play a role in the sleepiness of PD. In this study, we examined L-dopa and DA dose-response associations with MWT-defined alertness.

Methods: PD pts (n = 40) (X age = 64.2, 27 M, 13F) underwent a 48 hr sleep lab protocol of 2 PSG nts followed by 2 days of 4-nap MWT. MWT duration was held constant at 40 mins; we scored sleep latency to 3 consecutive epochs of sleep (SLAT3) and obtained means for each pt across naps. Of the 40 patients, 27 received DA (X pergolide dose equivalent = 2.6 mg, SD = 1.1) and 33 received L-dopa (X L-dopa daily dose = 539.4 mg, SD = 264.5) and 20 received both medication classes. Patients taking L-dopa were significantly older (65.6 vs 57.9, t = 2.09, p < .05) and those taking DA significantly younger (62.1 vs 68.6, t = 2.19, p < .04) when compared to pts not taking those medication classes.

Results: Across all 40 patients, higher L-dopa dose was positively correlated with longer latency to fall asleep SLAT3 (rho = .31, p < .05), however, higher pergolide equivalent dose was correlated with shorter latency to fall asleep (rho = -.34, p < .05). Comparisons of patients receiving only L-dopa (n = 13) and only DA (n = 7) confirmed longer sleep latencies in the former (23.9 vs 14.1 mins, t = 2.01, p = .059).

Conclusion: These data suggest that the two major classes of medications used to treat PD patients may have divergent effects on daytime alertness in this patient population, although preferential age-dependent patterns of prescribing may confound the effect.

Support (If Any): R01 NS-050595; KL RR-025009 (ACTSI)

0640

PILOT STUDY ON THE EFFECTS OF POOR SLEEP ON EXECUTIVE FUNCTIONING IN ESSENTIAL TREMOR AND PARKINSON'S DISEASE

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Introduction: Beyond motor symptoms, essential tremor (ET) and Parkinson's disease (PD) have comparable high levels of executive dysfunc-

tion and sleep complaint. The brain relies on compensatory mechanisms to maintain cognitive performance following poor sleep. Increased dopamine and greater cerebellar activity each correlate with better cognitive performance during sleep loss in healthy adults. A popular hypothesis is that cerebellar hyperactivity leads to downstream thalamo-cortical dysfunction in ET. Likewise, ET patients may be cognitively resistant to poor sleep. Conversely, dopamine depletion and neurologic compromise in PD may lead to greater cognitive vulnerability to poor sleep.

Methods: The Frontal Systems of Behavior (FrSBe) questionnaire and Center for Epidemiologic Studies Depression Scale (CES-D) were administered to a convenience sample of 94 idiopathic PDs and 10 ETs recruited during routine clinic visits at the UF Movement Disorders Center. Poor sleep was determined by self-report response to the CES-D question "Over the last week my sleep was restless?" Patients also completed the Beck Depression Inventory and the State Anxiety Index and were included as covariates in a 2(ET vs. PD) x 2(not restless vs. restless sleep) analysis of covariance (ANCOVA). The dependent variable, executive functioning, was computed for each participant based on self-report responses to several FrSBe items and converted to t-score controlling for age and education.

Results: Analysis revealed a significant interaction, but no main effects, for neurologic condition and restless sleep, $F(1,98)=4.12, p<.05, \eta2=.04$. Executive functioning was rated as more impaired in PDs with restless sleep and ETs without restless sleep, M=62.04(1.49),M=60.65(6.14) than ETs with restless sleep and PDs without restless sleep, M=52.22(5.01),M=53.40(2.35), respectively.

Conclusion: Restless sleep is related to worse executive functioning in PDs but better functioning in ETs. One interpretation may be that PDs are cognitively vulnerable and ETs cognitively resistant to the effects of poor sleep. A larger sample of ETs is needed to confirm these results.

0641

POST-STREPTOCOCCAL ANTIBODIES ARE ASSOCIATED WITH METABOLIC SYNDROME IN A POPULATION-BASED SAMPLE OF HEALTHY ADULTS

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Introduction: Disturbed Sleep is associated with metabolic syndrome (MetS) but the pathogenesis is still elusive. Recently, we found associations between anti-Streptolysin O antibodies and narcolepsy and between post-streptococcal autoantibodies against Protein Disulphide Isomerase (PDI), an enzyme involved in insulin degradation, and insulin resistance. This led us to speculate that post-streptococcal immunity may be involved in the sleep-MetS association.
Methods: Metabolic data (HDL, triglycerides, fasting glucose, blood pressure, waist circumference, BMI, smoking); post-streptococcal antibodies (anti-Streptolysin O (ASO) and anti-PDI), and C-reactive protein (CRP, as a general inflammatory marker), were assessed in 1158 participants of the Wisconsin Sleep Cohort Study every 4 years for a total of 2471 visits. The cohort consists of healthy adults with an over-sampling of habitual snorers to ensure an adequate distribution of sleep-disordered breathing.
Results: Of 2471 visits, anti-PDI antibodies were found in 591 (23.9%), ASO$\geq$ 100 in 412 (16.7%), and 806 (32.6%) were positive for either or both anti-PDI antibodies and ASO. CRP did not differ between groups. Both the ASO and anti-PDI anti-streptococcal antibodies were independently associated with MetS [anti-PDI: OR 1.40 (95% CI 1.15, 1.70), p= 0.0010; ASO: OR 1.36 (95% CI 1.10, 1.67), p= 0.0042; anti-PDI and/or ASO: OR 1.38 (95% CI 1.16, 1.64), p= 0.0003; adjusted for age, gender, education, smoking]. Strikingly, these anti-streptococcal antibodies were also longitudinally associated with MetS [anti-PDI: OR 2.35 (95% CI 1.24, 4.46), p= 0.0090; ASO: OR 2.11 (95% CI 1.08, 4.16), p= 0.0296; anti-PDI and/or ASO: OR 2.36 (95% CI 1.33, 4.16), p= 0.0030].
Conclusion: The anti-streptococcal antibodies ASO and anti-PDI are associated with MetS in both cross-sectional and longitudinal studies, identifying a novel risk factor with potential for population screening and primary prevention. These data are in line with a growing body of evidence linking sleep, infections, immunity and metabolism.

0642

EXCESSIVE DAYTIME SLEEPINESS IS ASSOCIATED WITH HIGHER HBA1C IN TYPE 2 DIABETES: THE GLYCOSA STUDY

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Introduction: Despite the growing awareness that sleep quality can impact glucose metabolism, associations between sleep parameters and glycemic control in type 2 diabetes are not well defined. Using baseline data from an ongoing multi-center study, the current analysis examined whether obstructive sleep apnea (OSA) severity or sleepiness are associated with HbA1c in type 2 diabetes.
Methods: The current analyses are based on the GLYCOSA study, an ongoing multi-center study evaluating the effects of positive airway pressure for OSA in type 2 diabetes. Patients with type 2 diabetes not on insulin were screened for OSA with an ApneaLink™(ResMed). Other assessments included the Epworth Sleepiness Scale (ESS) and HbA1c levels. To determine whether OSA severity or ESS were independently associated with HbA1c, generalized linear regression models were used.
Results: The sample consisted of 796 participants with data on HbA1c, ESS, and ApneaLink-derived apnea hypopnea index (AHI) and oxygen desaturation index (ODI). The sample was predominantly male (62.2%) with a mean age of 61.3 years and BMI of 32.2 kg/m². The median AHI and ODI were 16 events/hr and 12 events/hr, respectively. The median and mean ESS scores in the sample were 9.0 and 9.5, respectively, with an interquartile range of 6-12. No association was observed between HbA1c and AHI or ODI. ESS was associated with higher HbA1c levels even after accounting for confounding factors (age, sex, race, clinic site, BMI, and waist). Comparing the two lower ESS quartiles (< 9), participants in the third (ESS:10-12) and fourth quartiles (ESS>12) had higher HbA1c levels by 0.11 and 0.26 percentage points, respectively, independent of age, sex, race, clinic site, and BMI (p<0.0001 for linear trend).
Conclusion: Severity of OSA as indexed by the AHI or ODI is not associated with glycemic control in type 2 diabetes. However, self-reported sleepiness is independently associated with higher HbA1C levels.
Support (If Any): Funding for the GLYCOSA study was provided by ResMed.

0643

RELATIONSHIP OF SLEEP DEFICIENCY TO PERCEIVED PAIN AND PHYSICAL DISABILITY IN HOSPITAL PATIENT CARE WORKERS

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Introduction: Sleep deficiency (insufficient sleep duration and/or inadequate sleep quality) has consequences for pain and work function. In this study of hospital workers employing a socioecological framework, we tested the hypothesis that sleep deficiency is associated with self-reported pain, functional limitations, and work-interfering physical limitations, controlling for relevant confounders.
Methods: Patient Care Unit workers from two large academic hospitals in the Boston metropolitan area completed a workplace health survey that included measures of socio-demographics, workplace factors, psychological distress, sleep, pain, and physical limitations. Sleep deficiency was the presence of insufficient sleep duration (<6h/day) or inadequate sleep quality (poor sleep often or always, insomnia symptoms, or apnea symptoms). Self reported outcomes included 1) pain in any body part, last 3 months, 2) moderate or greater degree of work interference due to this pain 3) functional limitation on an activities of daily living scale. Association of sleep deficiency with each outcome was assessed by multiple logistic regression analysis [odds ratios (OR)±95% confidence intervals].
Results: The sample of 1572 respondents was 90% women, mean age 41 years (s.d.=12), mean BMI 26 kg/m² (s.d.=5). Seventy percent reported sleep deficiency, 73% reported pain in the last 3 months, 33% reported work interference, 17% reported functional limitation. Sleep deficiency, was associated with higher rates of pain (OR=1.5, CI:1.1-2.0, p=0.009), work interference (OR=1.7, CI:1.3-2.3, p=0.0004) and functional limitation (OR=2.1, CI:1.4-3.2, p=0.0008), controlling for ethno-racial category, gender, age, BMI, shift, work hours, occupation,

job demands, psychological distress, coworker support, and supervisor support.

Conclusion: Sleep Deficiency is significantly associated with pain, functional limitation and workplace interference. Future studies will assess causal direction. These findings suggest that sleep, work-related bodily pain, and resulting functional and work limitations are potentially modifiable outcomes for a workplace health and safety intervention, or related avenues of approach for intervention studies.

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0644

ASSOCIATION BETWEEN LONG SLEEP DURATION AND INCREASED LEFT VENTRICULAR MASS

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Introduction: Sleep duration has a U shape relation with cardiovascular risk. Also, long sleep ($\geq$10 hours) is associated with increased risk of incident stroke. Increased left ventricular mass (LVM) is a risk factor for cardiovascular morbidity and stroke, but its relation to sleep duration is not established. Our aim is to evaluate the relation between sleep duration and LVM.

Methods: A cross-sectional analysis was conducted among the participants of the population-based Cardiovascular Abnormalities and Brain Lesions study (CABL). Left ventricular mass on transthoracic echocardiogram was computed according to the modified ASE formula: LVM = 0.8 [1.04 (LVDD + IVS+PWT) 3 - (LVDD) 3] +0.6. Sleep duration was assessed by reported hours of sleep on a diary kept during 24-hour blood pressure monitoring. Multivariate linear regression models were constructed to assess the relation between sleep duration and LVM indexed by height$^{2.7}$, after adjustment for demographics, depression score and established cardiovascular risk factors (hypertension, diabetes, and smoking). Analysis of sleep duration categories (less than 6 hours, 6 to 11 hours, and more than 11 hours) was performed.

Results: Among 756 participants (mean age 71$\pm$9 years), 60% were women and 71% Hispanics. The majority had hypertension(71%); diabetes was present in 29%. The mean sleep duration was 8.5 $\pm$1.8 hours. The mean LVM index was 51 $\pm$ 14 g/m2.7. There was an exponential univariate relation (J shaped) between sleep duration (parameter estimate= 0.28; p =0.01) and LVM index. This relation did not persist after adjusting for covariates. In fully adjusted models, long sleep ($\geq$11 hours) was associated with increased LVM index (parameter estimate=4.8; p=0.002).

Conclusion: In this population-based study, long sleep was associated with increased LVM after controlling for possible confounders. Primary sleep disorders (e.g. sleep apnea) and fragmented sleep may explain the relation between long sleep duration and increased LVM.

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0645

MODERATE TO SEVERE OBSTRUCTIVE SLEEP APNEA IS A RISK FACTOR FOR MORTALITY IN SARCOIDOSIS

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Introduction: Obstructive sleep apnea (OSA) is an indicator of poor outcomes in patients with COPD. The impact of sleep disorders in patients with sarcoidosis is poorly defined. We aimed to study the characteristic and impact of sleep disorders in patients with sarcoidosis.

Methods: Patients with sarcoidosis who underwent polysomnography (PSG) at our Sleep Center between January 2004 and August 2010 were included in the analysis. Data on demographics, sarcoidosis characteristics, and PSG variables were collected from the electronic medical record system and the Sleep Database. Patients with AHI <15 (N=41) were compared to patients with AHI $\geq$15 (N=45). Data are presented as mean$\pm$SD.

Results: In the period between January 2004 and August 2010, 86 patients with sarcoidosis underwent PSG and formed our study cohort (Age 54$\pm$14 years, males 30[35%], BMI 40$\pm$38 kg/m2, ILD 7[9%]). The most common reasons for PSG were daytime somnolence (N=60) and snoring (N=65). Overall prevalence of OSA was 78% (N=67). Compared to patients with AHI <15, those with AHI $\geq$15 were older (56 vs. 52 years; p=0.05), had higher neck circumference (p<0.001) and BMI (p=0.04), and have higher Friedmann score (p<0.001). There were no significant differences between the groups for pulmonary function characteristics or left ventricular ejection fraction (60% versus 55%; p=0.3). Of the 6 (6.9%) patients who died, 5 were in the AHI$\geq$15 group.

Conclusion: There was a high prevalence of OSA in our cohort of patients with sarcoidosis who had symptoms of daytime somnolence or snoring. Known identifiers of OSA such as BMI and neck circumference may be used to screen for OSA in patients with sarcoidosis. Moderate to severe OSA may be a risk factor for mortality in patients with sarcoidosis. Further studies are needed to better evaluate the impact of OSA in patients with sarcoidosis.

0646

SLEEP RELATED GASTROESOPHAGEAL REFLUX AND SLEEP QUALITY

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Introduction: In GERD patients with nighttime heartburn it is well established that they have a marked increase in sleep complaints, and GI symptom scores increase with the severity of insomnia. Treatment of nighttime heartburn has also been shown to produce an improvement in subjective sleep complaints. The aim of this study was to determine if differences in sleep measures are accompanied by different patterns of gastroesophageal reflux (GER) in patients with and without complaints of nighttime heartburn.

Methods: Subjects (n=25) with complaints of nighttime heartburn, daytime heartburn alone (n=13), and normal volunteers (n=25) were studied. All subjects completed the Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS). All subjects were studied with combined polysomnography and 24-hour pH monitoring.

Results: The PSQI scores were highest in the nighttime heartburn group (p < .01). The daytime heartburn group and the controls were not significantly different. The nighttime heartburn group showed a significantly increased nighttime acid contact time and average duration of reflux events (p < .05) compared to the other groups. No significant group difference was noted in daytime acid contact time. Total sleep time, sleep onset latency, and sleep efficiency were not significantly different among the three study groups. The number of subjective awakenings reported was greatest in the nighttime heartburn group (p < 0.05). Nighttime heartburn patients reported lower quality of sleep compared to control subjects (p < 0.05).

Conclusion: 1. GERD patients with nighttime heartburn show a unique pattern of subjective sleep disturbance and objectively documented sleep related GER. 2. These data support the notion that sleep related GER is a cause of a significant sleep disturbance, and sleep related GER should be considered as a potential cause of otherwise unexplained sleep complaints.

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0647

SLEEP DURATION AND VISUAL IMPAIRMENT: ANALYSIS OF THE 2009 NATIONAL HEALTH INTERVIEW SURVEY

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Introduction: This study ascertained the independent association of visual impairment (VI) with sleep duration using the National Health Interview Survey (NHIS) data.

Methods: Analysis was based on the 2009 NHIS, providing valid sleep and vision data for 19,985 volunteers (ages: 18-85). The sample was 87% white and 13% black; 55% women; and 70% had a family income <$35,000. The NHIS is a cross-sectional household interview survey utilizing a multistage area probability design. Probability samples of the civilian population of all 50 states and DC were obtained. Trained personnel from the US census bureau gathered data during face to face interviews. Volunteers provided socio-demographic and subjective data; physician-diagnosed chronic conditions were also elicited.

Results: Prevalence of VI was 13% (cataract=11%, glaucoma=3%, macular degeneration=2%, and diabetic retinopathy=1%); 31% were short sleepers ($\leq$6hrs) and 15%, long sleepers (>8hrs); 33% were obese ($\geq$30kg/m^2); and 34% reported negative moods (depression/anxiety). Long sleep was more common among blacks [18% vs. 14%, p<0.001], whereas VI was more common among whites [13% vs. 10%, p<0.001]. Multivariate adjusted logistic regressions showed stronger independent associations of VI with long, rather than, short sleep [OR=1.51, p<0.001, OR=1.07, p<0.001, respectively]. Since our first regression model indicated that obesity and mood also had strong associations with long sleep, we ascertained interactions of those factors with VI on long sleep. Among blacks, greater odds of being a long sleeper were observed for individuals with VI and obesity, rather than with VI and mood [OR=1.43, p<0.001, OR=1.01, p<0.001, respectively]. Among whites, greater odds were noted for individuals with VI and mood, rather than with VI and obesity [OR=1.59, p<0.001, OR=1.20, p<0.001, respectively]. Sociodemographic and medical factors were adjusted.

Conclusion: Findings suggest that analysis of epidemiologic sleep data should consider visual impairment in assessing odds of long sleep. Plausibly, individuals with visual impairment spend more time at home, providing more opportunity to spend time in bed, likely increasing sleep time.

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0648

PREVALENCE OF OBSTRUCTIVE SLEEP APNEA AND CARDIOVASCULAR MORBIDITY IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction: The high prevalence of obstructive sleep apnea (OSA) in end stage renal disease patients compared to the general population is well documented. Data regarding OSA in post transplant recipients are limited. However, previous studies reported a prevalence of up to 27%. We sought to evaluate the prevalence of OSA in our kidney transplant (KT) recipients and the relationship to blood pressure changes and cardiovascular events.

Methods: This is a prospective study where patients one month post KT were screened for OSA using overnight oximetry and questionnaire. Patients with a history of OSA, multi-organ transplant, or an iothalamate glomerular filtration rate of < 50 ml/min were excluded. Those who had a high probability for OSA based on questionnaire and an abnormal overnight oximetry were referred for polysomnography. Other data collected included ejection fraction and left ventricular mass index by echocardiography, 24-hour ambulatory blood pressure measuring diurnal and nocturnal systolic and diastolic blood pressures, and cardiovascular events defined as stroke, arrhythmia, or acute coronary syndrome.

Results: Seventy-five patients were enrolled into the study. Twenty-eight (37%) had an abnormal overnight oximetry. Of these, 15 underwent polysomnography which identified OSA in 13 (17%). Of the remaining 13 patients, polysomnography is pending in 4 and 9 refused evaluation. The mean apnea-hypopnea index was 27.5 ± 18.8. Patients with abnormal overnight oximetry were older (59.2 ± 11.1 vs. 52.9 ± 14.0, p=0.05), more likely to be men (60% vs. 30%, p=0.02), and had higher nocturnal systolic blood pressure (132.8 ± 14.4 vs. 126.4 ± 10.8, p=0.04). During a follow up of a median of 8.9 (1.1-23.7) months, 3/13 (23%) with OSA and 2/52 (4%) with no OSA developed cardiovascular events (p< 0.05).

Conclusion: OSA is common among patients post kidney transplant. Thorough evaluation to identify these patients is important since they may be at increased risk for cardiovascular events following KT compared to patients without OSA.

0649

SLEEP-DISORDERED BREATHING AND RENAL FUNCTION IN VETERANS

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Introduction: Sleep-disordered breathing (SDB) and kidney disease are common among veterans and both lead to increased cardiovascular risk and mortality. To date, however, no study has examined the relationship between SDB and renal function among veterans.

Methods: We retrospectively reviewed the charts of 450 veterans who presented consecutively to the NF/SGVHS since 2006 and underwent polysomnography(PSG). We included in our analysis the subset of these veterans(n=330) with usable PSG data and a measure of renal function, serum creatinine(SCr), within 3 months of PSG. We estimated renal function using the Modification of Diet in Renal Disease estimated glomerular filtration rate(eGFR). Chronic kidney disease(CKD) was defined as eGFR<60 ml/min/1.73m2. All covariate data was collected from the VA electronic medical record.

Results: Mean age was 59.5±10.3 years; 95% were male, 72% were white, 11% black and 17% other. Mean body-mass index(BMI) was 34.2±7.3. Median apnea-hypopnea index(AHI) was 23.1 (IQR 11.9-52.1); 7% had AHI <5, 26% had AHI 5-14.9, 26% had AHI 15-29.9 and 42% had AHI≥30. Mean eGFR was 81.8±23.4 ml/min/1.73m2; 13% had CKD. Veterans with higher tertile of geometric mean AHI had lower mean eGFR (mean eGFR[95%CI] Q1 88.0 [83.8-92.3], Q2 82.8 [78.5-87.0], Q3 79.4[75.2-83.7], p trend 0.005). This association persisted after adjustment for age and race (p trend=0.039). After further adjustment for BMI, this association persisted but was of borderline statistical significance (p=0.07). Neither age nor BMI modified the association between SDB and renal function (p interaction = 0.80 and 0.93, respectively).

Conclusion: SDB is common among veterans referred for PSG at our institution. Greater severity of SDB was associated with lower eGFR but this association was partially explained by greater BMI among veterans with higher AHI. Prospective study in a population unselected for sleep disorders and with a spectrum of renal function is required to better understand the association between SDB and renal function.

0650

SLEEP SYMPTOMS AMONG PATIENTS WITH END-STAGE RENAL DISEASE BY DIALYSIS TREATMENT IN CENTRAL MEXICO

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Introduction: Prevalence of sleep disorders in persons with end-stage renal disease (ESRD) is higher compared to the general population. Little is known about sleep disorders of Mexican patients with ESRD. This pilot study describes sleep symptoms reported by Mexican patients with ESRD on peritoneal dialysis (PD) or hemodialysis (HD).

Methods: Patients residing in central Mexico receiving PD or HD provided demographic data and completed the Spanish-language validated Sleep Heart Health Study Sleep Habits Questionnaire (SHQ). The SHQ contains 12 sleep symptoms, including difficulty falling and staying asleep, daytime sleepiness and insufficient sleep. Data were analyzed using frequencies and chi-squared tests with PASWv17 to address the study aim.

Results: Demographics and health status showed participants (N=30) to be 37% women, a sample mean age of 59±12 years, an average 10th grade education, 73% married and a mean BMI of 25±6. Of the sample, 83% had doctor-diagnosed Type 2 diabetes. A majority of patients (67%) were receiving PD. HD patients were significantly more likely to report feeling tired during the day no matter how many hours of sleep they had compared to patients on PD (60% versus 15%, p<0.05). HD patients also reported more insufficient sleep (30%, p<0.05); no PD patients reported this problem. There was a borderline significant finding for HD patients to report excessive daytime sleepiness compared to PD patients (30% versus 5%, p<0.10). There were no differences for insomnia symptoms, periodic limb movements, leg pains or use of sleep aids between groups.

Conclusion: Preliminary findings suggest that HD patients have more difficulty with unrefreshing sleep, daytime sleepiness and sleep insufficiency compared to PD patients that could be a function of treatment delivery. These preliminary findings may help develop culturally and clinically responsive sleep interventions for dialysis modality in Mexico.

0651

PREVALENCE OF RESISTANT HYPERTENSION AND OSA RISKS IN A CROSS-SECTIONAL SURVEY OF THE US POPULATION

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Introduction: Patients with risk factors for and self-reported diagnosis of obstructive sleep apnea (OSA) are more likely to develop hypertension (HTN), require greater pharmacologic therapy for HTN, and are more likely to be resistant to outpatient HTN management. Resistant HTN (RHTN) is defined as failure to achieve blood pressure <140/90, or <130/80 if patient have diabetes or with chronic kidney disease while on >3 medications with optimal dosages, including a diuretic (American Heart Association, 2008). Hypothesis: Self-reported symptoms suggesting OSA risk (snoring or snorting over 3-4 times/week) as well as self-reporting OSA diagnosis by a physician are predictors of RHTN.

Methods: Cross-sectional analysis of a stratified multistage probability sample of nationally representative US adults 18 years and older (N=10,526 adults) enrolled in the National Health and Nutrition Examination Survey (NHANES) between 2005 -2008. Age-adjusted prevalence rates of RHTN and adjusted odds ratios of RHTN were calculated using weighted analysis.

Results: 3306 adults in the sample were found to have HTN, including 112 with RHTN: (94 of which were diagnosed with diabetes or chronic kidney disease with >=130/80 on 3 or more medications, including a diuretic). Age adjusted prevalence rate of resistant HTN in US population was 0.7 % in both men and women. Adjusted logistic regression models for socio-economic characteristics, behavioral risk factors, health status and depression, showed increased odds of RHTN with poverty [OR=2.1, 95%CI (1.2-3.8)], lower education [OR=2.4, 95%CI (1.3-4.2)], overweight/obesity [OR=3.3, 95%CI (1.5-7.3)], self-reporting poor health status[OR=6.2, 95%CI (3.2-12.1)], and depression [OR=2.2, 95%CI (1.0-4.7)], but no association between RHTN and self-reported symptoms of OSA was seen in this database.

Conclusion: This study showed that self-reported symptoms of OSA were not found as significant predictors of RHTN in the general US population.

0652

DIFFERENTIAL RACIAL/ETHNIC EFFECTS ON THE LINK BETWEEN SLEEP AND HYPERTENSION

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Introduction: Blacks are more likely to report short sleep (≤6hrs) or long sleep (>8hrs) and are characterized by a greater prevalence of hypertension than their white counterparts. This study examined differential racial/ethnic effects on link between sleep and hypertension using data from the 2009 National Health Interview Survey (NHIS).

Methods: Participants' age range was 18-85 years; 87% were white and 13%, black; 55% were women. NHIS is a cross-sectional household interview survey using a multistage area probability design. Probability samples of the civilian population of all 50 states and DC were obtained. Data was collected by personnel from US census bureau in face-to-face interviews, using computer-assisted personal interviewing (CAPI). Respondents (n=25,352) provided socio-demographic and subjective data as well as data on physician-diagnosed chronic conditions. They estimated their habitual sleep duration and provided mood ratings. Final weights were applied to analyses to adjust for use of complex design in the NHIS.

Results: Compared with individuals of the white race/ethnicity, a greater prevalence of obesity (BMI ≥25kg/m2) [OR=1.42, p<0.0001], hypertension [OR=1.40, p<0.0001], and diabetes [OR=1.60, p<0.0001] was observed for individuals of the black race/ethnicity. However, blacks were characterized by a lower prevalence of heart disease [OR=0.74, p<0.0001]. Logistic regression analysis indicated that black short or long sleepers were more likely to have hypertension than their white counterparts [OR=1.43, p<0.0001; OR=1.80, p<0.0001], respectively. Adjusting for effects of age, sex, education, obesity, diabetes, and heart disease increased risk of hypertension for black short sleepers [OR=1.66, p<0.0001], but did not affect risk for of hypertension for black long sleepers [OR=1.78, p<0.0001].

Conclusion: Finding of greater risk of hypertension for individuals of the black race/ethnicity, relative to whites, is consistent with data suggesting that blacks may be at greater risk for metabolic conditions associated with short sleep. Moreover, they suggest that risk of hypertension may also be greater among black long sleepers.

0653

THE EFFECT OF ENDOSCOPIC SINUS SURGERY ON SLEEP-RELATED QUALITY OF LIFE AND SEVERITY OF INSOMNIA IN CHRONIC RHINOSINUSITIS

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Introduction: In chronic rhinosinusitis, the sleep disturbance is the one of the troublesome clinical manifestations, and may be caused by various sinusitis-related symptoms such as nasal congestion, posterior nasal drip, cough and so on. The aim of this study is to investigate the effect of endoscopic sinus surgery (ESS) on sleep related quality of life and severity of insomnia in patients who has chronic rhinosinusitis.

Methods: Subjects were 28 patients diagnosed as chronic rhinosinusitis and who underwent endoscopic sinus surgery from December 2007 to January 2009. To reveal the change of sleep disturbance after the surgery, the questionnaires about the sleep related quality of life, and insomnia such as Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI) were performed before and after the surgery.

Results: Most sino-nasal symptoms and sinusitis related quality of life were improved significantly after the surgery (P<0.01). Sleep related quality of life was significantly improved postoperatively (P<0.01). In addition, there was significant improvement in total scores of insomnia severity index, particularly, in scores of sleep onset and sleep maintenance difficulties (both nocturnal and early morning awakenings) (P<0.01).

Conclusion: We reveal that endoscopic sinus surgery can significantly improve sleep related quality of life and severity of insomnia in chronic rhinosinusitis.

0654

FEASIBILITY OF COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA IN COPD

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Introduction: Fatigue is associated with functional decline in COPD and patients report sleep continuity disturbances which likely contribute to fatigue. Cognitive behavioral therapy for insomnia (CBT-I) has been particularly effective in people with chronic illnesses. However, people with COPD have unique disease-related features such as breathlessness, hypoxia and increased mucus that interfere with sleep and may lessen effectiveness of traditional CBT-I. The purpose of this study was to examine the feasibility of CBT-I for people with COPD and to estimate preliminary effects on sleep continuity, sleep quality and fatigue.

Methods: We used a one-group prospective, pre-post design. Participants received six, 1hour sessions of CBT-I (stimulus control, sleep restriction, sleep hygiene, cognitive therapy and relaxation) provided by a trained doctorally prepared nurse. Using sleep diaries, outcomes included sleep latency (SL), wake after sleep onset (WASO), total sleep time (TST) and sleep efficiency (SE), plus measures of sleep quality and fatigue. Participants completed the Insomnia Treatment Acceptability Scale (ITAS) at the last CBT-I session.

Results: Eight participants enrolled with a (mean±SD) age of 64±4 years and (mean±SD) FEV1% predicted 68±9. Baseline (mean±SD) score on the Sleep Impairment Index was 15+5 (scores range from 0 to 28, high scores indicate greater insomnia) and baseline SL was 27+26 minutes. There were no dropouts from the study and no sessions were missed. Pre-post mean differences were: -10 minutes for SL, -56 minutes for WASO, +26 min. for TST and +11% for SE. Significant differences from pre to post treatment occurred for sleep quality (t=3.35, p=.012) and insomnia severity (t=5.9, p=.001) and fatigue decreased by a mean of 14%. Participants found the treatment acceptable.

Conclusion: Results suggest that using CBT-I in COPD is feasible and provokes positive sleep and fatigue outcomes that compare favorably to those obtained in primary insomnia.

0655

EFFECT OF PULMONARY REHABILITATION ON SLEEP OUTCOMES AND QUALITY OF LIFE IN CHRONIC LUNG DISEASE

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Introduction: Sleep-related disorders are common in patients with chronic lung diseases (CLD). In other populations exercise has been shown to improve sleep. In patients with CLD, pulmonary rehabilitation (PR) produces important health benefits in symptoms, exercise tolerance, and quality of life (QOL). However, little is known about the effect of PR on sleep in CLD. The aim of this study was to evaluate the effect of PR on sleep in patients with CLD.

Methods: Patients with moderate-to-severe CLD enrolled in the UCSD PR program were asked to participate. A 6-minute walk test (6MW) and questionnaires related to symptoms, QOL, and sleep quality were obtained before and after an 8-week PR program. Outcome measures included: UCSD Shortness of Breath Questionnaire (SOBQ); SF-36 Physical (PCS) and Mental (MCS) Component Scores; Self-efficacy for Walking (SEW); and Pittsburgh Sleep Quality Index (PSQI).

Results: 86 patients participated: 49% male; mean(SD) age=68(10); diagnoses=73% obstructive, 20% restrictive,7% mixed lung disease; 44% on long-term oxygen; 17% with obstructive sleep apnea; and abnormal spirometry [FEV1 % pred=50 (18), FVC % pred=72 (19), FEV1/FVC %=54 (19)]. At baseline, 58% had poor sleep quality (PSQI ≥ 5). Changes after PR [Pre/Post mean(SD)] demonstrated improved sleep quality [PSQI Global Score 6.9 (3.9)/6.0 (3.9), p=0.02]. PSQI sub-score analyses showed significant improvement only in Sleep Disturbances [1.4 (0.6)/1.2 (0.6), p=0.03]. Both the SF-36 MCS and PCS scores improved significantly after PR [MCS: 54.1 (8.6)/57.9 (6.4), p=0.002; PCS: 31.2 (7.7)/35.5 (9.5), p<0.001] as did 6MW, SOBQ, and SEW.

Conclusion: Sleep quality in patients with CLD is poor. PR had a significant positive impact on overall sleep quality, particularly in sleep disturbances. PR also produced improvement in both mental and physical components of QOL, dyspnea, and exercise tolerance. PR may be considered as a non-pharmacologic treatment for sleep complaints in this population.

0656

IMPACT OF ABNORMAL LUNG FUNCTION ON SLEEP ARCHITECTURE AND LONG TERM OUTCOMES IN OBSTRUCTIVE SLEEP APNEA: A COHORT STUDY

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Introduction: The impact of abnormal pulmonary function in patients with OSA has not been adequately studied. We aimed to assess the impact of abnormal pulmonary function on short and long-term outcomes in patients with OSA.

Methods: Adult patients with polysomnographically (PSG) confirmed OSA (defined as AHI >5) between July 2005 and August 2010 who underwent pulmonary function testing (PFT) within 12 months of PSG were identified using electronic medical records. Of these, 250 patient charts [normal PFT (N=100), obstructive PFT (N=50), restrictive PFT (N=50) and mixed PFT (N=50)] were reviewed to obtain demographic and PSG variables. OSA patients with normal PFTs were compared to patients with OSA and abnormal PFTs.

Results: We identified 823 patients who formed our study cohort: 440 (53%) females, 597 (72%) Caucasian and 182 (22%) African Americans. Of these, 333 (43%) had mild OSA, 216 (32%) had moderate OSA and 189 (25%) had severe OSA. Compared to patients with normal PFTs, patients with abnormal PFTs had reduced survival at 1, 2, and 5 years (96.9%, 94.2%, and 85% versus 98.7%, 97.6%, and 90.2%; P = 0.018). Compared to patients with normal PFTs, those with abnormal PFTs had lower overall AHI (median 16 vs. 21.9, p=0.01), lower NREM-AHI (median 13 vs. 22.1, p=0.003), and lower total number of respiratory events (median 85.5 vs. 125). There were no significant differences between the two groups in terms of BMI, Epworth Sleepiness Scores, total sleep time (TST), sleep efficiency, total arousals, percentage of TST in N1, N2, N3 and REM sleep stages, percentage of TST spent with oxygen saturation below 90%, or percentage of TST with end tidal CO2 (EtCO2) above 50%.

Conclusion: In patients with OSA, those with reduced measures of pulmonary function have reduced survival compared to patients with normal pulmonary function.

0657

QUALITY OF LIFE IN PATIENTS WITH OSA AND ABNORMAL LUNG FUNCTION: A RETROSPECTIVE STUDY

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Introduction: Sleep disordered breathing (SDB) is seen in variety of patients with lung disorders. The impact of dual disease burden of OSA and abnormal lung function on quality of life has not been adequately studied. This study was undertaken to evaluate quality of life, fatigue, and depression in patients with OSA and abnormal lung function based on a self reported outpatient questionaire.

Methods: As part of their visit, all patients complete a Sleep clinic questionnaire consisting of validated tools for measuring quality of life, subjective sleepiness, fatigue, and depression at our institution. Adult patients with polysomnographically (PSG) confirmed OSA (defined as AHI >5) between January 2008 and August 2010 who underwent pulmonary function testing (PFT) within 12 months of PSG and completed the Sleep clinic questionnaire were identified using electronic medical records and the Sleep Center database. Data on demographics, PSG variables, and Sleep clinic questionnaire [European Quality of life (EQ5D) Index, PHQ-9 scores for depression, Total sleep time (hours), Epworth sleepiness score (ESS), Fatigue Severity Score (FSS) and Functional Outcomes of Sleep Questionnaire (FOSQ) scores] were collected. OSA

patients with normal PFTs were compared to patients with OSA and abnormal PFTs.

Results: We identified 154 patients who formed our study cohort [90(58.44%) were females; 110(71%) Caucasians, and 39 (25%) African Americans]. 55 (36%) had normal PFT and 99 (64%) had abnormal lung function. Compared to patients with normal lung function, OSA patients with abnormal lung function had lower EQ5D [median (25th, 75th) = 0.8 (0.7, 0.8) vs 0.8 (0.8, 0.8);p=0.028] and lower Intimate Relationships and Sexual Activity FOSQ [1.3 (1.0, 3.3) vs 3.0 (1.0, 3.9); p=0.027]. No significant differences were noted in terms of PHQ-9 Scores, Total Sleep time in hours, ESS, FSS, and overall FOSQ scores.

Conclusion: In patients with OSA, abnormal lung function can result in reduced quality of life (EQ5D) and FOSQ scores. Larger prospective cohort studies are needed to understand the quality of life indicators in OSA and abnormal lung function.

0658

ATRIAL FIBRILLATION IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA AND ISCHEMIC STROKE - A CASE CONTROL STUDY

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Introduction: Obstructive sleep apnea (OSA) has recently been shown to be an independent risk factor for ischemic stroke. Atrial fibrillation (AF), a strong risk factor for stroke, has also been linked to OSA. Whether OSA plays an intermediary role in the relationship between AF and stroke is unknown. To explore this, we aimed to study the association between AF and first-time stroke in patients with OSA.

Methods: Olmsted county residents with a new diagnosis of OSA based on polysomnography (PSG) between 1/1/2005-1/1/2010 (N=2980) who suffered a first-time ischemic stroke during the same period were identified as cases. Controls with no history of stroke were randomly chosen from the same PSG database. Multiple logistic regression was performed with age, gender, AF, BMI, smoking, hypertension, hyperlipidemia, diabetes and CAD as co-variates with the diagnosis of OSA as the variable of interest.

Results: A total of 108 subjects were analyzed. Mean age of cases (n=34) was 73 years +/-12.3 years and 53% were men. Among controls (n=74), mean age was 61 +/-15.5 years, 55% were men. After controlling for confounders, AF was more common in the stroke cases than among controls (50.0% vs 10.8%, corrected odds ratio 7.89, p<0.001).

Conclusion: Patients with OSA who had a stroke had higher rates of AF even after accounting for potential confounders. Further studies are needed to establish the temporal relationship between AF and occurrence of stroke in this group of patients, and whether targeted therapy of OSA impacts outcomes.

0659

THE INCIDENCE OF CORONARY HEART DISEASE IN SLEEP-DISORDERED BREATHING IN THE WISCONSIN SLEEP COHORT STUDY

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Introduction: Sleep-disordered breathing (SDB) has been associated with coronary heart diseases (CHD) in observational and clinic based studies. However, only one population-based study to date assessed the relationship of objectively-measured SDB with incident CHD. To further examine evidence for a causal association between SDB and CHD,

we investigated the incidence of CHD in the Wisconsin Sleep Cohort Study (WSCS).

Methods: The population-based WSCS sample consisted of 1198 adults, free of CHD at baseline and not treated for SDB, followed longitudinally over 20 years. SDB was defined by the apnea-hypopnea index (AHI) using overnight polysomnography. We used baseline log (AHI+1) as the predictor variable in survival analysis models predicting incident CHD. Incident CHD was defined by new reports of myocardial infarction, cardiac revascularization procedure, congestive heart failure or coronary heart disease death obtained using detailed health history questionnaire repeated at 4-year intervals and mortality data.

Results: Participants' mean age was 47 (range: 30-70) years; 54% were men. The incidence of CHD in the WSCS was 7.14/1000 person-years. The mean time to event was 9.2 ± 4.9 years. Using AHI as categorical data, the unadjusted incidence of CHD per 1000 person-years was, 4.57 and 10.47 in AHI 15-30 and AHI $\geq$30 respectively, compared with 6.21 in those with AHI <5. Using survival analysis models predicting CHD events, and adjusting for age, sex and body mass index, calculated hazard ratio (95% confidence intervals) for AHI 15 vs. 0 was 1.32 (1.06-1.65), and for AHI 30 vs. 0 was 1.41 (1.07-1.86).

Conclusion: In our study, SDB was significantly associated with incident CHD. Those with moderate to severe SDB (AHI $\geq$30) in the general population were estimated to have a 41% greater incidence of developing CHD compared to those without SDB. Our findings support the postulated adverse effects of SDB on CHD.

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0660

THE SPECTRUM OF SLEEP DYSFUNCTION IN POSTURAL TACHYCARDIA SYNDROME (POTS)

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Introduction: Postural-tachycardia syndrome (POTS) represents a selective autonomic failure and typically presents with orthostatic intolerance (OI) associated with postural tachycardia without significant orthostatic hypotension. Sleep dysfunction is an important non-orthostatic intolerance component but has been largely neglected in the literature. Because of proximity of autonomic and sleep-wake generating neurons it is logical to have concomitant sleep dysfunction with OI symptoms.

Methods: We describe the spectrum of sleep dysfunction in seven patients (6 women ages 19-53 and one man aged 38) who presented with symptoms of orthostatic intolerance in the upright posture, and non-OI symptoms (sleep dysfunction, fatigue, and gastrointestinal symptoms) for 4-15 years. Sleep dysfunction included repeated awakenings, night sweating, witnessed apneas (38 M), fearful dreams, excessive daytime somnolence, and late bedtime and late rise time in one woman. Examination was normal except orthostatic tachycardia without significant orthostatic hypotension.

Results: Autonomic function tests were consistent with the diagnosis of POTS. PSG study confirmed sleep maintenance insomnia and abnormal sweating in two women and central apnea (CSA) with ataxic breathing in the man. Actigraphy documented evidence of excessive movements in sleep and delayed sleep phase state in one woman.

Conclusion: Sleep dysfunction in these patients revealed heterogeneity similar to the protean manifestations of POTS. Treatment may improve quality of life and therefore it is important to pay attention to sleep dysfunction in patients with this entity, the nature of which is still a mystery.

0661

RISK OF OBSTRUCTIVE SLEEP APNEA DETECTED BY THE BERLIN QUESTIONNAIRE PREDICTS HEMODYNAMICALLY SIGNIFICANT CORONARY LESIONS

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Introduction: Obstructive sleep apnea (OSA) has been increasingly recognized as an independent risk factor for coronary heart disease (CHD), but remains underdiagnosed in the cardiology setting. The Berlin Questionnaire is a validated screening test for OSA and has shown appropriate diagnostic performance in detecting OSA among patients with resistant hypertension. The present study aims to investigated whether the risk for OSA identified by the Berlin questionnaire is associated with CHD diagnosed by coronary angiography in a case-control study.

Methods: Cases were patients referred for elective coronariography to investigate stable CHD. They were additionally classified by presence or absence of significant coronary lesion (stenosis $\geq$ 50% in any epicardial artery). Controls were individuals without symptoms or diagnosis of CHD, selected from a population-based sample and matched to cases by age and gender. All subjects responded to the Berlin Questionnaire.

Results: Berlin Questionnaire positive for OSA was identified in 135 out of 328 cases (41.2%), a percentage significantly higher than in control subjects, 151 out of 439 (34.4%; p=0.03). Multinomial logistic analysis, adjusting for confounding factors as age, gender, skin color, years of education, smoking, alcoholic beverages consumption, and diabetes was utilized to compare cases and controls with and without significant coronary lesion. The risk for OSA identified by the Berlin questionnaire was independently associated with CHD exclusively in cases with lesions of at least 50% (OR 1.53; 95%CI 1.02-2.30; P=0.04). In individuals with significant coronary lesions, the risk for OSA in Berlin questionnaire was higher in younger subjects (40-59 years; OR 1.76; IC95% 1.05-2.97; P=0.03). Almost four times higher risk of significant lesion was detected in women with positive Berlin Questionnaire (OR 3.56; IC95% 1.64-7.72; P=0.001).

Conclusion: High risk for OSA identified by the Berlin questionnaire is associated with risk for significant coronary arterial lesions, mostly in middle-aged patients and women. Key words: Sleep apnea, coronary disease, heart catheterization.

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0662

SLEEP APNEA AND ANXIETY AMONG PATIENTS WITH METABOLIC SYNDROME

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Introduction: This study assessed risk of Obstructive Sleep Apnea (OSA) and anxiety levels among patients with metabolic syndrome.
Methods: Data for the present study was obtained from a larger study investigating effects of OSA treatment in the primary-care setting. A total of 254 patients with metabolic syndrome provided subjective data

for the analysis. Patients were diagnosed with metabolic syndrome using criteria articulated in the joint interim statement for harmonizing the metabolic syndrome (Circulation; Nov. 4, 2009). Their average age was 63 ± 15 years; 63% were female, and all were of black race/ethnicity. We assessed OSA risk using the Apnea Risk Evaluation System (ARES), defining high risk as an ARES score ≥6. Patients also rated their anxiety level using the Beck Anxiety Inventory (BAI). Data was coded and analyzed by an experienced statistician using SPSS 18.0.

Results: Of the sample, 88% were diagnosed with hypertension, 69% with diabetes, 83% with dyslipidemia, and 90% were overweight/obese; 37% had a history of heart disease and 11% had a stroke. Seventy-three percent of the patients reported finishing high school, and 43% reported annual income <10K. Using the ARES screener, we estimated that 39% were at high risk for OSA; based on the BAI, the average anxiety level was 9.03 ± 9.11. To test the hypothesis that individuals with high OSA risk have higher levels of anxiety, we used ANCOVA. Results showed that patients at high OSA risk had significantly higher levels of anxiety (F=7.70, P<0.001); model adjusted for effects of age, gender, income, and education.

Conclusion: Our finding of an OSA risk of 39% may be explained by the fact that all of the patients had metabolic syndrome, which is a strong predictor of OSA. Our results suggest that patients with metabolic syndrome and are at high risk for OSA should be screened for the presence of anxiety.

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0663

ASSOCIATION BETWEEN SLEEP ARCHITECTURE, SLEEP DISTURBANCE AND METABOLIC SYNDROME: A STRUCTURAL EQUATION MODEL ANALYSIS

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Introduction: Metabolic syndrome contributes to the patho¬genesis of many chronic or severe diseases, and affected approximately 25% to 40% adults. Sleep disturbances, including obstructive sleep ap¬nea (OSA), sleep deprivation, and sleep fragmentation, have been shown to be associated with it. However, relation between sleep architectures, sleep disturbance, and metabolic syndrome is still unclear. We evaluated the relationship between sleep architectures, sleep disturbance, and presence of the metabolic syndrome with a structural equation model (SEM) to clarify the contribution of sleep factors to metabolic syndrome.

Methods: 553 participants were recruited from community comprised of 238 female (43%) with mean age of 44.32 (±13.98), and 315 male (57%) with mean age of 44.83(±13.09). They underwent one night polysomnography (PSG) recording and evaluation for metabolic syndrome. Logistic regression was first applied to examine the sleep factors increase risk to develop metabolic syndrome. SEM was then conducted to evaluate the goodness of fit of the model.

Results: Logistic regression shown significant association between age (p=0.002), AHI (p =0.035), arousal index (AI, p =0.043), sleep efficacy (SE, p =0.004) and metabolic syndrome (R2=0.35). When using SEM to exam the hypothesis model, we found a good overall model fit ($\chi2/100$ = 1194.23; CFI = 0.76; RMSEA = 0.14) and found that factor loading in the model included TST, SE, stage1+2 percentage, but percentage of slow wave sleep (SWS), REM sleep were excluded. As well as the presence of sleep disturbance, included AHI, duration of SaO2 lower than 90%, AI were strongly correlated to metabolic syndrome, but the PLM, DI were excluded.

Conclusion: Our results demonstrate that sleep architecture and disturbance co-ag¬gregate for the development of metabolic syndrome. Although this model needs further validation, it still provides a compre-

hensive model for future studies on the effects of sleep-related factors on metabolic syndrome.

0664

EFFECT OF POSITIVE AIRWAY PRESSURE COMPLIANCE ON MANAGEMENT OF DM AND LIPID DISORDERS

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Introduction: OSA is associated with lipid disorders and glucose intolerance. There is lack of information on role of PAP in control of hyperlipidemia and DM.

Methods: Retrospective study. We reviewed electronic records at VAMC Milwaukee of patients with PAP data download and established diagnosis of DM or hyperlipidemia between January - June 2009. Total cholesterol, LDL, HDL,TG and HbA1C at 6-18 months after treatment were compared with levels 0-12 months before treatment. Statistical analysis: 2 tailed T-test

Results: Total number = 50. Male/Female = 46/4 21 patients had good compliance. Of these, 8 had DM and 15 hyperlipidemia. Baseline mean levels with standard deviation (SD): HbA1c = 7.6% (SD1.6) , total cholesterol = 170 (SD 31.3) , LDL = 98.8 (SD 21.3) , HDL = 44.13 (SD 11.7) and TG = 135.06 (SD 68.5). 29 subjects (58%) had poor compliance. Of these, 10 had DM and 25 had hyperlipidemia. Baseline mean levels with standard deviation (SD): HbA1c = 6.69% (SD ± 0.4), total cholesterol = 183.1 (SD 51.9), LDL = 110.0 (SD 45.3), HDL = 42.6 (SD10.6) and TG = 152 (SD 85.4). In patients with hyperlipidemia: Group with good PAP compliance had decreases in total cholesterol and LDL by 14.0 (p=0.041) and 13.1 (p= 0.049) respectively. Group with poor PAP compliance had no significant change There was no significant difference in HDL and TG values in either group. In patients with DM: There was no significant change in HbA1C in either group: group with good PAP compliance had decrease in HbA1C by 0.86% (p = 0.09) and poor compliance group had decrease by 0.2% (p= 0.23).

Conclusion: There was a significant change in total cholesterol as well as LDL in patients with hyperlipidemia and good compliance to PAP. There were no significant changes in HDL and TG. There was a trend towards decrease in HbA1c in patients with DM and good compliance to PAP. There was no significant difference in number or dosages of medications used before and after treatment in either group.

0665

SLEEP AND GLYCEMIC CONTROL IN PATIENTS WITH TYPE 2 DIABETES

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Introduction: Sleep problem is common in type 2 diabetics. Poor sleep quantity and quality may affect glucose tolerance and homeostasis, hence affecting glycemic control. This study examined sleep patterns in patients with type 2 diabetes.

Methods: One hundred and thirty-one (55 males and 76 females) type 2 diabetics aged 30-81 years (mean ± SD = 61.8±10.7) voluntarily participated in this cross-sectional study. The average duration of diabetes since diagnosed was 9.7±7.3 years. Sleep quality was assessed by the Pittsburg Sleep Quality Index (PSQI). Glycemic control was assessed by hemoglobin A1c (HbA1c).

Results: In participants, 70.2% of diabetics had poor glycemic control (HbA1c >7). The mean global PSQI score was 7.0±4.2, and 62.6% of participants were identified as poor sleepers (PSQI□5). Their mean sleep efficiency was 82.8±14.8% with an average sleep of 6.2±1.5 hours a night. The leading causes to disturb night time sleep were nocturia

(87%) and cough or snoring (56.5%). In contrast, only 3.1% claimed having more than 9 hours of sleep a night. There was no correlation between sleep and glycemic control in these diabetics (r=0.038 p= 0.666).
Conclusion: Patients with diabetes suffer from poor sleep quality. Majority of patients experience nocturia and cough during night time.

0666

A PILOT STUDY TO IDENTIFY GENETIC VARIATIONS OF RESTLESS LEGS SYNDROME IN PERSONS WITH TYPE 2 DIABETES

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Introduction: Restless Legs Syndrome (RLS) is a highly heritable syndrome with an identifiable phenotype, variable expressivity, and high penetrance. RLS is reported in 44% of persons with type 2 diabetes (t2D). Genetic variations may impact the onset of RLS symptoms. The purpose of this pilot was to compare genetic variations of RLS in persons with t2D.
Methods: This is a pilot study to examine a genome wide association, typing cases and controls on a single set of arrays. 41 patients with t2D were recruited from the PENN Rodebaugh Diabetes Center. Participants were screened using the telephone diagnostic interview for RLS. Data was collected on ferritin, glycosylated hemoglobin (HgA1c), and genetic testing (analyzed at the Molecular Diagnosis and Genotyping Facility at UPENN). Genetic variations for RLS were based on findings in literature 6-9 including: BTBD9 (rs9296249, rs9357271, rs3923809), MEIS1 (rs2300478), MAP2K5 (rs12593813, rs11635424, rs4489954, rs3784709, rs1026732), LBXOR1 (rs6494696), PTPRD (rs4626664).
Results: Sample size was 41 (26 males; 15 females), mean age 64(SD=9.8). Participants with RLS were younger, had higher HgA1c and lower ferritin levels. One SNP on the MAP2K5 gene at locus rs3784709 was different between the 2 groups (p=0.005) with C risk allele on locus rs3784709 more frequently identified in persons with RLS than those without. Limitations of the study include sample size. as we did not have power based on odds ratio and allele frequency to detect associations with the SNPs.
Conclusion: It is uncertain why some people with t2D may develop RLS and others do not if the genetic variations are no different between the two groups. The progression of RLS after the diagnosis of t2D warrants further investigation. Studies examining the genetic variation of RLS and the association with t2D may improve diagnosis and treatment of RLS and t2D.
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0667

CHARACTERIZING THE RELATIONSHIP SHARED BY SLEEP DISORDERS AND DIABETES

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Introduction: Research has demonstrated that sleep disorders (SDs) are associated with prolific health problems. The extent of these relationships has not been clearly ascertained because of significant rates of under or inadequate diagnoses along with a multitude of intervening variables associated with disease symptomatology. Investigations are further constrained by difficulty in acquiring valid data from people whose diagnoses are based on a complete nocturnal polysomnography (NP) and/or multiple sleep latency tests (MSLT). Researchers are beginning to examine relationships shared by SDs and diabetes to illuminate relevant covariance. It is estimated that 23.6 million people in the United States have diabetes and an additional 57 million people have pre-diabetes. Daily self-management is essential for controlling diabetes and its associated complications. Comorbidity of diabetes with SDs may present unique challenges for daily self-management because SDs may compromise cognition, emotional well-being, and general health.
Methods: We constructed an 111-item questionnaire to use in conjunction with nocturnal polysomnography studies (NPS), multiple sleep latency tests, the Epworth Sleepiness Scale (ESS), and medical chart reviews of people referred for evaluation of SDs.
Results: We analyzed data from 658 people (290 female, 368 males). 101 had a history of diabetes and were diagnosed with SDs. Analyses of the diabetes versus no diabetes groups provided characterizations of those with SD and diabetes. For example, comparisons of the groups during NPS revealed significant differences in prevalence of diagnoses of poor sleep efficiency and nocturnal hypoxemia. People with diabetes had higher BMI; slept fewer hours; spent more time in stage 1 sleep and less in stages 3 and 4; reported greater incidents of pain, depression, high blood pressure, heart failure, heart attack, chronic lung disease, thyroid disease, stroke, and bed wetting.
Conclusion: We hope identification of diabetes risk/predictor variables associated with SD will contribute to facilitating prevention, early diagnosis, and effective treatment modalities.

0668

PREVALENCE OF VITAMIN D INSUFFICIENCY/DEFICIENCY AMONG SLEEP MEDICINE PATIENTS COMPLAINING OF SOMATIC PAIN AND CORRELATION WITH DAYTIME SLEEPINESS

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Introduction: Vitamin D deficiency/insufficiency (VDDI) affects > 1 billion persons worldwide, predisposing to nonspecific musculoskeletal pain and painful myopathy. Vitamin D levels are inversely correlated with systemic inflammatory markers. Chronic pain and systemic inflammation contribute to sleep disruption and daytime impairment symptoms, including excessive daytime sleepiness (EDS), though the potential contribution of VDDI to these problems in a sleep medicine population has not been systematically investigated. We postulated that VDDI may be highly prevalent amongst sleep medicine patients complaining of pain, and sought to determine whether there is a correlation between 25-hydroxyvitamin D level and EDS.
Methods: Consecutive patients evaluated at an academic sleep disorders center from 4/1/08 to 3/31/09 were questioned about the presence of musculoskeletal pain. 69 patients who answered in the affirmative, and who agreed to VDDI screening via venous sampling, were included. Epworth Sleepiness Scale scores (ESSS) were analyzed if obtained within 2 weeks of the blood test. Vitamin D deficiency was defined as a 25-hydroxyvitamin D level of <20 ng/mL, insufficiency as ≥20 but <30 ng/mL, and sufficiency as ≥30 ng/mL.
Results: Deficiency was found in 34 patients (49%), insufficiency in 22 (32%), and sufficiency in 12 (17%). Among those with BMI ≥ 30 (n=44), 25 (57%) were deficient, 13 (30%) insufficient, and 6 (14%) sufficient. Deficiency/insufficiency was more common in African American patients (68% and 23%, respectively) than in white patients (42% and 38%). Scatter plot analysis suggested an inverse correlation between ESSS and 25-hydroxyvitamin D level, with a best-fit slope of -0.57 ESS points/ug/mL 25-hydroxyvitamin D.
Conclusion: Amongst sleep medicine patients who complain of pain, VDDI is common. ESSS may be inversely related to 25-hydroxyvitamin D level. Whether sleep medicine patients should be more broadly screened for VDDI—and whether remediation of identified deficits might improve EDS in such a population—requires further study.

0669

RELATIONSHIP BETWEEN INSOMNIA, PAIN SENSITIVITY AND PAIN INHIBITION IN OLDER ADULTS WITH AND WITHOUT KNEE OSTEOARTHRITIS

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Introduction: Quantitative sensory testing (QST) suggests that osteoarthritis patients demonstrate generalized hyperalgesia and impaired endogenous pain inhibitory capacity, but the correlates of these sensory alterations are poorly understood. The present investigation examines whether insomnia may be associated with hyperalgesia and reduced pain inhibition in osteoarthritis (OA).

Methods: In this quasi-experimental study, we used polysomnography and knee radiography to carefully diagnose 4 groups of older adults according to research diagnostic criteria for sleep and knee osteoarthritis. We compared standardized indices of pressure pain threshold (PPT) and pain inhibition in 100 participants meeting criteria for: 1) Normal-Sleep/No-OA (n=22); 2) Normal-Sleep/+OA (n= 14); 3) Primary-Insomnia/No-OA (n=15) and 4) Insomnia/+OA (n=49). Baseline PPT was measured bilaterally via algometry at the trapezius. Pain inhibition was assessed via a diffuse noxious inhibitory control (DNIC) paradigm quantifying percent change in trapezius PPT from baseline relative to trapezius PPT assessed during contra lateral hand immersion in a 4°C, circulating ice water bath (DNIC index).

Results: ANOVA s demonstrated a significant omnibus effect for group status on both PPT and DNIC (p<.05). Follow up comparisons, controlling for age, sex, and BMI demonstrated that the No-Insomnia/No-Osteoarthritis group displayed higher baseline PPT and a greater DNIC effect compared to the Insomnia/+OA group (M=444.59kPa, SD=±33.58 vs. M=346.71kPa, SD=±22.50; M=1.32, SD=±0.27 vs. M=1.17, SD=±0.21, respectively). Normal-Sleep/+OA and Insomnia/No-OA groups demonstrated comparable QST values to each other, but not significantly lower than the Normal-Sleep/No-OA or higher than the Insomnia/+OA, though trends were in the expected directions and data collection continues.

Conclusion: These preliminary findings demonstrate that insomnia in the context of OA is associated with heightened pain sensitivity and diminished pain inhibitory capacity. This suggests that insomnia may alter pain processing pathways that contribute to pain amplification in OA. Follow up work targeting insomnia as a treatment may offer a novel method for improving or preventing OA pain.

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0670

PRE-SLEEP AROUSAL AND PAIN CATASTROPHIZING IN COMORBID INSOMNIA AND CHRONIC PAIN

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Introduction: Over 50% of people with chronic pain experience significant symptoms of insomnia. This study examines the relationships among pain intensity, pain catastrophizing, and pre-sleep arousal with insomnia severity in chronic pain patients.

Methods: Forty-seven outpatients with chronic pain (duration ≥ 6 months) completed self-report measures of health, mood, pain, and sleep. Three separate hierarchical regression analyses were conducted with the Insomnia Severity Index as the outcome. All three analyses included demographic and health variables (age, sex, BMI, education level, and depression) in step one, and pain intensity ratings in step two. Model 1 added the Pre-Sleep Arousal Scale in step 3. Model 2 added the Pain Catastrophizing Scale in step 3. Model 3 included both variables together in last step.

Results: After controlling for covariates, adding pre-sleep arousal in model 1 significantly increased the variance explained in insomnia se-

verity, ΔR^2=.17, $F(1,39)$=8.93, $p<.001$. In model 2, adding pain catastrophizing in the last step also led to a significant increase in variance explained, ΔR^2=.086, $F(1,39)$=7.30, p=.01. Pain catastrophizing was significantly related to insomnia severity, β=.45, $t(39)$=2.70, p=.01. However, when pre-sleep arousal and pain catastrophizing were entered together in model 3, pain catastrophizing was no longer significant. Pre-sleep arousal was the strongest predictor, β=.54, $t(38)$=3.01, p=.005. Overall, model 3 accounted for 62.9% of the variance in insomnia severity, $F(8,38)$=8.07, $p<.001$.

Conclusion: This study highlights the important contributions of pre-sleep arousal and pain catastrophizing to insomnia severity, over and above the effect of pain intensity. Research and clinical work should explore how cognitive variables (such as pain catastrophizing) may be linked to pre-sleep arousal in comorbid insomnia.

0671

THE ASSOCIATION OF SLEEP DIFFICULTIES WITH HEALTH-RELATED QUALITY OF LIFE AMONG FIBROMYALGIA PATIENTS

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Introduction: Difficulty sleeping is common among fibromyalgia patients; however, its impact on health-related quality of life (HRQoL) among fibromyalgia patients is not well understood. The aim of the current study is to assess the burden of sleep difficulties on HRQoL among fibromyalgia patients.

Methods: The current study included data from the 2009 National Health and Wellness Survey (N=75,000), which is a cross-sectional, internet-based survey representative of the adult US population. Only patients who reported being diagnosed with fibromyalgia by a physician were included in the analyses (N=2196). Sleep difficulty symptoms included: difficulty falling asleep, staying asleep and waking up too early. Patients who reported regularly experiencing two or more of the symptoms (severe sleep difficulties; n=1353) or only one of the symptoms (general sleep difficulties; n=574) were compared with patients reporting no symptoms (n=269) in the past year. HRQoL was assessed using the Short Form 12-item (SF-12) health survey, controlling for demographic and health characteristics in multiple regression models.

Results: The overall fibromyalgia sample (N=2196) was mostly female (n=1841; 83.83%) and had a mean age of 53.32 (SD=12.63). Patients experiencing severe or general sleep difficulties were significantly more likely to be on disability (28.01% vs. 23.17% vs. 14.87%, respectively; p's<.05) and less likely to possess insurance coverage (87.09% vs. 90.07% vs. 93.68%, respectively; p's<.05) compared to patients without sleep difficulties. After controlling for demographic and health characteristics, patients experiencing severe or general sleep difficulties reported significantly lower mean mental (40.46 vs. 42.24 vs. 45.09, p's<.001) and physical (31.69 vs. 33.06 vs. 35.65, p's<.001) SF-12 component summary scores than patients without sleep difficulties.

Conclusion: Among the fibromyalgia population, sleep difficulties were independently associated with clinically-meaningful decrements in mental and physical HRQoL. These results suggest effective treatment may be necessary to adequately manage sleep difficulties among the fibromyalgia population.

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0672

EFFECT OF PREGABALIN ON HOME SLEEP AND DAYTIME ACTIVITY PATTERNS IN PATIENTS WITH FIBROMYALGIA AND SLEEP MAINTENANCE DIFFICULTIES

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Introduction: Sleep problems are common among fibromyalgia patients. Actigraphy, which provides objective measurements of sleep and daytime activity at home, was used to determine whether the beneficial effects of pregabalin measured in a sleep laboratory were detectable at home.

Methods: 119 patients with an ACR-defined fibromyalgia diagnosis received pregabalin (150-450 mg/d) and placebo in a randomized, double-blind, 2-period cross-over study (4 weeks treatment per period). A subgroup of 66 patients wore a Bodymedia Armband activity monitor (day and night) during week 4 of each treatment period. Standard algorithms used recorded activity (counts/min) to divide each 24-h day into rest and active periods, and then to estimate sleep efficiency (aEff [%]) and total sleep time (aTST [mins]). Activity data were also used to calculate activity endpoints during sleep (mean, 75th, 90th percentiles) and daytime (mean, 10th, 25th percentiles). Percentiles were derived from the recorded activity distribution of each patient. Data were compared with 17 healthy volunteers (HV) (not age- or weight-matched) who wore the activity monitor for 3 weeks. Values are mean±s.e.

Results: Pregabalin- vs. placebo-treatment increased aEff (91.9±0.3% vs. 90.7±0.4%; P<0.04) but not aTST (432.1±9.1 vs. 419.2±10.3 mins). aEff and aTST for HV were 91.2±0.4% and 415.0±10.4 mins. Pregabalin- vs. placebo-treatment decreased mean (13.7±0.6 vs. 16.4±1.2; P<0.05), 75th (7.2±0.5 vs. 10.9±2.2), and 90th percentile (34.6±2.5 vs. 43.3±3.5; P<0.05) sleep activity (counts/min). Pregabalin values were comparable with HV (14.4±0.8, 7.6±0.6, 36.5±2.3 counts/min, respectively). Pregabalin- vs. placebo-treatment increased low-level daytime activity (10th percentile: 60.3±6.8 vs. 41.9±3.8; P<0.02 and 25th percentile: 129.9±9.4 vs. 111.0±7.5 counts/min; P=0.053). HV daytime activity percentiles were 55.9±5.2 and 138.2±10.3 counts/min, respectively. No change was observed for mean daytime activity levels.

Conclusion: Pregabalin treatment improved (vs. placebo treatment) home-based, actigraphy measures of sleep and increased low-level daytime activity, giving values comparable with healthy subjects.

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0673

THE ASSOCIATION OF BREAST CANCER AND OBSTRUCTIVE SLEEP APNEA

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Introduction: We noticed a significant number of female patients had both obstructive sleep apnea and a history of breast cancer upon changing from a paper medical record system to an electronic medical record system This prompted further analysis of the relationship between the two.

Methods: Data were obtained from the Electronic Medical Record (EMR) system from a single physician's primary care medical practice which encompassed a total of 719 female patients, ages 45 years and older. Among this group of patients those found to have a history of breast cancer and obstructive sleep apnea (OSA) were isolated and data regarding their apnea and cancer was gathered and evaluated. The Fisher Exact Test was used to evaluate relationship between OSA and breast cancer.

Results: Of the 719 female patients, 45 had a history of breast cancer and 126 were found to have OSA. Eighteen patients were found to have both conditions. Using the Fisher Exact Test, a p-value of < .0001 was

obtained suggesting a strong relationship between breast cancer and obstructive sleep apnea in our sample. The degree of sleep apnea ranged from mild to severe. The majority of breast cancers were infiltrating ductal carcinomas, with one adenocarcinoma and two lobular carcinomas. There was no relationship between the severity of the apnea and the type of cancer. The majority of the patients were obese and the mean BMI was 29.1.

Conclusion: There is a high correlation between breast cancer and obstructive sleep apnea in women age 45 and older. A possible explanation for this observation is the presence of obesity as an independent risk factor for both sleep apnea and breast cancer. Further study is needed to confirm the concomitance between obstructive sleep apnea and breast cancer in a larger sample size. Obese patients with breast cancer should be carefully screened for possible OSA.

0674

VALUES AND RELATIONSHIPS AMONG CIRCADIAN ACTIVITY RHYTHMS WITH SUBJECTIVE SLEEP, FATIGUE, AND MOOD IN WOMEN ONE YEAR AFTER THE FIRST ADJUVANT BREAST CANCER CHEMOTHERAPY TREATMENT

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Introduction: This study examined circadian activity rhythms and their relationships with subjective sleep, fatigue, and mood (anxiety/depression) in women one year after the first adjuvant breast cancer chemotherapy treatment (Tx).

Methods: A secondary analysis was performed from a randomized clinical trial testing a behavioral therapy sleep intervention to a healthy eating control condition. Subjects (n=148 of the larger sample of 219) with actigraphy data were post-operative for Stage I -IIIA breast cancer, and post-anthracycline-based, with or without taxane adjuvant chemotherapy treatments. Measurements included: circadian activity rhythms (wrist actigraphy continuous for 1 week); perceived sleep quality (Pittsburgh Sleep Quality Index, PSQI); fatigue (Piper Fatigue Scale); and anxiety/depression (Hospital Anxiety and Depression Scale).

Results: Results are presented as one group because there were no significant differences between groups on these variables at 1 year. Mean circadian rhythm values for mesor, amplitude, peak activity, acrophase, circadian quotient, and 24-hr autocorrelation reflected synchronized rhythms comparable to those of healthy adults, however, individual results varied. PSQI scores were split to reflect self-reported good (≤5, n=76) or poor (≥5, n=72) sleep quality. There were no significant differences between the good and poor groups on actigraphy variables. However, t-tests showed that the poor sleepers' PSQI scores were associated with reports of higher fatigue (F=.4.61, p=.033), higher anxiety r=.6.46, p=.012), and more depressive symptoms (F=.12.85, p<.001).

Conclusion: Some of the relationships reflecting poor physical and mental health status during the week of Tx 3 continued one year after the first Tx, but others did not. Circadian activity rhythms were less commonly disrupted. However, the associations between reports of poor sleep, higher fatigue, and more anxiety and depressive symptoms continued and are of serious concern. Clinicians need to assess and intervene to reduce these distressing symptoms individually and as a cluster in breast cancer survivors.

Support (If Any): Funded by NIH, 5R01NR007762-05

0675

A RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED STUDY ON THE EFFECT OF SILDENAFIL IN AUTONOMIC NERVOUS SYSTEM RESPONSE DURING SLEEP IN OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: We have previously demonstrated that sildenafil can impair sleep related respiratory parameters, in obstructive sleep apnea syndrome (OSAS). Increase in obstructive events and desaturation of oxyhemoglobin may influence autonomic response during sleep. The objective of this study was to evaluate autonomic response in OSAS patients after sildenafil 50 mg, at bedtime.
Methods: Heart rate variability (HRV) was evaluated in the group of thirteen male OSAS patients of the previous study, who underwent all-night polysomnography after receiving sildenafil 50mg or placebo. Frequency-domain HRV was analyzed in 5-minute samples of stable SWS and REM including an apnea event and in 1-minute sample after recovery of respiration in NREM and REM sleep.
Results: Comparing to placebo, during sildenafil night, increase in central AHI occurred in non-REM sleep, increase in obstructive AHI and also decrease in oxyhemoglobin saturation occurred in both non-REM and REM sleep. Additionally, arousal index and in LF/HF component of HRV were higher in REM sleep. Increase in HF and decrease in LF/HF in SWS and decrease in TP in REM were observed in the five-minute samples analysis. Regarding apnea and post apnea one-minute period evaluation, increase in HF occurred in post apnea, and TP variation was not significant nether in NREM, nor in REM sleep, with the use of sildenafil. Modifications of HRV and respiratory parameters of sleep were also evaluated. Correlation was found between modification TP in NREM sleep during apnea and AHI, between modification of HF in REM sleep and AHI, and arousal index. Multivariate analysis showed association of changes in LF/HF in REM sleep post apnea with modification of mean saturation induced by sildenafil.
Conclusion: In severe OSA, the use of sildenafil 50 mg at bedtime plays a detrimental role on respiratory parameters in both non-REM and REM sleep, with fragmentation in REM sleep, increase in parasympathetic activity and blunted heart rate variability during apnea and a prolonged increase in LH/HF component of HRV after resumption of ventilation.
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0676

SLEEP QUALITY AND ASTHMA CONTROL IN NON-SEVERE AND SEVERE ASTHMA

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Introduction: Sleep disturbances are commonly reported by individuals with asthma and are more severe in those with poorly controlled asthma. Gastroesophageal reflux disease (GERD) is considered a probable cause of poor sleep in asthma. We sought to determine if poor sleep quality can be explained entirely by GERD and whether sleep quality is associated with asthma control and asthma quality of life after controlling for GERD and other risk factors.
Methods: Adults with severe asthma (SA), non-severe asthma (NSA), and normal controls (NC) enrolled in the Severe Asthma Research Program (SARP) completed the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and Asthma Quality of Life Questionnaire (AQLQ). Asthma control consisted of items comparable those in the Asthma Control Questionnaire. Individuals using CPAP or BiPAP and/or were at high risk for obstructive sleep apnea were excluded.

Results: A total of 333 patients (109 SA, 164 NSA, 60 NC) were included in the analyses. On average, SA had worse sleep quality (PSQI: 10.1 ± 3.1) than NSA patients (8.7 ± 3.1) and each group had worse sleep quality than NC (6.8 ± 2.5). SA patients had worse asthma control (3.9 ± 1.3) and quality of life (4.2 ± 1.3) than NSA $(5.1\pm1.1$ and $5.1\pm1.1)$. The majority of asthma patients had poor sleep quality regardless of GERD (with GERD; PSQI> 5: 93.6% and without GERD; PSQI> 5: 87.7%). Poor sleep quality was associated with poor asthma control and worse asthma quality of life, independent of age, gender, GERD, body mass index, ESS, and oral corticosteroid use, in both NSA (β=-0.38, p<.001; β=-0.33, p<.001) and SA (β=-0.26, p<.01; β=-0.29, p<.01).
Conclusion: These findings suggest that GERD does not entirely explain poor sleep quality in patients with NSA and SA. Future research is warranted to determine whether specific treatment for sleep disturbances improve asthma control or quality of life.

0677

POTENTIAL GAINS IN TREATING SLEEP APNEA COMPARED TO HYPERLIPIDEMIA IN THE PREVENTION OF CARDIAC DISEASE

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Introduction: Our objective was to compare the effect size estimates of the impact of hyperlipidemia with the impact of obstructive sleep apnea (OSA) on primary and secondary coronary artery disease (CAD) events. Data from well-defined cohort studies and randomized controlled trials (RCTs) were compared with the number needed to treat statistic (NNT).
Methods: A structured literature search collected eligible cohort studies and randomized trials with exposures of hyperlipidemia or OSA. The populations were required to be either primary or secondary CAD with follow-up of at least 3 years and outcomes of incident cardiac events including myocardial infarction and sudden death. The attributable risk (AR) was calculated for cohort studies and the absolute risk reduction (ARR) was calculated for RCTs. The NNT was chosen as a comparator statistic and was applied to cohort studies with the assumption that the AR between the highest and reference risk categories estimates the potential impact of an entirely effective intervention or 'potential' NNT. The risk difference was adjusted across studies for an estimated 5 year risk.
Results: RCT estimates were found for only the treatment of hyperlipidemia on primary CAD and secondary CAD. The impact from cohort studies of hyperlipidemia on primary CAD revealed potential NNTs of 15 to 252 and on secondary CAD a potential of 26. The RCT estimates for treating hyperlipidemia preventing primary CAD events ranged from 44 to 82 and secondary events the NNT was 13 to 42. The impact from the few existing cohort studies of OSA revealed potential NNTs on primary CAD of 18 and on secondary CAD of 8.4.
Conclusion: The potential impacts of hyperlipidemia on CAD estimated from cohorts was higher than in RCT as would be expected. The potential impact of OSA on both primary and secondary CAD events appears to be stronger than hyperlipidemia. The actual impact of treating OSA remains to be studied.
Support (If Any): Mount Sinai Hospital

0678

ATRIAL FIBRILLATION DETECTION USING A PHOTOPLETHYSMOGRAPH WAVEFORM

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Introduction: Atrial fibrillation (AFIB) is the most common sustained arrhythmia, increases with age, and presents with a wide spectrum of symptoms and severity. The diagnosis of AFIB is currently based on either full electrocardiography (ECG) or by Holter ECG device which is recording one or two ECG leads most commonly over relatively short periods of time (24-28hr). The photoplethysmograph (PPG) waveform is used for recording arterial oxygen saturation. However, PPG signals may also allow obtaining several additional parameters as heart rate and cardiac cycle, respiration characteristics and even depth of anesthesia and blood loss. The present research is examining the hypothesis that the PPG waveform can be referred as a useful tool for screening, detecting and diagnosing of atrial fibrillation.

Methods: 109 Patients were recruited from HF center, the division of Cardiology, Lady Davis Carmel Medical Center, Haifa, Israel. Each patient was detected at home for an entire night with 12 leads ECG and pulse oximeter for the recording of the PPG signal. Results were automatically analyzed by a PPG innovative algorithm for AFIB detection (WideMed Ltd., Herzliya, Israel). The ECG data was given to a technician for marking the AFIB annotation (gold standard).

Results: The annotations of AFIB from the automatic analysis of the PPG were compared with the gold standard manual annotations and achieved a gross duration sensitivity and positive predictive value of 96%.

Conclusion: In this study we found a collaborating support for the potential usage of the PPG signal to detect irregular heart rate including episodes of atrial fibrillation. Since this mode of detection is convenient for the patients, it may allow the treating physician to obtain prolonged periods of monitoring and give important information for treatment decisions.

Support (If Any): WideMed Ltd.

0679

SEVERITY OF OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH AND WITHOUT CARDIOVASCULAR-RELATED DISEASES

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Introduction: Previous studies often investigated association of obstructive sleep apnea (OSA) with cardiovascular morbidity and mortality, systemic inflammation and impaired glucose metabolism but the possibility of reverse causation (i.e., metabolic abnormalities such as diabetes mellitus leading to sleep apnea) was not clearly defined. Our aim is to examine if presence of any of the cardiovascular-related dis-

eases including hypertension, diabetes mellitus, coronary artery disease and/or cerebrovascular disease worsens the severity of OSA compared to absence of all the cardiovascular-related diseases. The secondary aim is to evaluate if the Epworth Sleepiness Scale (ESS) score was different between these two groups.

Methods: This is a retrospective study where all patients aged ≥ 18 years referred to sleep laboratory for suspected OSA from January, 1st 2010 to June, 30th 2010 were included. The full-night baseline and split night polysomnographic reports were reviewed. Data was then evaluated by logistic regression analysis to compare between two groups, the severity of OSA (RDI < 15 and RDI ≥ 15), other polysomnographic variables and daytime sleepiness score (ESS <10 and ≥ 10).

Results: 145 patients were analyzed. After adjusting for age, sex and body mass index (BMI), the patients with any of the cardiovascular-related diseases had more severe sleep apnea (RDI>15) with adjusted odds ratio (OR) of 2.5. The increase in RDI was primarily from increase in total obstructive apneic index (OAI ≥ 5) and hypopneic index (HI ≥ 5) (adjusted OR of 2.6). Sleep efficiency and mean oxygen saturation (≥ 95%) were better in the group without any of the cardiovascular-related diseases (adjusted OR of 2 and adjusted OR of 2.9, respectively). However, there was no statistically significant difference between the two groups when compared other polysomnographic variables or ESS score.

Conclusion: Patients with any of the cardiovascular-related diseases are at a higher risk of having moderate to severe OSA without significant increase in daytime sleepiness despite adjusting for age, sex and BMI. Therefore, we suggest that patients with any of the cardiovascular-related diseases should be screened for OSA even if they are asymptomatic.

0680

OVERNIGHT PHARYNGEAL NARROWING IN PATIENTS WITH CONGESTIVE HEART FAILURE AND SLEEP DISORDERED BREATHING

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Introduction: The mechanisms of sleep disordered breathing (SDB) in congestive heart failure (CHF) are not well understood. Lower extremity oedema may predispose CHF patients to spontaneous fluid displacement during the night, which may in turn result in an increase in upper airway collapsibility, and decreased pharyngeal cross-sectional area (XSA) . The aim of this study was to test the hypothesis that sleeping supine is associated with pharyngeal narrowing in CHF patients with SDB.

Methods: Overnight visualisation of the upper airway was performed in 4 CHF patients (3 female; median (range), age: 38.5 (35-43) years; BMI: 37 (26.4-46.2) kg/m^{2}; neck circumference: 37.3 (34.5-45.5) cm; LVEF: 27.5 (5-45) %; NYHA I-III) with SDB (AHI: 36.5 (16-46.4) events/hour), predominantly central sleep apnoea (central apnea index: 10.3 (1.3-20.4) events/hour). The retropalatal XSA was visualised using a fibreoptic bronchoscope; pharyngeal pressure was measured using a pressure transducer placed at the palatal rim; airflow was measured using a pneumotachometer; neck circumference was measured using inductance plethysmography. Expiratory pharyngeal compliance was calculated as the slope of the relationship between XSA and pharyngeal pressure. Patients slept in a supine posture and data was sampled from periods of stable NREM sleep as close to the beginning and end of the study as possible. The median (range) time between the start and end of the night was 2.0 (1.5-3.6) hours.

Results: Neck circumference was unchanged overnight (start of night: 37.1 (32.6-45.8) cm vs. end of night: 37.3 (32.6-44.5) cm), whereas retropalatal XSA decreased overnight (start of night: 11.6 (5.4-72.9) mm[2] vs. end of night: 6.7 (2.5-67.5) mm[2]), as did expiratory pharyngeal com-

pliance (start of night: 3.2 (-0.03-6.56) mm^2/cmH$_2$O vs. end of night: 0.7 (-0.03-3.02) mm^2/cmH$_2$O).

Conclusion: CHF patients with central SDB experienced progressive pharyngeal narrowing overnight, which may predispose them to an increased likelihood of upper airway collapse, due to increased surrounding pressure.

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0681

EVALUATING FOR MODERATE-SEVERE SLEEP DISORDERED BREATHING IN PATIENTS WITH AT RISK FOR CORONARY HEART DISEASE

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Introduction: Sleep disordered breathing (SDB) is common in coronary heart disease (CHD). We examined the utility of the Berlin Questionnaire (BQ) and common SDB risk factors to screen patients with or at risk for CHD for moderate-severe SDB.

Methods: Analyses were based on 449 patients with CHD or at least 3 CHD risk factors meeting initial screening criteria for the Heart Biomarker Evaluation in Apnea Treatment study and had portable monitoring. Patients had an Epworth Sleepiness Scale (ESS)<16 and a high-risk BQ. Sleepiness was defined as ESS≥11. Logistic regression was used to determine associations of moderate-severe SDB with the BQ and its individual components, and age, BMI, sex, and sleepiness.

Results: 1,886 patients were screened of which 1,370 (73%) had high-risk BQ scores. 449 patients then had a sleep study. The sample was predominantly men (72%) with hypertension (87.7%). The mean age was 61.5 years, BMI was 32.2 kg/m2 (64% obese), and ESS was 8.8 (ESS≥11: 38.5%). The positive predictive value of a high-risk BQ for moderate-severe SDB (AHI≥15) was 46.7%. The presence of sleepiness did not improve the predictive value of a high-risk BQ for moderate-severe SDB. In contrast, significant associations between moderate-severe SDB and a positive category 1 of the BQ (i.e. presence of obstructive breathing symptoms) (OR:2.10), BMI (OR:1.1), age (OR:1.03), and male sex (OR:1.76) were observed. ROC analyses demonstrated an AUC of 0.65 with a sensitivity of 74.1%, specificity of 44.0%, a positive predictive value of 60.4%, and negative predictive value of 59.5%.

Conclusion: In patients with or at risk for CHD, high-risk BQ, and mild to moderate sleepiness, the prevalence of SDB (84.6%) and moderate-severe SDB (46.7%) was high. Traditional SDB risk factors including age, BMI, male sex, and obstructive breathing symptoms in patients with a high-risk BQ were associated with moderate-severe SDB.

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0682

RISK OF OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH PACEMAKERS AND IMPLANTABLE CARDIOVERTER DEFIBRILLATORS

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Introduction: Obstructive Sleep Apnea (OSA) affects 2-4% of the adult population and has been associated with increased long term cardiovascular mortality. Patients with OSA have a higher incidence of arrhythmias e.g. in Sleep Heart Health Study atrial fibrillation, non-sustained ventricular tachycardia, and complex ventricular ectopy were more common in patients with OSA. The prevalence of OSA in patients being treated for arrhythmias with pacemakers or implantable cardioverter defibrillator (ICD) is not clear although a prevalence of 59% was suggested in the European Multicenter Polysomnography Study. Our goal was to assess risk for OSA using the Berlin Questionnaire (BQ) in patients presenting to the Oregon Health and Science University (OHSU) arrhythmia clinic for pacemakers or ICD implantation.

Methods: We found 648 patients who had pacemakers or ICD implanted between June 2007-June 2010 (37 months) at OHSU arrhythmia clinic. After IRB approval, we were able to get phone consent from 196(30.2%) patients to mail them a BQ with return envelopes. We received a response back from 121 subjects (61.7%). BQ Data was analyzed to evaluate for risk for sleep apnea.

Results: There were 54(44.6%) females and 67(53.4%) males with average age of 66±15 years. Body mass index was 26.5±7.2 kg/m2. Fifty five (45.5%) patients had history of hypertension. 71(58.7%) patients had 2 or more categories positive on the BQ suggesting a high risk for OSA while 50 (41.3%) patients had one or no categories positive on the BQ suggesting a low risk for OSA.

Conclusion: The risk for OSA is high in subjects presenting to the arrhythmia clinics for placement of pacemakers or ICD's. This population should be screened for OSA as the presence of OSA is likely to increase arrhythmogenesis and cardiovascular mortality.

0683

SLEEP APNEA AND CARDIAC ARRHYTHMIA: A POPULATION BASED STUDY

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Introduction: Obstructive sleep apnea (OSA) exerts strong modulatory effects on the autonomic nervous system through several mechanisms. While profound vagal activity may lead to bradyarrhythmias, sympatho-excitation could favor ventricular arrhythmia; and whether these differ in individuals with and without sleep apnea remains unclear. The goal of this study is to analyze arrhythmias of such individuals who participated in the Sao Paulo Epidemiologic Sleep Study.

Methods: : A total of 1042 participants (95% response rate) visited the sleep laboratory, were clinically evaluated and had a full-night polysomnography (PSG) recorded. The electrocardiographic (ECG) channels were analyzed with a Holter system provided by Cardios (Cardio Smart - Cardio Sistemas, São Paulo, Brazil). ECG characteristics included were: Heart rate, QT and PR intervals, ventricular and atrial arrhythmias, pauses and heart rate time domain variability. The apnea-hypopnea index was used to determine the presence (AHI>5) and severity of OSA (Mild: 5<AHI<15; Moderate: 15<AHI<30; Severe: AHI>30).

Results: : A total of 767 participants were included in analyses, after unreadable artifacts were excluded. At least one type of cardiac rhythm disturbance (atrial or ventricular arrhythmia and/or pause) was found in 62.7% of them, and OSA in 35.9%. Both ventricular and atrial arrhythmia were 6 times more frequent among severe OSA individuals than controls (92.3% vs. 53.3% and 85% vs. 47%, respectively; p<0.001), whilst among mild and moderate cases were less frequent, but still, twice as higher than in controls. Similarly, the QT interval was significantly greater in severe cases than in controls [387.1±(SE=5.1) vs. 371.9±1.5; p=0.01]. Heart rate variability, on the other hand, was found with decreasing pNN50 as OSA severity increased (20.3 vs. 13.7, 12.9 and 10.8; p<0.001). In fully adjusted models, OSA was an independent predictor of ventricular and atrial arrhythmias.

Conclusion: The occurrence of atrial and ventricular arrhythmia was greater in OSA individuals. The parasympathetic tonus seems to be involved.

Support (If Any): AFIP, FAPESP

0684

PREVALENCE AND PRELIMINARY OUTCOMES DATA OF UNDIAGNOSED SDB IN CARDIAC SURGERY PATIENTS

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Introduction: The perioperative management of surgery patients can be seriously complicated by SDB. Cardiac surgeries are of particular importance due to the strong link between SDB and cardiac disease and the large number and high cost of these procedures. Yet, a prospective investigation of the impact of SDB on cardiac surgery outcome has not been performed.

Methods: 107 patients admitted for CABG or valve replacement surgeries underwent polysomnography (PSG) pre-operatively at the Cleveland Clinic (CC) and Johns Hopkins Hospital (JHH). Studies were performed in the hospital room and remotely monitored in real time from the sleep laboratory using a wireless, 14-channel PSG acquisition system. 65 patients at CC and 42 patients at JHH completed testing and had outcome data available. Several outcomes were tracked post-operatively during a 30 day follow-up including length of ICU stay. PSG reports were generated typically within 24 hours of study completion and made available to the surgical team.

Results: Conducting PSG in the patient room was found feasible with sufficient sleep time and data quality in most cases. Average sleep time was 247 minutes (CC), 197 minutes (JHH) and sleep efficiency was 61.4% (CC), 52.3% (JHH). A high prevalence of SDB (AHI > 5) was found (72% at CC; 71% at JHH) with a significant percentage of the population exhibiting severe SDB (AHI > 30; 32% at CC; 29% at JHH). Cardiac surgery patients with severe SDB stayed in the ICU longer than those without SDB (0.7 days longer at CC, 1.1 days longer at JHH). More detailed analysis of outcome data is underway.

Conclusion: While the results are preliminary, this study shows that SDB is common in patients undergoing cardiac surgery procedures and may lead to extended ICU stay. The study also confirms the feasibility and quality of pre-operative PSG recorded in the hospital and monitored remotely.

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0685

RATIONALE AND DESIGN OF THE RANDOMIZED INTERVENTION WITH CPAP IN CORONARY ARTERY DISEASE AND SLEEP APNEA - RICCADSA TRIAL

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Introduction: Obstructive sleep apnea (OSA) is common in coronary artery disease (CAD) and a possible cause of increased mortality. To date, there is a lack of randomized controlled trials to draw the conclusion that all CAD patients should be investigated for OSA and subsequently be treated with continuous positive airway pressure (CPAP). The RICCADSA study is an on-going Swedish single-center (two sites) trial started in December 2005 addressing the impact of CPAP in newly revascularized CAD patients and concomitant OSA (Apnea-Hypopnea-Index [AHI[≥15/h] without daytime sleepiness (Epworth Sleepiness Scale <10). The primary end-point is the combined rate of new revascularization, myocardial infarction, stroke and cardiovascular mortality over a mean period of 3-years. Secondary outcomes include impact of CPAP on cardiovascular biomarkers, cardiac function, maximal exercise capacity and quality of life measures at 3-month- and 1-year follow-up as well as adherence to CPAP treatment in OSA patients.

Methods: A total of 244 CAD patients with non-sleepy OSA are randomly assigned to one treatment and one control group. The mean follow-up for patients will be three years. CAD patients with sleepy OSA (n=155) are offered CPAP treatment and included in the trial as positive controls, and non-OSA patients (n=110) as negative controls. The enrollment is expected to be completed in the current month of 2010.

Results: Among 1305 revascularized CAD patients, 654 (50.1%) underwent a sleep study by November 30, 2010. OSA was prevalent in 419 (64.1%), of whom 259 (61.8%) were regarded as non-sleepy. Borderline OSA (AHI 5-15/h) was found in 97 (14.8%), non-OSA (AHI<5/h) in 118 (18.8%) and dominantly Cheyne-Stokes respiration in 20 (3.1%), respectively.

Conclusion: Our results suggest a markedly increased prevalence of OSA in a revascularized CAD cohort while the majority of those subjects do not report daytime sleepiness. When completed, the RICCADSA-trial will contribute to define the impact of CPAP as a non-pharmacological intervention for CAD patients with OSA regardless of subjective sleepiness.

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0686

PHOTOPLETHYSMOGRAPHY AS A SOURCE FOR ANALYSIS OF SLEEP DISORDERED BREATHING IN PATIENTS WITH SEVERE CARDIOVASCULAR DISEASE

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Introduction: Sleep Apnea, Sleep-Disordered Breathing (SDB) and Cheyne-Stokes Breathing (CSB) are often not diagnosed, especially in cardiovascular patients. The prevalence of SDB in patients with heart failure is around 50%. Moreover, SDB and CSB were shown to have prognostic value for hospitalization and mortality in heart failure patients. In this study, we examined an automated analysis system based on photoplethysmographic signals that might provide a convenient screening and show a good potential as a diagnostic solution for patient evaluation at home or in an ambulatory setting.

Methods: We compared the Apnea Hypopnea Index (AHI), respiratory event detection and classification obtained by full polysomnography

(PSG) manual scoring "gold-standard" to the automated analysis in 74 subjects. Each subject underwent overnight PSG, 60 in a hospital cardiology department and 14 while being tested for suspected SDB in a hospital sleep laboratory. The automatic analysis is based on photoplethysmographic and saturation signals only. Those two signals were recorded for the entire night as part of the full overnight PSG sleep study.

Results: The sleep and respiratory parameters measured by the analysis correlated very well with the corresponding results obtained by the full PSG. The sensitivity of AHI 15 cutoff-level measurement by the analysis was 98% (95%CI: [87.1% - 99.6%]) and its specificity was 96% (95% CI: [79.8% - 99.3%]). CSB analysis sensitivity was 92% (95% CI: 78.6%-98.3%) and specififcity 94% (95% CI: 81.3%-99.3%). Regression and Bland-Altman plots revealed good agreement between the two methods.

Conclusion: Relative to gold-standard PSG, the use of the tested system in this study yielded an acceptable analysis of sleep- and/or respiratory-related breathing disorders. Accordingly, and given the convenience and simplicity of its application, the new system can be considered suitable for home and ambulatory screening and potentially diagnosis in patients with cardiovascular disease.

Support (If Any): WideMed Ltd.

0687

SLEEP DURATION MODIFIES THE HERITABILITY OF BODY MASS INDEX

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Introduction: Previous research has found that short sleep duration (< 7 hrs/night) is associated with elevated body mass index (BMI). The current study examined whether sleep duration modified genetic and environmental influences on BMI.

Methods: Participants were drawn from the University of Washington Twin Registry, a population-based sample of U.S. twins (N=1811 pairs, 933 MZ, 878 DZ; 63% female; M age = 36.6 years, SD=15.8 years). Participants provided self-report survey information on height and weight (used to calculate BMI; M=25.4 kg/m^2, SD=5.43) and habitual sleep duration (M=7.18 hrs/night; SD=1.24). Data were analyzed using behavioral genetic interaction models.

Results: The heritability of sleep duration was 32%; shared environmental influences on sleep duration were negligible (rMZ = 0.34; rDZ = 0.12). As previously reported, longer sleep duration was associated with decreased BMI (b = -.24, SE = .09, P < .01). Behavioral genetic modeling indicated that there were significant interactions between sleep duration and both genetic [a_0 = 9.35, a_x = -.71, both P < .05, where total genetic variance = a_0 + a_x*(sleep duration)] and shared environmental influences [c_0 = -4.99, c_x = 0.94, both P < .05, where total shared environmental variance = c_0 + c_x*(sleep duration)] on BMI. The heritability of BMI when sleep duration equaled 7 hours (h^2 = 70%) was more than twice as large as the heritability of BMI when sleep duration equaled 9 hours (h^2 = 33%).

Conclusion: Shorter sleep duration is associated with increased BMI and increased genetic influences on BMI, suggesting that shorter sleep duration may increase expression of genetic risks for high body weight. At the same time, longer sleep duration may suppress genetic influences on body weight. Future research aiming to identify specific genotypes for BMI may benefit from considering the moderating role of sleep duration.

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0688

SLEEP QUALITY AND DAYTIME SLEEPINESS IN RHEUMATOID ARTHRITIS

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Introduction: Sleep quality (SQ) and daytime sleepiness are important patient-reported outcomes in rheumatoid arthritis (RA). Chronic pain can negatively affect aspects of sleep which in turn are associated with -among other- impaired immune function. The assessment of sleep as an important factor of quality of life is gaining interest when prescribing a pharmacologic intervention for RA. This study aimed at describing the relationship betweeen RA disease activity and different dimensions of SQ.

Methods: This was an observational, cross-sectional, multi-center study with 300 RA patients in Belgium. The patients represented a heterogeneous sample using classical or biological disease-modifying antirheumatic drugs (DMARDs). Patients were distributed into a "Remission-Low" (DAS28≤3.2) or "Moderate-High" (DAS28>3.2) group. SQ was assessed with the Pittsburgh Sleep Quality Index (PSQI) and the Athens Insomnia Scale (AIS); daytime sleepiness with the Epworth Sleepiness Scale (ESS).

Results: Proportions of patients in Remission-Low and Moderate-High groups were 44.4 and 55.6% respectively. 56.4% of the patients received conventional DMARDs and 43.6% biological DMARDs. Mean (SD) scores were: PSQI 7.75 (4.3); AIS 6.75 (4.79) and ESS 7.30 (4.67). Moderate-High patients had significantly lower SQ than Remission-Low patients on the PSQI and AIS (p<0.001) but no difference was observed on the ESS. Cross-validation of the ESS with questions on daytime sleepiness in the PSQI and AIS confirmed the validity of the results: the higher the chance of dozing (ESS) the higher the daytime sleepiness (AIS) and the more difficulties to stay awake (PSQI) reported. Compared to Remission-Low patients, Moderate-High patients had higher pain scores (p<0.001).

Conclusion: PSQI and AIS are valid tools to assess sleep quality in RA patients. The ESS does not discriminate between patients with high versus low DAS28 scores, possibly due to an alerting effect of the chronic pain condition.

0689

POST-INFECTIOUS FATIGUE AS REVERSIBLE SLEEP DYSFUNCTION

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Introduction: Post-infectious fatigue (PIF), usually with musculoskeletal aches, cognitive dysfunction, and abnormal sleep, persists in 20% at 2 months and 10% at 6 months after mononucleosis (IM) or Lyme disease (LD). We evaluated 6 PIF cases: 2 had had IgM+ LD (C1,5) and 4 had acute EBV IM (C2-4,6). Cases (age/sex-PIF duration): C1 (23F-5 wks), C2 (18M-6wks), C3 (17F-16mos), C4 (15M-8mos), C5 (55M-40mos), C6 (29F-14yrs). C1-5 had a PIF-associated onset of leg restlessness (LR) typical of restless legs syndrome (RLS). Our ongoing research has found that injection of bilateral distal foot nerve entrapments (neuromas) improves RLS associated sleep dysfunction and fatigue. After informed consent, C1-6 were studied.

Methods: Baseline and post-injection sleep parameters, fatigue, and LR were assessed by daily sleep logs/visual analogue scales (VAS) and by validated questionnaires (score range): International RLS rating scale (IRLS 0-40), Pittsburgh Sleep Quality Index (PSQI 0-21), Fatigue Severity Scale (FSS 9-63), Multidimensional assessment of fatigue (MAF 1-50), and Flinders Fatigue Scale (FFS 0-31). Bilateral 3rd and 4th inter-

space neuromas confirmed by ultrasound were each injected with 1 ml lidocaine/bupivacaine/methylprednisolone/dexamethasone/ 4% alcohol. **Results:** Within 48 hours of injection, sleep logs/VAS in 5 of 6 cases showed improving sleep quality and fatigue levels. QUESTIONNAIRE baseline (B) score: C1-6 mean (range), % Improvement (% I) at 7-14 days post-injections: C1-6 mean/(range): IRLS (C1-5 only) B: 31(25-39), % I: 68% (21-96); PSQI B: 12(8-17), % I: 51% (0-88); FSS B: 48(39-56), % I: 53% (6-78); MAF B: 36(28-43), % I: 57% (13-78); FFS B: 22(13-30), % I: 61% (22-100). Treatment benefit continued over 1-4 months' follow-up.

Conclusion: PIF in 5 of 6 cases was sleep-related and largely reversible by neuroma injections. Despite 2 distinct triggering infections, the PIF/ LR symptom complex and its prompt progressive improvement were similar. We recommend further study of PIF as reversible sleep dysfunction.

0690

BEDTIME VERY LOW DOSE (VLD) CYCLOBENZAPRINE INCREASES NIGHTS WITH NORMALIZED CYCLIC ALTERNATING PATTERN (CAP) A2+A3 RATE ≤ 33% IN FIBROMYALGIA SYNDROME (FMS) WHICH CORRELATES WITH IMPROVEMENTS IN FATIGUE AND MOOD

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Introduction: Fibromyalgia Syndrome (FMS) is characterized by chronic pain, tenderness, unrefreshing sleep, fatigue and depressed mood. Disordered sleep in FMS has increases in the periodic nonREM sleep known as the Cyclic Alternating Pattern (CAP) (Rizzi, Sarzi-Puttini et al. 2004, Moldofsky et al 2010). Subtypes CAP A2 and A3 are indices of sleep instability while subtype CAP A1 is a measure of sleep stability. Previously, we showed that very low dose (VLD) cyclobenzaprine (CBP) improved core symptoms of FMS (Moldofsky H 2002). In a retrospective analysis, we tested whether VLD CBP decreases CAP A2+A3 and whether such changes potentially correlate with improvements in FMS symptoms.

Methods: Our double blind placebo-controlled study (n=36) of VLD CBP (mean dose = 3.1 mg) in FMS for 8 weeks (average 54 days) included self-reported measures of pain, fatigue, tenderness (dolorimetry) and mood (Hospital Anxiety and Depression [HAD] scale). Polysomnography was performed at screen, baseline and weeks 2, 4 & 8. EEG sleep CAP was measured by Embla automated CAP analysis system. CAP sleep response was calculated by CAP (A2+A3 rate)/(A1+A2+A3 rate) ≤ 33% (normalized CAP A2+A3) which we found to separate treatment effects by analyzing a range of normalized CAP A2+A3 values from 10% to 50%. Effects of treatment were analyzed by Last Observation Carried Forward (LOCF).

Results: VLD CBP treatment improved bedtime musculoskeletal pain (p=0.010), tenderness (p=0.006), bedtime fatigue (p=0.039), HAD (p=0.017), HAD depression subscale (p=0.017), and change in self-rated (p=0.001) and clinician-rated fatigue (p=0.004). Placebo subjects showed no improvement in these measures. VLD CBP also increased nights with normalized CAP A2+A3 rate ≤ 33% (p=0.020) while placebo did not. For those receiving VLD CBP, the increase in nights with normalized CAP A2+A3 rate ≤ 33% was correlated to bedtime fatigue (p=0.006), total HAD (p=0.033), HAD depression (p=0.017), and self-rated (p=0.007) and clinician-rated change in fatigue (p=0.011). Improvements in pain and tenderness did not appear significantly correlated with nights with normalized CAP A2+A3 ≤ 33%.

Conclusion: 1. Bedtime VLD CBP treatment is associated with increased nights with normalized CAP A2+A3 rate ≤33% which is correlated with improvements in fatigue and mood. 2. The normalized CAP A2+A3 rate may provide a novel biomarker for assessing treatment

effects on nonrestorative sleep and associated subjective somatic and mood symptoms in FMS.

Support (If Any): Supported by TONIX Pharmaceuticals

0691

OBSTRUCTIVE SLEEP APNEA, SLEEP DURATION, AND DIABETES SELF-MANAGEMENT AMONG PATIENTS WITH POORLY CONTROLLED DIABETES

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Introduction: Obstructive sleep apnea (OSA) and short sleep duration have been associated with poorer metabolic control. The goal of this study was to evaluate associations between OSA risk, sleep duration and diabetes self-management.

Methods: Data were from a behavioral intervention for poorly controlled diabetics at federally qualified health centers. The sample included 559 patients (66% women, age M(SD)=54.5 (11.0) years. Time since diagnosis was M(SD)=1.06 (0.38) years. The majority, (79%) reported oral medications and 44% used insulin. OSA risk was determined by the Berlin Questionnaire and short sleep duration was determined as habitual sleep time <6 hours. Depression and anxiety were assessed by the 8-item PROMIS measures. Adherence was assessed by 4 items including forgetting doses, mistakes, and intentional non-adherence. Self-efficacy for healthcare communication was assessed using the Communication and Attitudinal Self-Efficacy Scale and diabetes self-efficacy was measured by the Diabetes Self-Efficacy Scale. Data were analyzed using chi square, logistic regression, and t-tests.

Results: Prevalence of high risk for OSA was 65% and short sleep duration was 21%. Both risk for OSA and short sleep duration were associated with higher rates of poor adherence (60% vs. 45%, p=0.007 for OSA risk and 68% versus 51% for short sleep duration, p=0.01), higher anxiety (p<0.001) and depression scores (p<0.001). Effects of OSA risk on adherence remained significant after controlling for depression and anxiety (p= 0.01) but effects of sleep duration were attenuated after controlling for depression and anxiety (p=0.06). Short sleep duration was associated with poorer self-efficacy for healthcare communication (p=0.01) and, diabetes (p=0.003) and remained significant after controlling for depression and anxiety. OSA risk was not associated with self-efficacy.

Conclusion: Results demonstrate that OSA and short sleep duration may reflect poorer psychological functioning as well as poorer medication adherence in patients with diabetes. These results suggest sleep disruption may affect diabetes not only through metabolic processes but also through poorer behavioral self management.

Support (If Any): Missouri Health Literacy and Diabetes Communication Initiative

0692

SLEEP AND TYPE 2 DIABETES: HOW MUCH ARE THEY ASSOCIATED?

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Introduction: In the recent years, some studies have pointed out the increased risk of developing Type 2 diabetes for people who slept less than six hours per night and also in people with obstructive sleep apnea syndrome (OSAS). This study aims to examine 1) if such associations can be found in the general population and 2) if the presence of a type 2 diabetes treatment changed the associations.

Methods: This cross-sectional telephone study involved 15,945 individuals representative of the American adult general population (≥ 18 years) living in 15 states. Participants were interviewed on medical conditions (ICD-10), sleep disorders (ICSD) and mental disorders (DSM-IV) using Sleep-EVAL.

Results: A total of 5% of the sample reported Type 2 diabetes; the prevalence increased with age reaching nearly 15% in the ≥ 65 years. Proportion of treated Type 2 diabetes individuals sleeping less than 6 hours per night was comparable with non-diabetic participants (17.6% vs. 17.1%) but it was higher among untreated type 2 diabetes subjects (22.1%). Prevalence of OSAS was significantly higher in both treated (8.4%) and untreated (7.4%) type 2 diabetes subjects compared to non-diabetic individuals (4.3% p< 0.001). Logistic regression models were calculated to control for the effects of age, sex, high blood pressure and BMI on the observed associations. After adjusting for these variables, short sleep duration was no longer significantly associated with type 2 diabetes. On the other hand, OSAS remained significantly associated with type 2 diabetes (OR: 1.8; p<0.05).

Conclusion: Type 2 diabetes and OSAS appeared to be independently associated but not short sleep. Mediator variables such as age and obesity, better account for the apparent relationship between short sleep and Type 2 diabetes.

0693

OVERWEIGHT, OBESITY, DIABETES AND EXERCISE ASSOCIATED WITH SLEEP DISTURBANCE AND DAYTIME FATIGUE IN THE AMERICAN POPULATION

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Introduction: Previous studies have demonstrated that both obesity and diabetes are related to sleep outcomes. Exercise may also influence sleep and daytime function. We extend these findings by examining how general sleep-related complaints are associated with body mass index (BMI), diabetes history, and exercise in a large, nationally-representative sample.

Methods: Participants were respondents to the Behavioral Risk Factor Surveillance System (BRFSS). The present analysis focuses on nighttime complaints of sleep disturbance (SLEEPDIST) and daytime complaints of tiredness/fatigue (DAYFATIGUE). SLEEPDIST(N=156,252) was measured with: "Over the last 2 weeks, how many days have you had trouble falling asleep or staying asleep or sleeping too much?" DAYFATIGUE(N=155,761) was measured with, "Over the last 2 weeks, how many days have you felt tired or had little energy?" Responses were dichotomized, with ≥6 days indicating complaint. All analyses were stratified by gender and adjusted for age, race/ethnicity, income, and education. Predictors included BMI (25-29.9=overweight/30+=obese), Diabetes (self-report), and Exercise (any in past 30dys).

Results: Regarding SLEEPDIST, obesity was predictive in women(OR=1.35;p<.0001), and diabetes was predictive in both men(OR=1.39;p<.0001) and women(OR=1.38;p<.0001). Regarding DAYFATIGUE, being overweight was predictive in women only(OR=1.71;p=.0002). Obesity was predictive in both men(OR=1.19;p<.0001) and women(OR=1.57;p<.0001). Diabetes was also predictive in both men(OR=1.49;p<.0001) and women(OR=1.50;p<.0001). Any exercise in the past 30 days did not attenuate any of these relationships. However, exercise was independently associated with ~35% decreased odds of SLEEPDIST in men(OR=0.64;p<.0001) and women(OR=0.68;p<.0001), as well as ~50% decreased odds of DAYFATIGUE in men(OR=0.53;p<.0001) and women(OR=0.49;p<.0001).

Conclusion: These results suggest that (1)diabetes is a significant predictor of sleep and daytime complaints, and (2)there is a positive relationship between obesity and sleep disturbance for women and daytime fatigue in both sexes. Finally, a broad exercise measure was independently associated with much fewer complaints of both outcomes in both genders.

0694

IMPROVED DRIVING SIMULATION PERFORMANCE AFTER GERD TREATMENT WITH ESOMEPRAZOLE: A PROSPECTIVE PILOT STUDY

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Introduction: Gastroesophageal reflux disease (GERD) with heartburn appears to disturb sleep, quality of life, sleep quality, next day functionality, and work productivity. Disturbed sleep also impairs simulated driving (SD) performance. We hypothesized GERD treatment with a proton pump inhibitor (PPI) would improve SD.

Methods: Fourteen healthy patients (mean age = 49 years, 32-60, 11 women,) with typical nocturnal GERD symptoms participated after informed consent. Inclusion criteria were age < 60 yr, reported GERD sleep disturbance with 3+ episodes/wk, duration of problem > one month, and moderate to severe heartburn. We excluded patients with other sleep disorders, significant psychiatric and significant medical disorders. Hypnotics, anxiolytics, antihistamines, benzodiazepines were allowed if the dose had been stable for > 3 months. Driving studies were performed from 1000-1300 hr using the System Technology Inc. simulator. We prohibited caffeine and nicotine within 3 hr of the drive. After a 10-minute practice city drive, participants completed a 60 minute country drive. The standard deviation of lane position (SDLP) was compared across six consecutive 10-minute periods using a mixed ANOVA. Secondary measures included Epworth Sleepiness Scale (ESS) and GERD symptom score. Patients drove before and after treatment with ESO.

Results: Treatment reduced the percentage of nights with reported GERD induced sleep dysfunction to 10% from 63% (p<0.001), ESS decreased to 6.0 from 7.8 (p=0.036), and SDLP decreased by a mean of 0.11 ft for each of the six 10-minute periods (p = 0.038).

Conclusion: Treatment with ESO corresponded to reduced GERD induced sleep disturbance, reduced sleepiness, and improved DS performance. Possibly, treating GERD may improve highway safety for some patients. This is a rare demonstration of pharmacotherapy potentially improving sleep and next day performance, something hypnotics do not do. Follow-up randomized blinded controlled trials with polysomnography are warranted to validate these findings.

0695

ANGIOTENSIN CONVERTING ENZYME POLYMORPHISM AND ERECTILE DYSFUNCTION COMPLAINTS IN THE BRAZILIAN POPULATION: DATA FROM A SLEEP DISORDER SURVEY

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Introduction: Erectile dysfunction (ED) is increasingly recognized as a public health problem. Indeed, ED or sexual complications are common in men with cardiovascular disease and both diseases have overlapping risk factors, etiology and clinical outcomes. Angiotensin-converting enzyme (ACE) is the major regulator of circulatory homeostasis. An insertion-deletion polymorphism in the ACE gene has been associated with marked differences in serum ACE levels and with various cardiovascular diseases. We sought to evaluate a potential association between ACE polymorphisms and ED complaints and its relationship with sleep disorders in a population-based sample in São Paulo, Brazil.
Methods: A total of 449 men were enrolled in the Epidemiologic Sleep Study (EPISONO) and answered an 8-item questionnaire to ascertain sexual performance/ED and satisfaction. ACE polymorphisms were genotyped using a standard polymerase chain reaction method.
Results: No significant case-control difference was observed for the ACE I/D polymorphism either by genotype or allele-wise. The inclusion of Obstructive Sleep Apnea Syndrome (OSAS) diagnosis in the analyses did not provide evidence of an association with ED phenotype or with OSAS itself. Because age is a significant risk factor for ED complaints in our sample, we carried out analyses stratifying the sample by age group. The ID and II genotypes were significantly more frequent in ED complaint cases (88.9%) compared to controls (57.1%) in the men between 40 and 55 years of age. The frequency of the I allele was also significantly higher in individuals complaining of ED (66.7%) compared to men with no complaints (39.0%) (OR=3.12; 95%IC=1.48-6.59). Correction for potential confounding variables, including genetic ancestry, did not affect the strength of the association.
Conclusion: The findings of the present study suggest that the I/D polymorphism or another variant in close linkage disequilibrium with it may play a role in the development of ED in a specific age group and provides progress towards the understanding of the interaction between genetic factors, sleep and the risk of ED.
Support (If Any): AFIP, FAPESP/CEPID, CNPq.

0696

DAYTIME PULSE-OXIMETRY MEASUREMENTS DO NOT PREDICT NOCTURNAL DESATURATIONS IN ADULT SICKLE CELL PATIENTS

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Introduction: Low nocturnal saturations in sickle cell patients have been associated with increase pain crisis and first cerebrovascular accident. This study evaluated the relationship of daytime pulse-oximetry and nocturnal desaturations in adult sickle cell disease (SSD).
Methods: Retrospective analysis of 43 patients referred from sickle cell clinic. Inclusion criteria were presence of Hemoglobin SS (homozygous), age >21, overnight pulse-oximetry or overnight sleep study. Nocturnal desaturation was defined as spending >5 mins below 89% at night. Daytime saturations were considered normal if > 95%. Patient's baseline characteristics were documented. Fisher's exact test was used for comparing the normal and low daytime saturation groups.

Results: Of the 43 patients identified, 16 did not meet inclusion criteria. The mean age of the group was 40 (22-65). Of the 27 patients, 17 (63%) had normal daytime saturations (>95%) and 10 (37%) had low daytime saturations (95% or less). 6/10 (60%) of patients with low daytime saturation had nocturnal desaturation compared to 7/17 (41%) in the normal saturations group (p=0.44). Baseline characteristics were similar between groups. When compared with a random group with good daytime saturations, the sickle cell group with normal daytime saturations demonstrated significant oxygen desaturations (p<0.0072). Low daytime saturation in sickle cell patients also did not help in predicting obstructive sleep apnea (OSA).
Conclusion: We find that having normal or high daytime oxygen saturations does not rule out nocturnal desaturations in adult sickle cell patients. Low daytime saturations also do not predict presence of OSA in adult SSD as has been suggested in pediatric literature. Clinical Implications: Daytime oxygen saturations should be used with caution when evaluating adult sickle cell patients for nocturnal desaturation or OSA.

0697

SLEEP-DISORDERED BREATHING IN PATIENTS WITH SICKLE CELL ANEMIA AND PRIAPISM

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Introduction: Priapism is a sustained, painful, and unwanted erection of the penis and its prevalence in sickle cell anemia (SCA) is of 30 to 45% of the cases. Considering that priapism events are frequently described during sleep and that physiological penile erections occur preferentially in rapid eye movements (REM) sleep, when sleep apnea events are also more frequently observed, we hypothesize a relationship between priapism in SCA and sleep-disordered breathing. This study was performed to demonstrate the relationship of penile rigidity during sleep with apnea-hypopnea and oxyhemoglobin desaturation events.
Methods: We studied 33 male patients with SCA:17 who experienced priapism during the previous year and 16 controls. Groups were paired by age (25±8 vs.29±5 yr), body mass index (21.7±1.1vs. 20.0±2.9 kg/m2), hemoglobin (10.3±2.1vs. 9.9±1.8 mg%), fetal hemoglobin (3.6±1.4 vs. 3.8±2.7 mg%), and ferritin (117.8±105.1vs. 269.9±252 mg/ml). After clinical evaluation and an adaptation night to the Sleep Laboratory, PSG (Somnologica , EmblaTM) was performed concomitantly with penile rigidity recording (Rigiscan Plus, TimmTM).
Results: Comparing to controls, SCA patients with priapism history presented increase in arousals and apnea-hypopnea index and in desaturation index. Penile rigidity events occurred both in sleep stage 2 and REM in SCA patients with priapism history, whereas in controls it was more frequent in REM sleep. In addition, SCA patients with priapism presented correlation of rigidity in REM sleep % with desaturations in this sleep stage and with arousal, and also correlation of mean total rigidity with arousals.
Conclusion: Association of penile rigidity and sleep disordered breathing was observed in SCA patients with recent history of priapism.
Support (If Any): FAPESP 2009/14202-9

0698

AUTONOMIC NERVOUS SYSTEM ACTIVITY PRECEDING NOCTURIA IN OLDER ADULTS

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Introduction: Pathological nocturia is a frequent cause of morbidity and is the leading cause of sleep disruption in older adults1. Yet, the mechanisms of sleep disruption remain poorly understood. The proposed study aims to improve our understanding of these mechanisms by examining the autonomic nervous system2, 3 during sleep preceding nocturia.

Methods: Heart rate variability was measured over 5-minute segments of artifact-free ECG data in order to compute post-hoc the ratio of low-frequency to high-frequency spectral power (LF/HF), where greater LF/HF indicates sympathovagal activation. We analyzed data from the first void of the night where the following 3 segments of ECG data were available: S3, during the last 5 minutes of sleep prior to the awakening preceding the nocturic event; S2, during the last 5 minutes of sleep prior to the last non-micturition-related awakening preceding S3; and S1, during the first 5 minutes of sleep following either the prior void or sleep onset. Differences in LF/HF between S3-S2 and between S3-S1 were compared between 6 overactive bladder (OAB) subjects (Ss) and 4 primary insomniacs.

Results: There were no notable differences between OAB and insomnia groups for age (65.2 ± 4.8 vs. 58.8 ± 11.0 years), BMI (25.7 ± 5.5 vs. 23.4 ± 3.6), and gender distribution (4:2 vs. 3:1 F:M ratio). In OAB subject, the relative change in LF/HF between S2 and S3 was greater than in insomniacs ($165.1 \pm 134.9\%$ vs. $-17.7 \pm 26.1\%$; $p<0.03$). Similarly, the relative change in LF/HF between S3 and S1 was greater in OAB Ss than in insomniacs (147.6 ± 259.8 vs. $76.8 \pm 118.0\%$).

Conclusion: Evidence of sympathovagal activation prior to nocturia in OAB Ss contrasting with the lack thereof amongst insomniacs strongly suggest that sympathovagal activation may be specific to micturition-related awakenings in older OAB Ss.

Support (If Any): This study was undertaken with a research grant from Astellas Pharma US Inc. and GlaxoSmithKline.

0699

FLOPPY EYELID SYNDROME IS ASSOCIATED WITH OBSTRUCTIVE SLEEP APNEA SYNDROME: A PROSPECTIVE STUDY ON 113 PATIENTS

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Introduction: Recent studies suggest an association between obstructive sleep apnea/hypopnea syndrome (OSAS) and ocular pathologies such as floppy eyelid syndrome (FES), chronic glaucoma, anterior ischemic optic neuropathy, papillar oedema and keratoconus. The purpose of this study is to determine whether the FES and eyelid laxity are associated with OSAS and to evaluate the prevalence of FES in OSAS.

Methods: We performed a cross-sectional monocentric study which included 113 consecutive patients (42% of women and 58% of men) referred to the Strasbourg University Sleep Clinic for symptoms of respiratory sleep disorders. All patients completed sleep questionnaires, underwent a clinical examination, an ambulatory respiratory polygraphy and a comprehensive ophtalmological examination (visual acuity, intraocular pressure, corneal thickness, OCT fiber analysis, corneal topography, visual field Hymphrey 30-2 and an eyelid examination). The

polygraphic recordings were analyzed by two independent scorers and the ophthalmologist was not aware of the polygraphic results.

Results: Subjects were divided in 4 groups based upon their obstructive apnea+hypopnea index (AHI) during overnight respiratory polygraphy: No OSAS (AHI<5, n=34), Mild OSAS (AHI = 5-15, n=39), Moderate OSAS (AHI = 15-30, n=23), and Severe OSAS (AHI>30, n= 17). Independently of age, sex and body mass index, FES prevalence increased with OSAS severity (p<0.05) and was higher in severe OSAS (47.1%, p<0.01) than in other groups (17.4, 28.2, 17.6 in moderate, mild and no OSAS group, respectively). A multivariate analysis was conducted using a principal component analysis (PCA) taking into account colinearities between variables allowed to reduce the large number of factors to a few principal components, from which the first one accounting for most of the data variability regrouped all OSAS parameters analyzed. A multiple regression analysis showed a significant correlation between FES and the first principal component (OSAS; p=0,002), as well as second component (mostly age, p<0.05). Eyelid laxity significantly correlated with the same components.

Conclusion: OSAS severity is associated with FES or eyelid laxity and has an effect on FES prevalence. This finding suggests a common biological basis (tissue elasticity) for both disorders and raises the question whether an ophthalmological evaluation is needed for all patients affected with severe OSAS.

0700

SLEEP DISTURBANCES IN PATIENTS UNDERGOING TREATMENT FOR NONSMALL CELL LUNG CANCER

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Introduction: Sleep disturbances in lung cancer are common. One challenge is determining whether sleep disturbances are pre-existing. This study provides longitudinal data on sleep patterns before, during and after treatment in patients with inoperable non small cell lung cancer. This interim analysis provides results of sleep patterns from pretreatment to one cycle of chemotherapy.

Methods: Participants completed the following: Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), 7-day sleep diary and 7-day motionlogger actigraph (Ambulatory Monitoring, Inc.). Descriptive and inferential statistics were used.

Results: Among 26 participants, mean age was 65 years (sd = 9, Range = 47-84), with 61.5% male, and 85% Caucasian. All participants were diagnosed with non small cell lung cancer (58% adenocarinoma) and 90% were stages III/IV. Pretreatment self-reported sleep parameters did not differ significantly following the first cycle of chemotherapy: total sleep time 6.8 (sd=1.4) versus 6.7 (sd=1.1) hours, sleep onset latency 20 +/- 14 minutes versus 22 +/- 14 minutes. Motionlogger actigraph data revealed similar nonsignificant results: total sleep time 5.8 (sd=2.4) versus 6.8 (sd=2.2) hours, sleep onset latency 59 +/- 50 minutes versus 40 +/- 65 minutes and sleep efficiency 74% (sd=17) versus 80% (sd=20). The most common reasons for self-reported sleep disturbances included wakefulness after sleep onset (85%), nocturia (75%), and pain (50%). Additionally, 38% reported symptoms of sleep disordered breathing (SDB) at diagnosis (e.g. loud snoring, long pauses between breaths while asleep). Only half of the participants who reported SDB had an ESS >8.

Conclusion: Patients with non small cell lung cancer may constitute a subgroup of cancer patients most at risk for sleep disturbances at diagnosis, including sleep disordered breathing. Sleep disturbances do not appear to worsen after one cycle of chemotherapy. Research to confirm these findings in a larger sample is warranted.

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0701

PTSD SYMPTOM SEVERITY PREDICTS TOTAL SLEEP TIME IN COMORBID POSTTRAUMATIC STRESS DISORDER AND DEPRESSION

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Introduction: A number of studies have objectively examined sleep in Posttraumatic Stress Disorder (PTSD), however results are mixed. Approximately 50-80% of individuals with PTSD have Major Depressive Disorder (MDD), and many PTSD studies include individuals with comorbid PTSD+MDD. Uncontrolled depression may complicate our understanding of sleep problems in PTSD. Exploring the role of each disorder in sleep may inform our understanding of their interaction in this unique population. We examined relative contributions of PTSD vs. MDD symptoms as predictors of sleep disturbance in patients with PTSD+MDD.

Methods: Scores from the Clinician Administered PTSD Scale (CAPS) and the Hamilton Depression Rating Scale (HamD) were used to predict actigraphic sleep indices from 45 male participants (M age = 50.96 years, SD = 13.76 years). Participants were asked to wear actigraphs for one week (M = 6 nights, SD = 1.97 nights). Linear regression techniques were used to examine the relationship between CAPS and HamD scores (with sleep items excluded) and actigraphy data.

Results: PTSD symptoms scores were a better predictor of total sleep time (TST) than depression scores (β CAPS = -1.89, SE = .78, p > .05). A trend emerged indicating that depression was a better predictor of WASO (β HamD = -3.05, SE = 1.56, p = .06) than PTSD symptoms. No significant relationships were observed between HamD or CAPS scores and bedtime, wake-time, onset latency, mean duration of awakenings, or number of awakenings.

Conclusion: In PTSD+MDD, severe PTSD symptoms were associated with shorter TST. These results are in line with our previous study showing shorter TST in PTSD+MDD vs. controls. Trend findings correspond with research showing an association between MDD severity and sleep continuity. Our outcomes support the conclusion that sleep disturbance type may be explained by different disorders, or rather that MDD impacts fragmentation whereas PTSD impacts sleep quantity.

0702

FUNCTIONAL NEUROIMAGING OF REM SLEEP IN RETURNING VETERANS WITH PTSD: AN [18F]-FDG PET STUDY

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Introduction: REM sleep disturbances are the hallmark of Posttraumatic Stress Disorder (PTSD), and may arise from the persistence of dysregulation of brain regions involved in arousal regulation and fear responses, including the amygdala and medial prefrontal cortex. We compared relative regional cerebral metabolic rate of glucose (rCMRglc) in REM sleep relative to wakefulness in combat-exposed veterans with and without PTSD returning from the conflicts in Iraq and Afghanistan.

Methods: Six medication-free combat-exposed veterans with current PTSD (M age = 29.1 years old, SD = 4.6) and 6 without PTSD (M age = 29.3 years old, SD = 5.4) completed in-lab PSG and 18F-FDG positron emission tomography (PET) studies during wakefulness and REM sleep. Relative rCMRglc was compared between groups across wakefulness and REM sleep using SPM8.

Results: Objective sleep parameters on the baseline night did not differ between the two groups of veterans, except for REM density (t(10) = 2.11 p = .06) and % REM sleep (t(10) = 2.7, p = 0.02), which were greater in veterans with PTSD. Veterans with PTSD showed significantly greater relative rCMRglc during both wakefulness (Z = 4.70, p < .001) and REM sleep (Z = 4.44, p < .001) in large clusters that included the cerebellum, brainstem, precuneus, thalamus, dorsal striatum, and posterior, dorsal, anterior, and subgenual cingulate cortices, as well as amygdala, orbitofrontal cortex, and the occipitotemporal and parahippocampal gyri compared to veterans without PTSD.

Conclusion: The preliminary findings support the hypothesis that hyperactivation of brain regions involved in arousal regulation and fear responses persists from wakefulness to REM sleep in combat-exposed veterans with PTSD compared to those without PTSD. Persistent activity in these brain regions may subserve trauma-related nightmares.

0703

SLEEP DISTURBANCE IN VETERANS OF THE IRAQ AND AFGHANISTAN CONFLICTS: A CARDIOVASCULAR DISEASE RISK FACTOR?

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Introduction: A high proportion of US Veterans deployed to Iraq or Afghanistan endorsed symptoms of insomnia upon their stateside return (64%). Up to 91% of those returning with PTSD are likely to endorse insomnia. The risk of hypertension (HTN) in those with insomnia is more than 3 times that of normal sleepers. However, research on sleep and HTN is lacking in this escalating Veteran population. We sought to: 1) examine relationships between HTN, sleep quality, and nightmares; and 2) determine if trauma symptoms and sleep quality synergistically impact risk of HTN diagnosis in recently deployed Veterans.

Methods: Participants were Veterans (N=589; 79.9% male) serving since September 11, 2001, deployed at least once (84.5%), and aged 37.04 years (SD=10.13). About ¼ endorsed a diagnosis of HTN (27%), and about ¼ met criteria for current PTSD (27%). Clinically significant sleep quality impairment (PSQI≥5), PTSD symptoms (DTS≥32), nightmare frequency (≥2 nights per week), and nightmare severity (≥moderate severity) were reported by 77.1%, 49.3%, 37%, and 38.4% respectively.

Results: After controlling for age, gender, race, and smoking status, logistic regression revealed that Veterans reporting a HTN diagnosis were more likely to report clinically significant sleep quality impairment (OR=1.68, 95% C.I.=0.95-2.97), PTSD symptoms (OR=2.1, 95% C.I.=1.40-3.15), nightmare frequency (OR=1.86, 95% C.I.=1.24-2.79), and nightmare severity (OR=2.08, 95% C.I.=1.39-3.12). Veterans having both clinically significant PTSD symptoms and impaired sleep quality were more likely to endorse a HTN diagnosis (OR=3.31, 95% C.I. =1.68-6.52) than Veterans having neither of these conditions.

Conclusion: Results suggest that: 1) sleep quality, nightmares, and PTSD symptoms are associated with HTN diagnosis in recently deployed Veterans; and 2) impaired sleep quality and trauma symptoms may combine to increase HTN risk. Further research is needed to determine if treating sleep disturbance reduces the risk of HTN in returning Veterans.

0704

A PLACEBO-CONTROLLED STUDY OF THE EFFECTIVENESS OF A BEHAVIORAL SLEEP INTERVENTION AND PRAZOSIN FOR SLEEP DISTURBANCES IN MILITARY VETERANS

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Introduction: To compare the relative effectiveness of cognitive-behavioral and pharmacological therapies targeting nightmares and insomnia specifically in military combat veterans, we undertook this randomized trial comparing a behavioral sleep intervention (BSI) (that combined imagery rehearsal therapy for nightmares, stimulus control therapy, and sleep restriction for insomnia) against prazosin treatment and a separate placebo pill condition.

Methods: Fifty US veterans (mean age 40.9 years old, SD=13.2 years) with chronic sleep disturbances were randomized to prazosin (n=18), placebo (n=15), or the BSI (n=17). Participants kept a sleep diary throughout the 8-week treatment. Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), and PSG sleep measures were collected pre- and post-treatment. Response criteria comprised an ISI scale reduction of > 6 points, or a PSQI score decrease of > 3 points, or a nightmare frequency reduction of > 50%.

Results: Improvements in sleep latency (p = .04), sleep efficiency (p < .001), and nightmare frequency (p = .009) were greater with BSI compared to prazosin and placebo on diary measures. Greater reductions in insomnia were observed in the BSI and prazosin groups compared to the placebo group (p=.005) on the PSQI and ISI. PSG measures were uninformative. Post-treatment, 78.6% of participants receiving the BSI or prazosin met response criteria, whereas only 35.7% of those receiving placebo did so (p=.02).

Conclusion: BSI was associated with greater sleep improvements relative to prazosin and placebo on sleep diary measures. BSI and prazosin were associated with greater treatment response rates. Larger comparative effectiveness trials are required to determine predictors of treatment response in combat-exposed military veterans.

0705

EVIDENCE FOR BODY TEMPERATURE DYSREGULATION IN CHILDREN WITH FEAR OF HARM PHENOTYPE OF PEDIATRIC BIPOLAR DISORDER

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Introduction: The Fear of Harm phenotype (FOH) describes a cluster of psychiatric, behavioral, and physiological symptoms that characterize approximately 1/3 of children with a community or DSM-IV diagnosis of bipolar disorder (BD). Prominent among these symptoms are sleep initiation difficulties, and altered temperature perception. Reported here are initial data characterizing relationships between sleep and body temperature in children with FOH.

Methods: The distal-proximal gradient (DPG) in skin temperature and nocturnal sleep were measured at home on 37 nights in 15 subjects aged 5-12y with DSM-IV diagnoses of BD and FOH (FOH; n=11; 28 nts) or controls (CTL; n=4; 9 nts). Subclavicle and lower calf temperature were recorded from 1h pre-bedtime to 20 min post-waketime with wireless sensors (Vitalsense, Minimitter Respironics, Inc.). Sleep was recorded with an Actiwatch (Minimitter Respironics, Inc.). The interval from bedtime (BT) to the time at which the DPG was 0 degrees (DPG0) was compared between FOH and CTL, as were sleep variables, including parent-estimated sleep onset latency (SOL) and actigraphy sleep efficiency (SE).

Results: DPG0 occurred at 21:55±1:42 in FOH+ vs. 21:03±0:40 in CTL (n.s.), although on 6 nts from 4 different FOH Ss no DPG0 was ever reached, as proximal temperature remained high throughout the night. The mean BT-DPG0 interval was 0:55±0:83 in FOH vs. 0:13±0:16 in CTL (p<.001). SOL was significantly longer in FOH (0:32±0:22) than in CTL (0:09±0:05) (p<.001), and SE was significantly lower in FOH (83±9%) vs. CTL (92±5%) (p<.01). A significant correlation was found between the BT-DPG0 interval and SOL (Spearman's rho=.65, p<.01) but not SE (rho=-.46).

Conclusion: In CTL, a slow decrease in proximal temperature typically preceded BT, with a sharp increase in distal temperature at BT. Despite usual increases in distal temperature at BT, proximal temperature remained elevated at sleep onset (and throughout the night) in several FOH children, contributing to the longer BT-DPG0 interval, which was associated with significantly longer SOL in FOH. Changes in skin temperature around sleep onset have been shown to be functionally related to sleep initiation, and manipulating heat loss, which alters the DPG, can interfere with or facilitate sleep onset. Temperature patterns observed here in FOH but not CTL may reflect similar problems with heat balance that have been reported, and shown to affect sleep, in narcoleptics, women with vasospastic syndrome, and sleep onset insomniacs.

0706

TEEN SLEEP AND SUICIDALITY: RESULTS FROM THE YOUTH RISK BEHAVIOR SURVEYS OF 2007 AND 2009

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Introduction: Suicide in adolescents is a tragic and preventable cause of death. Previous studies have found that long and short total sleep time (TST) is associated with suicidal ideation in the adult population. We examined TST as a risk factor for suicidality ranging from ideation to attempts in a large national sample of adolescents.

Methods: We addressed this aim using the Youth Behavior Risk Surveys from 2007 and 2009, which consist of nationally representative school-based samples (N=12,154 for 2007, N=14,782 for 2009). Sleep was measured by the question: "On an average school night, how many hours of sleep do you get?" Outcomes included: serious ideation; planning of suicide; suicide attempt; and attempt resulting in injury. Logistic regression models were used to assess the relationship between the different types of suicidality and sleep after adjusting for age, sex, race/ethnicity, feelings of sadness, and substance abuse.

Results: Of the total sample, roughly 15% reported suicidal ideation, 10% planned suicide, 5% attempted and 2% reported an attempt requiring treatment. Teens who reported sleeping <5 or >10hours had a significantly higher risk for suicidality compared to those with a TST of 8hrs. The largest odds ratios were found among the most severe forms of suicidality (attempt requiring treatment) with odds ratios of 5.9(95% C.I 2.8-12.6) in 2007 and 6.5(95% C.I. 3.2-13.0) in 2009 for a TST of 4hrs or less and 4.8(95% C.I. 1.3-17.1) in 2007 and 6.1(95% C.I. 2.3-16.5) in 2009 for a TST of 10hrs or more.

Conclusion: Both short and long TST are risk factors for suicidality among teens with the greatest risk being seen for more serious suicidality. Self-reported sleep duration may be a useful screening question to assess suicide risk. Future studies should examine whether sleep duration is a causal and/or modifiable risk factor for suicidality in teens.

0707
DEVELOPMENTAL COURSE OF EARLY-LIFE TRAUMA: LATER-LIFE SLEEP AND TRAUMATIC STRESS

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Introduction: Trauma exposure during childhood can lead to specific physiological, behavioral, and psychological trajectories that influence sleep and functional outcomes. The present study evaluated the relations between the timing of trauma exposures, objective REM sleep measures, subjective sleep report, and daytime Post-Traumatic Stress Disorder (PTSD) symptoms among a sample of combat-exposed military veterans.

Methods: Participants (N=173) with a primary diagnosis of PTSD (63.0%; 42.9, [SD±13.0] years-old; 92.7% men), insomnia (30.6%; 36.1 [SD±12.4] years-old; 84.9% men), or who were healthy controls (6.4%; 28.4 [SD±4.0] years-old; 92.3% men) were included in this sample. Participants completed the Clinician-Administered PTSD scale, the Pittsburgh Sleep Quality Index (PSQI), the PSQI-Addendum for PTSD (to assess disruptive nocturnal behaviors), and completed overnight polysomnography. The Trauma History Questionnaire provided a retrospective account about variety of traumatic events experienced before age 18 (early-life trauma), and after age 18 (later-life trauma).

Results: Early-life trauma was associated with fragmented REM sleep (r=.43, p<.001), later-life trauma (r=.28, p<.001), and daytime PTSD severity (r=.17, p<.05). Later-life trauma was associated with daytime PTSD severity (r=.47, p<.001), disruptive nocturnal behaviors (r=.32, p=.001), and sleep quality (r=.31, p<.01). Later-life trauma mediated the relations between early-life trauma and daytime PTSD severity (Sobel=3.3, p=.001), sleep quality (Sobel=2.5, p=.01), and disruptive nocturnal behaviors (Sobel=2.5, p=.01).

Conclusion: Early-life trauma exposure was associated with later-life fragmented REM sleep, but not subjective sleep measures. Early-life trauma had an indirect influence on later-life PTSD and subjective sleep disturbances. These findings suggest that early-life trauma may affect the development of sleep physiology, which may partially explain reported discrepancies between subjective and objective sleep measures in PTSD. More broadly, investigating the impact of early-life trauma exposure on sleep may provide novel insights into sleep as a mechanism for stress resilience, which may inform prevention strategies to improve functional outcomes among trauma exposed individuals.

0708
INTIMATE PARTNER VIOLENCE: ASSOCIATIONS WITH CHILD SLEEP AND ADAPTIVE FUNCTIONING

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Introduction: Exposure to intimate partner violence (IPV) impacts child cognitive, behavioral, and emotional functioning. Sleep is associated with these outcomes, but is heretofore under evaluated among this population. The present study examined parent-reported child sleep problems and adaptive functioning in the context of IPV exposure.

Methods: Participants were females exposed to IPV (N=50; M=37.6, SD±5.2 years), attended a domestic violence support group or shelter, and mothered a child between 6-13 years (M=10.0, SD±2.1). Participants reported their: experience of physical and verbal IPV in the presence of their child (O'Leary-Porter Scale); psychopathology symptoms (Brief Symptom Inventory); their child's behavioral and emotional functioning (Behavioral and Emotional Rating Scale); and their child's

behavioral problems (Child Behavior Checklist), which provided 6 sleep-items (3 parasomnia and 3 sleep quality items) that were summed to create a 'child sleep problems' component.

Results: Increased maternal physical (r=.37, p=.009) and verbal (r=.35, p=.01) IPV was associated with increased maternal psychopathology symptoms. Increased maternal psychopathology symptoms were associated with increased child sleep problems (r=.44, p=.002). Maternal psychopathology symptoms mediated the relations between maternal physical IPV and child sleep problems (Sobel=2.1, p=.03) as well as maternal verbal IPV and child sleep problems (Sobel=2.1, p=.04). Children who did not exhibit sleep problems (36%) had significantly better behavioral and emotional functioning (M=131.7, SD±17.1) than children who exhibited ≥1 sleep problems ([M=109.3, SD±33.4]; t[1,47]=6.9, p=.01).

Conclusion: Maternal physical and verbal IPV were associated with maternal psychopathology, which mediated the relations between both types of IPVs and child sleep problems. Children who did not exhibit sleep problems demonstrated better adaptive functioning than children who did exhibit sleep problems. Adequate child sleep may promote resilience against some of the adverse outcomes typically caused by child trauma exposures. Sleep could potentially function as a target treatment mechanism to facilitate child behavioral and psychological recovery from IPV exposure.

0709
SLOW-WAVE ACTIVITY (SWA) REGULATION IN DEPRESSED 20-40 YEAR OLD MEN AND WOMEN

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Introduction: Recent research has shown that the sleep EEG abnormalities typically seen in individuals with major depressive disorder (MDD) vary by sex, with depressed men showing deficits in SWS and delta (.5- 4 Hz) EEG activity not evident in depressed women (Armitage et al 2000;2001; Armitage 2007). These findings suggest sleep homeostasis may differ between men and women with depression. This study explores the effects of a mild seep challenge, a 3-hour sleep delay on SWA in healthy controls (HC) and individuals with depression.

Methods: 160 participants (80 MDD and 80 HC) were recruited after undergoing a psychiatric interview. Prior to sleeping in the laboratory, subjects wore an actigraph to confirm maintenance of an 11pm-6am sleep schedule with no napping. Subjects then slept in the laboratory for three consecutive nights, including an adaptation night, and a baseline night. On the third night in the lab, subjects stayed awake for an additional three hours, with a 9 am wake up time. SWA was quantified with power spectral analysis and sorted by NREM sleep episode (excluding Stage 1 sleep), and compared across groups.

Results: Repeated-measures MANOVA revealed a significant group (MDD, HC) by sex (M, F) by NREM period interaction (p<.001). MDD men showed the lowest SWA in response to sleep delay, compared to all other groups (p<.03). MDD women showed the largest SWA response to sleep delay (p<.05). Among the HC group, women showed a larger SWA response to challenge than men (p<.05).

Conclusion: SWA homeostasis was impaired in MDD but was in opposite directions for men and women. A larger homeostatic response was also observed in HC women, but the magnitude of the sex difference was significantly smaller than those with MDD. We are currently exploring the clinical relevance of these findings.

0710

HIGH-FREQUENCY SLEEP EEG IN ABSTINENT ALCOHOLICS COMPARED TO HEALTHY CONTROLS

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Introduction: The underlying neurophysiological mechanisms of sleep disturbances in recovering alcoholics and their relationship to relapse are poorly understood. We tested the hypothesis that high-frequency sleep EEG would be increased in alcohol-dependent (AD) participants compared with healthy controls (HC), particularly among those who relapsed. We also examined sex and race differences in high-frequency sleep EEG.

Methods: Fifty-three ADs (36.6 ± 10.8 years, 10 women, 12 African American, 34 Caucasian) in early recovery (39.8 ± 19.1 days abstinent) and 19 age-matched HCs (35.6 ± 10.0 years, 4 women) participated. Following a 2300 - 0600 hours at-home sleep schedule and screening, participants underwent a baseline (2300 - 0600 hours) sleep night with polysomnography (PSG). Power spectral analyses were conducted on all 30-second artifact-free epochs and averaged by hour of the night in the beta frequency band (β=16-30 Hz). We examined raw and relative beta power (beta power/total power) across the entire night and by hour of the night. Alcoholic participants returned after 12 weeks to assess abstinence vs. any drinking with the Time Line Follow Back interview.

Results: Relative beta power across the night was significantly higher in AD compared to HC participants ($4.1 \pm 0.7\%$ vs. $3.7 \pm 0.7\%$, p < .05) and in African American compared to Caucasian subjects ($4.6 \pm 0.8\%$ vs. $3.9 \pm 0.6\%$, p < .04). AD men had higher relative beta power than HC men (p < .05), but no differences were found among women. AD participants who relapsed during the 12-week follow-up had higher relative beta power than abstinent AD and HC participants (p < .05). No other demographic, sleep, or alcohol-related variables were associated with relapse.

Conclusion: High-frequency sleep EEG was increased in AD vs. HC subjects, particularly among relapsers. CNS hyperactivity may be one mechanism of sleep disturbance in AD subjects that predicts relapse during recovery.

0711

THE EFFECT OF QUETIAPINE ON SLEEP DURING ALCOHOL ABSTINENCE

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Introduction: Insomnia is highly prevalent in the recovering alcoholic patient, and has been shown to be a risk factor for relapse. Quetiapine, a novel antipsychotic medication with hypnotic properties, is frequently prescribed on an "off-label" basis for insomnia in these patients. The effect of quetiapine on objective and subjective sleep in the recovering alcoholics is currently unknown.

Methods: Male alcoholics (N = 24), within the first year of recovery were recruited in an 8-week, double-blind, placebo-controlled trial. Participants were randomized to receive either 400 mg/day at bedtime, of quetiapine (N = 12), or placebo (N = 12). Two baseline polysomnograms were conducted before and after 8 weeks of treatment. The primary outcome measure was Sleep Efficiency on an in-laboratory polysomnogram. The principal secondary outcome measure for subjective sleep was the Insomnia Severity Index (ISI) total score. In addition, during this treatment trial, participants were evaluated for neuro-behavioral assays, addiction, and psychiatric variables using standardized instruments. They also received the standardized psychotherapy called Medical Management to help them cope with their urge to use alcohol.

Results: We report the preliminary study results on the participants who completed the study [quetiapine (N = 10), and placebo (N = 10)]. Sleep

Efficiency, on an in-laboratory polysomnogram, before and after the treatment showed a trend for the effect of Time, $F(1, 19) = 3.99$; p = 0.06; no effect of Medication status was seen. In addition, there were significant effects of time, without any effect of medication status, for the following variables: Insomnia Severity Index, PHQ-9 scores, Beck's Anxiety Inventory, and the Penn Alcohol Craving Scale. There were no differences between the groups for the number of Lapses, or the 10% Fastest Reaction Time scores on the psycho-motor vigilance task. Analysis of the participants with baseline insomnia [ISI total score ≥ 8, quetiapine (N = 10), placebo (N = 7)] showed a differential improvement in insomnia (ISI total score) over time with quetiapine as compared to placebo [Drug $F(1,13) = 7.77$, p = 0.015, Time $F(8,101) = 20.35$, p < .001, Drug * Time $F (8, 101) = 1.90$, p = .06; AIC = 653].

Conclusion: Quetiapine was associated with improvement in subjective insomnia ratings only in the alcohol dependent participants with baseline insomnia.

0712

DIM LIGHT MELATONIN ONSET (DLMO) IN ALCOHOL-DEPENDENT (AD) MEN AND WOMEN VS. HEALTHY CONTROLS

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Introduction: Sleep disturbances in AD patients may persist for years despite abstinence from alcohol. Although the mechanisms are not well understood, dysregulation of circadian rhythms has been suggested. One study in African-American men showed a delay in peak melatonin volumes in AD vs. healthy control (HC) subjects (Kühlwein et al., 2003), but DLMO has not been assessed in either Caucasians or women with alcoholism.

Methods: Forty-four AD participants (AD, mean age 36.8 ± 10.5 years, 10 women) in early recovery (mean abstinence 57.7 ± 19.5 days) and 19 age- and sex-matched controls (HC, mean age 34.8 ± 10.7 years, 5 women) participated. Following a 2300 - 0600 hours at-home sleep schedule, a screening and a baseline night of polysomnography, participants underwent a 3-hr extension of wakefulness (0200 - 0900 hours) during which salivary melatonin samples were collected every 30 minutes beginning at 1930 hours. The time of DLMO was the primary variable. Other variables included area under the curve (AUC) and course of melatonin values across time points.

Results: No significant differences between the AD and HC groups were found for any outcome variable, analyzing men and women together. Likewise, no significant differences were seen in women with and without AD. In men, however, DLMO was significantly delayed in AD vs. HC subjects [21:17 (0:44) vs. 20:51 (0:28) hr; t=-2.4, p=.025]; the AUC was higher in HC than AD subjects [111.5 (61.7) vs. 78.4 (43.4) pg/ml; t=2.1, p=.046]; and repeated measures ANOVA revealed a main effect for diagnosis on mean melatonin volume [$F(1, 38)=6.3$, p=.016]. When analyzing Caucasian men only (30 AD & 17 HC), DLMO remained significantly delayed in AD subjects.

Conclusion: These results extend the findings of Kühlwein et al. to Caucasian men. Further research should consider sex differences in the mechanisms underlying sleep disturbances in AD.

0713

INSOMNIA SYMPTOMS AND CARDIOVASCULAR RISK AMONG RESPONDENTS WITH BIPOLAR DISORDER IN THE NATIONAL COMORBIDITY SURVEY-REPLICATION

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Introduction: In the past decade, there has been increasing concern about the elevated prevalence of cardiovascular risk factors in bipolar disorder. Parallel to these findings, epidemiologic evidence suggests that insomnia symptoms (e.g. difficulty falling or staying asleep, or waking up too early) are independently associated with higher rates of cardiovascular risk factors in the general population. Given that sleep is pervasively disturbed in bipolar populations, the aim of the study was to examine the association between insomnia symptoms and cardiovascular risk factors in patients with bipolar disorder in the National Comorbidity Survey - Replication (NCS-R).

Methods: The NCS-R is a nationally representative survey of the U.S. population (ages 18+) conducted between 2001 and 2003. From this sample, 176 respondents with a lifetime bipolar disorder diagnosis were identified for the present study. The prevalence of self-reported cardiovascular risk factors (obesity, hypertension, and diabetes/high blood sugar) was compared across three subgroups of respondents with bipolar diagnoses, based on the presence of (a) chronic insomnia symptoms, (b) acute insomnia symptoms, or (c) no sleep problems in the past year. Prevalence estimates, as well as odds ratios adjusted for demographic and clinical variables (AORs) in logistic regression analyses, were corrected for the complex survey design.

Results: Rates of obesity and hypertension were statistically greater in bipolar patients with chronic (41.8%; 28.8%) and acute (43.7%; 24.1%) insomnia symptoms compared to bipolar patients with good sleep (19.7%; 5.9%). Diabetes/high blood sugar prevalence did not significantly differ between groups. Insomnia symptom duration remained a significant predictor of obesity (AOR=1.5) and hypertension (AOR=2.2) after controlling for clinical and demographic factors.

Conclusion: Insomnia symptoms, particularly those that are chronic in nature, may confer risk for obesity and hypertension in bipolar disorder. Thus, sleep disturbance may represent one pathway contributing to the high rates of CVD observed in bipolar disorder.

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0714

DIURNAL VARIATION IN RELATIVE BRAIN GLUCOSE METABOLISM WITHIN THE REWARD CIRCUIT IN ADULTS WITH PRIMARY INSOMNIA

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Introduction: Converging evidence indicates that reward motivation shows circadian modulation. Self-reported positive affect, as well as reward-related behaviors and physiology, show circadian rhythms, with lowest levels in the morning and peaks in the evening. These rhythms may be particularly salient for insomnia patients, who have altered diurnal variation in mood and arousal. However, no prior studies have examined the neural underpinnings of circadian-reward interactions in insomnia patients. The aim of these analyses was to characterize diurnal variation in relative brain glucose metabolism of regions within the reward circuit in adults with insomnia.

Methods: [18F]-fluorodeoxyglucose positron emission tomography scans were conducted during quiet wakefulness in the morning and evening in 23 adults with primary insomnia. Statistical parametric mapping was used to compare relative glucose metabolism during the two scans. Region-of-interest (ROI) analyses focused on reward-related regions, including the medial prefrontal cortex (mPFC) and striatum (caudate, putamen, and nucleus accumbens), using a threshold of p<.05 and minimum extent of 10 contiguous voxels.

Results: Relative glucose metabolism in the striatum was significantly higher in the evening than in the morning, consistent with higher levels of reward motivation. No areas within the striatum showed significantly higher relative metabolism in the morning. However, a large cluster within the mPFC (peak voxel in the right medial BA9) showed significantly lower relative metabolism in the evening, consistent with diminished top-down cortical control of the striatum during the time of peak reward motivation. A smaller cluster within the mPFC (peak voxel in the left medial BA9) showed the opposite pattern of higher relative metabolism in the evening.

Conclusion: Diurnal variation of regional glucose metabolism in reward-related brain areas predictably parallels the circadian patterns of self-report, behavioral, and physiological measures of reward motivation. This preliminary evidence implicates the mPFC and striatum as part of the neural mechanisms underlying the circadian modulation of reward motivation. Replication and comparison with healthy subjects will determine the specificity of this finding to insomnia.

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0715

IMPROVEMENT IN SLEEP QUALITY OF PATIENTS COMPLETING A PSYCHIATRY PARTIAL HOSPITALIZATION PROGRAM (PHP)

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Introduction: Sleep difficulties are common in patients with psychiatric disorders. Psychiatry Partial Hospitalization Programs (PHPs) provide intensive milieu treatment that represents a midpoint along the treatment intensity continuum between an inpatient and an outpatient service. We aimed to determine if the sleep quality of patients with insomnia and co-morbid psychiatric disorders improve after completing a PHP that includes a course of Cognitive Behavioral Therapy for Insomnia (CBT-I).

Methods: Patients referred to PHP typically attend the program for one month. The program includes recovery-oriented treatment, groups focusing on CBT-I and medication management. As part of a continuous quality improvement project, the Pittsburg Sleep Quality Index (PSQI) was administered to consecutive patients at the time of their entry into the PHP program and after a month of PHP.

Results: One hundred and eighty four consecutive patients who participated in the program from Nov 2007 to March 2009 were included. Baseline PSQI score was 12.5 ±4.8. After completion of PHP, PSQI scores improved by a mean of 3.14 points (95%CI; 2.5-3.8; p<0.001).

Conclusion: Our data show that patients experience a clinically significant improvement in sleep quality after one month of PHP, as indicated by a mean reduction of 3 points on the PSQI. This is one of the few studies to describe the effect of group CBT-I on quality of sleep in the context of a milieu treatment, in this case a PHP. These preliminary observations support the feasibility and potential impact of disseminating CBT-I in PHP settings for military veterans with psychiatric comorbidities and sleep disturbances. Further examination of the specific predictors of improvement in sleep quality is required.

0716

AN OPEN TRIAL OF COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA (CBT-I) RESULTS IN SIGNIFICANT POSTTREATMENT REDUCTIONS IN SUICIDAL IDEATION

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Introduction: Suicide represents a global disease burden, accounting for 57% of all violent deaths in the world annually. Sleep complaints are listed among the top 10 warning signs of suicide by SAMHSA, and a growing body of evidence suggests that self-reported insomnia and poor sleep quality constitute modifiable risk factors for suicide. Despite these findings, a study has yet to evaluate the impact of a sleep intervention on suicidal ideation.

Methods: Participants (57% female) included 303 community outpatients, aged 18-88 years (M=48) who completed group cognitive behavioral therapy for insomnia (CBT-I). Patients were not excluded on the basis of comorbid psychiatric, medical, or sleep disorders. The Beck Depression Inventory (BDI) was administered at both baseline and posttreatment. Treatment sessions were delivered weekly, with the exception of the final two sessions (scheduled biweekly). All procedures were HIPPAA compliant, and pre-approved by the Institutional Human Subjects Review Board.

Results: Paired t-tests were conducted to test the hypothesis that an open trial of CBT-I would result in posttreatment reductions in BDI total scores and suicidal ideation. Results revealed significantly lower BDI scores (sleep item removed) posttreatment [t(295)=12.11, p<.001; 95% CI 3.35-4.65]. Next, among the 65 individuals endorsing a score >0 on the suicide ideation item (BDI item 9), CBT-I produced a statistically significant posttreatment reduction in suicidal ideation [t(64)=9.41, p<.001; 95% CI 0.52-0.80]. Regarding the size of this effect, the within-subjects ES for suicidal symptoms was large [cohen's d = 1.83].

Conclusion: To our knowledge, this is the first investigation to show that a non-mental health treatment is associated with a posttreatment symptom reduction in suicidal ideation. Suicide is a preventable public health problem, yet efficacious interventions are scarce. These preliminary data provide rationale for the development and testing of a sleep-oriented intervention for the prevention of suicidal behaviors.

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0717

ARE STRESS LEVELS AFFECTED BY SLEEP QUALITY AND PERCEIVED HEALTH VALUES?

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Introduction: It is widely accepted that stress plays a central role in adverse health consequences. The causes of stress vary according to demands and appraisal, with poor sleep a potential contributing factor. Health beliefs, values, and behaviors can factor into health choices and decisions, including sleep habits and stress. The current study assesses the relationship between health values, sleep quality, and perceived stress levels.

Methods: Men and women primarily from a Midwest metropolitan area and between the ages of 18-65 years completed an online survey. The survey included demographics, sleep hygiene (SH) measure, Perceived Stress Scale (PSS), Pittsburgh Sleep Quality Index (PSQI), Health Associations Scale (HAS), Value on Health Scale (VHS), and the Perceived Health Competence Scale (PHCS).

Results: A total of 264 surveys were completed. Using a stepwise regression, global PSQI (F= 17.87, p< .001), age (F= 19.36, p< .001),

PHCS (F= 16.83, p< .001), and VHS (F= 15.61, p< .001) all entered the model to predict stress (PSS) and accounted for 19.4% of the variance. Thus, poorer sleep quality, younger age, and poorer health self-efficacy and value predict higher stress scores. Using a split median the sample was divided into low stress (Lst) and high stress (Hst) groups. The Hst group reported significantly higher PSQI scores (p< .01), poorer sleep behaviors (SH) (p= .012), and lower PHCS scores (p< .01). Interestingly, the groups did not rank the importance of sleep differently as a key health indicator for poor health, but the Hst group did significantly rank poor sleep more relevant as a health outcome (p= .028).

Conclusion: The results suggest that more negative health self-efficacy and values and poorer sleep quality are associated with increased stress. The Hst group did report poorer sleep related behaviors and subsequent poorer sleep quality. These results can be important to better understand the impact poor sleep can have on adverse health consequences, including stress, as well as the relevance of perceived health values and lifestyle choices on poor sleep and stress.

0718

BURNOUT CLUSTERS AND SLEEP-RELATED SYMPTOMS

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Introduction: Burnout is a work-related stress syndrome that is linked to sleep disturbances. The most common measure for burnout is the Maslach Burnout Inventory (MBI) which covers three dimensions of burnout syndrome: emotional exhaustion (EX), cynicism (CY) and reduced professional self-esteem (PROF). In this study we explored if naturally occurring MBI clusters correlate with different aspects of sleep.

Methods: Our Finnish population-based study sample consisted of 3224 workers with information on MBI, sleep length, early morning awakenings, fatigue and Global Seasonality Score. We performed clustering analysis for 16 items of MBI using k-means algorithm separately for males and females. The stability of the results was ensured. Correlations of clusters and sleep traits were analysed.

Results: We found analogous stable 4 cluster solutions for both sexes. The biggest group ("C-Low ") consisted of individuals with generally low scores. Individuals with symptoms of cynicism and exhaustion were clustered together and formed two clusters based on the degree of the symptoms ("C-Intermediate" and "C-High"). Individuals with problems of PROF constituted another cluster ("C-Prof"). Correlations of sleep measures and MBI clusters were highly significant. Sleep was the shortest and the most fragmented, and complaints about fatigue were the most common in the cluster C-High. Individuals in C-Prof had slightly elevated symptom scores relative to those in C-Low, but lower than among those in C-Intermediate.

Conclusion: Data mining of MBI showed stable clusterings separating individuals with different degrees of symptoms from the subscales EX and CY from the individuals with the most prominent symptoms from the subscale PROF. Individuals differed in sleep related traits according to their cluster such that individuals in the high and intermediate clusters exhibit most symptoms. Our results support the view that altered sleep is an important aspect of burnout syndrome. The study will comprise a template for subsequent molecular genetic analyses.

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0719

SLOW-WAVE SLEEP DISRUPTION AND THE RECOGNITION OF POSITIVE WORDS

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Introduction: Recent research has suggested that sleep deprivation may bias attention to negative stimuli in non-depressed individuals (Yoo et al., 2007). The purpose of this study was to explore how slow-wave sleep disruption affects positive and negative word recognition in healthy controls and participants with major depressive disorder.
Methods: 12 participants (6 diagnosed with Major Depressive Disorder (MDD) and 6 healthy controls) were recruited. Subjects were trained on a word recognition paradigm before bedtime. Following baseline sleep, subjects underwent one night of selective slow-wave sleep (SWS) disruption by auditory stimuli. Reaction time to a recognition word list was assessed in the morning. The participants were also asked to rate the emotional valence of each word presented from 1(extremely negative) to 9 (extremely positive).
Results: A repeated-measures ANOVA revealed a significant interaction (p=.029) between word valence (positive, negative) and condition (baseline, interruption), with positive words recognized faster than negative words after interruption in healthy controls. There were no significant patterns in those with MDD. No significant effect of slow-wave sleep interruption was found for accuracy of positive or negative words in either MDD or HC groups. Additionally, reaction time and emotional valence of words were not correlated (r=.04) at baseline. However, after slow-wave sleep interruption, the relationship between reaction time and valence showed a small but significant increase in HC (r=-.14). There was no relationship between reaction time and valence at baseline or after interruption for those with MDD.
Conclusion: Slow-wave sleep interruption improved speed and accuracy of positive word recognition in HCs but not in those with MDD. These results may reflect increased sensitivity to emotional stimuli after selective slow-wave sleep deprivation.

0720

SLEEP QUALITY PREDICTS FUTURE POSITIVE AFFECT IN A PROSPECTIVE STUDY OF POLICE ACADEMY RECRUITS

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Introduction: Positive affect represents a state of psychological well-being and has been associated with better health outcomes, possibly mediated by neuroendocrine, autonomic, and immune systems. Cross-sectional studies have demonstrated that poor sleep is associated with decreased positive affect. Although prospective studies indicate that poor sleep quality predicts later depression, there is limited information on whether sleep quality predicts future affect states.
Methods: The PSQI and PANAS were administered to 375 police academy recruits during academy training (baseline). The PANAS was subsequently administered at 12, 24, and 36 months. Subjects were asked to respond to PANAS items in reference to the prior month. Mixed-model analyses were performed to test the hypothesis that better subjective sleep quality at baseline predicts higher positive affect at 12, 24 and 36 months, even when controlling for baseline positive affect. We also tested the hypothesis that worse subjective sleep quality at baseline predicts higher negative affect at future time points.
Results: At baseline, PSQI score (where higher score indicates worse sleep quality) was weakly and negatively correlated with positive affect score (R=-.11) and moderately correlated with negative affect score

(R=.22). Baseline subjective sleep quality predicted future positive affect (β=-.15, p=.002) and negative affect (β=.18, p=.001) in the hypothesized directions. Better subjective sleep quality also predicted future higher positive affect score even when controlling for baseline positive affect (β=-.09, p =.046). When controlling for negative affect at baseline, the relationship between baseline subjective sleep quality and future negative affect was no longer significant (β=.06, p=.23).
Conclusion: Most studies that have examined sleep as a predictor have focused on future development of psychopathology. These results support findings indicating a cross-sectional relationship between sleep quality and affect state. Additionally, they indicate that better sleep quality may have a long-term impact on resilience factors such as positive affect.

0721

SLEEP DISTURBANCES AND ADVERSE CHILDHOOD EXPERIENCES IN ADULTS

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Introduction: Sleep disturbances are associated with an increased risk for many chronic diseases and unhealthy behaviors. A history of adverse childhood experiences (ACEs) is also associated with similar adult health outcomes. We studied the relationship between multiple ACEs and the likelihood of experiencing sleep disturbances in adulthood.
Methods: We used data from the Adverse Childhood Experiences (ACE) Study, a retrospective cohort study of 17,337 adult health maintenance organization members in California who completed a survey about 8 ACEs, which included childhood abuse and growing up with various forms of household dysfunction. The sleep disturbances measured included ever having trouble falling or staying asleep and feeling tired after a good night's sleep. We used an integer count of the number of ACEs (the ACES Score) to assess the cumulative impact of these experiences on the likelihood of sleep disturbances.
Results: Thirty-three percent of the cohort reported trouble falling or staying asleep while 24% reported tried after sleeping. All eight ACE categories were associated with an increased likelihood of sleep disturbances (p<0.05). Compared to persons with an ACE record of 0, those with ACE Score of 5 or more were 2.1 (95% CI: 1.8-2.4) times more likely to report falling or staying asleep and 2.0 (95%CI: 1.7-2.3) frimes more likely to report feeling tired after a good night's sleep. The trend for increasing odds for both types of sleep disturbance with increasing ACE Scores was statistically significant (p<0.0001).
Conclusion: Adverse childhood expriences were strongly related to sleep disturbance in adulthood, and the ACE Score had a graded relationship to these sleep disturbances. A history of ACEs should be obtained for patients with sleep disturbances to coordinate services that ameliorate the long-term effects of these events

0722

THE EFFECT OF BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA ON CAREGIVER'S SLEEP

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Introduction: Caregiving for a person with dementia (PWD) is a stressful role that often results in negative health outcomes. Quality sleep is a resource that provides physical, mental, and emotional energy for caregiving; however, caregivers 'sleep is often disrupted by nighttime behaviors of the PWD.
Methods: This was a descriptive cross-sectional study of 80 family caregivers (71 female, 9 male, 39 spousal, 33 adult children) over the age of 21 years, providing care to a community-dwelling PWD. Caregivers were excluded if diagnosed with depression, or sleep disorder

(other than insomnia) prior to caregiving. Caregiver's were interviewed for responses to the frequency of behavioral/psychological symptoms of dementia, PSQI, Perceived Stress Scale (PSS), and CESD.

Results: Caregiver's reported poor sleep (PSQI = 7.51, sleep efficiency 80.5%, total sleep 6.4 hours). Caregivers reported moderate levels of stress (PSS = M38.1, SD9.4) and depression scores below the 15 cut score for depressive symptoms (CESD = M12.9, SD 9.31). Sleep correlated with caregiver stress (r = .35, p <.001), caregiver depression (r = .42, p <.001) and made a unique contribution to the variance in caregiver stress ((Fmodel [4,75] = 5.768, p < .001) and depression (Fmodel [4,75] = 11.584, p < .001). Sleep quality eroded with increasing number of night time disruptions by the PWD (r = .22, p = .02). Caregivers reported lower global PSQI scores with increased frequency of PWD's apathy (r = .23, p <.05); and lower scores on the single item "sleep quality" with increased PWD agitation (r = .27, p <.01), apathy (r = .33, p <. 01) and depression (r = .26, p <.05).

Conclusion: The nighttime behaviors of the PWD disrupt and erode the caregiver sleep quality. Additionally, caregiver sleep is negatively affected by PWD daytime behaviors. Caregiver's sleep quality contributed to caregiver perceived stress and depression levels.

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0723

FUNCTIONAL PRINCIPAL COMPONENT ANALYSIS REVEALS DISRUPTED ACTIVITY RHYTHM IN INDIVIDUALS WITH ALZHEIMER'S DISEASE AND APATHY

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Introduction: Apathy is the most frequently occurring neuropsychiatric co-morbidity in individuals with Alzheimer's disease (AD). It is associated with earlier institutionalization and faster functional and cognitive decline. Although specific apathy scales are available, apathy remains difficult to diagnose and an objective test could be of significant clinical value. Lower overall daytime motor activity has been reported for individuals with AD and apathy, but whether there is a pattern to this diminution is unknown.

Methods: We examined the 24-hour pattern of gross motor activity (1 minute wrist actigraphy) in a group of AD subjects (aged 76.7 ± 6.54 yrs; 19 men, 26 women) with (n=17) or without (n=28) apathy (defined as NPI apathy subscore ≥ 4). Data were analyzed using functional principal component analysis (fPCA) on 9-parameter spline curves fit to the raw actigraphy data.

Results: The first fPCA component explained 38.4% of the variance and was significantly different between those with (-911 ± 924) and those without (553 ± 730) apathy (p<0.0001, t-test). In those without apathy, the activity pattern in this component exhibited a morning peak and a slightly lower plateau throughout the day. In those with apathy, there was a pronounced early afternoon dip in activity.

Conclusion: Although overall daytime activity levels are lower in AD with apathy, fPCA indicates that in individuals with AD, a dramatic decline in midday activity differentiates those with and without apathy, possibly representing a weakened interaction between the circadian pacemaker and the sleep/wake homeostat.

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0724

SLEEP STRUCTURE IN MEDICATED SCHIZOPHRENIA - A PILOT STUDY USING CYCLIC ALTERNATING PATTERN METHOD -

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Introduction: Schizophrenia is a chronic psychosis accompanying severe insomnia. In terms of sleep parameters of schizophrenics, previous studies have reported 1) prolonged sleep latency, 2) sleep discontinuation, 3) decreased Stage 3+4 (especially in Stage4), and 4) decreased REM latency. However, the specific feature of sleep structure is not revealed. Cyclic alternating pattern (CAP) is a periodic sleep EEG sequence occurring mainly during non-REM sleep. CAP study on schizophrenia has not reported yet. To clarify the CAP sleep structure of schizophrenic, we recorded polysomnography (PSG) in medicated patients with schizophrenia under the permission of the ethical committee of our college.

Methods: Subjects were 7 patients, who met the criteria for schizophrenia in ICD-10. (m/f 4/3: age 15 to 51 years) PSG was recorded 4 weeks after subjects' acute psychosis have recovered without any dose of antipsychotics. Subjects were also evaluated with Positive and Negative syndrome scale (PANSS) and Pittsburgh Sleep Quality Index. The PSG data were analyzed with R&K method and CAP method by the same expert.

Results: 1)The CAP rate significantly correlated with age (r=0.812), and the duration of the disease(r=0.789). 2)CAP rate had no correlation with PANSS scores. 3)Concerning subjective sleep quality, the number of CAP sequences had an inverse correlation with the subjective sleep quality score(r=-626). 4)Regarding amount of drugs, there was no correlation between CAP rate and benzodiazepines, but the number of CAP subtype A1 had a significant correlation with the amount of antipsychotics(r=0.761).

Conclusion: From the results, the CAP oscillating system, which is composed of the arousal-related neurons, such as serotonergic, histaminergic, and dopaminergic neurons, might gradually impaired by age in schizophrenia patients. It was also suggested that it could result from long-term use of antipsychotic drugs which act as an antagonist of arousal neurons.

0725

EFFECT OF REPORTED SLEEP AND ATTENTION SYMPTOMS ON NEUROPSYCHOLOGICAL TESTING PERFORMANCE IN ADULT DIAGNOSED ADD/ADHD POPULATION FROM THE YEARS 1991-2008

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Introduction: To investigate the influence of sleep and attention related symptoms on neuropsychological testing performance in a diagnosed ADD/ADHD population.

Methods: A total of 1262 adults age 15 to 80 years were included in the sample. This sample included 802 males and 451 females;935 of which were diagnosed with ADD and 305 of which were diagnosed with ADD plus an additional disorder (i.e. sleep and/or impact to brain function). Patients were originally referred for ADD/ADHD, with brain insult/injury referrals being excluded. A neuropsychological test battery was utilized to assess attention variables and self-report measures were employed to assess sleep and other health factors. The self-report measures included the Personal Problems Checklist for Adults, Personal History Checklist for Adults, Patient Behavior Checklist for ADHD Adults and Physical Complaints Checklist for ADHD Adults. Neuropsychological Test measures included Stroop Color-Word Test, Symbol Search,

NART-R, WTAR, Symbol Digit Modalities Test, Trail Making Test parts A & B, Seashore Rhythm Test, Speech Sounds Perception Test and the PASAT.

Results: Preliminary results revealed a significant interaction between the self-reported symptom of being tired with type of ADD diagnosed (i.e. ADD vs. ADD Plus) on PASAT trial 1 scores $F(1,1106)=6.10$, $p=.014$ and on PASAT trial 2 scores $F(1,1095)=6.35$, $p=.012$. Post hoc tests revealed an opposing effect of being tired for diagnosis of ADD vs. ADD plus on performance scores for both trials. A significant main effect for the self-reported symptom of finding it difficult to complete tasks was found to influence performance on PASAT trial 3 scores $F(3,873)=3.45$, $p=.016$.

Conclusion: Findings indicate that tiredness and attention symptoms affect performance differentially in the two groups ADD and ADD plus.

0726

SLEEP INFLUENCE ON CARDIAC ACTIVITY IN ADULTS WITH AUTISM

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Introduction: Poor sleep is a frequent finding in autism and it has been shown to interfere with daytime functioning, using either behavioral (Limoges et al., 2005) or EEG measures (Daoust et al., 2004). Literature in typically developing individuals (TD) shows that sleep also influences the regulation of the autonomic nervous system so that the sympathovagal tone is normally higher in the morning compared to evening values. Studies of electrocardiographic (ECG) recordings suggest that there might be disequilibrium between sympathetic and parasympathetic activity in autism (Ming et al., 2005) but it is not known whether this observation is related to sleep or not.

Methods: Fifteen men with ASD (22.3 ± 3.5 years) and 18 typically developing individuals (TD: 21.0 ± 4.2 years) were evaluated over two consecutive nights in a sleep laboratory. ECG samples were taken for 5 minutes at bedtime and just before final rise time in the morning. Spectral analysis of the ECG signal was performed using a commercial software and the following four variables were extracted: total spectral power, low frequency power (LF: sympathetic tone), high frequency spectral power (HFabs: parasympathetic tone), normalized values of high frequency spectral power (HFnu). Groups were compared with Student's t-tests.

Results: Significant differences between evening and morning values were found only in the TD group, with lower evening values for total spectral power ($p=0.008$), LF ($p=0.007$) and HFabs ($p=0.040$) were all lower in the evening compared to morning. In the morning, significantly lower HFabs ($p=0.043$) and HFnu ($p=0.027$) values were found in ASD vs. TD groups.

Conclusion: These results suggest that the effect of nocturnal sleep differs in TD and ASD individuals and that the parasympathetic tone is lower in ASD at rise time. Further analyses will focus on ECG activity during sleep, for each of the sleep stages.

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0727

POOR SUBJECTIVE SLEEP WITH NORMAL OBJECTIVE SLEEP DURATION INCREASES RISK OF SUICIDAL IDEATION AND/OR ATTEMPTS

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Introduction: Subjective sleep disturbances are associated with suicidal ideation and/or attempts (suicidal behavior =SB). Similarly, objective sleep disturbances were found to be associated with SB in clinical samples. One actigraphic study in non-clinical sample (n=49; ages 19-24) found sleep variability to be associated with SB, but was limited by lack of polysomnographic data. In this study we examined the association of polysomnographic (PSG) and subjective sleep with SB in general population.

Methods: A subsample of 1741 (age >20) out of 16,583 randomly selected adults from general population underwent comprehensive assessment (history, physical examination) including suicidal ideation/attempts (SB) and PSG.

Results: The prevalence of lifetime SB was 5.7%. Females ($p=.011$) and subjects with poor subjective sleep ($p<.001$) were more likely to report SB. SB was significantly higher in subjects with poor subjective sleep and >/=6hr of PSGsleep in comparison to poor subjective sleep and <6hr of PSGsleep and controls with <6hr or >/=6hr of PSGsleep ($p<.001$). Subjective poor sleep with >/=6hr of PSGsleep was significantly associated with SB even after controlling for age, BMI, gender, race, alcohol, years of education, marital status, obstructive apnea/hypopnea index, medical disorders, or lifetime depression. The odds of SB in subjective poor sleep with >/=6hr of PSGsleep was 2.52 (CI:1.22-5.19).

Conclusion: Subjective poor sleep with normal PSG sleep duration (>/=6hr) is associated with increased risk of suicidal behavior. It is possible that individuals with poor subjective sleep but normal objective sleep may have underlying poorer coping resources and more anxiety/rumination which may increase the risk of suicide.

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0728

SHARED METACOGNITIVE PROCESSES IN INSOMNIA AND ALCOHOL DEPENDENCE

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Introduction: Alcohol-dependent (AD) individuals typically report sleeping poorly. Investigations of the relationship between AD and insomnia largely focus on the impact of alcohol on brain function and on self-medication. However, a feature common to insomnia and addiction is ruminative preoccupation with sleep or alcohol, respectively. Such intrusive thought processes can be interpreted as metacognitions similar to depressive rumination. This investigation assessed whether abstaining alcoholics with insomnia (AD-INS) differed from alcoholics without insomnia (AD-NINS) and healthy controls (HCs), in their preoccupation with sleep quality.

Methods: All subjects were recruited from the community. HCs (N=11) had no Axis I disorders. The AD-INS group (N=16) met research diagnostic criteria for insomnia, and the AD-NINS (N=15) did not. Both AD groups stopped drinking 3-12 weeks before the study; all participants adhered to an 11p-6a sleep schedule and completed daily sleep diaries at home for 1 week. Instruments included 3 ruminative scales—the Anxiety and Preoccupation about Sleep Questionnaire (APSQ), Response

Styles Questionnaire (RSQ), and Obsessive-Compulsive Drinking Scale (OCDS), and the Insomnia Severity Index (ISI) for insomnia.

Results: Independent of insomnia diagnosis, alcoholics scored higher on the ISI (p=.001) and OCDS (p=.002), but only the AD-INS group rated higher than controls on the APSQ (p=.008) and the RSQ (p=.003). In ADs only, and controlling for insomnia diagnosis, APSQ was significantly correlated with ISI (R2=.693), RSQ (R2=.525), and with the 'obsessive thoughts' OCDS subscale (R2=.488). RSQ was not correlated with the ISI or OCDS.

Conclusion: These findings suggest that subjects with AD-INS have global ruminative thought processes that encompass self-focused depressive thoughts (RSQ), preoccupation with sleep (APSQ), and preoccupation with alcohol (OCDS). Conversely, depressive rumination was not associated with thinking about drinking. Combined, these observations can be interpreted to indicate that primary insomnia and alcohol dependence share common cognitive processes that play a role in maintaining the disorders.

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0729

SLEEP DISTURBANCES AMONG FORMER HEROIN ADDICTS WITH AND WITHOUT METHADONE MAINTENANCE TREATMENT: A CASE-CONTROL STUDY

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Introduction: Poor sleep quality has been reported to be commonly seen among heroin addicts. Although methadone maintenance treatment (MMT) could help patients in recovery from heroin dependence, the majority of MMT patients remained suffering from sleep disturbances. However, studies in this field have received little attention. Thus, this study aims to investigate the distributions of sleep disturbances and their associations with psychological distresses and quality of life among MMT patients, compared with former heroin addicts without MMT.

Methods: The study cohort included 82 MMT patients. Besides, 88 previous heroin addicts not receiving MMT were collected for comparison. All subjects received overnight ECG monitoring at home for the assessment of cardiopulmonary coupling during sleep. Patients filled out valid questionnaires including the Chinese Pittsburgh Sleep Quality Index (CPSQI), the Epworth Sleepiness Scale (ESS), the Insomnia Severity Index (ISI) and WHO Quality of Life-Brief version (WHOQOL-BREF) at next morning. Specific sleep disorders and comorbid psychiatric disorders were assessed by clinical interview.

Results: More than two thirds (67.9%) of MMT patients suffered from poor sleep quality and one forth (25.6%) of them reported excessive daytime sleepiness. Compared to patients not receiving MMT, MMT patients were more likely to have poor sleep quality indicated by higher mean scores in CPSQI, ESS and ISI. MMT patients reported poorer quality of life. There were no significant differences in the distribution of specific sleep disorders and cardiopulmonary coupling during sleep between former heroin addicts with and without MMT.

Conclusion: Our study indicated that MMT patients were more likely to suffer from sleep disturbances than previous heroin addicts not receiving MMT. Furthermore, poor sleep quality among MMT patients could lead to poor quality of life. The associations between sleep disturbances and psychiatric co-morbidities were also demonstrated among this specific population.

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0730

SLEEP CONTINUITY IS IMPAIRED AS A FUNCTION OF AVERAGE NUMBER OF DAILY CIGARETTES AND TIME SINCE SMOKING ONSET IN OTHERWISE HEALTHY SMOKERS

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Introduction: Cigarette smoking is the most important cause of preventable morbidity and premature death in the United States. In addition to adverse effects on respiratory, cardiovascular and cerebrovascular systems, cigarette smoking may also increase morbidity by impairing sleep. Most of the empirical evidence on the detrimental effects of smoking on sleep is based on population surveys and self-report measures. Moreover, virtually no study to date has investigated the effects of cigarette smoking on sleep by segregating them from the effects of smoking-related medical comorbidities, such as sleep disordered breathing. The aims of this study are 1) to objectively investigate behavioral correlates of sleep by means of wrist actigraphy in otherwise healthy smokers and 2) explore the relationship between sleep characteristics and smoking history.

Methods: 10 otherwise healthy smokers, who had been smoking at least 10 cigarettes/day for the past year, wore a wrist actigraph on their non-dominant arm to objectively establish habitual sleep patterns for two weeks. Time since onset of smoking, maximum amount of cigarettes per day and current amount of cigarettes per day were derived from the Smoking History Form (SHF II)

Results: Current average number of cigarettes per day and time since smoking onset were associated with higher sleep fragmentation index (r-.86, p=.006 and r=.84, p=.008 respectively) after adjusting for age.

Conclusion: Cigarettes smoking impairs sleep continuity even in the absence of sleep disordered breathing and other medical comorbidities. The degree of impairment is related to current severity and duration of smoking.

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0731

EFFECTIVE TRANSLATION OF THE PITTSBURGH SLEEP QUALITY INDEX INTO URDU

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Introduction: The Pittsburgh Sleep Quality Index (PSQI) is a questionnaire used in English speaking countries for assessment of sleep quality and disturbances in patients with psychiatric disorders. The instrument has been translated into many languages; it has not yet been validated in the Urdu-speaking population. Our purpose was to translate and validate the PSQI for use in Urdu-speaking countries.

Methods: The original PSQI was translated into Urdu (PSQI-Ur) in three phases: translation and back-translation, committee-based translation, and testing in bilingual individuals, before final approval of the PSQI-Ur version. Subsequently, a prospective study was performed in healthy bilingual subjects to assess the validity of the PSQI-Ur version compared to the original PSQI in the English version.

Results: Both English and Urdu versions of the PSQI were administered to 89 bilingual subjects (67% female, age range 15-70 years) in random order. The mean (± s.d.) global PSQI score was 5.73 ± 2.54 in English language and 5.63 ± 2.59 in the PSQI-Ur (p=1.00). The PSQI-Ur score was highly correlated with the English PSQI (rho=0.944, p<0.01).

Conclusion: Our study validates the PSQI-Ur scale as equivalent to the English language version in measuring sleep quality in Urdu-speaking populations. Future studies to evaluate the PSQI-Ur in assessing sleep quality in Urdu-speaking psychiatric patients need to be undertaken.

0732

PSYCHIATRIC CO MORBIDITIES IN AFRICAN AMERICAN PATIENTS PRESENTING TO SLEEP DISORDERS CLINIC

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Introduction: Psychiatric disorders are common in patients presenting in primary care clinics and sleep disorders clinics. There is bidirectional relationship between sleep disorders and psychiatric disorders. Investigation of the psychiatric dimension of sleep disorders can provide important information regarding pathophysiology and clinical management of both psychiatric and sleep disorders. There have been numerous studies assessing the psychiatric co morbidities and relationship between sleep disorders and psychiatric disorders. Sleep disorders, particularly sleep disordered breathing, has been found to be commonly prevalent in patients of African-American decent. There is no study in the medical literature evaluating the burden of psychiatric disorders in African-American patients presenting in sleep disorders clinic. This study evaluates psychiatric co-morbidities in patients presenting for evaluation in our sleep disorders clinic

Methods: 1.All African-American patients seen in our sleep disorders clinic from January 1,2010 till June 30,2010 were identified through clinic records 2.Chart review of these patients 3.Data were collected regarding their reasons for referral, demographics, medications, and diagnoses of various psychiatric disorders as documented in their charts 4.Review of PSG data of patients who underwent sleep studies

Results: All patients who presented to our sleep disorders clinic for evaluation were included in this review. Mean age was 52.6 years. M: F ratio was approximately 1:2. Commonly encountered psychiatric co-morbidities included Major depressive disorder, Anxiety disorders, Substance abuse, Schizophrenia and Schizoaffective disorders. Snoring, excessive daytime somnolence and insomnia were the most common presenting features.Significant number of patients presenting with insomnia had co-morbid psychiatric disorders.Psychiatric diagnoses were less common when the results were compred to other similar studies of general population.

Conclusion: This study showed that significant number of patients presenting with insomnia had co-morbid psychiatric disorders and suggested that all patients who present with insomnia should be evaluated for presence of co-morbid or underlying psychiatric disorders.Psychiatric disorders in African American patients presenting to our sleep disorders clinic may be underdiagnosed or less prevelant as comapred to general population.

0733

THE NIGHTTIME CHAOS OF OEF/OIF MILITARY-RELATED POSTTRAUMATIC STRESS DISORDER

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Introduction: Subjective sleep disturbances are well documented in PTSD, although objective sleep problems are less clear. Little data has been published on sleep characteristics of Operation Enduring Freedom/ Operation Iraqi Freedom (OEF/OIF) Veterans with PTSD. Here, we present baseline sleep data from OEF/OIF Veterans prior to treatment.

Methods: To be eligible, subjects must have been deployed at least once to OEF/OIF, experienced a military-related trauma, and meet DSM-IV criteria for PTSD, chronic insomnia, and nightmare disorder. At baseline, subjects completed self report questionnaires of sleep, as well as wore an actigraph and completed sleep diaries for 1 week. We report data from 21 subjects (age=32.6+/-7.6yrs, 19M, 10 with multiple deployments).

Results: Subjects reported 6.2+/-4.4 nightmares/week, with moderate levels of associated distress. They scored 9.3+/-3.9 on the PSQI-Addendum, well above the cutoff of 4. On the CAPS, nightmares were the most frequent and intense of the reported intrusive symptoms. Global PSQI scores were significantly elevated (mean=14.2+/-3.2), as were reports of insomnia on the ISI (mean=18.6+/-3.7) and CAPS (frequency of sleep difficulty: 100% reported "daily or almost every day"). Diary data also showed subjectively poor sleep: TST=5.8+/-1.8hrs, SE=77+/-14%, SL=42+/-8.2min, WASO=68.8+/-56.6min. Actigraphy showed similar data: TST=6.1+/-1.5hrs, SE=78+/-9.4%, WASO=73+/-28.5min. Of note, there was considerable inter- and intra-individual variability in these sleep measures.

Conclusion: Both subjective and objective sleep is highly disturbed in OEF/OIF Veterans with PTSD and this is the first study to demonstrate consistency between subjective and objective assessments in this cohort. As with other PTSD cohorts, nightmares occur almost daily, on average. Insomnia-related sleep disruptions are seen at levels roughly equivalent to insomnia patients from our lab and depressed patients in the literature. Night-to-night variability in sleep, at both group and individual levels, was greater in PTSD than the other samples. These marked sleep disruptions may relate to daytime function and/or treatment outcome.

0734

PAP COMPLIANCE IN HISPANIC VETERANS WITH PSYCHIATRIC DISORDERS

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Introduction: Psychological symptoms are recognized as contributing factors in PAP treatment compliance for sleep disordered breathing (SDB). We explored PAP compliance rates in Hispanic veterans with and without psychiatric co-morbidities.

Methods: Consecutive Hispanic patients were recruited from the Miami VA Sleep clinic as part of a sleep education in Hispanics study. Participants completed questionnaires, screening for SDB, sleep quality (PSQI), health-related quality of life (HRQOL) and for presence of anxiety and depression symptoms (HADS). SDB diagnosis and severity was confirmed by in-lab polysomnography. Patients were categorized in 2 groups (Psychiatric disorders present or not) based on Axis 1 diagnoses obtained from electronic records. One week after PAP distribution compliance data was downloaded from PAP memory card. Means and SDs and frequencies are reported. Group comparisons were made using Chi-square or student t test as appropriate.

Results: Sixty-one veterans (2% female) were enrolled with mean age 50± 13, BMI of 34±6 and HRQOL score 59.6±21.5. The mean HADS Depression score was 8±4 and anxiety score 9±5. Axis I diagnosis were found in 64% of the cohort, 30% had mood disorders, 18% with PTSD, 2% substance abuse, 2% psychoses, and 13% with multiple diagnoses. Poor sleep quality was reported by 95% of the cohort with mean PSQI score of 11±4 and 92% screened high risk for SDB and confirmed mean AHI was 41±32 events per hour. At 7 days, mean total hours of PAP usage was 30±18. During this time, 35% of the cohort had used PAP greater than 4 nights, more than 4 hours each night. There was a trend towards less PAP usage in patients with psychiatric disorders although it did not reach statistical significance.

Conclusion: Psychiatric disorders may play a role in determining PAP compliance. Longer term compliance data is needed to confirm this trend.

0735

NARRATIVE EXPOSURE TREATMENT FOR POSTTRAUMATIC STRESS DISORDER DECREASES INSOMNIA SYMPTOMS AND NIGHTMARES

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Introduction: Insomnia and nightmares are core features of PTSD, yet clinically significant sleep disturbance persists in approximately 40% of patients who complete cognitive-behavioral therapy for PTSD. This study examined the extent to which a novel treatment for PTSD improved trauma-related insomnia and nightmares.

Methods: Participants were randomized to either a narrative exposure treatment (NET; n = 22) or a waitlist condition (WL, n = 23). All participants completed assessments at baseline, post-treatment (6 weeks for WL), and 3 month follow-up (or 18 weeks for WL). Trauma-related sleep disturbance was examined using two items from the Clinician Administered PTSD Scale.

Results: The baseline assessment revealed that the NET and WL groups did not differ significantly in severity of sleep disturbance. At baseline, 80% of the sample reported clinically significant insomnia (sleep onset latency ≥ 30 min several times a week), and 20% reported clinically significant nightmares (severely distressing nightmares with difficulty returning to sleep at least once or twice per week). However, group differences were observed following treatment. Individuals who completed NET had significant decreases in sleep disturbance, with 22% reporting significant insomnia and 4% reporting significant nightmares. These sleep improvements were maintained through 3 month follow-up. In contrast, 65% of the WL group reported significant insomnia and 43% reported significant nightmares at 6 week follow-up.

Conclusion: These findings indicate that NET reduces sleep disturbance to sub-clinical levels of severity in a majority of patients. Furthermore, the degree of sleep improvement following NET compares favorably to reported sleep improvements following other cognitive-behavioral treatments for PTSD.

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0736

THE EFFECT OF BRIGHT LIGHT THERAPY ON POSTTRAUMATIC STRESS DISORDER RELATED SLEEP DISTURBANCES

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Introduction: Sleep disturbance is perhaps the most common complaint of posttraumatic stress disorder (PTSD) patients, and may play a role in precipitating and/or perpetuating the symptoms of PTSD. Treatment of disturbed sleep could provide an important means of improving mental health in PTSD patients. The objective of our ongoing study is to examine whether bright light therapy will elicit reductions in clinical and self assessment of PTSD symptom severity, and related morbidity, including depression and disturbed sleep.

Methods: Following a 1-week baseline, twenty-four veterans of the current conflicts in Iraq and Afghanistan diagnosed with combat-related PTSD were randomized to one of two, 4-week treatments: (1) bright light (daily 10,000 lux for 30 min; n=12) or (2) a placebo inactivated negative ion generator (NIG; n=12). A Clinician-Administered PTSD Scale (CAPS-2) was administered at baseline and within 1-3 days following the intervention. At weekly intervals, depression was assessed with the Beck Depression Inventory (BDI-II), self-reported PTSD symptoms were assessed with the PTSD Checklist-Military Version (PCL-M), and sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI), plus addendum for PTSD-related sleep problems.

Results: Preliminary results showed a greater reduction in CAPS-2 [Effect Size (ES)=0.89 vs. 0.07] and PCL-M (ES= 0.92 vs.0.27), following bright light vs. NIG, respectively. PTSD-related sleep complaints were also reduced more following bright light (ES=1.14) vs, NIG (ES=-0.16), partly due to a reduction in frequency of nightmares following bright light (from 2X/wk to < 1x/week), but no change following NIG . A greater reduction in BDI-II (ES=0.83 vs. 0.49) was also observed following bright light vs. NIG.

Conclusion: Preliminary results suggest benefits of bright light for PTSD and associated morbidity, including depression and PTSD-related sleep disturbances.

Support (If Any): VA Merit Award

0737

EFFICACY OF A COGNITIVE-BEHAVIORAL TREATMENT FOR INSOMNIA AMONG AFGHANISTAN AND IRAQ (OEF/OIF) VETERANS WITH PTSD

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Introduction: High rates of post-traumatic stress disorder (PTSD) are being diagnosed in veterans who served in Afghanistan and/or Iraq in Operation Enduring Freedom and Operation Iraqi Freedom (OEF/OIF). Sleep disturbances are a core and salient feature of PTSD and can maintain or exacerbate associated symptoms. Recent research demonstrates that sleep-focused behavioral interventions with a component for nightmares improve sleep disturbances as well as PTSD symptoms. Studies to date have focused primarily on civilian PTSD participants, with some recent pilot work on older veterans with PTSD. This study examines the efficacy of cognitive behavioral therapy for insomnia (CBT-I) in significantly improving sleep and reducing PTSD severity in younger OEF/OIF combat veterans.

Methods: Participants included 27 (mean age = 36.8, 85% male) OEF/OIF combat veterans with clinically significant insomnia and PTSD, recruited from the mental health clinic at the McGuire Hunter Holmes VA Medical Center. Participants were randomized to either a treatment group or a wait-list control group. Those in the treatment condition participated in four CBT-I sessions over a six-week period including sleep restriction, stimulus control, cognitive restructuring, sleep education, sleep hygiene and imagery rehearsal therapy to address nightmares. Participants completed measures at baseline and post-treatment. Participants in the treatment condition also provided three-month follow-up data. Outcome measures included: Sleep Diary (sleep efficiency, wake after sleep onset, sleep latency, total sleep time), Insomnia Severity Index (ISI), Pittsburgh Sleep Quality Index (PSQI), Pittsburgh Sleep Quality Index- Addendum (PSQI-A, a measure assessing PTSD related sleep disturbances), PTSD Symptom Scale, Disbeliefs and Attitudes About Sleep, Profile of Mood States, and Patient Health Questionnaire. Actigraphy was measured for participants in the treatment group at baseline and post treatment.

Results: Repeated measures ANOVAs revealed a significant improvement between groups, for the following variables: sleep efficiency, p < .001; sleep latency, p < .05; PSQI, p < .001; PSQI-A, p = .01; ISI, p < .001; PTSDSS, p = .001. Actigraphy data was collected and will be presented at the time of the conference along with remaining outcome measures.

Conclusion: CBT-I is an effective treatment for insomnia, nightmares and PTSD symptoms in OEF/OIF veterans with combat related PTSD and should be used as an adjunctive therapy to standard PTSD treatment.

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0738

ALTERED SLOW WAVE AND SPINDLE RANGE ACTIVITY IN MAJOR DEPRESSION: PRELIMINARY HIGH-DENSITY EEG FINDINGS

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Introduction: Abnormalities in slow wave activity (SWA) and sleep spindle activity have been previously described in major depressive disorder (MDD). We utilized high-density EEG (hd-EEG) to investigate topographic differences in these parameters between MDD and control subjects during sleep.

Methods: Unmedicated MDD subjects (n=28; 10 men) and age and sex-matched controls were recruited. Subjects underwent overnight hd-EEG (256 channel) polysomnography. The EEG data were filtered, FFTs performed, and data visually inspected and manually cleaned of artifact. Unpaired t-tests and statistical non-parametric mapping (SnPM) were used to evaluate for topographic differences in SWA and spindle range activity (SRA).

Results: All-night SWA normalized to the power in all channels was greater in frontal and lower in posterior channels in MDD subjects relative to controls. SnPM using cluster threshold confirmed the posterior decrease, but not the frontal increase in SWA in MDD. Normalized all-night spindle range activity (12-15 Hz) was greater in frontal regions in MDD subjects relative to controls, but SnPM did not confirm this result. Neither SWA nor SRA findings correlated with age or depression severity.

Conclusion: These preliminary findings suggest altered topographic SWA and SRA activity in depression. Further research is indicated to confirm these findings and determine if these findings are specific to subtypes of depression.

0739

ALTERED SLOW-WAVE ACTIVITY HOMEOSTASIS IN MAJOR DEPRESSIVE DISORDER WITH HYPERSOMNOLENCE: A HIGH DENSITY EEG PILOT STUDY

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Introduction: Hypersomnia is a common symptom of major depressive disorder (MDD) that increases the risk of incident depression and may be a residual symptom after resolution of a depressive episode. The pathophysiologic mechanisms underlying hypersomnia in mood disorders are unknown. This post hoc pilot study explored possible high density EEG (hd-EEG) markers that might distinguish MDD with hypersomnolence (MDD-HYS) from healthy controls and MDD with insomnia (MDD-INS).

Methods: MDD-HYS subjects (n=8; 5 men) and age- and sex-matched MDD-INS subjects and controls were selected from a larger study on sleep homeostasis in depression. Hypersomnia was defined as a self-report of sleeping $\geq$10 hours per day; insomnia as subjective report of difficulty initiating or maintaining sleep. Subjects underwent overnight hd-EEG (256 channel) polysomnography. EEG data were filtered, FFTs performed, and data visually inspected to remove artifact. Statistical analysis included ANOVA and post hoc unpaired t-tests to explore dif-

ferences between groups in absolute and normalized slow wave activity (SWA; 1-4.5 Hz) during NREM sleep.

Results: Left frontal all-night SWA normalized to the power in all channels was significantly higher in MDD-HYS (1.57±0.30) compared to controls (1.15±0.19, p=0.005) and MDD-INS (1.28±0.12, p=0.024). When examining absolute SWA in frontocentral regions for the first 30 minutes of NREM sleep, power was significantly lower in MDD-HYS compared to MDD-INS (29.6μV±13.7 vs. 66.6μV±23.9, p=0.016). No differences in absolute SWA were evident at the end of the night, suggesting a greater homeostatic dissipation of SWA in MDD-INS compared to MDD-HYS.

Conclusion: This pilot study suggests there may be alterations in SWA topography and dissipation across the night that segregate depressed subjects with hypersomnia from those with insomnia and healthy controls. Further research is indicated to replicate this finding and determine if hd-EEG findings correlate with hypersomnia severity.

0740

CORDANCE AS A BIOMARKER IN SLEEP-EEG FOR DEPRESSION: DIFFERENCES IN RESPONDERS VERSUS NON-RESPONDERS - A NATURALISTIC STUDY AFTER ANTIDEPRESSANT MEDICATION

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Introduction: Cordance is a relatively new quantitative EEG-method, which has shown usability as a biomarker for depression within the resting-state in wake patients. Sleep EEG shows distinctive alterations in a depressive episode and changes after antidepressants. We wanted to test whether differences in Cordance derived from sleep EEG exist between responders and non-responders after antidepressant medication.

Methods: 20 in-patients with a depressive episode [ICD-10 F 31.4, F 32.1-3, F 33.1-3] were treated with various antidepressants of "doctor's choice". The change of the Hamilton depression scores between the first and fifth week of treatment provided evidence about response. Response to treatment was defined as a $\geq$ 50 % reduction of Hamilton score. Cordance values for the prefrontal theta-EEG were calculated from sleep EEG during the first week with active medication.

Results: Results showed significant differences: 8 responders compared to 12 non-responders showed higher Cordance values in prefrontal EEG-sites (z-score -1,57 ± 0.79 versus -2,64 ± 0,69, p = 0.0055).

Conclusion: These results suggest that Cordance derived from sleep EEG provides a biomarker for depression.

0741

DIFFERENCES IN SPONTANEOUS WAKING EEG BETWEEN CONTROLS AND SUBJECTS WITH DEPRESSION

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Introduction: Abnormalities in slow wave activity (SWA) have been described in major depressive disorder (MDD), suggesting altered sleep-wake homeostasis. Little is known, however, about how waking EEG tracings in MDD are affected by sleep. We examined spontaneous waking high-density electroencephalogram (hd-EEG) recordings and their relationship to slow wave activity during sleep.

Methods: 12 right-handed MDD subjects (9 female) and 12 age and sex matched controls were analyzed, taken from a larger study on sleep homeostasis in depression. Two minutes of spontaneous waking hd-EEG (256 channel) was collected in the evening prior to sleep and the morn-

ing after sleep with subjects seated and eyes closed. The intervening sleep was recorded. Analyses used unpaired t-tests and Pearson correlations.

Results: When examining global EEG power in the evening and morning, no differences were found between controls and MDD subjects. However, MDD subjects had a weaker low frequency power (2-8Hz) frontocentrally, both in the evening and morning. Next we examined the decline in waking power from evening to morning. Control subjects showed an overnight decline in low (1.5-7.5Hz) and high (9.5-37Hz) frequencies, whereas MDD subjects did not show a decline below 8 Hz, although they did decline in the 10-33Hz range. In controls, overnight change in waking theta and alpha power correlated to sleep SWA in the frontocentral region. In contrast, MDD subjects did not exhibit global or regional correlations of changes in waking theta and alpha power with sleep SWA.

Conclusion: This study suggests that changes in waking EEG traces in healthy subjects that correlate with sleep homeostatic decline are altered in MDD. Further studies are needed to better assess altered sleep-wake homeostasis in depression and to determine if these findings are specific to subtypes of depression.

0742

OVERNIGHT CHANGES IN AUDITORY EVOKED POTENTIAL AMPLITUDE REFLECT ALTERED SLEEP HOMEOSTASIS IN MAJOR DEPRESSION

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Introduction: Previous research has demonstrated that waking auditory evoked potential (AEP) amplitude declines after a night of sleep and that the overnight reduction in AEP amplitude correlates with the amount of sleep slow wave activity (SWA), suggesting that changes in the AEP waveform may reflect a homeostatic process related to sleep. Because major depressive disorder (MDD) may involve altered sleep homeostasis, we investigated overnight changes in AEPs and their relation to sleep SWA in MDD and matched controls.

Methods: As part of a larger study on sleep homeostasis in depression, pre- and post-sleep single-tone, waking AEPs and all-night sleep recordings with 256-channel high-density EEG were analyzed for 11 right-handed, non-medicated MDD participants (8 female) and 11 age- and sex-matched controls. Overnight changes in amplitude and latency for N1 and P2 components were analyzed with paired t-tests for each group, while their relationships with sleep spectral power were calculated with a Pearson correlation.

Results: A significant pre- to post-sleep decline in N1 amplitude was observed for healthy controls (p < .05), but not for the MDD group. Moreover, the overnight change in N1 amplitude correlated with sleep SWA (1-4.5Hz) only for the control group (p < .02); more SWA predicted a greater reduction in amplitude. No significant differences before and after sleep were detected for P2 amplitude, N1 latency, or P2 latency for either group.

Conclusion: These results support the notion that the overnight decline in N1 amplitude may reflect a sleep-related homeostatic process and suggest that MDD involves altered regulation of such homeostasis. Importantly, these findings indicate that single-tone AEPs, combined with high-density EEG, may provide a useful measure for investigating sleep homeostasis in depression. Subsequent research is required to corroborate these findings, and to examine the potential utility of AEPs in categorizing MDD in terms of subgroups and predicting treatment response.

0743

EFFECTS OF EARLY AND LATE PARTIAL SLEEP DEPRIVATION ON SLEEP AND SLOW-WAVE ACTIVITY (SWA) IN MAJOR DEPRESSIVE DISORDER

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Introduction: Acute total and partial sleep deprivation improve mood in more than half of major depressive disorder (MDD) patients, but relapse is common following recovery sleep and its practicality is limited in outpatient settings. We compared sleep PSG and SWA in MDD participants assigned to a more modest repeated early or late partial sleep deprivation (6 hours TIB) vs. no sleep deprivation (8 hours TIB) in conjunction with antidepressant medication.

Methods: Twenty-two subjects meeting DSM-IV criteria for MDD (25.2 ± 6.7 years of age, 9 women, baseline HAMD-17 score 20.2 ± 1.8) have participated to date. Subjects received 8 weeks of fluoxetine 20-40 mg and were randomized to two weeks of no sleep deprivation (NSD, n=7), early partial sleep deprivation (E-PSD, 2-hour delay of bedtime, n=7) or late partial sleep deprivation (L-PSD, 2-hour advance of rise time, n=8). Following an 8-hour at-home sleep schedule, subjects underwent PSG at baseline, on the first and last experimental nights, and on the first recovery night (8 hours TIB).

Results: No group differences were found on baseline sleep variables. Total sleep time was reduced in the E-PSD and L-PSD groups compared to NSD on experimental nights vs. baseline (p < .001). Stage N3% increased in the E-PSD group and decreased in the L-PSD and NSD groups (p < .03). REM latency and Stage N1% were elevated and SWA power was decreased on the last experimental night compared to baseline and the first experimental night (p < .001). REM% increased during recovery sleep in the L-PSD group while Stage N2% increased in the E-PSD and NSD groups.

Conclusion: The sleep manipulations increased SWS and SWA in the E-PSD group, while fluoxetine increased Stage N1 and prolonged REM latency in all three groups. We are evaluating how the sleep manipulations combined with fluoxetine influence self- and clinician-rated mood.

0744

OBJECTIVE VS. SUBJECTIVE MEASUREMENTS OF SLEEP IN DEPRESSED INSOMNIACS: FIRST NIGHT EFFECT OR REVERSE FIRST NIGHT EFFECT?

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Introduction: Many individuals experience worse sleep during their first night in a sleep laboratory compared to succeeding laboratory nights. This "first night effect" is typically characterized by increased sleep onset and REM latency, less REM stage sleep, and lower sleep efficiency. In contrast, other studies have observed a "reverse" first night effect, in which individuals sleep better the first night at the laboratory compared to later nights. Studies investigating laboratory adaptation effects have typically focused on comparing the first night in the laboratory with successive nights in the same environment. This study compared sleep in the laboratory with sleep at home, before and after laboratory monitoring, in depressed insomniacs undergoing treatment.

Methods: A double-blind, randomized, placebo-controlled clinical trial was performed with 60 depressed, insomniac outpatients receiving one week of open-label fluoxetine, followed by 8 more weeks of fluoxetine and either eszopiclone or placebo at bedtime. Patients underwent actigraphic monitoring with sleep diaries over a continuous 10-week period. After one week of baseline monitoring, subjects spent one night in the laboratory with actigraphy monitoring and sleep diaries. At the end of 10 weeks, subjects underwent a second night of laboratory monitoring. Actigraphic and diary sleep measurements for the weeks before and after laboratory nights were compared with laboratory night measurements.

Results: Actigraphically recorded laboratory sleep during both nights in the laboratory was found to be improved relative to sleep at home, with less wake time and greater sleep time and sleep efficiency occurring in the laboratory. In contrast, sleep diaries indicated a worsening of sleep in the laboratory compared to home, with significantly more awakenings and less sleep time on laboratory nights compared to the weeks at home.

Conclusion: Objective and subjective sleep measurements seen in depressed insomniacs may be influenced by the monitoring setting and the measurement modality.

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0745

SUBJECTIVE, BUT NOT OBJECTIVE, SLEEP DISTURBANCES ARE ASSOCIATED WITH AN INCREASED RISK OF DEPRESSION IN OLDER MEN

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Introduction: Depression and insomnia are common complaints in older adults. Prior studies have suggested that subjective sleep disturbances are associated with increased risk of recurrent and new onset depression, but longitudinal relationships between objective sleep disturbances and depression are uncertain.

Methods: Subjective sleep quality and daytime sleepiness were measured in 2,510 non-depressed men aged 67 and older, enrolled in the MrOS Sleep Study at baseline using the Pittsburgh Sleep Qualty Index (PSQI) and Epworth Sleepiness Scale (ESS). Objective sleep was measured at baseline using wrist actigraphy for an average of 112+18h. Depressive symptoms were measured at baseline and an average of 3.4+0.5 years later, with the Geriatric Depression Scale(GDS) using the following cut-points: 0-2(normal); 3-5(some depressive symptoms); >=6(depressed).

Results: Of the 2,510 men with GDS<6 at baseline, 116(4.6%) were depressed and 495(19.7%) had some depressive symptoms at the follow-up exam. After adjusting for multiple potential confounders, men with subjective sleep disturbances had a 43-75% greater odds of having a greater level of depressive symptoms at follow-up than men without subjective sleep disturbances. There were significant associations between subjective difficulty initiating sleep and odds of greater level of depressive symptoms, but subjective short sleep duration or sleep fragmentation were not associated with depressive symptoms at follow-up. There was a moderate association between objectively measured prolonged sleep latency and greater level of depressive symptoms in cross-sectional, but not longitudinal analyses. There was no association between other ob-

jectively measured sleep parameters and level of depressive symptoms at follow-up.

Conclusion: There was evidence of a temporal association between subjective sleep disturbances and worsening depressive symptoms over time. Men who reported subjective sleep disturbances at baseline had moderately greater odds of endorsing more depressive symptoms at follow-up. In contrast, there was no temporal association between objective sleep disturbances and greater level of depressive symptoms in older men.

0746

PREDICTORS OF HOPELESSNESS IN MAJOR DEPRESSION

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Introduction: While all symptoms of major depressive disorder (MDD) result in significant impairments, sleep disturbance is one of the most common and is consistently described by patients as the most incapacitating of all. This is not surprising given that research reliably shows that sleep disturbance directly compromises cognitive-emotional functioning (Dinges et al., 1997). Given the strong relationship between sleep and well-being, it is also not surprising that sleep disturbance is strongly related to suicidality. Previous studies have established that poor subjective sleep quality reported by patients with MDD is predictive of increased suicidal ideation and attempts (Agargun, Kara, & Solmaz, 1997). The present study evaluated the relationship between objective sleep measures and suicidal ideation.

Methods: 7 patients diagnosed with MDD were recruited for an overnight sleep study. All were symptomatic and medication-free at enrollment. Sleep EEG was recorded over two consecutive nights in the lab and the Beck Depression Inventory (BDI), and the Beck Hoplessness Scale (BHS) quantified depressive symptoms.

Results: Scores on the BHS were entered as the dependent variable into a hierarchical linear regression with sleep architectural measures as predictors. Results indicated that 74.3% of the variance in BHS scores was accounted for by a combination of REM latency and minutes of REM sleep across the total night. Additionally, those who showed high suicidality as indicated by the Structured Clinical Interview for the DSM-IV also showed reduced REM activity and increased hopelessness. NREM sleep measures did not predict BHS scores.

Conclusion: Results suggest that REM sleep may be uniquely associated with hopelessness and increased suicidal ideation in those with MDD. If confirmed, these findings may be of clinical relevance in choosing treatments and interventions that target REM sleep.

0747

OBSTRUCTIVE SLEEP APNEA (OSA) IN MAJOR DEPRESSIVE DISORDER

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Introduction: Patients with OSA have been shown to have elevated levels of depressive symptoms. Less is known about the prevalence of OSA among depressed patients. The aim of this study was to examine the prevalence of OSA and its relationship to poor sleep and depression severity among patients with major depressive disorder (MDD).

Methods: Participants were 77 healthy individuals (36.4% male) who met DSM-IV criteria for MDD and insomnia disorder and did not meet criteria for other primary psychiatric diagnoses. Participants underwent ambulatory screening polysomnography (PSG) and were not taking hypnotic, antidepressant or other medications that affect sleep or mood. The mean age was 48 (SD=11); 6.5% were Hispanic; 74% Caucasian; 40% were married or cohabitating. Insomnia and depression severity were measured using the Insomnia Severity Index (ISI) and the Hamilton Rating Scale for Depression (HRSD), respectively.

Results: The mean (SD) HRSD was 22.3 (4.1) and the mean ISI was 22.8 (3.5). PSG data revealed mean (SD) sleep onset latency 31 minutes (69); wakefulness after sleep onset 85 minutes (60); Apnea Hypopnea Index (AHI) 9 events/hour (11). AHI≥15 was present in 18.2% of the sample and AHI≥10 was present in 27.3% of the sample. AHI was not significantly correlated with HRSD or ISI (p-values > .77). As expected, male gender was associated with greater likelihood of AHI>15 (one tailed p=.036).

Conclusion: The frequency of OSA with an AHI ≥15 in this sample of depressed individuals with insomnia was higher than observed in a large-scale epidemiological study in the United States, which found 9% of men and 4% of women (age 30-60) had an AHI ≥15. Our results may underestimate the true prevalence of OSA in patients with MDD and insomnia, as individuals with an existing diagnosis of OSA and those with probable OSA were excluded.

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0748

CO-EXISTING MOOD AND ANXIETY DISORDERS ARE ASSOCIATED WITH AN ELEVATED PREVALENCE OF INSOMNIA SYMPTOMS IN THE NATIONAL COMORBIDITY SURVEY-REPLICATION

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Introduction: Insomnia symptoms are highly prevalent in mood and anxiety disorders, yet little is known about rates of insomnia symptoms in co-existing mood and anxiety disorders. In this study, we examined the association between insomnia symptoms and co-existing mood and anxiety disorders in the National Comorbidity Survey - Replication (NCS-R).

Methods: The NCS-R is a nationally representative survey of the U.S. population (ages 18+) conducted between 2001 and 2003. Difficulty initiating sleep (DIS), difficulty maintaining sleep (DMS), and early morning awakening (EMA) in the past year were assessed as dichotomous variables. A variable (ANY) was created to signify the presence of at least one insomnia symptom (DIS, DMS or EMA). Mood disorders (major depressive disorder, dysthymia, bipolar disorder) and anxiety disorders (panic disorder, agoraphobia, specific phobia, social phobia, generalized anxiety disorder, posttraumatic stress disorder) occurring in the past year were assessed using DSM-IV criteria. A sample of 5692 respondents was divided into four groups: no mood or anxiety disorder (N=3711), mood disorder only (N=327), anxiety disorder only (N=1137), and co-existing mood and anxiety disorder (N=517). Prevalence estimates, and odds ratios adjusted for demographic and clinical variables in logistic regression analyses, were corrected for the complex survey design.

Results: Respondents with co-existing mood and anxiety disorders had significantly higher rates of at least one insomnia symptom (ANY=62.8%), as well as specific insomnia symptoms (DIS=45.4%; DMS=48.4%; EMA=40.1%), compared to the other three groups. Insomnia symptom prevalence in the mood disorder only group (ANY=45.6%; DIS=31.2%; DMS=36.2%; EMA=24.5%) did not significantly differ from the anxiety disorder only group (ANY=46.5%; DIS=25.2%; DMS=31.7%; EMA=27.5%); however, both groups more frequently endorsed insomnia symptoms compared to respondents

with no such diagnosis (ANY= 23.3%; DIS=12.4%; DMS=15.3%; EMA=12.9%). This pattern of findings remained significant after controlling for clinical and demographic factors.

Conclusion: Co-existing mood and anxiety disorders are associated with high rates of insomnia symptoms.

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0749

CHANGE IN QUALITY OF LIFE AFTER BRIEF BEHAVIORAL THERAPY FOR REFRACTORY INSOMNIA IN RESIDUAL DEPRESSION: A RANDOMIZED CONTROLLED TRIAL

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Introduction: Insomnia concurrent with depression is not only a major subjectively distressing factor for patients, but also exacerbates daytime fatigue and somnolence, which leads to deterioration in quality of life in patients. Moreover, insomnia often persists despite pharmacotherapy in depression and represents an obstacle to its full remission. The added value of brief Behavioural Therapy for insomnia (bBTi) over treatment as usual (TAU) has been confirmed for residual depression and refractory insomnia in terms of the severity both of insomnia and depression (in press), but to date the impact of bBTi on Quality of Life (QoL) have not been appropriately evaluated. The study aimed to examine what aspects of QoL changed among patients with residual depression and refractory insomnia treated with bBTi.

Methods: Thirty-seven outpatients (average age of 50.5 years) were randomly assigned to TAU alone or TAU plus bBTi, consisting of 4 weekly 1-hour individual sessions. QoL was evaluated using the Short Form 36 at baseline and the 8-week follow-up. Each of the eight QoL domains was quantified. Analysis of covariance was used to test group effects while controlling for the baseline scores.

Results: The mean scores of all the domains increased in the bBTi plus TAU group at the 8-week follow-up, while those in four domains decreased in the TAU alone group. bBTi plus TAU resulted in significantly lower scores in terms of the physical functioning (P=.006), the social functioning (P=.002) and the mental health (P=.041) domains than TAU alone at 8 weeks. No significant differences were observed in the other domains.

Conclusion: In patients with residual depression and treatment refractory insomnia, adding bBTi to usual clinical care produced statistically significant and clinically substantive added benefits in terms of some aspects in QoL.

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0750

SLEEP AND CIRCADIAN ALIGNMENT IN BIPOLAR DISORDER

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Introduction: Neural circuitry regulating the circadian and sleep-wake systems may be dysregulated in individuals with bipolar disorder, which may result in sleep-circadian misalignment. The Phase Angle Difference (PAD) between Dim Light Melatonin Onset (DLMO) and the midpoint of sleep is a robust measure of sleep-circadian alignment. To our knowledge PAD has not been assessed previously in individuals with bipolar disorder. We evaluated the presence of circadian misalignment among this population using PAD.

Methods: We examined the timing of sleep over 5 to 6 days using sleep diary and wrist actigraphy in 10 euthymic individuals with a lifetime diagnosis of bipolar I disorder. The following night, salivary melatonin was sampled every half hour from 4:30pm until 2 hours after habitual bedtime, from which DLMO was calculated. PAD was calculated as the difference between DLMO and the average midpoint of sleep.

Results: Data for one participant was not considered valid. Of the remaining 2 males and 7 females, most showed relatively normal DLMO (median= 21:16). PAD values ranged from 05:35h to 09:04h (mean=06:42). Three participants had PAD values that deviated from the benchmark "normal" value of 6 hours by at least 60 minutes. Furthermore, we observed marked night to night variability in the timing of sleep, both with respect to sleep onset times (mean= 24:01h, SD= 1:14h) and sleep offset times (mean=7:45h, SD=1:12h). The average within-subject variability in sleep onset and sleep offset times was 1:02h and 00:55h respectively.

Conclusion: It is feasible to measure PAD in euthymic patients with bipolar I disorder, and some individuals show evidence of circadian misalignment. Within-subject variability of sleep measures also suggests circadian instability. Safe, controlled experimental challenges to the circadian system may further elucidate the nature of circadian dysregulation in bipolar patients.

0751

SLEEP IN BIPOLAR DISORDER: AN EXAMINATION OF SLEEP DISTURBANCE ACROSS THE COURSE OF THE ILLNESS

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Introduction: Evidence is accruing that sleep may be an important but understudied mechanism of bipolar disorder. First, sleep disturbance is symptom of mood episodes and sleep disturbance persists during the inter-episode period. Second, sleep disturbance is a common prodrome of mania and depression. Third, sleep deprivation triggers the onset of hypo/mania in a large proportion of bipolar patients. Despite the severity and prevalence of bipolar disorder and the unequivocal role of sleep, very little is known about the course of the disorder and related sleep disturbance. This study aims to elucidate the prevalence of intra and inter-episode sleep disturbance across the course of bipolar disorder.

Methods: Twenty-four patients with a diagnosis of bipolar disorder and co-occurring sleep complaints (age: 37.0±12.4 years; 8 males) were administered a modified NIMH-Life Chart. The Life Chart documented the number and duration of individual mood episodes and intra and inter-episode sleep disturbance. The types of sleep disturbance examined were insomnia, hypersomnia, delayed sleep phase, reduced sleep need and irregular sleep patterns.

Results: Participants reported experiencing mood episodes for an average of 16.3±9.2 years with an total of 3.9±4.5 manic episodes (duration: 4.5±3.7 months) and 6.3±6.8 depressive episodes (duration: 6.8±6.7 months). Seventy-one percent of manic episodes included reduced sleep need. Fifty-eight percent of depressive episodes included insomnia and 56% included hypersomnia. The most common sleep disturbance experienced during the interepisode period was insomnia and this was reported by 79% of the participants interviewed. The other inter-episode sleep disturbances reported were: 58% hypersomnia, 4% reduced sleep need, 29% delayed sleep phase and 25% irregular sleep patterns. Twenty-nine percent of participants reported that their sleep disturbance preceded their diagnosis of bipolar disorder.

Conclusion: Sleep disturbance is a prevalent and complex feature of bipolar disorder. The type and prevalence of sleep disturbance experienced varies across individuals.

0752

EFFECTS OF CAFFEINE AND NIGHTTIME TECHNOLOGY USE ON SLEEP QUALITY IN COLLEGE STUDENTS

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Introduction: Poor sleep quality has been consistently rated as a top impediment to academic performance in college students. The purpose of this study was to examine the effect of nighttime technology use such Internet and cable television and caffeine intake on sleep quality in college students.

Methods: College students were recruited by email messages and completed an internet-based survey. Sleep quality was primarily examined by the Pittsburgh Sleep Quality Index (PSQI), including questions related to subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. This survey also included questions for technology use after 9 pm on school nights, timing and number of caffeinated beverages consumed per day, and self-reported GPA. Relationships among these factors were examined via Pearson correlation, t-test, or Mann-Whitney U, as appropriate.

Results: The majority of the participants (n=440) were female (66.4%), non-Hispanic (90.9%) white (80.2%). Based on the cut-off point of 5 on the PSQI Global score, 75% were "poor" sleepers, and 66.3% self-identified as a "night owl". After 9 pm on school nights, 54.1% of the students watched television, 59.3% reported text messaging, 72.7% were online with friends (AIM, Facebook, Myspace), 38% talked on the phone, 14.8% played video games, 28.4% watched DVDs/video, and 44.3% listened to Ipod/MP3. On average, the students engaged in over 2 of these activities while doing schoolwork. Higher multitasking index (total number of hours spent across all the activities) was correlated with shorter school night sleep duration (r=-0.221, p<0.001), greater daytime dysfunction (r=0.119, p=0.013), and lower GPA (r= -0.257, p<0.001). Higher total amount of daily caffeine intake was correlated with poorer subjective sleep quality (r=0.109, p=0.022) and a higher multitasking index (r=0.123, p=0.010). Students who reported to usually drink caffeinated beverages after 4pm (30.7%) had a poorer overall sleep quality, shorter sleep duration, and greater daytime dysfunction than those who didn't (p<0.05).

Conclusion: Many college students used multiple forms of technology late into the night while consuming caffeinated beverages, leading to poor sleep quality, as well as daytime dysfunction and poor academic performance. These findings have important implications for programs intended to improve sleep quality in young adults.

0753

PREVALENCE RATES FOR SUBJECTIVE SLEEP DISTURBANCE AND DAYTIME FATIGUE ACROSS THE USA

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Introduction: Social and demographic influences are important for sleep attainment. Geographic location has not been previously explored.
Methods: Data from the 2006 Behavioral Risk Factor Surveillance System (BRFSS) were used for this analysis (N=157,319). The BRFSS is an annual, state-based, random-digit-dialed telephone survey of American adults. Subject weights for sex*age*race/ethnicity*region maximized reliability/validity. Participants answered a question on Sleep Disturbance and Daytime Fatigue. The following states/regions provided data on these items: Alabama, Alaska, Arkansas, California, District of Columbia, Delaware, Florida, Georgia, Hawaii, Indiana, Iowa, Loui-

siana, Maine, Michigan, Minnesota, Mississippi, Missouri, Montana, Nevada, New Hampshire, New Mexico, North Dakota, Oklahoma, Oregon, Puerto Rico, Rhode Island, South Carolina, Tennessee, Texas, Utah, Vermont, Virgin Islands, Virginia, West Virginia, Wisconsin, and Wyoming. Prevalence estimates were adjusted for age, sex, ethnoracial group, education, income, employment status, general health, healthcare access, and depression. To evaluate national and regional differences, chi-square Global Tests for Differences were conducted across states and census regions.

Results: Adjusted prevalence rates of Sleep Disturbance differed across states/regions overall (chi-square=412.3, p<.0001), as well as separately for men (chi-square=139.5, p<.0001) and women (chi-square=350.0, p<.0001), as did rates of Daytime Fatigue overall (chi-square=245.7, p<.0001), as well as separately for men (chi-square=117.5, p<.0001) and women (chi-square=181.2, p<.0001). When Census regions were compared, no differences were found for Sleep Disturbance. Differences existed for Daytime Fatigue overall (p<.0001), as well as for men (p<.001) and women (p<.0001) when examined separately, with the West reporting the least complaints and the South reporting the most.

Conclusion: These results demonstrate that reports of sleep-related complaints (and potentially sleep disorders) vary by geographic region, independent (at least partially) of factors that influence circadian rhythms (e.g.,latitude). This geographic disparity can inform differential allocation of health resources and services in relation to sleep health programs at various levels (national/regional/state).

0754

SHORT SLEEPER SYNDROME (SSS): A POSSIBLE SLEEP-DURATION, CIRCADIAN, METABOLIC, AFFECTIVE, PAIN-TOLERANCE, NORMAL VARIANT IN HUMANS

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Introduction: Circadian clock genes are thought to have pleiotropic effects. Our group reported a missense mutation in human CK1δ causing familial advanced sleep phase syndrome associated with asthma, depression, and skin flushing. In 2009 we reported a missense mutation in human DEC2 causing short total sleep time (TST), and possibly increased behavioral drive. Here we report the results of extending our phenotyping method to a larger sample of self-described short-sleepers without insomnia complaint.

Methods: Thirty seven participants (20 female; ages 28-84; mean=55.6) in 26 kindreds had 24-hour weekend TST ≤ 6.5 hours with onset by age 30. Mood, behavioral activation, and sleepiness were assessed by Beck Depression Inventory (BDI), activation questionnaire developed by CRJ (AQ), and Epworth Sleepiness Scale (ESS). Chronotype, TST, weekend wake up (WU), body mass index (BMI), and pain-tolerance (PT) were assessed using the Horne-Ostberg Morningness/Eveningness Questionnaire (MEQ), 10-day wrist actigraphy, and structured but open-ended telephone interviews. Thirty seven age and gender-matched participants with conventional sleep-duration and circadian entrainment served as controls.

Results: Significant differences between short sleepers (SS) and conventional sleepers (CS) were found in TST, MEQ, WU, and AQ (all p<.001). TST: SS mean=5.55 hours (range=3.0-6.5); CS mean=8.21 hours (6.75-10.25). MEQ: SS mean=68.87 (56-79); CS mean=60.12 (41-76). WU: SS mean=05:03 (02:30-08:00); CS mean=07:02 (05:20-10:15). AQ: SS mean=71/100 (43-99); CS mean=57/100 (25-89). Trends toward lower BDI, ESS, and BMI did not reach significance. BDI: SS mean=3.97 (0-19); CS mean=6.36 (0-29). ESS: SS mean=7.24 (1-16); CS mean=8.40 (1-17). BMI: SS mean=26.04 (17.04-36.02); CS

mean=27.49 (19.15-57.37). PT: 20 SS reported high PT, 5 SS "normal", 7 SS low.

Conclusion: Preliminary phenotyping of self-described short sleepers suggests a multifaceted, potentially familial syndrome. Therefore, SSS may present a particularly high-yield opportunity to explore clock gene pleiotropy, including the importance of sleep genetics to human biology and clinical medicine.

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0755

HABITUAL SLEEP DURATION AND INSULIN RESISTANCE IN A COMMUNITY SAMPLE OF MIDDLE-AGED AND OLDER ADULTS

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Introduction: Acute sleep restriction in normal subjects has been shown to decrease insulin sensitivity. The primary aim of this study was to determine whether habitual sleep duration is associated with insulin resistance after accounting for several other factors such as age, sex, body mass index, and the severity of sleep apnea in a general community sample.

Methods: The current analyses are based on data collected by Sleep Heart Health study. From the baseline sample of 6,441 participants, only those with measurements of fasting glucose and insulin were included in this analysis. Habitual sleep duration during the work week was assessed by self-report. Insulin resistance was quantified by the homeostasis model assessment index (HOMA-IR = fasting glucose x fasting insulin/22.5). Multivariable regression methods were used to model log(HOMA-IR) as a function of habitual sleep duration while adjusting for age, sex, body mass index (BMI), and sleep apnea severity.

Results: The study sample consisted of 1,130 participants (mean age: 62.8 years; mean BMI: 28.8 kg/m^2). The distribution of sleep duration was as follows: $\leq$ 6 hrs (24.3%), 7-8 hrs (68.2%) and $\geq$ 9 hrs (7.5%). HOMA-IR values were lowest in participants reporting $\leq$ 6 hours/night of habitual sleep compared to those reporting 7-8 hours/night of habitual sleep (2.87 vs. 3.20; p<0.04). This difference was most evident in participants with a BMI $\geq$ 25 kg/m^2 (3.10 vs. 3.60; p<0.007). After adjustments for age, BMI, sex, and sleep apnea severity, the difference in HOMA-IR between short and normal sleepers remained significant only in those participants with a BMI $\geq$ 25 kg/m^2.

Conclusion: In a community-based sample of middle aged and older adults, self-reported habitual short sleep duration ($\leq$ 6 hours/night) is associated insulin resistance independent of other factors such as age, sex, obesity and sleep apnea. The association between short sleep duration and insulin resistance is most notable in overweight and obese people.

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0756

BIOPSYCHOSOCIAL PREDICTORS OF INSUFFICIENT REST OR SLEEP IN THE AMERICAN POPULATION

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Introduction: As social/behavioral determinants of health become increasingly recognized, understanding how these play a role in sleep becomes increasingly important. Insufficient sleep is a potentially important indicator, capturing elements of sleep duration and disturbance--both linked to many health outcomes. The present analysis explored whether specific biopsychosocial health predictors are predictive of insufficient sleep.

Methods: The 2009 Behavioral Risk Factor Surveillance System(BRFSS) was used(N=323,047), which included a survey item detailing days/week of perceived insufficient rest or sleep. We hypothesized that specific modifiable and unmodifiable factors contribute variance to insufficient sleep, encompassing several domains: demographics (age, sex, race/ethnicity, marital status, Census-region), socioeconomics (crowding, education, income, employment, health insurance), health (physical health, mental health, BMI, emotional support, general health), and healthy behavior (minutes of exercise, alcohol intake, servings of fruits/vegetables, general physical activity, heavy drinking, smoking). Linear regression adjusted for all predictors.

Results: Being female was a predictor, as was being Hispanic/Latino or Asian/Other (Black and Multiracial were trends). Age was negatively related to sleep insufficiency. The youngest groups reported the most insufficient sleep (significantly higher than 80+: 18-24,25-29,30-34,35-39,40-44,45-49,50-54,55-59,60-64,65-69). South and Northeast Census-region were positively associated with insufficient sleep. Lack of high-school diploma and low income($10,000-$15,000, $20,000-$25,000, and $25,000-$35,000) were predictors. Being retired or unemployed were predictors. There was a trend for access to health insurance. Physical and mental health, as well as all levels of general health (versus Excellent), were predictive. Obesity was a predictor. Crowding was a predictor, as was being Never Married. All levels of Emotional Support (versus Always) were predictive. Minutes of moderate/vigorous activity was a predictor, but larger effects were seen for broadly-assessed exercise. Alcohol was not a predictor, but daily and former smoking were. Number of fruits/vegetables was not a predictor. For all predictors together R-squared=17.55.

Conclusion: A number of factors across the biopsychosocial spectrum are associated with insufficient sleep.

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0757

INFLUENCE OF RAMADAN ON SUBJECTIVE SLEEP QUALITY AND DAYTIME SLEEPINESS IN POST-OPERATIVE ATHLETES LIVING IN QATAR

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Introduction: Healthy adults require between 7-9 h of sleep for optimal health and daytime functioning. Athletes, especially those recovering from surgery, may require increased sleep demand to aid in recovery but little is known regarding the influence of Ramadan. Therefore, the aim of this study was to characterize the subjective sleep quality and daytime sleepiness in post-operative athletes and to examine changes associated with the observance of Ramadan.

Methods: Male athletes status post-anterior cruciate ligament (ACL) surgery (3-6 months) (n=9, 26 ± 4.6 y, 27 ± 5.7 BMI) attending outpatient physiotherapy in Qatar. Sleep quality and daytime sleepiness was assessed 1-week before Ramadan (PRE) and during the last week of Ramadan (POST), between Aug-Sept 2010, using standardized questionnaires: Pittsburgh Sleep Quality Index, PSQI; Insomnia Severity Index, ISI; and Epworth Sleepiness Scale, ESS. Physiotherapy measurements for pain, swelling, muscle bulk, hamstring length, and peak leg-press load were obtained retrospectively by chart review. Data were compared using Wilcoxon Signed Ranks Tests for related samples. Spearman Rho was used to assess correlations between quantitative sleep and physio-

therapy measures. P<0.05 was used for significance for all two-tailed tests.

Results: There were no differences between PRE-POST measurements of PSQI, ISI, or ESS. Total sleep time was reduced from PRE (6.6 ± 1.5 h) to POST (5.4 ± 1.5 h, P=0.04). Peak leg-press load increased from PRE (46.7 ± 11.2 N-m) to POST (65.6 ± 10.1 N-m, P=0.01). Changes in sleep were not correlated with physiotherapy measures.

Conclusion: Among this post-operative athlete group, the total sleep duration was lower than recommended in adults and was further reduced during Ramadan, whereas peak leg-press load increased. Additional studies with a control group are needed to investigate whether sleep duration during Ramadan limits functional improvement during physiotherapy in order to assist in program assessment.

0758

THE EFFECTS OF HAVING A TELEVISION IN THE BEDROOM ON SUBJECTIVE SLEEP QUALITY AND QUANTITY: A POPULATION BASED STUDY

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Introduction: Having a television (TV) in the bedroom has been associated with reduced sleep duration and obesity in children. However, the effect of a bedroom TV has not been extensively studies in adults. We evaluated the effect of having a TV in the bedroom on subjective sleep quality and quantity in adults living in San Diego County. We hypothesized that a TV in the bedroom would result in lower subjective sleep quality.

Methods: Subjects were recruited using random digit dialing as part of the Sleep Health and Knowledge in U.S. Hispanics Study. Participation was limited to non Hispanic Whites (NHW) and Hispanics of Mexican Descent (HMD). The Pittsburgh Sleep Quality Index (PSQI) was administered. Demographic and anthropometric data were obtained and the presence of a bedroom TV was determined.

Results: Participants included 333 subjects (176 NHW and 157 HMD). Of the total sample, 220 (66.1%) had a TV in the bedroom. There was no significant difference between those with and without a bedroom TV in reported sleep latency (23.2±22.7 vs. 19.8±31.8 minutes), sleep duration (7.03±1.4 vs. 7.07±1.4 hours), sleep efficiency (88.8±21.3 vs. 89.2±23%), PSQI global score (6.4±3.6 vs. 6.0±3.9), PSQI score >5 (64.2% vs. 55.1%) or BMI (28.1±6.3 vs. 26.9±6.3 p>0.13). Those with a bedroom TV were younger (48.8±18 vs. 53.4±20, p=0.03). Women had worse sleep quality than men (PSQI global score 6.6±3.9 vs. 5.6±3.3, p=0.016), but a TV in the bedroom did not affect sleep quality in either gender. Hispanics reported a bedroom TV more frequently than NHW (77.1% vs. 56.3%, p<0.001), however, ethnicity did not affect sleep quality in either group.

Conclusion: A bedroom TV was common in this survey, especially among HMD. However, for this sample of non-insomniacs, having a TV in the bedroom did not affect subjective sleep quality or quantity regardless of gender or ethnicity.

0759

SOCIAL DETERMINANTS OF SHORT SLEEP AMONG BLACK AND WHITE AMERICANS

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Introduction: Conditions in which people are born, grow, live, work and age, and the available healthcare system comprise WHO-defined social determinants of health. This study assessed social determinants of short sleep in the US population.

Methods: Data from the 2009 Behavioral Risk Factor Surveillance System (BRFSS) were used. BRFSS is a CDC sponsored project, representing the world's largest ongoing, state-specific, randomized survey that measures behavioral risk factors among adults in the United States [mean age=56±16years, female=63%]. Analysis focused on telephone interviews conducted in six representative states, soliciting sociodemographic, medical, sleep, and health-risk data, yielding observations for 31,059 respondents. BRFSS-provided weights were applied to analyses to adjust for use of complex design.

Results: Of the sample, 52% were employed with an average family income of up to 50K; 42% were not married and 8% had no HS degree. Prevalence of hypertension was 40%; diabetes, 12%; high cholesterol, 43%; overweight/obesity, 65%; cancer, 14%; and arthritis, 36%. Prevalence of short sleep (≤6hrs), referenced to average sleep (7-8hrs), was 35%. A multivariate adjusted logistic regression analysis ascertained associations of 4 factor sets with short sleep. They included Demographic:Age,sex,race/ethnicity, education; Personal:Care-giving, emotional support, hours worked, number of adults/children in the household, and geographic residence; Medical:Hypertension, diabetes, high cholesterol, overweight/obesity, heart disease, arthritis, cancer, and depression/anxiety; and Health risk:Smoking, drinking, physical inactivity, lack of fruit/vegetable, and no regular physical exams. Analysis showed significant* social determinants of short sleep were: working >40hrs [OR=1.72, 95% CI:1.44-2.06], black race/ethnicity [OR=1.42, 95% CI:1.12-1.80], care-giving to family/friends [OR=1.23, 95% CI:1.44-2.06], and lack of emotional support [OR=1.21, 95% CI:1.12-1.31]; *p<0.001.

Conclusion: Findings expand literature addressing factors associated with short sleep. Social determinants of health also have unique contribution in explaining risk of short sleep. They should be considered when developing programs to increase awareness of ill effects of short sleep

0760

SHORT SLEEP AND DYSFUNCTIONAL BELIEFS AND ATTITUDES TOWARD SLEEP AMONG BLACK MEN

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Introduction: Barbershops are an ideal location for health screening and wellness promotion among black men. It is used successfully to

screen for the presence of hypertension, diabetes, and prostate cancer. The present study assessed associations of short sleep with dysfunctional beliefs and attitudes toward sleep among black men in the barbershop.

Methods: Respondents were black customers (n=120; mean age=42±15 years) attending barbershops in Brooklyn, NY. They provided sociodemographic data and estimated habitual sleep time. The Apnea Risk Evaluation System (ARES) was used to identify men at high OSA risk; this is recommended for populations with a large pretest probability for OSA. The Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS) was used to quantify strength of endorsed attitudes/beliefs toward sleep. DBAS is a Likert-type scale requiring men to indicate from 0 (strongly disagree) to 10 (strongly agree); higher scores indicated more dysfunctional attitudes/beliefs about sleep.

Results: Of the sample, 25% reported hypertension, 11%, diabetes, and 3%, heart disease; 68% were overweight/obese. They also reported caffeine intake (22%) and alcohol consumption (29%). Estimated rates of sleep-related problems were: nap=36%, DIS=23%, DMS=24%, and sleep medicine=6.2%. Rate of short sleep ($\leq$6h) was 57%; 34% were satisfied with their sleep. ARES data showed 29% were at high OSA risk (cut-off: >5). The mean DBAS score was 4.26±1.99; log-transformed values were used in ANCOVA, adjusting for effects of age, BMI, HTN, DM, mood, and sleep variables. Short sleepers did not have greater DBAS scores than average sleepers (7-8h) [$F_{1,92}$=0.89, NS]. Rather, men at high OSA risk had greater DBAS scores [$F_{1,92}$=13.68, p<0.001] and tended to report greater rate of sleep dissatisfaction [36% vs. 21%, χ^2=2.59, NS].

Conclusion: Findings suggest that ARES can be used to screen black men in the barbershop. That black men at high risk for OSA have dysfunctional beliefs about sleep might explain low adherence rates to physician-recommended sleep assessment in that population.

0761
RACIAL DIFFERENCES IN PERCEIVED STRESS, SLEEP HABITS AND DAYTIME SYMPTOMS

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Introduction: Racial disparities are important to understand in order to design effective programs for evaluation and intervention. We hypothesized that important racial differences exist in subjects enrolling in a heart health program.

Methods: The Integrative Cardiac Health Project (ICHP) is a heart health program that includes goals of improving sleep and stress management. At program entry, participants complete validated questionnaires, specifically the Berlin Questionnaire for sleep apnea, Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), fatigue visual analog scale (FVAS) and the Perceived Stress Scale. Subjects also submit to anthropomorphic measures and a cardiac-relevant lab panel. Differences between whites and blacks were compared using unpaired t-test and Wilcoxon rank sum test (2-tailed) as appropriate.

Results: Of 350 consecutive subjects (mean age 55.1 yrs, 28% men), there were 133 white (38%), 105 black (30%), 90 mixed race/undeclared, 14 Latino, and 8 others. For this analysis, only white and black subjects were considered. White subjects were somewhat older (57.4+12.6 yr vs 52.1+12.4, p=0.001) and included more men (47% v 34%, p=0.04). BMI was similar between groups (29.5+5.1 kg/m2 vs 30.6+6.6, p=0.18). White subjects had lower perceived stress (PSS=19.4+9.6 vs 23.6+6.8, p<0.001), better sleep quality (PSQI=6.1+4.1 vs 7.1+3.9, p=0.05), and less daytime sleepiness (ESS=8.0+4.9 vs 9.8+5.0, p=0.01). White subjects tended to have less fatigue (FVAS=3.9+2.5 vs 4.5+2.4, p=0.08) and longer sleep duration (20 min longer per night, p=0.07). However, there was no difference in sleep latency (24.4 min vs 23.0, p=0.85) or likelihood for sleep apnea (Berlin positive 44% vs 51%, p=0.40).

Conclusion: There are important differences in levels of perceived stress, sleep quality and daytime sleepiness between white and black subjects in our program. These differences deserve explanation and may be valuable in designing interventions tailored for specific groups.

0762
SLEEP DISTURBANCE AND DAYTIME FATIGUE ASSOCIATED WITH PERCEIVED RACIAL DISCRIMINATION

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Introduction: Perceived discrimination is associated with adverse physical and mental health outcomes. Sleep may serve as an important pathway linking discrimination with health.

Methods: Data from the 2006 Behavioral Risk Factor Surveillance System (BRFSS) were used. The BRFSS is an annual, state-based, random-digit-dialed telephone survey of American adults. Michigan and Wisconsin (N=7093) were the only states to collect both sleep and racism data. Subject weights for age*sex*race/ethnicity*region maximized reliability/validity. Perceived racism was assessed with: "Within the past 12 months when seeking health care, do you feel your experiences were worse than, the same as, or better than for people of other races?" Responses were dichotomized as either "Worse" or "Same-or-Better." Outcomes included subjective Sleep Disturbance and Daytime Fatigue. Responses were dichotomized, with those indicating complaints $\geq$6days vs. <6days. Covariates included age, sex, race/ethnicity (White and Black/African-American), education, income, employment and depression. Models were evaluated with and without depression, since depression correlates very highly with both perceived racism and sleep-related outcomes.

Results: Perceived racism was associated with nearly a 2-fold increased risk of having Sleep Disturbance (OR= 1.97; 95%CI=1.35-2.89). After adjusting for depression, this relationship was attenuated but remained significant (OR=1.61;95%CI=1.03-2.51). Perceived racism was associated with a 57% increased risk of Daytime Fatigue (OR= 1.57; 95%CI=1.11-2.23); however, additional adjustment for depressive symptoms, reduced this association to non-significance. There were no significant Race/Ethnicity*Racism interactions for either outcome.

Conclusion: Perceived racial discrimination is associated with significantly increased risk of sleep disturbance, even after adjusting for socioeconomic factors and depressive symptoms. The effect of perceived racism on daytime fatigue was explained by depressive symptoms. These findings add to our understanding of how perceived racism may ultimately influence heath disparities.

0763

RACE/ETHNICITY, SLEEP DURATION AND QUALITY OF LIFE: ANALYSIS OF THE BEHAVIORAL RISK FACTOR SURVEILLANCE SYSTEM

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Introduction: Sleep disturbance is independently associated with declining physical and mental health-related quality of life (QOL). We examined whether sleep duration (short and long) is related to QOL and whether short sleep among blacks augurs greater likelihood for dissatisfaction with life.

Methods: Analysis was based on the Behavioral Risk Factor Surveillance System (BRFSS) data obtained in 2009. BRFSS is a CDC sponsored project and represents the world's largest ongoing, state-specific, randomized survey that measures behavioral risk factors among adults in the United States [mean age=56±16years, female=63%]. Analysis focused on telephone interviews conducted in six representative states, soliciting sociodemographic, health, and sleep data, yielding data for 31,059 respondents. Data analysis was performed using SPSS 18.0.

Results: Prevalence of short sleep (≤5hrs), long sleep (≥9hrs) and dissatisfaction with quality of life among whites and blacks were: 9.8% vs. 18.9%, 11.1% vs. 15.7%, and 5.1% vs. 7.7%, respectively (p<0.001). Multivariate adjusted logistic regression analysis showed that short and long sleep durations were associated with dissatisfaction with QOL [OR=2.44, 95% CI=2.10-2.84, p<0.001; OR=1.28, 95% CI=1.07-1.54, p<0.001, respectively]. Results of regression analysis testing interactions between race/ethnicity and short sleep showed that black short and long sleepers were more likely to report dissatisfaction with QOL, relative to their white counterparts [OR=1.84, 95% CI:1.65-2.06, p<0.001 and OR=1.11, 95% CI=0.96-1.29, NS, respectively]. Covariates adjusted in the analyses included age, sex, income, education, marital status, physical activity, smoking and/or alcohol consumption, depression, anxiety, and a history of diabetes, hypertension, heart disease, cancer, or arthritis.

Conclusion: Our analysis indicated that both short and long sleep durations were associated with dissatisfaction with quality of life, but black short sleepers were at increased risk of reporting dissatisfaction with quality of life compared with white short sleepers. These findings are consistent with data suggesting that blacks are at greater risk for metabolic disorders associated with short sleep.

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0764

SLEEP QUALITY, SLEEP DISORDERED BREATHING, AND INSOMNIA IN US HISPANIC PATIENTS

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Introduction: There is a paucity of information on the epidemiology of sleep disorders in Hispanics. We determined the prevalence of sleep disorders in a cohort of Hispanics in South Florida.

Methods: Hispanic patients were recruited from 3 University of Miami, Sleep, Internal Medicine(IM) and Pulmonary clinics as part of a study on Sleep Knowledge and Compliance in Hispanics. Participants completed validated questionnaires, evaluating sleep quality (SQ, PSQI), health-related quality of life (HRQOL), risk of sleep disordered breathing (SDB), and prevalence of insomnia (ISI). Group comparisons were made using Chi-square or one way ANOVA as appropriate.

Results: 156 participants, 63% female, with Hispanic origin distribution of 46% Cuban American, 29% Central American, and 25% from South America were enrolled with mean age 58±15, BMI of 30±6 and HRQOL score 69.4±19.4. Poor SQ was reported by 67% of the cohort with mean PSQI score of 7±5; 65% screened high risk for SDB. Moderate to very severe difficulty in initiating sleep was reported in 28% of patients, with 35% having difficulty maintaining sleep, and 25% reporting waking up too early. Poor SQ was more common in Hispanic patients seen in Sleep clinics (89%, mean PSQI 10±4) compared with IM clinic participants (53%, mean 6±4) and pulmonary patients (71%, 8±5). The prevalence of increased risk for SDB was greatest in Sleep clinic patients (90%) compared with IM clinic (52%), and pulmonary clinic patients (59%).

Conclusion: This is one of the first studies to show that poor sleep quality, SDB and insomnia are prevalent in a diverse cohort of US Hispanic patients.

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0765

STUDY OF SLEEP QUALITY IN WOMEN BASED ON THE USE OF DIFFERENT TYPES OF SANITARY PADS DURING MENSTRUATION

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Introduction: Sleep complaints in women are evident during their menstrual periods. This suggests that external factors may further compromise one's quality of sleep during menstruation. The Objectives were to evaluate sleep quality (questionnaires) and objectively (polysomnography) in women using two different types of sanitary pads.

Methods: Seventeen volunteers (18-40 years) with menstrual cycles of 28-30 days, and reports of moderate to intense menstrual flow, and have a body mass index between 18 and 27 kg/m2 were included in this crossover study. The sleep assessments were made by polysomnography and by means of validated questionnaires (severity index of insomnia, Pittsburgh questionnaires, Berlin questionnaires, and restless leg syndrome). The first evaluation of sleep was performed during the follicular phase (7-10th day of the cycle - control situation). There were subsequent evaluations during the 2nd and 3rd day of the menstrual period, and a different type of absorbent (A or B) was used on each day. The volunteers were randomly assigned to an order of absorbent type use, AB or BA.

Results: The use of absorbent A or B did not affect the parameters of sleep (polysomnography) or the quality of sleep (questionnaires). All results obtained with the use of the absorbents were not statistically different from the control situation and were within the normal limits.

Conclusion: In this study, we found no significant difference in sleep quality between the follicular phase and the menstrual period, and further, the use of absorbent over consecutive nights during the same menstrual cycle was not associate with sleep changes.

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0766

LIVING WELL: DO HEALTH EDUCATION COLLEGE STUDENTS SLEEP BETTER?

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Introduction: College students are widely believed to be sleep-deprived, but students who chose an elective Health and Wellness course may self-select healthier behaviors. We sought to learn about the sleep and health habits of Health and Wellness students at a major US University.

Methods: Students enrolled in an elective general education "Living Well" class in the school of Health, Physical Education and Recreation were asked to take a voluntary, anonymous, online survey about sleep and health behaviors. Data were collected for one month. This project received IRB exemption from Indiana University and the University of Kentucky.

Results: Of a possible 86 students (45 women), 46 (54%) took the survey. Of these, 72% were women, their mean age was 18.6 years and their mean BMI was 22.8 Kg/m2. Their mean high school GPA was 3.7. Only 6.5% were smokers; 4.3% were abstinent from alcohol. The mean Epworth sleepiness score was 9. Hours of sleep on week nights correlated inversely with Epworth score (p<0.0001, linear model). 44% got < 6 hours of sleep on weeknights, and 35% got > 9 hours of sleep on weekend nights. Students who slept > 8 hours on week nights had lower Epworth scores (p<0.005, t-test), but lower high school GPAs (p<0.05, t-test). Students who exercised more were less sleepy (p=0.05, t-test). One third had been in a crash in which they were the driver. Students who reported dozing when a passenger in a car on the Epworth were more likely to report crash (p<0.05, logistic regression). Only 13% of students never napped, and there was a relationship between napping and self-reported crash (p<0.05, logistic regression).

Conclusion: Even college students in an elective health class have erratic sleep schedules. Napping is related to crash risk.

0767

IS HEALTHY BEHAVIOR ASSOCIATED WITH BETTER SLEEP?

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Introduction: Although many studies have demonstrated that population-level short sleep duration is related to negative health outcomes, these measures do not account for differences in sleep need. One way to assess short sleep duration relative to need is to measure perceived sleep insufficiency. Another important health predictor is healthy behavior (related to diet, exercise, smoking and alcohol). It may be the case that one pathway that healthy behavior exerts impact is through insufficient sleep. To investigate this, the current analysis explores how healthy behaviors are related to sleep insufficiency.

Methods: Data from the 2009 Behavioral Risk Factor Surveillance System (BRFSS) were used. BRFSS is an annual, state-based, random-digit-dialed telephone survey of American adults(18+). Analyses included only those who provided data on all items (N=324,722). Insufficient sleep was measured with: "During the past 30 days, for about how many days have you felt you did not get enough rest or sleep?" Health behaviors included diet (fruit/vegetable servings per day, 5+ servings, category[0,<3,<5,5+]), exercise (any past month, any leisure-time past month, minutes vigorous, minutes moderate, minutes total), current smoking, and alcohol (drinks/month, heavy drinking). Covariates included age, sex, education, income, race/ethnicity, and BMI.

Results: Covariates accounted for 51% of insufficient sleep (F(10,324711)=1735.8,p<.0001). Together, health behaviors (diet/exercise/smoking/alcohol) accounted for an additional 16% (Fpart(12,324699)=474.250,p<.0001). Individually, diet accounted for 1% (Fpart(3,32708)=120.9,p<.0001), exercise 10% (Fpart(6,324705)=558.9,p<.0001), smoking 8% (Fpart(1,324710)=2719.2,p<.0001), and alcohol <1% (Fpart(2,324709)=45.5,p<.0001) above covariates. In a fully-adjusted model (all covariates/predictors), all predictors are significant except moderate physical activity, servings of fruit/vegetables, drinks/month and heavy drinking. In stepwise analysis, current smoking (Fpart(1,324710)=2719.216,p<.0001) and leisure-time exercise (Fpart(1,324709)=2066.217,p<.0001) explained a combined 14% above covariates.

Conclusion: Health behaviors (diet/exercise/smoking/alcohol) were individually and collectively associated with insufficient sleep, after controlling for socioeconomic and demographic factors. Interestingly, broad measures of current smoking and any leisure-time activity in the past month were the best unique predictors.

0768

IDENTIFICATION OF NATURAL SHORT SLEEPERS BASED ON BOUT LENGTH DATA OBTAINED FROM POLYSOMNOGRAPHY

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Introduction: Traditionally "natural short sleepers" are defined by reported habitual sleep time. This approach can't differentiate short sleepers from chronic sleep restricted individuals. Theoretically the duration of sleep bouts track sleep drive and duration of wake bouts reflects wake drive. Natural short sleepers should have short sleep and be alert during wakefulness, while sleep restricted individuals would have short sleep but low wake drive. We hypothesize that on an 8.5 hour polysomnogram (PSG), individuals with short sleep bout duration and long wake bout duration are short sleepers and those with long sleep bouts and short wake bouts are sleep restricted. We identified short sleepers based on bout lengths on all night PSG and verified this using an MSLT and sleep-wake reports.

Methods: From a population based sample (n=618) 86 randomly selected subjects were evaluated with sleep dairy, sleep-wake symptoms, 8.5 hour PSG and MSLT. From PSG data, 4 phenotypes were created based on a median split of sleep(19.38 min) and wake(2.18 min) bout lengths. We hypothesized that the Short Sleep /Long Wake group would characterize short sleepers and the Long Sleep/Short Wake group would characterize insufficient sleepers. We compared these two groups in terms of traditional sleep measures, MSLT, and daytime symptoms.

Results: The PSG Sleep efficiency for SS/LW group was 70%(SD±12) and for LS/SW was 96%(SD±2.5)(p<01). The ESS for SS/LW was 7.3(SD±3) and LS/SW was 9.7(SD±4.9)(p>.10) and the MSLT for the SS/LW group was 14.3 min(SD±3.84) and LS/SW group was 9.8 min(SD±4.87) (p<01). Diary data showed similar reported total sleep time (7.0 hours) and nap time (15-26min) in both groups. The frequency of insomnia symptoms did not differ between the groups (p>0.1).

Conclusion: Bout length data is a useful measure in identifying different sleep phenotypes such as natural short sleepers.

0769

TRACKING THE DYNAMICS OF THE EFFECTIVENESS OF SLEEP

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Introduction: Sleep physiology and pathology can be tracked by several methods-such as multiple nights of polysomnography, oximetry, and actigraphy. A new method of estimating sleep quality is the ECG-spectrogram, where high frequency cardiopulmonary coupling is the biomarker of effective and restorative sleep. This biomarker associates strongly with relative rather than absolute delta power, periods of stable breathing, strong sinus arrhythmia, and blood pressure dipping. The M1 (Embla) is a device with multi-night recording capability for actigraphy, ECG and body position.

Methods: 2 weeks of nightly recordings with the M1 were obtained from 5 healthy adult subjects (age range 22-32, 2 female) screened with polysomnography to exclude sleep apnea, and one 58-year old male with sleep apnea. Summary metrics and intra-class coefficients (ICC) were calculated. Data from 10 subjects (each) with and without sleep apnea are expected to be available for the meeting. Sleep periods were estimated from actigraphy.

Results: Analysis of variance showed that within individual night-to-night variability was not, but variability between subjects were, statistically significant. With just 6 subjects, the ICC for high, low and very low frequency % (of estimated sleep period) and duration were, respectively: 0.41, 0.44, 0.13, 0.32, 0.08, and 0.18

Conclusion: Sleep quality can be readily tracked across multiple nights using the ECG-spectrogram. Intra-individual variability of high frequency coupling is relatively low, and may represent a stable phenotype. Effects of sleep therapies could be assessed in a non-intrusive and cost-effective manner.

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0770

STABILITY AND REPRODUCIBILITY OF SLEEPINESS AND SLEEP PROBLEM PHENOTYPES OVER 4-YEAR INTERVALS IN THE WISCONSIN SLEEP COHORT STUDY

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Introduction: It is not clear whether sleep-related characteristics—including objective and subjective sleepiness, insomnia symptoms, and symptoms associated with narcolepsy—represent "stable phenotypes" in generally healthy populations unselected on clinical features. To investigate stability of these sleep-related phenotypes, we examine longer-term (4-year) consistency of these characteristics in Wisconsin Sleep Cohort Study participants.

Methods: The Wisconsin Sleep Cohort sample comprises 1524 subjects (45% female, 33-71 years old) who had baseline in-laboratory sleep evaluations and sleep-health interviews. Subjects have repeat studies at 4-year intervals. To examine propensity to fall asleep, we used a subset of 440 subjects who underwent Multiple Sleep Latency Tests (MSLT) and completed the Epworth Sleepiness Scales (ESS) twice in a 4-year period. In addition, an overlapping subset of 841 subjects completed sleep-health interviews assessing narcolepsy and insomnia symptoms, also at 4-year intervals. We created binary categorizations of the sleep variables according to standard criteria (e.g., MSLT<5 minutes; ESS<8) as well as using self-reported symptom frequency to categorize subjects as having narcolepsy symptoms (3 individual symptom items examined) and insomnia symptoms (4 symptom items). We calculated Kappa statistics to examine consistency of the sleep-related characteristics over the 4-year intervals.

Results: Comparing baseline and 4-year follow-up studies within-subjects, the kappa statistics for categorizing subjects as MSLT<8 minutes was 0.33 (95% CI=0.24-0.42); for MSLT<5 minutes, kappa=0.23 (95% CI=0.12-0.34); and for ESS>10, kappa=0.57 (95% CI=0.49-0.65). Self-reported narcolepsy and insomnia symptom reproducibility ranged from kappa=0.36-0.47, and kappa=0.34-0.46, respectively.

Conclusion: There is considerable longer-term intra-subject variability in objectively and subjectively-assessed propensity to fall asleep, and in self-reported narcolepsy and insomnia symptoms. The most stable characteristic was propensity to fall asleep as measured by the Epworth Sleepiness Scale. While there is moderate intrasubject stability in sleep-related phenotypes over 4-year intervals, extrinsic factors and measurement variability are important contributors to within-subject variation.

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0771

EFFECT OF TOTAL SLEEP TIME ON QUALITY OF LIFE AND DEPRESSION

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Introduction: Sleep duration has been associated with an increased risk of mortality, but there is little research looking at how sleep duration affects quality of life and depression. This study looks at the relationships between sleep duration, quality of life and depression.

Methods: Since January 2008, the Cleveland Clinic Sleep Disorders Center has collected patient-entered validated questionnaires, including an assessment of overall quality of life, the EuroQol (EQ-5D) and a screening tool for depression, the Patient Health Questionnaire (PHQ-9). This study analyzed data from January 2008 to May 2010. Sleep time categories were defined as: short sleep - <6 hours per night, long sleep - > 9 hours per night, normal sleep - 6-9 hours per night. A multi-variable logistic regression model was fit to adjust for demographic differences. The model included sleep time categories, age, gender, race, marital status and visit type (new vs. established). Generalized estimating equations were used to account for multiple visits per patient.

Results: 10,654 records were analyzed (4737 new, 5917 established). Mean age was 51.6 years (SD 14.8), and 52% were female. Fifty-nine percent were married, and 79% were Caucasian. Short and long sleepers had higher scores on the PHQ-9 and lower scores on the EQ-5D compared to those who slept for 6-9 hours, indicating greater depression severity and lower quality of life. The amount of change between short and long sleeper groups with normal sleepers was similar (mean PHQ-9 scores: <6 hours: 10.6, 6-9 hours: 6.6, >9 hours: 10.5, mean EQ-5D scores:< 6 hours: 0.69, 6-9 hours: 0.74, >9 hours: 0.68). Short and long sleepers were significantly different than normal sleepers in all cases (p < .0001 for all comparisons).For patients who reported having perfect health (based on an EQ-5D score of 1), there was a higher percentage who slept for 6-9 hours (30.8%), and the PHQ-9 scores were significantly lower compared to short and long sleepers (in the perfect health group).

Conclusion: Short and long sleepers have a lower quality of life and screen higher for depression. The amount of change in quality of life and depression are similar for short and long sleepers.

0772

ASSESSING THE INTERACTION BETWEEN SLEEP, STRESS AND CATECHOLAMINES: A HOME-BASED FEASIBILITY STUDY

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Introduction: Emerging research suggests that psychological stress and sleep disruption synergistically activate biological stress systems. We report a feasibility study of this interaction in a naturalistic setting, focusing on urine catecholamines as a physiological marker of stress.

Methods: A convenience sample of 5 women and 5 men was studied. Outcome variables included: Surveys on stress and sleep (PSS - perceived stress scale; Pittsburgh Sleep Quality Index - PSQI); sleep diaries, actigraphy, and two 12 hour urinary catecholamine samples (day:8 AM to 8 PM, night: 8 PM to 8 AM). Actigraphy data covered 48 hours. Surveys were completed during day 1 of actigraphy. Urine collection coincided with the second day of actigraphy. Urine catecholamines (norepinephrine - NE; epinephrine - Epi) were analyzed with HPLC.

Results: Catecholamines (normalized to creatinine) demonstrated the expected diurnal differences. Daytime NE (196.4 ± 23.2) and Epi (87.5 ± 21.2) were greater than nighttime NE (144.8 ± 7.4) and Epi (41.7 ± 13.4) ($p = 0.048$; 0.084, respectively). The day/night ratio of NE was significantly correlated with day 1 sleep onset latency and sleep efficiency ($r = 0.79$, $p = .006$; $r = -0.6$, $p = .064$, respectively). The day/night ratio of Epi was significantly correlated with day 2 sleep efficiency and wake after sleep onset ($r = 0.83$, $p=.005$; $r= -0.68$, $p=.045$, respectively). PSS score was not significantly associated with any catecholamine measure, however, PSS was positively correlated with daytime dysfunction due to poor sleep on PSQI ($r = 0.71$, $p = 0.022$).

Conclusion: Trends towards significant relationships between sleep variables and catecholamine excretion were observed, but these inferences are exploratory, given the small, homogeneous sample. These pilot results support the feasibility of collecting data on stress, sleep, and sympathetic activity in a community-dwelling sample. Sleep variables tended to correlate with diurnal rhythms of urine catecholamine levels. As sleep loss is a stressor, this suggests that urine catecholamines can be responsive to prior or concurrent sleep loss.

0773

THE RELATION BETWEEN SEDENTARISM, SLEEP AND CARDIAC RHYTHM: A POPULATION BASED STUDY

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Introduction: The sympathetic nervous activity is believed to increase in sedentary healthy individuals, while vagal tonus decreases in those who habitually perform exercise. It seems that autonomic outflow is regulated in a state-specific manner during sleep and exercise. Nevertheless, the effect of sedentarism on sleep is not well established. Therefore, the aim of this study is to evaluate the influence of regular physical activity and sedentarism on autonomic nervous system and sleep parameters in a general population.

Methods: A sample size of 1041 volunteers was defined in order to allow for prevalence estimates with 3% precision. A full-night PSG was performed on a digital system at the Sleep Institute of Sao Paulo, Brazil. Clinical evaluation was performed before preparation for the PSG. The ECG channel of PSG was analyzed in a Holter system (Cardios®, São Paulo, Brazil). The ECG characteristics included: Heart rate, QT and PR interval, ventricular and atrial arrhythmias, pauses and heart rate time domain variability. The population was divided into sedentary

and non-sedentary using a questionnaire. ClinicalTrials.gov (Identifier NCT00596713). Statistical analysis: General linear model, Chi-Square, Binary Logistic Regression, values in mean and standard error, $p \leq 0.05$

Results: Of the 1041 participants, 786 were sedentary (43.8% male) and 255 non-sedentary (47.8 % male; $p=0.2$). The mean age were 41.2 ± 0.6 years in sedentary and 45.3 ± 1.0 years in non-sedentary, $p<0.001$. There were differences in PSG parameters between sedentary and non-sedentary demonstrated by AHI (7.9 ± 0.5 events/h vs. 10.2 ± 0.9; $p=0.02$), stage 2 ($54.3 \pm 0.4\%$ vs. 56.0 ± 0.6; $p=0.01$) and REM sleep ($19.3 \pm 0.3\%$ vs. 18.1 ± 0.4; $p=0.01$). The incidence of ventricular arrhythmia were higher in sedentary (14.2 ± 2.6) compared to non-sedentary (3.3 ± 4.6; $p=0.04$). Heart rate variability demonstrated lower SDNNIDX in sedentary compared to non-sedentary (70.4 ± 2.0 ms vs. 66.2 ± 1.1 ms, respectively; $p=0.05$). These variables were included in the binary logistic regression model. We observed that SDNNIDX ($p=0.02$) was significantly associated to sedentarism (OR: 1.007; IC: 1.001-1.013). Sleep variables were not associated to sedentarism.

Conclusion: Physical activity reduces ventricular arrhythmias in a general population. This study suggests that heart rate variability, but not sleep variables, is associated to sedentarism.

0774

COLD EXTREMITIES DURING DAYTIME PREDICT NOCTURNAL BLOOD PRESSURE DIPPING: FIRST EVIDENCE FROM A STRUCTURED-DAYTIME AMBULATORY STUDY

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Introduction: Subjects whose blood pressure (BP) does not reduce at nighttime - non-dippers - are at greater risk for cardiovascular morbidity. Recent controlled lab studies have shown that nocturnal decline in BP is primarily caused by sleep. Important determinants of systemic BP include peripheral vascular resistance. However, the contribution of the peripheral skin blood flow has not been studied under real life conditions. The aim of the study was to show whether the diurnal patterns of skin temperatures (ST, indirect measure for skin vascular resistance) and BP are related, and whether ST can predict nocturnal BP dipping.

Methods: Participants were 56 subjects (f:m= 35:21, age: 58 ± 2yr: BMI 25.3 ± 0.6, medication: 66%, diagnosis: 70% glaucoma) who stayed in the University eye hospital of Basel for a two-day eye investigation under structured daytime activities (meal times; habitual bedtimes). During 24 hours, ambulatory recordings of ST (11 probes on distal and proximal sites, 1min intervals), BP and heart rate (half-hourly) were carried out (data collected over one year).

Results: ST exhibit highest levels during sleep phase and a bimodal daytime pattern with a peak around midday and a trough in the late morning and in the afternoon. In contrast, systolic, diastolic, mean arterial (MABP) BP and heart rate showed an inverse pattern, whereby the pattern of MABP nearly mirrored that of distal-proximal ST gradient (linear mixed effect model, AR(1), $p<0.001$; 24-hour mean values were not related). Nocturnal dipping ((wake phase MABP - sleep phase MABP)/ wake phase MABP)) was significantly correlated with low distal ST (but not with proximal ST) during daytime (10-16hr) ($p<0.002$). This finding was not confounded by gender, age, BMI, diagnosis, or medication.

Conclusion: It can be hypothesised that distal vasoconstriction during daytime (10-16hr) is functionally related to nocturnal BP dipping and maybe a predictor of clinical relevance.

0775

FEWER SPONTANEOUS AROUSALS IN INFANTS WITH APPARENT LIFE THREATENING EVENT

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Introduction: A deficit in arousal process has been implicated as a mechanism of Sudden Infant Death Syndrome (SIDS). Compared with control infants, SIDS victims showed significantly more subcortical activations and fewer cortical arousals than matched control infants. Apparent life threatening event (ALTE) is often considered as an aborted SIDS event. The aim of this study was to study the arousal characteristics of ALTE infants during the first months of life.

Methods: 35 ALTE infants were studied with nighttime polysomnography at 2-3, 5-6 and 8-9 months of age. 18 of the infants had mothers who smoked. The infants were born full-term and were usually supine sleepers. Sleep-state and cardiorespiratory parameters were scored according to recommended criteria. Arousals were differentiated into subcortical activations or cortical arousals, according to the presence of autonomic and/or electroencephalographic changes. The results were compared with those of 19 healthy infants with non-smoking mothers.

Results: During NREM sleep, the ALTE infants had fewer total arousals, cortical arousals and subcortical activations at 2-3 and 5-6 months ($p < 0.001$) than control infants. ALTE infants with smoking mothers had more obstructive apnea ($p = 0.009$) and more subcortical activations during REM sleep at 2-3 months of age ($p < 0.001$) than ALTE infants with non-smoking mothers.

Conclusion: Spontaneous arousals were differently altered in ALTE infants than in SIDS infants, suggesting an entity different from SIDS. ALTE infants with smoking mothers had arousal and respiratory characteristics that were similar to future SIDS victims, suggesting some common abnormalities in brainstem dysfunction.

0776

SUPPLEMENTAL MELATONIN DECREASES SLEEP LATENCY IN CHILDREN WITH AUTISM

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Introduction: Retrospective and small prospective studies have shown that supplemental melatonin promotes sleep in children with autism spectrum disorders (ASD). However, most studies have not used objective measures of sleep.

Methods: Children were ages 3-10 years, with a clinical diagnosis of ASD based on DSM-IV-TR criteria. Diagnosis was confirmed by the Autism Diagnostic Observation Schedule and by either clinical interview or the Autism Diagnostic Interview-Revised. All children had sleep delay, defined as inability to fall asleep within 30 minutes at least 3 nights a week. Medical causes of insomnia and primary sleep disorders were addressed prior to enrollment. Children on medications which affect melatonin pharmacokinetics were excluded. Parents were instructed in optimizing sleep habits prior to treatment. Objective measures of sleep were measured over 17 weeks with actigraphy (Phillips/Respironics/Mini Mitter) in conjunction with sleep diaries. All children received two weeks of an inert flavored liquid 30 minutes before bedtime and then began 1 mg of supplemental melatonin (Natrol ®). The child's response to melatonin was reevaluated every three weeks based on mean sleep latency (SL) Dose was increased every three weeks (from 1 mg, to 3 mg, to 6 mg, to 9 mg) until the child reached a satisfactory response (SAT-R), defined as SL within 30 minutes on 5 or more nights in the week. Once a SAT-R was achieved, the child remained on that melatonin dose for the remainder of the 17 weeks.

Results: Twenty-one children were included, two girls and 19 boys, with a mean age of 6 years [standard deviation (SD) = 2.2]. A SAT-R was reached in five children at 1 mg, 14 children at 3 mg, and two children at 6 mg. Mean sleep latency (minutes) improved with treatment compared to baseline [41 (SD 33.9) to 24.8 (SD 21.6); $p <0.0001$]; Wilcoxon-signed rank test. Improvements were also noted in sleep efficiency [73.9 (SD 9) to 78.3 (7.5); $p = 0.013$] and total sleep time (minutes) [430.4 (SD 73.1) to 460.5 (SD 66.5); $p = 0.029$] Fragmentation index, a measure of movement/restless sleep, did not improve. Actigraphy parameters did not change from when the SAT-R was achieved as compared to end of study. There were no adverse effects related to melatonin.

Conclusion: In this pilot work, we documented, with actigraphy, that supplemental melatonin decreases sleep latency and improves other sleep parameters, with stability over several weeks. Randomized clinical trials of supplemental melatonin appear warranted.

0777

NEUROCOGNITIVE MORBIDITY IN CHILDREN WITH DOWN SYNDROME AND OBSTRUCTIVE SLEEP APNEA

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Introduction: Children with Down syndrome (DS) are at increased risk for developing obstructive sleep apnea (OSA), and laboratory polysomnographic (PSG) studies estimate the prevalence to be between 30-79% (Dyken et al., 2003). In typically developing children, OSA is associated with increased subjective sleepiness and mood disturbance, behavior problems, and deficits in attention, memory, and executive functions (Owens et al., 2009).

Methods: Thirty-four children with DS (age range: 7-18 years, age M = 12.02; 17 girls) participated in this study. Nocturnal sleep was assessed with ambulatory in-home PSG. Neurocognitive abilities were assessed with the Arizona Cognitive Test Battery (ACTB) for DS (Edgin et al., 2010).

Results: Seventy-five percent of our sample (n = 25) met criteria for pediatric OSA (AHI > 1.5), and the mean AHI was 7.5. We found trends for an association between OSA severity and chronological age, and an association between age and performance on the ACTB. In order to assess effects of OSA on cognition, we divided our sample into 14 chronological age-matched pairs, in which one member of each pair had a higher AHI (M = 14.5, SD = 16.66) and the other member had a clinically less insignificant AHI (M = 1.8, SD = 1.41). Groups were equivalent on gender, IQ, and surgical status. Participants in the high AHI group performed worse on the CANTAB Intra-Extra Dimensional Set Shift task stages completed (t (10) = -2.354, p = 0.04; d = -0.93), and showed a trend toward worse performance on the CANTAB Paired Associates Learning task mean trials to success (t(13) = 1.937, p = 0.07; d = 0.59).

Conclusion: This study is the first demonstration of a relationship between OSA and neurocognitive morbidity in children with DS, emphasizing the importance of early detection and treatment of sleep apnea in this syndrome.

0778

OBJECTIVE ASSESSMENT OF SLEEP DURATION IN OBESE ADOLESCENTS

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Introduction: Obesity has reached epidemic proportions in children during the past 30 years as has insufficient sleep. Adolescents in particular often have insufficient sleep, which may promote obesity. Our group previously showed that in an adolescent obesity clinic, less sleep was associated with decreased response to weight loss intervention (B. Sallinen, Longer Sleep Duration Predicts greater 3 month Weight Loss in Obese Adolescents-PAS 2010). We therefore sought to characterize using objective data the amount of sleep typically obtained by these patients with attention to race and gender variables that have been associated with sleep durations in some studies.

Methods: Subjects were obese adolescents (BMI [body mass index] ≥ 95th percentile calculated at initial visit) aged 11-18 years who enrolled in a weight loss program. At enrollment total sleep time was measured with a SenseWear armband monitor worn for > 22 hours on each of 2 consecutive days (measuring weekday and weekend duration). The SenseWear Pro2 activity monitor includes a dual axis accelerometer and sensors that measure heat flux, galvanic skin response, skin temperature, and near-body ambient temperature and includes a validated algorithm to estimate sleep time and patterns. Average daily sleep was assessed in Caucasian and non-Caucasian adolescents by gender.

Results: Adolescents (n=58) included 38 girls; mean age was 14 ± 2 years; average BMI was 42.0 ± 9.4 kg/m2 and 37 (67%) were Caucasians. Among boys, Caucasians (n=14) and non-Caucasian (n=3) slept on average weekdays 6.8 ± 1.4 hours and 6.9± 1.2 hours respectively and on weekends 8.2 ± 1.1 hours and 8.7 ± 1.3 respectively. Among girls Caucasians (n=25) and non-Caucasian (n=16) slept 7.8 ± 0.7 hours and 6.4 ± 1.0 hours respectively on weekdays and 7.3± 1.7 hours (n=23) and 7.5 ± 1.3 hours on weekends.

Conclusion: Sleep duration is deficient for this age, in comparison to recommended amounts, both on weekdays and weekends, across races and for both genders. These data suggest an opportunity for improved sleep and possibly improved effectiveness of weight-loss interventions through efforts to increase sleep in these patients.

0779

VALIDATION OF A PARENTAL REPORT OF CHILD SLEEP VERSUS DIRECT ACTIGRAPHIC ASSESSMENT OF SLEEP

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Introduction: Diagnosis and treatment of pediatric sleep disorders as well as the determination of children's sleep in pediatric sleep research relies on accurate measurement of sleep. Parental reports of children's sleep are one of the easiest and least expensive methods for estimating sleep timing in children, particularly in large populations, but may or may not yield accurate results. A goal of this study was to validate prospective parental report of weekly child sleep duration versus actigraphy assessed over 1 week.

Methods: Seventy-five children (6-11 years of age) participated in the week-long study. Study procedures involved 1) a parent prospectively completing a 1-page questionnaire of their child's sleeping habits, obtained prior to actigraphy collection, 2) each child wearing an actigraph (Spectrum Respironics/Philips) on the non-dominant wrist for one week, and 3) a parent completing daily sleep diaries about their child during the week of actigraphy collection. We compared parental report of child sleep duration with the actigraphic sleep duration using correlation analysis and mixed model ANOVA.

Results: The mean±SD sleep duration from parental report (10.10h±0.70h) and actigraphy (8.95h±0.50h were significantly correlated (Pearson r=0.54, p<0.0001) with a mean difference of 1.12±0.57h. Parental report of sleep duration was significantly longer than actigraphic sleep duration (p<0.01). Mean diary Time in Bed (10.20±0.63) was more closely related to parental report of child sleep (Pearson r=0.60, p<0.0001), with a mean difference of 0.12±0.58h.

Conclusion: Parental report of child sleep duration was significantly and systematically longer than total sleep time using actigraphy. This overestimation by more than an hour appears to be due to parental reports of when children are "going to bed" rather than actually sleeping. These findings impact clinical diagnosis in pediatric patients and sleep research investigations where a parental report of child sleep duration is used.

0780

DAYLIGHT SAVINGS TIME AND THE IMPACT ON STANDARDIZED TEST SCORES IN EARLY ADOLESCENTS

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Introduction: Previous research has shown that sleep loss affects academic performance in youth. With the push towards "high stakes" standardized testing, there are concerns that external factors may unfairly bias results. As the shift to Daylight Savings Time (DST) has an acute affect on sleep, students and schools assigned to standardized testing in the days soon after the time shift may be at a disadvantage.

Methods: We used the Early Childhood Longitudinal Study - Kindergarten Class of 1998-1999 (ECLS-K) data, with sample weights employed for all analyses to approximate a nationally representative cohort. Students were included if they had data for the spring of both the 8th and 5th years following kindergarten (N = 8,821), corresponding to 8th and 5th grade for the majority of youth. Regression analyses examined the impact of testing dates in the week following the DST shift (March 11 - March 18, 2007) on standardized T-scores for the 8th year reading, math, and science tests. Analyses also controlled for student gender, scores from the 5th year tests, and the date of testing, the latter to take into account the fact that students testing later in the spring would have received more instruction and be expected to score higher than students testing earlier.

Results: The sample-weighted population was 52% male, with 86% in the 8th and 13% in the 7th grades. Test dates during the week immediately following the switch to DST were associated with significant decreases in T-scores for Math (-1.52, 95%CI -2.45 to -0.60) and Science (-1.13, 95%CI -2.07 to -0.18), but not Reading (-0.07, 95%CI -0.96 to 0.82).

Conclusion: The shift to DST is a significant risk factor for decreased math and science scores on standardized testing, most plausibly as a result of acute sleep loss. States and school districts should take this into account when setting testing dates.

0781

THE SUSTAINED IMPACT OF A HEALTHY MEDIA USE INTERVENTION ON PRESCHOOL CHILD SLEEP

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Introduction: While there are many causes of childhood sleep problems, recent research has highlighted the role of media use. We examined whether an intervention promoting healthy media use could impact preschool sleep problems.

Methods: We are conducting a randomized, controlled trial of an intervention aiming to improve the media diet (TV, movies, computer and video games) of children ages 3-5 by decreasing violent or age-inappropriate content, and replacing it with prosocial, developmentally positive content. Parent-report surveys were collected at baseline, 6 and 12 months. Sleep questions were drawn from the Child Sleep Habits Questionnaire, a validated measure assessing the frequency of problems with sleep onset latency, night awakenings, nightmares, difficulty waking in the morning, and daytime tiredness. Total sleep problem scores could range from 5-15. Linear and multinomial logistic regressions were used to test the impact of the intervention on the trajectory of sleep problem scores after controlling for baseline sleep and behavior problem scores.

Results: The study enrolled 615 children, of which 404 have completed all three timepoints; 13% have a trajectory of improvement, 5% of worsening, and 82% of stability. Children in the intervention group had significantly greater improvement in sleep problem scores between baseline and six months, with a difference in score change of 0.29 between groups (95%CI 0.05-0.54). The effect was sustained to month 12, where the difference between groups was 0.30 (95%CI 0.06-0.54). The intervention group was also significantly more likely to have a trajectory of improvement (OR=2.86, 95%CI 1.25-6.53). The intervention effect was significantly greater for boys (OR=9.00, 95%CI 2.38-33.93) than girls (OR=0.97, 95%CI 0.29-3.24).

Conclusion: A healthy media use intervention had a significant and sustained impact on child sleep, despite not directly targeting sleep habits. More research is needed on the mediators involved to explore why these effects were observed largely in boys.

0782

PRELIMINARY VALIDATION OF THE INSOMNIA SEVERITY INDEX FOR CHILDREN (ISI-C)

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Introduction: Most questionnaires assessing pediatric sleep disturbances are relatively long and address the whole spectrum of sleep disorders. There is a need for brief questionnaires targeting more specific conditions such as insomnia. The objective of this study was to validate a pediatric version of the Insomnia Severity Index (ISI).

Methods: The ISI for Children (ISI-C) was adapted from the adult version. The original version assesses, for the past month, insomnia symptoms, sleep satisfaction, noticeability of difficulties, distress, and daytime consequences. The wording of items was modified so that parents could answer for sleep difficulties experienced by the child. The noticeability item was dropped and the daytime consequences and satisfaction items were duplicated to assess these dimensions in both the parent and the child. The final version contained eight items rated on five-point scales (total score ranged from 0-32). It was administered to 62 healthy school-age children (32M/30F, mean age = 9.9 years old, SD = 1,75, range = 6-12), along with the Children Sleep Habits Questionnaire (CSHQ), sleep diaries, and actigraphy.

Results: Good internal reliability was suggested by a Cronbach's alpha coefficient of .79. Convergent validity was supported by a significant correlation with the CSHQ total score (r = .53, p < .001), as well as with

the Bedtime Resistance (r = .43, p < .01), Sleep Duration (r = .37, p < .01), and Night Wakings (r = .36, p < .01) subscales. The total ISI-C score did not correlate with actigraphic data, but its sleep onset insomnia item was correlated with sleep latency measured with actigraphy (r = .34, p < .01).

Conclusion: The ISI-C shows adequate psychometric properties and could be a useful assessment questionnaire of insomnia in children. Test-retest reliability remains to be documented, as well as its validation with clinical samples of children with sleep disorders.

Support (If Any): This research was supported by a student scholarship awarded to Vincent Moreau from the Canadian Institutes of Health Research.

0783

AGE-RELATED GENDER DIFFERENCES IN THE PREVALENCE OF INSOMNIA IN A COMMUNITY SAMPLE OF YOUNG CHILDREN

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Introduction: Few population-based studies have examined the prevalence of insomnia and its association with sociodemographic factors in children.

Methods: A sample of 700 children (6-12 yr) from The Penn State Child Cohort underwent a 9-hour polysomnogram, a physical examination and a parent completed sleep questionnaire. Insomnia was defined as a parent-reported difficulty falling (DFA) and/or staying (DSA) asleep.

Results: The prevalence of insomnia was 19.2%, with 44.7% reporting DFA, 26.0% DSA, and 29.3% both. There were no significant differences between girls (20.0%) and boys (18.3%) or between age groups of 5-7, 8-10, and ≥ 11 yr (21.2%, 16.5%, and 24.3%, respectively) in the prevalence of insomnia. However, significant age differences were found within girls so that those ≥ 11 yr showed a higher prevalence of insomnia (30.1%) as compared to those 5-7 (21.4%) or 8-10 yr (15.9%). Furthermore, similar findings were found in terms of insomnia subtypes: girls ≥ 11 yr had the highest prevalence of DFA (21.3%) as compared to those with 5-7 (8.2%) or 8-10 yr (7.1%) , followed by those with both DFA and DSA (with a prevalence of 9.4%, 4.8%, and 11.5% for those with 5-7, 8-10, and ≥ 11 yr, respectively). Consistently, within girls, those ≥ 11 yr had a higher prevalence of insomnia with "long" (≥ 21 minutes) sleep latency (26%) as compared to insomnia with normal (< 21 minutes) sleep latency (4.1%). In contrast, the prevalence of insomnia within boys was similar across the 5-7, 8-10, and ≥ 11 yr age groups (21.1%, 17.6%, and 17.5%, respectively) and did not change significantly when examined across insomnia subtypes, either based on subjective complaints or objective sleep latency.

Conclusion: These data suggest that gender differences in insomnia may start during the peripubertal period. These gender differences are most likely explained by hormonal and psychological changes associated with puberty, presented earlier in girls.

0784

CIRCADIAN MISALIGNMENT IN CHILDREN PRESENTING WITH INSOMNIA SYMPTOMS TO THE PEDIATRIC SLEEP DISORDERS CLINIC: DETECTION AND PREVALENCE

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Introduction: Evaluation and management of pediatric insomnia complaints often overwhelms the busy clinician. Circadian rhythm disturbances may play a significantly under recognized role in pediatric insomnia complaints. The purpose of this study was to estimate the prev-

alence of circadian misalignment in children referred for "insomnia" to a sleep specialist.

Methods: Data were collected by chart review of patients referred to a pediatric sleep medicine clinic in a tertiary academic medical center during a 12-month period. Patients with known chromosomal abnormalities were excluded. Insomnia symptoms included complaints of difficulty falling asleep and staying asleep/night wakings. Circadian misalignment (CM) was identified when the parent reported that the patient had difficulty falling asleep and had >2 hours difference in wake time on weekdays vs. weekends. Categorical data were assessed with Fisher's exact test and continuous data with unpaired t-tests.

Results: Sample characteristics: N=70, mean age 8.8 ± 5.7, 41 (58.6%) females. Of referrals received, 68% came from pediatricians and 32% from other specialists. Neurodevelopmental disorders were present in 44 (62.9%) of patients and psychiatric co-morbidities were seen in 20 (28.6%). Prior to consultation, hypnotic medication was prescribed for 19 (32.8%) patients. CM was present in 30 (42.9%) of the referrals. Children with CM were significantly older [mean age 12.9 ± 4.15 versus 5.7 ± 4.6 in the non-CM group (p< 0.0001)]. There were no group differences for gender, prior hypnotic treatment, or neurodevelopmental co-morbidities.

Conclusion: CM may masquerade as "insomnia" in a substantial proportion of children referred for insomnia evaluations. These results underscore the importance of regular sleep wake schedules in the pediatric population.

0785

WEEKEND SHIFTS IN SLEEP TIMING ARE ASSOCIATED WITH DIMINISHED REWARD-RELATED BRAIN FUNCTIONING IN HEALTHY ADOLESCENTS

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Introduction: Adolescents experience developmental changes in circadian phase (delays) that conflict with early school start times, leading them to adopt irregular weekday-weekend schedules. Their weekend sleep/wake timing tends to be later, and thus closer to that dictated by their circadian clock. This pattern can lead to recurring circadian misalignment, which has been linked to adult depression and adolescent substance abuse. Given the disrupted reward function in these disorders, these associations suggest that circadian misalignment alters reward processing. The present analyses investigated the neural mechanisms that underlie these circadian-reward interactions by examining the association between reward-related brain function and weekend shifts in sleep timing in a sample of healthy adolescents.

Methods: We tested associations between the weekend shifts in sleep timing and the neural response to monetary reward using actigraphy and functional magnetic resonance imaging with a monetary reward functional magnetic resonance imaging paradigm in 56 healthy adolescents (31 females, aged 10-14). Weekend shifts were operationalized as the shift in midsleep from Saturday to Sunday night. Region of interest (ROI) analyses focused on the medial prefrontal cortex (mPFC) and ventral striatum, both of which are implicated in reward function. Regression analyses tested associations between weekend shifts and reactivity in these ROIs during reward anticipation vs. baseline, reward outcome vs. baseline, and win vs. loss outcome—using a threshold of p<.05 and minimum extent of 10 contiguous voxels. All analyses were adjusted for pubertal stage and sex.

Results: As a whole, the sample showed Saturday-Sunday midsleep advances of nearly an hour (M=0.81±1.15 hr). Greater advances in midsleep were associated with decreased striatal and mPFC reactivity during both reward anticipation and reward outcome. These associations remained significant during reward outcome even after adjusting for

mean sleep duration. Finally, mPFC reactivity during win vs. loss correlated with the advance in midsleep, suggesting a reward-specific effect.

Conclusion: Findings suggest that adolescent weekend shifts in midsleep, as a proxy for circadian misalignment, are associated with diminished reward-related mPFC functioning, which could reflect difficulty regulating response to reward. Thus, circadian misalignment could contribute to reward-related outcomes such as substance abuse, as well as other risk-taking behavior.

0786

POLYSOMNOGRAPHIC DIAGNOSIS OF OBSTRUCTIVE SLEEP APNEA: PEDIATRIC VS. ADULT RESPIRATORY RULES IN ADOLESCENTS

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Introduction: The American Academy of Pediatrics recommends polysomnography as the gold standard in the evaluation of obstructive sleep apnea (OSA). American Academy of Sleep Medicine (AASM) published criteria for scoring respiratory events differ between pediatric and adult algorithms. Because of the relative scarcity of pediatric sleep labs, AASM recommendations permit the scoring of sleep studies in adolescents using either published criteria. In this study, we compared scoring of respiratory events using adult vs. pediatric AASM criteria in overweight/obese adolescents referred to a large regional pediatric sleep center.

Methods: Overweight/obese adolescents aged 13-18 yrs presenting with habitual snoring were selected as a population at high-risk of having clinically significant OSA. All subjects underwent physical examination to determine Tanner stage and completed overnight polysomnography. Pediatric Sleep Questionnaire and parent/teen Quality of Life Questionnaire data was obtained.

Results: Sleep study data from thirty-three overweight/obese adolescents were scored by a single sleep technician. Mean age±S.D. = 15.2±1.4 years, mean BMI Z-score = 2.3±0.47. Pediatric criteria consistently resulted in a higher obstructive apnea hypopnea index (O-AHI median=3.0, range 0.2-80.2) compared to adult criteria using either the recommended adult scoring algorithm for hypopneas (median=0.9, range 0.0-74.5, p=0.001) or the alternate adult hypopnea scoring algorithm (median=2.0, range 0.2-76.9, p=0.01). When categorizing sleep apnea as primary snoring (AHI <2 events/hr), mild OSA (2≤ AHI <5) or mod+ OSA (AHI ≥5), more adolescents were identified as having primary snoring or mild OSA when using adult criteria compared to pediatric.

Conclusion: Respiratory events are common in habitually snoring overweight/obese adolescents. Use of adult criteria in the scoring of respiratory events in adolescents results in the scoring of significantly fewer respiratory events. Further studies are needed to delineate whether OSA related sequelae and treatment outcomes are better predicted by polysomnographic events scored by adult or pediatric criteria in symptomatic adolescents.

0787

REFINEMENT OF A SCORING SYSTEM FOR AMPLITUDE-INTEGRATED EEG IN PRETERM INFANTS

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Introduction: The developing brain undergoes a time of rapid growth during the third trimester when preterm infants are most susceptible to neural disturbance and injury. Sleep-wake patterns are a vital element of brain activity, and reflect healthy brain maturation. Amplitude-integrated electroencephalography (aEEG) is limited channel EEG for continuous monitoring of brain activity. aEEG interpretation relies upon visual pattern recognition. However, there is no uniform classification standard, thus limiting generalizability for practice and research. The purpose of this study was to refine and operationalize an existing scoring system for preterm infant aEEG interpretation.

Methods: Single-channel aEEG was recorded in the neonatal intensive care unit from 16 medically stable preterm infants (mean postmenstrual age 34.1 ± 1.5 weeks, mean postnatal age 22.6 ± 8.5 days). Each infant was recorded once between caregiving and feeding episodes for approximately 3 hours. Tracings were evaluated visually and scored using a modified aEEG scoring system comprising four background variables (continuity, presence of cycling, amplitude of lower border, and bandwidth). Scoring varies by variable with ordinal ranges 0-2, 0-4, 0-5 and possible total score of 13. Two investigators independently completed scoring of each recording. Percent agreement for each variable was calculated for inter-rater reliability.

Results: 14 of the 16 recordings with satisfactory aEEG quality were analyzed. Percent agreement in each variable resulted in: continuity 100%, cycling 64% (9/14), amplitude of lower border 94% (13/14), and bandwidth 57% (8/14).

Conclusion: Findings indicate that of the four variables, cycling and bandwidth were more challenging to score. Although quantifiable and more readily measurable, the revised scoring was still quite subjective. A further refined aEEG scoring criteria may enhance the identification of preterm infant aEEG patterns. Reliable methods for objective scoring including presence and description of cycling between sleep and wake states hold promise for research in preterm brain monitoring.

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0788

EFFICACY OF AN INTERNET-BASED INTERVENTION FOR INFANT AND TODDLER SLEEP DISTURBANCES: ONE YEAR FOLLOW-UP

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Introduction: In a previous study, we found that an internet-based intervention for infant/toddler sleep disturbances was beneficial in improving multiple aspects of young children's sleep, as well as maternal sleep. The aim of this study was to assess the efficacy of this intervention one year later.

Methods: The initial study included 264 mothers and their children (6-36 months), with families randomly assigned to a control or one of two intervention groups [Customized Sleep Profile (CSP) or CSP + prescribed bedtime routine]. One year later, 171 (65%) completed a brief 10-question survey.

Results: Results of repeated measure ANOVAs (p<.001) demonstrated significant improvements in sleep latency, difficulty falling asleep, number/duration of night wakings, longest continuous sleep period, and maternal confidence in managing their child's sleep in the two intervention groups compared to baseline (effect sizes = 0.34 to 0.53). In addition, children in the CSP + prescribed routine group had significantly more total sleep time at night. Children in the control group, in which no changes were seen in the initial study, showed improvements in the number/duration of night wakings and longest continuous sleep period (ES = 0.25 to 0.46). Mothers in all groups were less likely to describe their child's sleep as a problem and reported improved sleep compared to baseline.

Conclusion: Initial completion of the internet-based intervention resulted in significant improvements in infant/toddler sleep, as well as maternal sleep. One year later, all improvements were maintained. Improvements were also seen in the control group compared to baseline for many, but not all of the indices, likely indicative of normal developmental changes. It appears that the intervention advances improvement as seen in the early results of the study, thus saving unknown time of more disrupted sleep, as well as provides additional benefits. These results suggest that brief internet interventions for early childhood sleep problems are effective in improving child and maternal sleep with improvements maintained one year later.

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0789

HYPERSOMNOLENCE DISORDERS IN CHILDREN: POTENTIAL LIMITATIONS OF CURRENT AASM CRITERIA

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Introduction: Narcolepsy in the pediatric population is well described, but little data exist about children with clinically significant hypersomnolence who do not meet AASM criteria for either narcolepsy or idiopathic hypersomnia. The purpose of this study is to characterize and compare these hypersomnolent children to children with narcolepsy or idiopathic hypersomnia.

Methods: Retrospective chart abstraction [clinic notes, polysomnography (PSG), multiple sleep latency testing (MSLT)] of hypersomnolent children, age of onset ≤ 18 years, in a tertiary pediatric sleep center between 2002 and 2010. Two groups were identified: children with narcolepsy or idiopathic hypersomnia (N+IH) and children with problem hypersomnolence (H) but whose symptoms and PSG/MSLT findings did not meet AASM criteria. Statistics: Fisher's exact test for binary data and T test analysis for continuous data.

Results: Sample included 78 children with hypersomnolence (55% female; mean age 11.8±3.6yr). In N+IH group [n=47(60%)], 23(49%) had narcolepsy with cataplexy, 16(34%) had narcolepsy without cataplexy, and 8(17%) had idiopathic hypersomnia. The H group included 31/78(39%) children. Mean sleep latencies were significantly lower in N+IH group vs. H group (3.87±2.89 vs.11.7±2.38, respectively; p <0.0001). Sleep occurred in ≥3 naps during MSLT similarly in both groups (100% vs. 97%). Epworth sleepiness scale scores (pediatric modification) were significantly higher in the N+IH group vs. H group (16.7±4.27 vs.13.41±5.21, respectively; p = 0.007). There were no group differences in age at diagnosis [12 ± 3.5yr (N+IH) and 11.5±3.6yr (H)], gender, race or comorbidities (neuropsychiatric or autoimmune disorders). In the H group, during MSLT, 30(96.8%) fell asleep in ≥3 naps, 21(67.7%) had sleep in ≥4 naps and 10(32%) had ≥2 sleep onset REM periods.

Conclusion: While narcolepsy and idiopathic hypersomnia can be diagnosed in children based on AASM diagnostic criteria, a substantial proportion (~40%), will not meet these criteria but who suffer significant sleepiness and daytime dysfunction and may benefit from alerting therapy.

0790

EVALUATION OF A SINGLE CHANNEL AIRFLOW DEVICE FOR DIAGNOSIS OF OBSTRUCTIVE SLEEP APNEA SYNDROME IN OBESE PEDIATRIC PATIENTS

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Introduction: Obstructive sleep apnea syndrome (OSAS) is highly prevalent in obese children. The ApneaLink is a portable single channel airflow device that measures air flow, respiratory effort and pulse oximetry. The device has proven useful in OSAS screening in adult patients. In the current study, we asked whether this device could be used to screen for OSAS in the pediatric population.

Methods: We performed simultaneous attended sleep-laboratory polysomnography (PSG) and measurements using the portable device on obese pediatric patients referred for snoring (age 9-18 years, BMI>95th percentile for age/gender). We compared the obstructive apnea hypopnea index (OAHI) obtained from PSG to the OAHI obtained from the portable device scored both manually by the investigators and automatically by the device.

Results: 15 subjects (10 males, mean age 12.6 ± 2.8 years, BMI z score 2.42 ± 0.37, OAHI on PSG 18.2 ± 35.0 events/hour) were studied. The OAHI of the PSG correlated with the OAHI of the device scored automatically ($r = 0.97$, $p < 0.001$) and manually ($r=0.94$, $p < 0.001$). The results demonstrate highest sensitivity and specificity of the OAHI from the portable device auto score compared with the OAHI from the simultaneous polysomnogram at an OAHI of > 10 events/hour (AHI > 1.5: sensitivity 100%, specificity 40%; AHI > 5: sensitivity 83%, specificity 78%, AHI > 10: sensitivity 100%, specificity 91%).

Conclusion: The single channel device used in this study is a sensitive screening tool for evaluation of suspected OSAS in obese pediatric patients age 9 - 18 years. Our data suggest that the device may be most effective in pediatric patients when a cut off OAHI of > 5 or > 10 events/hour is applied to diagnose OSAS. We speculate that it can be used in pediatric patients, for evaluation for referral to attended sleep-laboratory PSG, clinical research, and inpatient sleep studies when an attended PSG is not feasible.

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0791

CYCLIC ALTERNATING PATTERN IN INFANTS WITH CONGENITAL HYPOTHYROIDISM AND CENTRAL SLEEP APNEA

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Introduction: Cyclic Alternating Pattern (CAP) is a neurophysiological event during NREM sleep. This pattern has been found in pediatric population and adults. Pioneer studies suggested a relationship between CAP and instability during sleep. In some sleep disorders, as obstructive apnea, changes on CAP distributions have been described. On the other hand, infants with congenital hypothyroidism have a high index of central sleep apnea. This experiment was designed to determine the presence and distribution of CAP in infants with congenital hypothyroidism and their relationship with central sleep apnea.

Methods: A two hours polysomnographic analysis was done in congenital hypothyroidism (CH) infants with hormonal replacement therapy (these infants belong to a development and early intervention program) (n = 15), low risk (LR) infants (n = 15) and high risk (HR) infants by high apnea central index with out congenital hypothyroidism (these infants belong to a development and early intervention program) (n = 15). Both sexes were represented in each group (age range: 24 days- 722 days old). After an early wake up, recordings were done in the morning immediately after breakfast. Thus, at least two sleep cycles were obtained. Sleep scoring was performed following Rechstschaffen and Kales' criteria with corrections for this age. CAP subtypes for phase A were identified following the Terzano and cols' criteria. Concerning the phase B of the CAP, particular software especially designed for this task (Somnium) was used. Statistical analysis was done using a linear correlation analysis and ANOVA followed by Newman-Keuls test.

Results: Infants with CH have a similar sleep macro structure, however by LR, the microstructure analyzed by subtypes of phase A of CAP is different between groups and age. CH infants have more A3 subtype and less A1 than LR infants.

Conclusion: The differences in subtypes A of CAP found between groups could be an evidence to use CAP like a new tool for sleep analysis on pediatric population. At the moment is not clear a relationship between CAP, breathing disorder and congenital hypothyroidism.

0792

AN OBJECTIVE MEASURE OF SLEEPINESS IN EARLY CHILDHOOD: FACIAL ANALYSIS OF CHILDREN'S EXPRESSED SLEEPINESS (FACES)

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Introduction: Few measures for assessing sleepiness in early childhood currently exist. This gap is likely due to young children's inability to self-report, regular and developmentally-appropriate napping, and no normative data utilizing standard objective methods (e.g., MSLT, waking theta activity). As sleepiness is linked to cognitive/mood disorders, research on its prevalence/determinants in children is needed to inform the prevention/treatment of sleep and behavioral problems. The purpose of this study was to develop an objective measure of sleepiness in young children.

Methods: Nine healthy children (3 M; 30-36 months) with no sleep/emotion/behavioral problems followed a strict sleep schedule for 5 days before sleepiness assessments, which optimized sleep (12.5+ hrs TIB/24hrs) and entrained the circadian system. Assessments (20min) occurred on 2 afternoons in the home: one after an afternoon nap of at least 60min (verified w/ actigraphy), the other after nap deprivation. Children's faces were videotaped while viewing a neutral seascapes video for 4min followed by emotionally-eliciting pictures/movies. A review of the literature related to behavioral manifestations of sleepiness led to identifying facial features for coding: yawning, head-nodding, eye-rubbing, sleep-verbalizations, laying-head down, incomplete blinking, and complete blinking. Reliable coders performed millisecond video-based facial analysis of sleepiness behaviors. We hypothesized increased sleepiness behaviors with acute sleep restriction in young children.

Results: A Wilcoxon test revealed a significant difference in both measures of blinking across the assessment (ps<.05), although effects were most robust when children viewed the seascapes video (ps<.01). In this neutral context, children exhibited more incomplete blinks (Z= -2.7; Nap: M=3.9, SD=3.2; No nap: M=10.2, SD=6.5) and more complete blinks (Z=-2.4; Nap: M=4.7, SD=5.9; No nap: M=8.8, SD=7.2) when sleep restricted. Few incidents of other sleepinessn behaviors (e.g., yawning, head-nodding, eye-rubbing) were observed as a consequence of this relatively mild challenge.

Conclusion: These results are consistent with previous research on drowsy driving showing increased eye-blinks in association with sleep restriction/deprivation. We extend such findings to early childhood, which support further development of the FACES using more challenging experimental paradigms (e.g., late bedtimes), as well as with children diagnosed with clinical sleep disorders.

0793

QUANTITATIVE ASSESSMENT OF EPILEPTIFORM DISCHARGES IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)

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Introduction: To identify and quantify the distribution of epileptiform discharges in patients with Attention Deficit Hyperactivity Disorder (ADHD) presenting to a pediatric sleep medicine center for nocturnal video-polysomnography (PSG) because of a complaint of snoring, multiple awakenings, witnessed apneas, daytime sleepiness or restless sleep.
Methods: The PSG of fifty- five children with ADHD (33 male, 22 female and mean age= 6.8years) were identified retrospectively and evaluated from January 2008 to June 2010 for epileptiform discharges using scalp electroencephalography (EEG). Forty six patients were on stimulants. Fifty- five non-ADHD patient controls were age, sex, Respiratory Disturbance Index (RDI), and Periodic Limb Movement Index (PLMI) matched. Polysomnographs were studied for epileptiform discharges using the same montages.
Results: ADHD patients had a significant greater likelihood of EDs compared to controls (p= 0.000) specifically, 32 (58.18%) ADHD patients had epileptiform discharges (EDs) with a (range from 3- 984, and mean= 71), and 23 (41.82%) were normal. Nine (16.34%) controls had EDs with a (range from 4- 21 and mean= 10), and 46 (83.66%) were normal. Of the 46 ADHD patients who were on stimulants, 28(60.9%) had EDs with a (range from 3- 984, and mean= 77), and 18(41.86%) had no EDs. Of the 9 ADHD patients who were not on stimulants, 4(44.4%) had EDs with a (range from 8- 97 and mean= 32), and 5 (55.6%) had no EDs, (p=0.46).
Conclusion: Children with ADHD had more epileptiform discharges than age, sex, RDI, and PLMI matched controls. Our findings show that ADHD is associated with epileptiform abnormalities on EEG.

0794

EFFECTS OF A STANDARDIZED PAMPHLET ON SLEEP LATENCY IN CHILDREN WITH AUTISM

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Introduction: Sleep difficulties, particularly sleep onset insomnia, are common reasons why parents seek medical intervention in children with autism spectrum disorders (ASD). We determined the efficacy of a sleep education pamphlet on sleep latency (time to fall asleep) in children with ASD.
Methods: Children ages 2-10 years, enrolled in the Autism Treatment Network at Vanderbilt University Medical Center and Cincinnati Children's Hospital Medical Center, were eligible. All had a clinical diagnosis of ASD, with confirmation by the Autism Diagnostic Observation Schedule. Parents were randomly assigned to receive or not receive a sleep education pamphlet containing information about daytime habits, bedtime routine, and sleep environment. Children wore an actigraphy device, which measures activity and rest to estimate sleep parameters,

prior to receiving the pamphlet (baseline) and two weeks after randomization (treatment). Sample size of 36 participants was predetermined to detect a difference in time to fall asleep of at least 30 minutes in children whose parents received the pamphlet. Independent t-tests were performed to compare mean SL at baseline, as well as the mean change in SL by treatment.
Results: The group receiving the pamphlet showed improvement in SL [from 56.7 minutes ± 27.1 at baseline; mean ± standard deviation) to 49.5 minutes ± 26.7 with treatment]. The group randomized to not receive the pamphlet showed worsening in SL [from 52.1 minutes ± 25.1 at baseline to 61.3 minutes ± 47 with treatment). However, statistical significance was not reached in either group (p > 0.10).
Conclusion: Providing a sleep education pamphlet to parents of children with ASD did not significantly improve sleep latency. We are currently conducting studies to determine if more intensive education improves sleep patterns in this population.

0795

SLEEP HOMEOSTASIS IN ADOLESCENT DEPRESSION

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Introduction: Slow-wave activity (SWA) and sleep homeostasis show significant sex differences in adults with major depressive disorders (MDD). Men with MDD show a blunted SWA response to sleep challenge compared to healthy control men whereas women with MDD over-respond to a mild sleep challenge. The present study was undertaken to determine if sleep homeostasis was impaired in early onset MDD and if sex differences were also evident.
Methods: 50 physically mature (Tanner Stage 5) adolescents, 12-18years of age were recruited, including 30 symptomatic, un-medicated MDD (10 M, 20 F), and 20 healthy controls (HCs) with no personal or family history of MDD (HC: 7 M and 13 F). Participants maintained a regular sleep-wake schedule for 5 days, followed by 2 nights of PSG in the laboratory on the same schedule. On the sleep homeostatic challenge night, bedtime was delayed by 3 hrs, followed by recovery sleep. Power spectral analysis quantified SWA in NREM sleep (excluding Stage 1) on the baseline and sleep delay nights. SWA response to delay was compared across groups.
Results: Sleep latency was shorter after sleep delay in all groups, roughly half of baseline values and supported by a significant main effect (p<.01). Total SWA power was also increased by sleep delay, but showed a significant group by sex interaction (p<.03). HC females showed the largest response to sleep delay whereas MDD females showed the smallest response to sleep challenge.
Conclusion: In contrast to results in adults, this study found the smallest SWA response to challenge in adolescent females with MDD, not males, further supporting the view that SWA homeostasis is both disease- and sex- dependent.

0796

VALIDATION OF THE CHILD AND ADOLESCENT SLEEP CHECKLIST (CASC)

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Introduction: Assessment of sleep using a single questionnaire for children with a wide range of ages requires special considerations. The aim of this study was to make a validation of the newly developed sleep questionnaire for the community study of children and adolescents.
Methods: Child and Adolescent Sleep Checklist (CASC) is consisted of 36 questions commonly used from kindergartener up to high-school students. CASC has three versions; for caregivers, for elementary school children (6-11 years of age), and for high-school students (12-18 years of age). Caregiver version is used commonly for all age groups, elementary school version is to be filled out by the students under the instruction of teachers or caregivers, and high-school version is to be filled out by the students themselves. To validate the appropriateness of these questions, CASC sleep problem scores were compared with scores of Children's Sleep Habits Questionnaire (CSHQ) and Pittsburgh Sleep Quality Index (PSQI).
Results: Parental reports (preschoolers and elementary school children, n=26) were compared with CSHQ; CASC sleep problem score showed good correlation with CSHQ total score (r=0.770, p<0.001). Self reports (high school students, n=19) were compared with PSQI; CASC sleep problem score showed good correlation with PSQI score (r=0.599, p=0.007).
Conclusion: CASC score showed good correlation with scores of currently used sleep questionnaires. CASC has its advantage in making cross sectional screening of sleep problems in wide range of ages by using both parental and self report. CASC can be especially useful in interventional or cohort study as this questionnaire allows to use same question items throughout the study period.

0797

ACCURACY OF COMPUTER ALGORITHMS AND THE HUMAN EYE IN SCORING ACTIGRAPHY

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Introduction: While the use of actigraphy in evaluating certain sleep disorders has been validated, the details of scoring actigraphy are not well defined. The objective of this study is to determine the optimal scoring method and parameter settings of actigraphy by comparison to simultaneous polysomnography (PSG).
Methods: Fifteen studies of simultaneous PSG and actigraphy were completed in adolescents (mean age = 16.3 years) and analyzed. Visual scoring of the actigraphy by the human eye was compared to commercial computer software scoring across low, medium, and high wake thresholds and 4, 5, 10, and 15 minutes of immobility. Rest periods were set four ways: according to known times from the PSG, manual setting by a human, according to sleep diary times, and auto-setting the major rest interval using computer software. The PSG was considered the reference standard.
Results: There was a better correlation between actigraphy and PSG sleep start/end, total sleep time, wake after sleep onset (WASO), and sleep efficiency when the rest period was determined by the human (mean r = 0.6395) rather than auto-set by the software (r = 0.4060). The best results came when the rest intervals were set based on the PSG (r=0.6938). Scoring the printed actogram by the human eye was superior to the auto analyses as well (r = 0.5747). Higher correlations and lower biases were obtained from lower wake threshold settings (low and medium) and higher immobility times (10 and 15 minutes).
Conclusion: Accurate determination of the rest interval is important in scoring actigraphy. Scoring actigraphy by the human eye is superior to this computer algorithm when auto-setting major rest periods. A low wake threshold and 10 minutes of immobility for sleep onset and sleep end yield the most accurate results. Auto-setting major rest intervals should be avoided to set start/end of rest; adjustments for artifacts and/or a sleep diary for comparison are necessary.

0798

DIGITAL ORAL PHOTOGRAPHY FOR PEDIATRIC TONSILLAR HYPERTROPHY GRADING

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Introduction: Adenotonsillar hypertrophy is the most common etiology for pediatric sleep-disordered breathing. Visual tonsil grading is used, in part, to determine candidacy for adenotonsillectomy. Telemedicine improves access to specialized medical care among underserved rural populations and may be ideal for visual pediatric tonsillar hypertrophy grading. Our purpose was to determine the efficacy of digital photographs for pediatric tonsillar grading.
Methods: Using Brodsky's scale, 41 children (3.0-14.6 years) had in-person tonsil grading during a routine pediatric otolaryngology (ENT) physical examination. Oral photographs were obtained with a standard single-lens reflex digital camera, later graded by the same ENT physician and by a Pediatrician with sleep expertise. Both physicians were blinded and made photograph gradings independently.
Results: In-person ENT gradings were highly correlated with both ENT photograph grading (r=.578, p<0.001) and Pediatrician photograph grading (r=.623, p<0.001). Yet they also differed significantly (t=3.3, p=0.002, g=.46 for ENT; t=3.9, p<0.001, d=.51 for Pediatrician) with in-person gradings overestimating. However, photograph gradings did not differ between ENT and Pediatrician, suggesting that photographs provide unique and consistent information. Discrepancies between in-person and photograph gradings were not explained by child age. If decision to recommend tonsillectomy were based exclusively on ≥+2 tonsils, 31% of patients who would have surgery based on in-person grading would not have surgery based on photo grading and 12% who would not have surgery based on in-person grading would have surgery based on photo grading.
Conclusion: Photographs used to determine pediatric tonsillar grade provide unique and consistent information to independent healthcare providers, which may be different from that provided in vivo. This may be due to static image allowing more detailed mental calculations. If photograph gradings provide more accurate information than in-person gradings, they should be considered for both remote use, as well as an alternative to current in vivo estimates.

0799

CARDIOPULMONARY COUPLING MEASURES OF SLEEP STABILITY AND SLEEP QUALITY IN CHILDREN WITH PRIMARY SNORING

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Introduction: Cardio Pulmonary Coupling (CPC) is a measure of sleep stability linking autonomic and respiratory data obtained from overnight polysonomgraphy (NPSG). High Frequency coupling (HFc) and Low Frequency Coupling (LFc) along with their ratios give insight to sleep stability and quality. Children with primary snoring (PS) (Apnea-Hypopnea index (AHI<2)) are thought to have stable sleep. The purpose of this study was to examine CPC values in overweight/obese children (8 to 18 years of age) with habitual snoring taken from a larger prospective study.
Methods: NPSG from 20 children enrolled in a larger study diagnosed with PS were analyzed using the RemLogic CPC 1.0 analysis software.
Results: Data from 20 subjects (12 males); Mean age ±SD (12.7±2.9) BMIz score 2.1±0.53 ; AHI (1.0±0.5) were analyzed. LFc/HFc ratio (a measure of sleep instability) was significantly higher (0.6±0.4) than the normative cutoff value of 0.25 (p<0.05). HFc/LFc ratio(a measure of quality of sleep) was significantly lower (2.5±1.5) than the normative cutoff value of 4 (p<0.05) and also positively correlated with Pediatric Sleep Questionnaire (r=0.49; p<0.5) . Neither CPC measures correlated with BMIz score or AHI. When compared to quality of life data; LFc/HFc ratio significantly correlated inversely to parental report of physical functioning of the child on the PedsQL™ 4.0 (r=-0.46; p<0.05) and also trended inversely with social functioning (r=-0.38; p=0.09). No other components of the parent or child report of the PedsQL™ correlated with measures of sleep stability or quality.
Conclusion: Overweight and obese children with the diagnosis of PS have poor sleep quality and stability as measured by cardiopulmonary coupling but these values do not correlate with severity of obesity or symptoms of OSA. Further studies are needed to explore the relationships between CPC measures of sleep quality and stability and symptoms/sequelae associated with OSA and the response to therapeutic intervention.
Support (If Any): CPC module supplied by EMBLA.

0800

ACTIGRAPHIC SLEEP PATTERNS OF MINORITY ADOLESCENTS

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Introduction: Findings indicate that minorities have poorer daytime outcomes than Caucasians in several areas, and empirical evidence substantiates links between poor sleep and daytime impairment in the general population. Few studies, however, have studied the sleep of minority adolescents. The present study aims to investigate the sleep patterns of minority teens.
Methods: Actigraphy data corroborated with sleep diaries were analyzed for a sample consisting of 48 adolescents (aged 13-14, 50% minority). The participants indicated on sleep logs whether or not they slept in a bed, how many others slept with them, and how many others where in the room. Each main actigraphic sleep interval was assigned 1point for presence of short duration (less than 9 hours of sleep), late sleep onset (after 11:00 pm), sleep start variability (sleep onset time > 60 minutes discrepant from average), and fragmentation (wake bouts > 30 minutes). Four ratios (# of days scored 1/total # of days) were summed for the overall sleep problem index.

Results: Out of 9 demographic/environmental variables, only minority status was retained in a stepwise linear regression model, explaining 25.7% of the variance of sleep problems (*p* = .001). Minority status remained significant (*R*² = .176, *p*= .002) above and beyond sleep environment. Minority teens were 5.2 times more likely to be poor sleepers (OR = 5.2, CI = 1.45-18.71) compared with Caucasian peers. Minority adolescents had significantly less sleep (M = 435.05 [SD = 52.17] minutes versus 462.32 [35.3]) and later bedtimes (M = 11:52 pm [SD = 1.04] versus 10:47 pm [.81]) than their peers (*t* [47] = -2.152, 4.068; *p*'s < .05).
Conclusion: We found a strong association between minority status and sleep problems in adolescents after accounting for sleep environment. Other potential mediators should be investigated including stress. This study supports proactive sleep education for families of disadvantaged minority teens.

0801

SLEEP DISTURBANCE IN CHILDREN AND ADOLESCENTS WITH ADHD: UNIQUE EFFECTS OF MEDICATION, ADHD SUBTYPE AND COMORBID STATUS

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Introduction: ADHD is estimated to affect 3% to 5% of school-aged individuals, with 11% to 37% reporting sleep disturbance. Disturbed sleep can result in daytime sleepiness and behavioral difficulties that affect cognitive functions in children, including attention and memory, as well as exacerbate symptoms of ADHD. This study aimed to determine the prevalence of ICD-9 sleep disorders, prescribed sleep medication, and complaints of sleep problems as diagnosed by pediatric primary care providers in children and adolescents with ADHD across medication, ADHD subtype, and comorbid status.
Methods: Electronic medical records were reviewed for 3,478 children and 2,403 adolescents. Information was collected regarding ICD-9 sleep diagnoses, medications potentially used to treat sleep disorders, demographic variables, medications commonly used to treat symptoms of ADHD, ICD-9 ADHD subtype, and comorbidity. Reports of sleep problems were also examined in 280 children and 276 adolescents.
Results: Children were more likely to be diagnosed with a sleep disorder if they had ADHD with hyperactivity (ADHD-H; B = 0.554, p<.001) or an externalizing comorbidity (EC; B = 0.407, p<.05); adolescents were more likely to be diagnosed with a sleep disorder if they had an internalizing comorbidity (IC; B = 2.520, p<.01) or EC (B = 0.929, p<.001). Children were more likely to be prescribed a sleep medication if they had ADHD-H (B = 0.925, p<.001), IC (B = 0.975, p<.01), EC (0.848, p<.001), IC and EC (B = 1.547, p<.05), were prescribed a stimulant medication (SM; B = 0.433, p<.001), non-stimulant medication (NM; B = 0.619, p<.05), or SM and NM (B = 0.904, p<.001). Adolescents were more likely to be prescribed a sleep medication if they were also prescribed a SM (B = 0.942, p<.001), SM and NM (B = 1.077, p<.001), diagnosed with an IC (B = 1.291, p<.001), EC (B = 1.035, p<.001), or ADHD-H (B = 0.614, p<.001). Adolescents diagnosed with both an IC and EC (B = 2.515, p<.01) were more likely to report a sleep problem.
Conclusion: This is one of the first studies to highlight the subgroups of children and adolescents with ADHD more likely to exhibit sleep disturbance across a large primary care network. These risk factors and their subsequent effects on the severity of symptoms associated with ADHD must be considered when assessing and treating children and adolescents with ADHD. Future studies should investigate how sleep disturbance is evaluated and treated in this population in the primary care setting.

0802

CONTRIBUTIONS OF CIRCADIAN TENDENCIES AND BEHAVIORAL PROBLEMS TO SLEEP ONSET INSOMNIA IN CHILDREN WITH ADHD

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Introduction: Attention-deficit/hyperactivity disorder (ADHD) is characterized by impulsivity/hyperactivity and inattention. It is estimated to occur in 3-7.5% of school-aged children, thus making ADHD one of the most prevalent child psychiatric conditions. Although the presence of Sleep-Onset Insomnia has been noted among 1/3 of children with ADHD, the causes of such sleep issues remain unclear. Within the current literature, both biological and behavioral explanations for sleep problems in this population have been advanced, suggesting different interventional strategies, depending on the pathophysiological mechanism that is in fact at play. The goal of this study was to determine the relative contributions of biological (circadian tendencies) and behavioral (externalizing problems) factors to sleep onset insomnia experienced by children with ADHD.

Methods: 75 children (26 ADHD, 49 Controls), aged 7 to 11 years old (mean age = 8.61, SD = 1.27), participated in the study. Participants were asked to cease medication for the duration of the study and to avoid consuming products containing caffeine (such as chocolate or cola). Sleep was evaluated using polysomnography and the Child Sleep Habits Questionnaire. Externalizing problems were evaluated using the Child Behavioral Checklist and circadian tendency was evaluated using Child Morning-Evening Preference Scale. ADHD was diagnosed using DSM-IV criteria.

Results: Multiple Linear Regression Analyses was used to determine the contributions of externalizing problems versus circadian tendencies to sleep onset delay and bedtime resistance. Externalizing problems yielded significant independent contributions only to the explained variance in parental reports of bedtime resistance, whereas an evening circadian tendency contributed both to parental reports of sleep onset delay and to PSG-measured sleep-onset latency.

Conclusion: Externalization and circadian tendency were associated with a different bedtime problems. Thus, circadian phase delay and bedtime refusal may both be common, but are two distinct problems. As such, each may require a different interventional strategy.

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0803

ATTENTION AND HYPERACTIVITY SYMPTOMS AT KINDERGARTEN ENTRY ASSOCIATED WITH LESS SLEEP IN PRESCHOOL

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Introduction: Although Attention-Deficit/ Hyperactivity Disorder (ADHD) is not generally diagnosed until the school age years, the onset of developmentally inappropriate inattention and hyperactivity/impulsivity is often much younger. Sleep problems, particularly difficulty falling asleep and staying asleep, are frequently reported in children and adolescents with ADHD. However, the direction of causation, if any, has been difficult to determine. Longitudinal studies may provide a window into the direction of this complex relationship.

Methods: The analyses use data from the preschool and kindergarten waves of the Early Childhood Longitudinal Study - Birth Cohort (ECLS-B) study. The ECLS-B dataset includes a contemporary, representative sample of children and their families living in the United States and followed longitudinally. The sample consisted of approximately 6,860 children who had data on the variables of interest across the preschool and kindergarten waves. Parent-reported bedtime and wake time, obtained via interview at both time points, were used to calculate total nighttime sleep duration. Parents were also asked to rate their children's behavior on brief measures of attention/task persistence and hyperactivity/impulsivity.

Results: We performed two sets of regression analyses to identify whether (a) sleep duration in preschool-age children predicts attention and hyperactivity at kindergarten entry and (b) attention and hyperactivity symptoms at preschool predict sleep duration at kindergarten. Each analysis controlled for the outcome of interest at the preschool time point, as well as gender, ethnicity and family income. Less sleep at preschool significantly predicted worse parent-reported hyperactivity (β=-0.06, P<.02) and attention at kindergarten (β=0.06, P<.01). Conversely, parent-reported attention and hyperactivity at preschool did not predict parent-reported sleep duration at kindergarten (attention: β=0.04, P = .09; hyperactivity: β=- .01, ns).

Conclusion: Short sleep duration may contribute to the development or worsening of inattention and hyperactivity/impulsivity during early childhood, or may serve as an early warning sign of emerging behavioral difficulties.

0804

NIGHT-TO-NIGHT MOOD CHANGES OF ADOLESCENTS DURING EXPERIMENTAL CHRONIC SLEEP RESTRICTION

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Introduction: Adolescents often experience chronic sleep restriction on school nights, which can result in daytime sleepiness and mood difficulties. The pattern by which these symptoms develop over the course of multi-night sleep restriction is not known, though adult data suggest non-linear effects. This study characterizes the day-to-day changes in subjective sleepiness and moods of adolescents across 5 nights of sleep restriction.

Methods: 23 healthy adolescents aged 14-16.9 years completed a three-week experimental protocol that included a baseline week followed in counterbalanced order by a sleep-restricted week (SR; 6.5 hours in bed Monday-Friday nights) and an extended sleep week (ES; 10 hours Monday-Friday nights), with a two-night "washout" before each condition. Sleep duration was monitored by actigraphy and daily sleep diaries. The diaries also included self-reported moods (nervous, sad, angry, energetic, fatigued, able to concentrate, sleepy), each rated daily on a 5-point scale, as well items related to sleep onset latency and difficulty awakening each morning. Multivariate models examined change in scores over time, with paired t-tests comparing ratings for each day across conditions.

Results: Nightly sleep averaged 6.2 (SR) versus 8.6 hours (ES; p<.001). Ratings for nervous, angry, and energetic mood did not systematically differ across conditions or days. However, by Tuesday or Wednesday, ratings for fatigue, sleepiness, concentration problems, and sleep onset latency significantly differed across conditions (p<.05-.001), generally reflecting a rapid worsening during SR, followed by stability. Although slower to change, reported difficulty waking was evident by Thursday and subjective sadness by Friday (p<.01).

Conclusion: Chronic sleep restriction results in a rapid rise in teen-reported sleepiness, fatigue, and concentration problems that then tends to level off after a few days. It is not known if objective deficits continue to

worsen in the absence of continued change in self-perception, but if so, this would be similar to reports in adults.

Support (If Any): National Institutes of Health (R01 HL092149, UL1 RR026314)

0805

LEARNING, ATTENTION AND CONDUCT PROBLEMS AS SEQUELAE OF EXCESSIVE DAYTIME SLEEPINESS IN A COMMUNITY SAMPLE OF YOUNG CHILDREN

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Introduction: Although excessive daytime sleepiness (EDS) is a common problem in children with estimates of 15%, few studies have investigated the sequelae of EDS in young children. In this study, we investigated the association of EDS with objective neurocognitive measures and parent reported attention, conduct, and learning problems in a large general population sample of children.

Methods: A population based study of 508 school aged children (6-12 years) from The Penn State Child Cohort underwent a 9-hour polysomnogram, comprehensive neurocognitive testing and parent rating scales. Children were divided into two groups: those with and without parent reported EDS. Path analysis was used to examine whether processing speed and working memory performance would mediate the relationship between EDS and learning, conduct and school problems.

Results: Logistic regression models suggest that parent reported attention, conduct and school problems as well as objective measurement of working memory and processing speed are significant sequelae of EDS even when controlling for SDB and sleep latency. Path analysis demonstrates that working memory and processing speed performance are strong mediators of the association of EDS with school and attention problems, while to a lesser degree are mediators of the path from EDS to conduct problems.

Conclusion: This study suggests that in a large general population sample of young children, parent reported EDS is associated with neurobehavioral (school, conduct, and attention) problems, and poorer performance in processing speed and working memory. Impairment due to EDS in daytime cognitive and behavioral functioning can have a significant impact on children's development.

0806

BEDTIME SLEEPINESS OF CHILDREN WITH PSYCHOPATHOLOGICAL PROBLEMS

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Introduction: Sleepiness in children may present as irritability and hyperactivity rather than tiredness or lethargy, and therefore, excessive motor activity and inattention may de facto represent strategies to stay awake. Multiple sleep latency tests suggest that children with ADHD exhibit objective daytime somnolence, the latter being also a common complaint. Erratic sleep-wake patterns may enhance such complaints.

Methods: Sleep was continuously monitored by actigraphy for 7 days in children attending a summer program where parents and children spend the week days at camp where they are trained in behavior modification techniques to improve behavioral regulation. Self-reported sleepiness at bedtime, and at the beginning and the end of the camp day was collected in 16 children (14 boys, aged 9.4±1.7, Caucasian 87.5%, 12.5% Other ethnicity). All children were taking one or multiple medications. Categorized on parental reported diagnosis, the group comprised 5 ADHD, 8 ADHD with co-morbidity, and 3 children with Other psychopathology.

Results: Overall, during the study children had an average score on the Sleepiness Scale (2.87±1.6; i.e., min.: 0 - max.: 5.58). Self-reported

sleepiness at bedtime was unrelated to any of the sleep schedule parameters, except for Monday; i.e., sleepiness was related to Sleep Efficiency Index (r=0.67, p<0.01), to TST (r=0.53, p<0.05) and to Restlessness (r=-0.54, p<0.05). Children's sleepiness at the beginning of camp star day was unrelated to their sleep schedules. However, sleepiness at the end of the day correlates to sleep onset latency, sleep duration, immobile time and wake-up time. Noteworthy, self-reported sleepiness varied greatly among the children, and also varied across days within any given child.

Conclusion: Sleepiness varies daily among children with psychopathological problems, particularly on Mondays. Daily differences within individual sleep schedules may exacerbate such variability in reported sleepiness.

Support (If Any): Comer Children's Hospital Golf Classic Research Award

0807

SLEEPINESS, SLEEP AND FOOD PATTERNS IN CHILDREN WITH PSYCHOPATHOLOGICAL PROBLEMS

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Introduction: ADHD children have consistently manifested increased frequency of sleep complaints such as delayed sleep onset, numerous nocturnal awakenings and sleepiness on awakening. Erratic sleep-wake patterns may enhance such complaints. The issue of obesity and ADHD has recently gained substantial attention, whereby children with ADHD appear to be at increased risk for obesity. Although the increased prevalence of both obesity and ADHD are indisputable, these 2 conditions also share the frequent presence of excessive daytime sleepiness.

Methods: Sleep was continuously monitored by actigraphy for 7 days during a summer program where parents and children spend the week days at camp where they are trained in behavior modification techniques to improve behavioral regulation. Self-reported sleepiness was collected in 16 children (14 boys, aged 9.4±1.7, Caucasian 87.5%, 12.5% Other ethnicity), and parents filled out the food frequency and activity questionnaire. Weight and height (i.e., BMI) were measured. Categorized on parental reported diagnosis, the group comprised 5 ADHD, 8 ADHD with co-morbidity, and 3 children with Other psychopathology.

Results: Most children had normal BMI, except 2 children being overweight and 1 obese. Daily food patterns were characterized by bread, cereals, and starches (71%), fruits (64%), desserts and snacks (36%) and juices (36%). Both sleepiness and BMI were associated with sleep schedules and food patterns, sharing 76% of variance with mean WASO and WASO variability. No other associations with sleepiness and BMI set were found regarding sleep patterns, whereas desserts/snack and fast food were associated with increased sleepiness at the start of the day. In other words, sleepiness and BMI shared 97% of variance with the food patterns set.

Conclusion: Although the children included were of normal weight, their disrupted sleep patterns and sleepiness appears to favor unhealthy food patterns. Therefore, daytime somnolence may place children with ADHD at increased risk for obesity.

Support (If Any): Comer Children's Hospital Golf Classic Research Award

0808

DEPRESSION AND ANXIETY ARE RELATED TO SLEEP DISTURBANCES IN ADOLESCENTS

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Introduction: Some researchers suggest a relationship between depression and anxiety in adolescents and changes in their sleep patterns at that age. We verified whether depressive and anxious symptoms in high

school students were related to sleep disorders, sleep habits, and sleepiness during class.

Methods: 761 adolescents (13-19 years old) completed a questionnaire on sleep habits, sleep disturbances, excessive daytime sleepiness (EDS), the Brief Screen for Depression (BSD), and the Costello-Comrey Anxiety Scale (CCAS). Correlations were performed between the global scores on the BSD and CCAS and: total sleep time (TST) during school nights (SN) and weekend nights (WN), bedtimes during SN and WN, sleep disorders, sleep initiation difficulties, and EDS.

Results: There were significant correlations between BSD and CCAS scores and: TST during SN (BSD: r =-0.168, p< 0.01; CCAS: r =-0.116, p< 0.01), bedtimes during WN (BSD: r =0.121, p< 0.01; CCAS: r =0.113, p< 0.01), sleep disorders (BSD: r =0.413, p< 0.01; CCAS: r =0.413, p< 0.01), sleep initiation difficulties (BSD: r =0.383, p< 0.01; CCAS: r =0.321, p< 0.01), and EDS (BSD: r =0.438, p< 0.01; CCAS: r =0.398, p< 0.01). There were modest yet statistically significant correlations between BSD and CCAS scores and TST during WN (BSD: r =-0.090, p< 0.05; CCAS: r =-0.081, p< 0.05), and between BSD scores and bedtimes during SN (r =0.081, p< 0.05).

Conclusion: These results suggest that depressive and anxious symptoms might be strongly associated with sleep changes in adolescents. More specifically, extreme evening type (reflected by later bedtimes during WN), sleep debt (reflected by lower sleep duration on SN and EDS), and sleep disorders (reflected by higher sleep disturbances and sleep initiation difficulties) seem to be closely related to manifestations of depression and anxiety in teenagers.

0809

CHILDHOOD TRAUMA AND DEPRESSIVE SYMPTOMS ARE ASSOCIATED WITH IRREGULARITY OF SLEEP PATTERNS IN ADOLESCENTS

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Introduction: During adolescence, the development of sleep architecture crystallizes and begins to transition into adult-like patterns. Sleep restriction, poor sleep quality, and eveningness preference all have been associated with depressive symptoms in adolescence. We hypothesized that depressive symptoms and childhood trauma would each be independently associated with sleep irregularity in a community sample of adolescents ascertained from the greater San Antonio metropolitan area.

Methods: We recruited 996 adolescents: Gender: (Male:Female - 513:481), Race: (White:Hispanic:Others - 507:340:149) and Age (13.4±1.05). Sleep irregularity was measured by 7 likert-type questions assessing regularity of bedtimes, wake times, sleep duration and sleepiness via the Dimensions of Temperament Survey (DOTS). An overall sleep irregularity score was calculated. The Mood and Feelings Questionnaire (MFQ) assessed depressive symptoms during the prior two-week period. The Childhood Trauma Questionnaire (CTQ) assessed abuse and neglect covering childhood and adolescence. Data were analyzed using univariate ANOVAs in SPSS. The overall sleep irregularity score derived from the DOTS was the dependent variable. The predictors were total MFQ and CTQ scores controlling for age, sex, and race.

Results: The total MFQ score (F(1,989)=11.03, p=.001) and total CTQ score (F(1,989)=12.57, p=.000) independently predicted the overall sleep irregularity score. Gender had a significant main effect on the regularity of sleep (F(1,989)=3.92, P<.05). There were no significant effects of age, race or any significant two-way interactions among the predictor variables.

Conclusion: Our data shows that both increased childhood trauma and current depressive symptoms are significantly linked with irregular sleep patterns in adolescents aged 12 to 15 years. Further studies are needed to identify how affective dysregulation associated with childhood trauma and depressive symptoms directly leads to the irregularity of sleep observed in adolescents.

0810

SEX DIFFERENCES IN SLOW-WAVE ACTIVITY (SWA) IN ADOLESCENT DEPRESSION

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Introduction: Major depressive disorders (MDD) are associated with subjective and objective sleep disturbances. The initiation and consolidation of sleep and the distribution of REM and NREM sleep stages is abnormal in those with MDD. Sleep EEG measures have confirmed lower SWA in men with MDD with a blunted decay across the night but not in women with MDD. However, it is not clear whether early onset MDD is also associated with blunted SWA and if sex differences are also evident. The present study evaluated SWA and its time course in adolescents (12-18 years of age) with and without MDD.

Methods: 52 symptomatic, unmedicated MDD (20 M, 32 F), and 55 healthy controls with no personal or family history of MDD (HC: 22 M and 33 F) adolescents were studied. Participants maintained a regular sleep-wake schedule for 5 days, followed by 2 nights of PSG in the laboratory. Power spectral analysis quantified SWA in NREM sleep (excluding Stage 1) and the time course was compared by group and sex.

Results: SWA in the first NREM period was lower and the decay in SWA across the night more irregular in MDD male adolescents compared to HC males (p<.009). REM latency was also shorter in MDD males (p<.003). By contrast, SWA was equivalent in MDD and HC females. SWA was not significantly correlated with REM latency in any group.

Conclusion: These findings may reflect lower homeostatic sleep pressure in early onset MDD but only in adolescent males, consistent with findings in adults with MDD. Studying homeostatic response to sleep challenge is necessary to test this hypothesis.

0811

INTERNET ADDICTION AND ITS RELATION TO SLEEP AND DEPRESSION IN KOREAN ADOLESCENTS

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WITHDRAWN

0812

SUICIDAL BEHAVIOR AND SLEEP COMPLAINTS IN CHILDREN AND ADOLESCENTS WITH MAJOR DEPRESSIVE DISORDER

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Introduction: There is a strong relation between suicide behavior and sleep complaint during depressive disorders. The aim of this study was to investigate the suicidal behavior among children and adolescents correlated with sleep complaints in children and adolescents with Major Depressive Disorder (MDD).

Methods: 214 children and adolescents were diagnosed with current MDD. The Subjects were obtained from experienced two research interviewers and the psychiatric diagnoses were ascertained according to DSM-IV criteria. The signed consent from the parent or legal guardians was obtained. All analyses were performed by SPSS) using χ2 tests and Bonferroni correction.

Results: We evaluated patients who were moderate to severe depressed. Initial Insomnia was present in 58.9%, Night Awakening in 36%, Early

Awakening 29.9%, and Hypersomnia in 31%. Between patients with SB, 40.2% percent of them had Morbid Ideation, 30.8% Thoughts of Death, 32.7% had Suicidal Ideation, 23.4% had Suicidal Plan, and 13.3% had already had any Suicide Attempt. The correlations were: morbid ideations with initial insomnia; thoughts of death with initial insomnia and hypersomnia (all p<0.05); and suicidal thoughts with initial insomnia (p=0.05), night awakening and early awakening (p=0.005). Our logistic regression showed our patients that had more morbid ideation plus initial insomnia (OR=2.1) and early Awakening (OR=4.4) had more clusters of suicidal behavior (SB). We found that patients with SB also showed Initial Insomnia (OR=1.8), and Early Awakening (OR=4.3). Suicidal Ideation shown a very high association to SC (OR=9.8), to Initial Insomnia (OR=7.6) and Night Awakening (OR=3.9). Patients with Suicidal Plan had two times more chances to present Night Awakening and Hypersomnia (OR=2.0). Suicidal Attempt was 3.4 more correlated to Early Awakening.

Conclusion: Suicidal behavior was present in our pediatric patients with depression, and it was well associated with sleep complaints. The mean of the presence of the sleep complaints related to depression need to be clarified.

0813

POLYSOMNOGRAPHY AND NEUROBEHAVIORAL PROFILES OF INSOMNIA IN A COMMUNITY SAMPLE OF YOUNG CHILDREN

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Introduction: Despite the fact that approximately one in five children have parent reported insomnia-like symptoms, studies are limited and results inconsistent. Our objective was to examine the relationship between childhood insomnia and behavioral outcomes in a large general population sample of children.

Methods: A population based study of 695 school aged children (6-12 years) underwent a 9-hour polysomnogram and a parent completed global behavior rating scale. Children were initially divided into two groups: those with and without parent reported insomnia symptoms (e.g., difficulty falling and/or staying asleep). We then examined the relationship between types of insomnia complaint: no insomnia, difficulty falling asleep only, difficulty staying asleep only and both complaints. Finally, based on the child's objective sleep latency, we split the insomnia like group into two: "normal" sleep latency (<21 minutes) and "long" sleep latency ($\geq$ 21minutes).

Results: Children with insomnia-like symptoms demonstrated more problems on all neurobehavioral indices than children without. The parents who reported that their children had difficulty falling asleep and waking often during the night, rated them significantly higher in mood variability and school problems than children whose parents only reported difficulty falling asleep. Wakes often was not significantly associated with any neurobehavioral symptoms. Children with insomnia like symptoms and "normal" sleep latency showed a profile of predominately higher levels of conduct problems, attention deficit, inappropriate social behavior and mood variability whereas children with insomnia-like symptoms and "long" sleep latency showed none.

Conclusion: Severity of subjective insomnia complaint was associated with mood and cognition problems. Children with both a parent reported complaint of insomnia and objective "normal" sleep latency are more psychologically distressed than children with insomnia and objective "long" sleep latency. Objective sleep latency may be a useful marker in subtyping childhood insomnia.

0814

OBJECTIVE SLEEP ABNORMALITIES AS A POTENTIAL PATHWAY FROM CHILDHOOD GENERALIZED ANXIETY DISORDER (GAD) TO DEPRESSION IN ADULTHOOD

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Introduction: Up to 90% of children with GAD report problems sleeping but polysomnographic evidence of sleep abnormalities is available among adults with GAD only. In depressed patients, sleep abnormalities are well documented in adults while essentially normal sleep patterns are found in children. The current study therefore examined objective sleep patterns in children with GAD (without comorbid depression) compared to age-matched controls.

Methods: Non-medicated children with a primary GAD diagnosis (n=12) and healthy control children with no emotional/behavioral problems (n=10) were assessed (7-11 years; M = 8.7) based on structured diagnostic interviews, subjective sleep measures, and one night of standard polysomnography (PSG) in a sleep laboratory.

Results: Despite no differences in total sleep time or sleep onset latency, significantly shorter REM latencies and increased REM duration characterized children with GAD. Marginally-significant findings for a greater number of REM periods and reduced N2 sleep (p=.06) were also apparent in the GAD group. Perceived sleep onset latency (in minutes) in the lab corresponded with actual sleep onset latency for controls (r = .81; p<.05) but not GAD youth.

Conclusion: Results provide objective evidence of sleep abnormalities in prepubescent, non-depressed children with GAD. Significantly reduced REM latency and increased total REM correspond with sleep abnormalities documented in adults with depression more so than anxiety. Despite a small sample size, findings provide potential evidence of a specific physiologic pathway between childhood GAD and the later onset of depression.

0815

BEDTIME RESISTANCE AND SLEEP ANXIETY ARE RELATED TO PARENT ATTACHMENT IN PARENTS OF CHILDREN WITH DOWN SYNDROME

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Introduction: Children with Down syndrome (DS) have a high incidence of sleep problems (Carter et al., 2009). Previous studies have found a relationship between pediatric sleep problems and parenting stress in typically developing children (Crowe, Clark, & Qualls, 1996) and children with chronic illness (Meltzer & Moore, 2007), and we sought to replicate this relationship in children with DS.

Methods: Fifty-six parents of children with DS (age range: 7-18 years, age mean: 12.33 years; 24 girls) completed the 33-item Child Sleep Habits Questionnaire (CSHQ) and a subset of questions from the 101-item Parenting Stress Index (PSI). The CSHQ is a screening instrument for school-aged children based on common clinical symptom presentations of prevalent sleep disorders. The PSI screens for stress in the parent-child relationship, identifies dysfunctional parenting, and predicts the potential for parental behavior problems and child adjustment difficulties within the family system. It contains five child domain subscales and seven parent domain subscales. One of the latter subscales is attachment, which assesses the degree to which a parent feels a sense of emotional closeness with the child, with higher scores indicating insecure attachment.

Results: Eighty-eight percent of our sample (49 children) had total sleep disturbance scores in the clinical range (i.e., greater than 41). There were

no correlations between the total sleep disturbance scores and total stress scores, or PSI subscale scores. Bedtime resistance and sleep anxiety (two subscales from the CSHQ) were both positively correlated with the parent attachment subscale of the PSI (r = 0.370, p < 0.05; r = 0.438, p < 0.01, respectively).

Conclusion: These findings suggest that a child's level of bedtime resistance and sleep anxiety relate to parents' ratings of attachment with children with DS. These findings are consistent with literature demonstrating a relationship between sleep problems and parenting stress.

Support (If Any): Down Syndrome Research and Treatment Foundation, National Down Syndrome Society, Arizona Alzheimer's Research Consortium, The Lejeune Foundation, The Thrasher Research Fund

0816

EXOGENOUS MELATONIN FOR SLEEP DISORDERS IN CHILDREN WITH VISUAL IMPAIRMENT AND INTELLECTUAL DISABILITY: EVIDENCE GROWS BUT RESEARCH SHRINKS

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Introduction: Sleep disturbances in children with neurodevelopmental disabilities are common and frequently difficult to treat using conventional pharmacological and behavioural interventions. Exogenous melatonin is increasingly being used in a non-regulated manner for various pediatric sleep disorders.

Methods: A systematic review of the efficacy and safety of exogenous melatonin in participants aged 3 months to 18 years was conducted using 6 electronic databases and reference lists of relevant reviews of studies reported between 1980 and 2010, and associated professional sleep society abstracts from 1999 to 2010. Randomized controlled trials (RCTs) were assessed using the Jadad scale and the criteria of Schultz et.al, and non-randomized trials were assessed by the Downs and Black checklist. Inverse variance method was used to weight the studies and a random effects model was used to analyze the data in RevMan 2008 (Update Software)

Results: Two RCTs with 8 participants were retrieved for melatonin treatment of visually impaired children which reported improved effect on sleep latency (p=0.019 and p<0.05, respectively). However, a separate analysis for visual impairment was not conducted. Ten RCTs of 298 participants were retrieved for melatonin in children with an intellectual disability. Two RCTs that reported time-to-sleep onset showed a significant decrease (p<0.05) for this outcome. Study duration was short at a maximum of 8 weeks. Subjective and objective measures of sleep improvement were not standardized and were inadequate. No study evaluated the impact of exogenous melatonin on the pharmacokinetic profile and phase response of endogenous melatonin.

Conclusion: Despite limited RCT data, melatonin remains a commonly prescribed drug for sleep disorders in children with intellectual disability and visual impairment. Although there is evidence from small scale studies suggesting appropriately timed melatonin therapy is effective, an optimal dosing schedule has yet to be defined for improving sleep in this vulnerable, but less studied, pediatric population.

0817

EVALUATION OF A STANDARDIZED BEHAVIORAL PROTOCOL IN THE TREATMENT OF SLEEP PROBLEMS IN CHILDREN WITH ANGELMAN SYNDROME

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Introduction: Angelman syndrome is a neurogenetic developmental disorder characterized by a variety of behavior problems, including language deficits, hyperactivity, short attention span, and pervasive and persistent disturbances in sleep. Yet, despite the robust evidence base supporting the use of a number of behavioral treatments for pediatric sleep problems in typically developing children, there have been no controlled studies of behavioral sleep interventions in children with Angelman syndrome. Perhaps as a result, only a small minority of parents of children with Angelman syndrome ever receive behavioral recommendations for sleep problems. Consequently, the purpose of the current study is to evaluate the outcomes of a standard behavioral therapy protocol to address sleep disturbances in children with Angelman syndrome.

Methods: Participants included children between the ages of 4-11 years with Angelman syndrome. Participants were required to demonstrate frequent bedtime resistance, difficulty falling asleep without parental presence, and/or frequent night wakening. Parents maintained daily diaries to record disruptive bedtime behaviors, total sleep time, sleep latency, and night wakings, as well as actigraph monitoring. The treatment targeted three primary areas that have been linked to sleep impairment in children; the sleep environment, sleep-wake schedule, and parent-child interactions.

Results: Results were evaluated using two types of interrupted time series designs involving the intensive study of individuals across repeated observations before and after treatment. Results showed that for each subject, the introduction of treatment produced marked and sustained reductions in disruptive bedtime behavior, improved sleep latency, increased independent sleep onset, and fewer night-time awakenings. One and three-month follow-up data are currently being collected. Actigraph data will also be analyzed pre and post-treatment to evaluate subjective reports that children with Angelman syndrome often present with a reduced inherent sleep requirement.

Conclusion: Behavioral interventions should be considered as a viable treatment option to address sleep disturbances in children with Angelman Syndrome.

0818

ADDRESSING SLEEP PROBLEMS IN CHILDREN WITH AUTISM SPECTRUM DISORDERS AT A MULTIDISCIPLINARY AUTISM CENTER

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Introduction: Sleep problems are highly prevalent among children with Autism Spectrum Disorders (ASDs), particularly insomnia. Pediatric sleep problems are often overlooked in typically-developing children. It is unknown how often they are addressed in children with ASDs. Goals were to quantify how often children with ASDs had sleep problems addressed by their autism providers, and test for differences between children whose sleep problems were addressed versus not. It was hypothesized that children with snoring/apneas would have sleep addressed and those with insomnia would not consistently have it addressed.

Methods: This retrospective cross-sectional cohort included 122 subjects with ASDs from a single center, ages 2-17.5 years, 85% male, and

79% white. Problem sleep was defined by an intake item asking the extent to which sleep disturbance was a problem within the past month. Parents were administered the Children's Sleep Habits Questionnaire (CSHQ). Clinicians documented whether discussion of sleep and/or referral to subspecialty clinic occurred. Logistic regression models were performed to examine associations between sleep symptoms (sleep disordered breathing, insomnia) and discussion/referral of sleep problems.

Results: Twenty-six subjects (21%) were categorized as problem sleepers, twelve (46%) of whom had discussion (8), referral (1), or both (3). CSHQ Sleep Disordered Breathing Subscale score was not associated with problem sleep (p=0.1), but with increased likelihood of discussion or subspecialty referral (OR=1.7, confidence interval [CI]=1.1-2.8, P=0.03). Sleeping too little and night waking were associated with problem sleep (P<0.001), but not its discussion or referral. Sleeping in a parent's bed and prolonged sleep onset were not associated with problem sleep being identified or addressed.

Conclusion: Sleep issues in children with autism are not consistently addressed, even by experienced clinicians. Larger studies are needed to confirm results as well as explore factors affecting whether sleep problems are addressed and how to best train clinicians in this area.

0819

SLEEP DISORDERS IN A COHORT OF CHILDREN WITH AUTISM SPECTRUM DISORDER

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Introduction: Autism Spectrum Disorder (ASD) is one of the most devastating disorders of brain development, with a prevalence of 1 in 110 children. A common medical condition in children with ASD is chronic insomnia, with a prevalence of 60-80%. There are more than 80 sleep disorders in the ICSD-2 and identifying the underlying cause of insomnia in children with ASD is a complex and challenging task. The purpose of this secondary analysis of a descriptive cross sectional study of the sleep behaviors and sleep quality in children with ASD was to identify the specific sleep disorder for each child identified with insomnia on a case by case basis.

Methods: Children with ASD, ages 4-10, were randomly selected from a Regional Autism Center, n=59. ASD diagnosis was confirmed with the ADOS and DSM-IV-TR. Each child's sleep was evaluated with home observations, comprehensive medical, developmental and sleep history, including medication history, chart review, Children's Sleep Habit Questionnaire scores, 2 weeks of sleep diary and 10 nights of actigraphy.

Results: Based on subjective and objective measures, 66% of the participants were identified with insomnia. Sleep diagnoses identified were: sleep disordered breathing, n=1(2.5%), sleep terrors, n=3(7.7%), behavioral insomnia -sleep association type, n=12(31%), behavioral insomnia-limit setting type, n=6 (15%), medical condition, n=6 (15%) and 11(28%) children had adequate sleep hygiene, strong bedtime routines, fell asleep by themselves, and had no identifiable medical condition that could cause sleep disturbances. These 11 cases were not better explained by another sleep disorder and are best described as Insomnia due to ASD.

Conclusion: Intrinsic causes for insomnia in ASD population needs to be further explored. Hypotheses for intrinsic causes include: Arousal dysregulation due to synaptic pathway anomalies, abnormal melatonin rates and rhythms and clock gene mutations in ASD.

0820

POSSIBLE RELATION BETWEEN (A) H1N1 VACCINATION AND PEDIATRIC NARCOLEPSY

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Introduction: Narcolepsy is a condition which the precise cause is unknown, however it is generally considered to be triggered by a combination of genetic and environmental factors, including infections. Since the signal on a potential association between H1N1 vaccination and narcolepsy was raised in Sweden and Finland, additional cases have been reported in different countries over Europe and particularly in France. France was exposed to a large vaccination campaign from October to December 2009 specifically orientated towards children.

Methods: Pediatric data have been extracted from a National French multicentric research program on narcolepsy (PHRC AOM07-138) that has enrolled a cohort of 544 narcoleptic patients. Post H1N1 pediatric patients were investigated at the Pediatric Centre for Narcolepsy Robert-Debre in Paris (1) and at the Hospital Mere-Enfant in Lyon (2) between December 2009 and October 2010.

Results: Five patients (1) and 1 patient (2) (4 girls, 2 boys) aged from 9 to 13 yo were diagnosed with narcolepsy with cataplexy. All patients were both healthy and free of any morbid condition before the sudden occurrence of EDS, weight gain and clear-cut cataplexy triggered by emotion. Symptoms developed in all patients between December 2009 and October 2010. Patients had been vaccinated with one or two injections of Pandemrix 4 or Panenza 2. Other potential triggering factors had been excluded by history taking. Patients showed positive MSLT and normal brain MRI. All children were HLA DQB1*0602 positive, hypocretin deficient and Trib 2 negative (except in one single case with familial history of narcolepsy).

Conclusion: A severe and complete form of narcolepsy with cataplexy occured in all six children within a few weeks or months following (A) H1N1 vaccination. All children shared common clinical features including acute onset of symptoms. The role of the H1N1 vaccine in these cases is still unclear and currently under investigation.

Support (If Any): PHRC AOM07-138, French health Ministry; promotor: Assistance Publique - Hôpitaux de Paris.

0821

MODAFINIL IS AN EFFECTIVE AND SAFE TREATMENT FOR PEDIATRIC NARCOLEPSY

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Introduction: Narcolepsy with cataplexy occurs during childhood in approximately one third of the subjects. Considering the dramatic consequences of the disorder, medication may be required at an early stage. During the past decades, modafinil has been used as first line treatment in narcoleptic children. However, systematic data are lacking to evaluate the benefice/risk ratio of the drug.

Methods: Pediatric data have been extracted from a National French multicentric research program on narcolepsy (PHRC AOM07-138) that has enrolled a cohort of 544 narcoleptic patients.

Results: A total of 45 children among 49 affected with narcolepsy and 4 with idiopathic hypersomnia received modafinil. Mean age at onset of treatment was 10.9±3.5 years (age range: 3-16 yo). The average daily dose of modafinil was 388±158 mg (200 to 800mg). Duration of treatment varied from 28 days to 10 years (mean 933±965 days). The mean estimated improvement was 5.8±1.8 (self rating scale 0-9). Modafinil was interrupted in 12 children because of lack of efficacy (9), excessive cost (1), mild adverse effects (2). It was combined with other stimulants in 8 children (stimulants 6 and sodium oxybate 2). There were no reported adverse effects in 30/45 (66%) children. There were minor and transient adverse effects in 12 (26%) children, including headache (3), loss of appetite (2), dry mouth (2), irritability (1), tremor (1), hot flushes (1), tongue protrusion (1), and increased cataplexy (1). Treatment was interrupted due to an adverse effect in 2 children only.

Conclusion: Modafinil was first line treatment in 85% of narcoleptic children in our cohort, showing a positive benefit/risk ratio in 75% of the cases, with a mean duration of use of 3 years. No severe AE occurred and most of the reported side effects were transient and benign. In our pediatric cohort, Modafinil appeared to be safe, well tolerated and effective.

Support (If Any): PHRC AOM07-138, French health Ministry; promotor: Assistance Publique - Hôpitaux de Paris

0822

SLEEP DISORDERS IN THE SEVERELY MENTALLY HANDICAPPED: A REPORT CONCERNING THE REPERCUSSIONS FOR FAMILIES AND THE EXPERIENCES OF HEALTH PROFESSIONALS

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Introduction: The incidence of severe mental handicap in France is estimated at 3-4/1000 live births. Sleep disorders are frequent and often severe in this population of children. The aim of our study was to report on the current situation of families with severely mentally handicapped children and also medical staff who treat these children in France.

Methods: With the help of the Reseau Lucioles, we addressed an adapted version of the Children's Sleep Disturbance Scale (SDSC) questionnaire to the families of severely mentally handicapped children in France. We also distributed a questionnaire to paediatricians working with the Centre d'Action Médico Sociale Précoce , which is a centre for the prevention detection and treatment of mental handicap and also to paediatric neurologists present at the French Society of Neuropediatricians (SFNP) in 2010.

Results: We received replies from 292 families. The population was made up of 75.9% children: 26.4% Angelman syndrome, 14.7% Rett syndrome ,12% autistic disorders and 46.8% of other pathologies. 93.8% of the population who responded to the questionnaire stated that their child suffered from sleep disturbances. 43.8% classified the trouble as severe or very severe. We found a reported incidence of 70% concerning sleep onset insomnia , 51% reporting short sleep duration , 60% reporting night awakenings or sleep maintenance disorder, 12% with sleep respiratory disturbance, and 35% with excessive daytime sleepiness. Only 23% of people replying had found solutions to reported sleep disorders. 94.3% of parents and 41.1% of siblings estimated that they were "quite" or "very " bothered by sleep problems presented by the mentally handicapped member. We analysed 154 questionnaire replies from medical doctors, who estimated that less than 50% of their patients suffered from sleep disorders . They also expressed their difficulty in diagnosing and treating such pathologies.

Conclusion: Our study highlights the need for progress in the management of sleep disorders in the severely mentally handicapped children.

0823

SLEEP HYGIENE AND ACTIGRAPHICALLY EVALUATED SLEEP CHARACTERISTICS IN CHILDREN WITH IN CHILDREN WITH BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES

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Introduction: Sleep problems are frequent in epileptic children. Although several studies described the relationship between epilepsy and sleep, no studies investigated sleep hygiene (SH) in these children. Aim of this study is to investigate SH and sleep in children with Benign childhood epilepsy with centrotemporal spikes (BCECTS) where it is generally presumed that quality of life is not significantly affected.

Methods: A sample of 85 epileptic (mean age 7.6 years)and 182 typically developing children (TD) (mean age 7.8 years) were investigated. None of epileptics had frequent seizures and were drug-free. Parents completed Children's Sleep Hygiene Scale (CSHS, Harsh, 2001) and Children's Sleep Habits Questionnaire (CSHQ, Owens 2000). Sleep was actigraphically evaluated for 7 consecutive nights.

Results: ANOVA results showed that epileptic children scored significantly higher on CSHQ (Total 57 vs 43, Bedtime Resistance 10 vs 8, Night-Wakings 6 vs 3, Sleep Anxiety 8 vs 5, Parasomnias 12 vs 8, Sleep Duration 5 vs 4,p<.001) than TD. Actigraphic data showed that epileptics had significant later bedtime (21.55 vs 21.35; p<.005) more WASO (36 vs 10 min,p<.0001) and shorter nighttime sleep (567 vs 581 min; p<.01) than TD. Interestingly, they had significantly less weekend oversleep (38 vs 53 mins , p<.001) and showed better sleep hygiene than TD (SH Total 4.2 vs 3.7, Physiological 5.5 vs 4.9; Cognitive 4.8 vs 4, Emotional 0.96 vs 0.64 ; Bedtime Routine 4 vs 3.3; Stability 5.3 vs 4.9;p<.001).

Conclusion: Results suggest that despite children with BECTS have more sleep problems and sleep fragmentation, their sleep hygiene practices are more adequate than in controls. One potential reason is that good sleep hygiene practices derive from a higher parental anxiety resulting in more parental control, which habitually refrain children from a lot of practices that might possibly aggravate the course of epilepsy.

0824

PREVALENCE OF SLEEP DISORDERS IN CHILDREN WITH EPILEPSY REFERRED TO A SLEEP CENTER

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Introduction: Sleep and epilepsy are interrelated. Sleep disorders are increasingly recognized as a common comorbidity of epilepsy. Limited data exists about prevalence of these disorders in children with epilepsy. We performed a retrospective review to identify the referral reasons and diagnoses in this population.

Methods: The study was approved by the institutional review board at the Cincinnati Children's Hospital Medical Center. All patients with epilepsy, evaluated in sleep center from 2005 to 2009 with polysomnography (PSG), were identified and the records were reviewed.

Results: Total 69 patients met the criteria for the study including 43 males and 26 females, with ages 0.8 to 28.1 (9.9 ± 6.1), with 10 with generalized, 52 with focal and 7 with unclassified epilepsy. Forty six patients were referred for snoring, 7 for gasping/pauses in breathing, 4 for excessive daytime sleepiness, 7 for insomnia and 5 for movements in sleep. Fourteen patients had primary snoring and 9 did not have a sleep disorder. Thirty patients were diagnosed with OSA and 2 with Hypoventilation. One patient had central sleep apnea (CSA) and another one periodic limb movement disorder (PLMD) along with OSA. Five

patients were diagnosed with CSA who all had focal epilepsy. Seven patients were diagnosed with insomnia and 2 with PLMD.

Conclusion: In this referred population, the prevalence of OSA was 47.8%, CSA was 7%, insomnia was 10%, PLMD was 2.8%, primary snoring was 20% and no identifiable sleep disorder was 13%. OSA was identified in 56.5% the patients who snored and CSA in 14% with respiratory pauses. The most common referral reason was sleep related breathing problems and diagnosis was OSA. The reason for this may be more awareness and easy screening for these disorders. Further studies are needed to identify the true prevalence of sleep disorders in the patients with epilepsy.

0825

WAKEFULNESS AND SLEEP STATES PREDICT LOCALIZATION OF SEIZURE ONSET IN SEIZURES OF DIFFERENT SEMIOLOGIES

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Introduction: Recent evidence supports the notion that sleep and wakefulness may predict seizure semiology and localization. The aim of this study was to evaluate the relationship between semiology of seizures in children and adolescents to the corresponding seizure localization (focal/generalized) during wakefulness and sleep.

Methods: Charts of 380 consecutive pediatric epilepsy patients undergoing Video-EEG monitoring over 2 years were reviewed. Seizure semiology recorded during monitoring was classified according to ILAE seizure semiology terminology, and analyzed based on occurence during wakefulness/sleep and EEG onset (generalized/focal). Statistical analysis was performed for non-parametric measures. When appropriate odds ratio were calculated using 95% confidence intervals.

Results: A total of 1008 seizures were analyzed in 380 children, mean age was 8.5 years ± 5.7 (range 0-20), with 50% girls. A total of 547 (54%) seizures occurred in wakefulness and 461 (46%) occurred in sleep. Auras, gelastic, dyscognitive, atonic, myoclonic, hypomotor seizures, and epileptic spasms occurred more often in wakefulness, while tonic, tonic-clonic, automotor, and hypermotor seizures occurred more frequently in sleep. The most common seizure localization onset was generalized, seen in 374 of the 1008 seizures (37%). Overall, 66% of auras with focal onset occurred during wakefulness, while only 35% of generalized onset auras occurred during wakefulness (p<0.001). Focal onset auras were 3.7 times more likely to occur during wakefulness than generalized onset auras (OR 3.71, CI1.38-9.97). Additionally, 92% of myoclonic seizures with generalized onset occurred during wakefulness, while only 37.5% of focal onset myoclonic seizures occurred during wakefulness (p<0.001). Generalized onset myoclonic seizures were 19-times more likely to occur during wakefulness than focal onset myoclonic seizures (OR19.16, CI 4.54-80.74).

Conclusion: Sleep and wakefulness may predict whether auras and myoclonic seizures have focal or generalized onset. Semiology of seizures and data on occurrence during wakefulness or sleep can provide important information for epilepsy localization.

0826

SLEEP COMPLAINTS IN ADOLESCENT BRAIN TUMOR SURVIVORS

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Introduction: Survivors of pediatric brain tumors have reported increased rates of excessive daytime sleepiness (EDS). However, little data are available regarding the specific sleep disturbances of pediatric brain tumor survivors.

Methods: Adolescents (n = 49) ages 13 to 18 years who were at least 5 years from diagnosis and at least 2 years post treatment for brain tumor completed the Adolescent Sleep Hygiene Scale (ASHS) and the Modified Epworth Sleepiness Scale (ESS). Their parents completed the Kosair Children's Hospital Sleep Questionnaire and the Modified ESS.

Results: On adolescent self-report, 28% reported EDS, though they reported relatively good sleep hygiene, with the exception of the Sleep Stability subscale (Mean = 3.93 + 1.1). By parent-report, 17% had EDS on the ESS, and 16% were reported on the Kosair to appear fatigued frequently to almost always. Twenty percent were reported to snore frequently to almost always. The majority of adolescents (57%) were reported to sleep 8-9 hours per night, while 21% were reported to sleep less than 8 hours each night. Concordance between parents and adolescents reporting on EDS was only fair, with a kappa coefficient of 0.4125. While age at diagnosis was unrelated to EDS for self-report, older age at diagnosis was related to increased EDS by parent report.The type of brain tumor was unrelated to EDS.

Conclusion: Our sample reported similar rates of EDS to previous studies of pediatric brain tumor survivors. Concordance rates of EDS reporting between survivors and parents suggest that parents may not recognize their adolescents' significant sleepiness. A higher proportion of snoring was reported in our adolescent brain tumor survivors than is typical for adolescents.

0827

ASSESSMENT OF SLEEPINESS AND SLEEP DEBT IN ADOLESCENT POPULATION IN URBAN INDIA

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Introduction: Adolescence being a crucial and evolving phase of human life is subject to several unique intrinsic and extrinsic stressors contributing to an unstructured and inadequate sleep/wake routine. Its negative impact on cognitive impairment and body mass index has been well documented in the western population, the paucity of Indian literature in our young adults prompted us to undertake this study.

Methods: A questionnaire based cross sectional study in school going adolescents aged 13-15 years. Participants completed the Cleveland Adolescent Sleepiness Questionnaire as a measure of sleepiness after informed consent and documented hours of sleep obtained.

Results: Mean age of the participants was 13.8 years (Age range: 13-15). Gender ratio of the participants was M:F=3.4:1. Mean CASQ score was 36.3 ± 9.75. Age positively correlated for sleepiness as well as total scores (r=0.257, p<0.001)however gender showed no difference (p=0.769) in this study. Sleepiness statement score positively correlated with hours of sleep with a p value of <0.05. 24.8% of children obtained less than 6 hours of sleep. 43% of adolescents reported falling asleep in class in the morning and 21% felt sleepy while doing their school assignments at home.

Conclusion: Indian adolescents like their global counterparts also have excessive daytime somnolence and sleep debt which is largely unrec-

ognized warranting a study with a larger sample size and intervention with education.

0828

PREVALENCE AND CORRELATES OF POOR SLEEP QUALITY AMONG SURVIVAL ADOLESCENTS 18 MONTHS AFTER 2008 WENCHUAN EARTHQUAKE, CHINA

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Introduction: Sleep problems are prevalent among adolescents. Multiple psychosocial and biological factors are associated with increased risk for sleep problems in adolescents. However, little is known about sleep quality and its correlates among adolescents exposed to natural traumatic events. This study examined the prevalence and correlates of poor sleep quality among survival adolescents 18 months after 2008 Wenchuan earthquake in China.

Methods: Eighteen months after Wenchuan earthquake in 2008, a questionnaire survey was conducted in a sample of 1494 8th and 11th graders in Dujiangyan district, 20 kilometer away from the epicenter. A total of 233 adolescent students as a control group were sampled from a nearby school district where the students were not exposed to the earthquake. Participants were asked to fill out a self-administered questionnaire including the Pittsburgh Sleep Quality Index, Adolescents Self-rating Life Event Checklist, and Social Support Rating Scale for Children and Adolescents. Stepwise regression analysis was used to examine significant predictors of sleep quality.

Results: The mean total PSQI score was significantly higher in exposure group (Mean=5.89, SD=2.84) than in control group (Mean=4.82, SD=2.6) (p<.01). Using the total PSQI score of 8 as cutoff, the prevalence of poor sleep quality was significantly higher in exposure group (28.2%) than in control group (15.5%) (p<.01). Stepwise regression analysis showed that female gender (β=0.067), age (β=0.185) and, negative life events (β=0.371) were associated with increased risk for poor sleep quality; while subjective social support (β=-0.092) and utilization of social supports (β=-0.065) were associated with decreased risk for poor sleep quality.

Conclusion: Our results suggest that sleep quality among adolescents 18 months after earthquake exposure are still poor. Multiple psychosocial factors are associated with poor sleep quality among survival adolescents after earthquake.

0829

POOR SLEEP QUALITY ASSOCIATED WITH PTSD, ANXIETY, AND DEPRESSION AMONG ADOLESCENTS EXPOSED TO 2008 WENCHUAN EARTHQUAKE, CHINA

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Introduction: Adolescents are at risk for sleep problems. Numerous studies have shown that sleep problems are very common after natural disasters. Little is known about sleep and mental health problems among adolescents after natural traumatic events. This study examined the association between sleep quality and PTSD, anxiety and depressive symptoms among juvenile victims 18 months post 2008 Wenchuan earthquake, China.

Methods: A total of 1473 adolescents 18 months after the 2008 Wenchuan earthquake were sampled from Dujiangyan district, 20 kilometer

away from the epicenter. The mean age of the sample was 15.92 years (SD=1.33), 54.3% were female. Participants were asked to complete a questionnaire including the Pittsburgh Sleep Quality Index, Self-Rating Scale for Posttraumatic Stress Disorder, the Depression Self-Rating Scale for Children, the Screen for Child Anxiety and Related Emotional Disorders.

Results: The total PSQI score was significantly related to PTSD (r=0.396), depression (r=0.501) and anxiety score (r=0.470) (All p values<0.01). Using the total PSQI score of 8 as cutoff, the prevalence of poor sleep was 28.2%. The comorbidity of poor sleep with PTSD, depression, and anxiety were 7.5%, 15.5%, and 18.1%, respectively. The prevalence of PTSD (26.5% vs 6.9%), depression (55.5% vs 22.9%), and anxiety (63.9% vs. 29.7%) were significantly higher among poor sleepers than normal sleepers (all p values < .01).

Conclusion: Poor sleep quality is associated with PTSD, anxiety, and depressive symptoms among adolescent survivors after earthquake. Sleep assessment and intervention may be important in the prevention of mental health problems for adolescent survivors.

0830

IMPACT OF CHRONOBIOTIC CHAOS ON SLEEP AND DAYTIME FUNCTIONING IN PARENTS OF VENTILATOR-ASSISTED CHILDREN

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Introduction: Compared to parents of healthy children, parents of children with chronic illnesses have been reported to have more sleep disruptions, as well as more problems with daytime functioning (e.g., mood, fatigue). When caring for a child who requires mechanical ventilation, parent sleep is often disrupted due to required nighttime caregiving (e.g., suctioning, responding to vent alarms), which can negatively impact daytime functioning. This study examined sleep and daytime functioning in mothers and fathers of ventilator-assisted children.

Methods: Fifty-eight parents of ventilator-assisted children (VAC; 42 mothers and 16 fathers) and 21 comparison parents of typically-developing healthy children (TD; 13 mothers and 8 fathers) wore an actigraph for 14 nights to assess sleep-wake patterns and activity levels, as well as completed measures of health related quality of life (HRQOL; SF-36) and executive functioning (BRIEF).

Results: Both groups obtained 7.0 hours of sleep over a 24-hour period. However, from 22:00-06:00, VAC parents were significantly more active (mean activity: VAC=50.7, TD=33.5, p=.02) and obtained less sleep (mean TST: VAC=5.5 hours, TD=6.3 hours, p=.02). From 06:00-12:00, VAC parents slept more than TD parents (VAC=79 minutes, TD=50 minutes). Although not statistically significant, this 29 minute difference is clinically meaningful. A significant difference [$F_{(1,77)}$=6.5, p=.01] was found between groups for organizational aspects of executive functioning, as well as for the mental functioning and well being aspects of HRQOL [$F_{(1,77)}$=5.3, p=.02]. Executive functioning was significantly correlated with overnight sleep minutes [r=-.37, p=.002], suggesting that parents who had less sleep time from 22:00-06:00 reported more problems with organization during the day.

Conclusion: Although the total sleep time over 24-hours did not differ between parents of VAC and parents of TD children, the almost one hour sleep deficit during the typical sleep time of 22:00 to 06:00, as well as the increased activity levels overnight suggest that parents of VAC are experiencing "chronobiotic chaos." In addition, this disrupted sleep may be related to different aspects of daytime functioning, including organizational abilities. Additional support for VAC parents, including overnight in-home nursing care may help parents obtain greater quantity

and better quality sleep at night, consequently improving their daytime alertness and functioning.

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0831

MATERNAL SNORING DURING PREGNANCY DOES NOT AFFECT FETAL GROWTH

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Introduction: Snoring is common among pregnant women affecting up to 46% of women during the third trimester. Previous studies investigating the effect of maternal snoring on fetal growth have revealed conflicting results. Therefore, our objective was to examine the effect of maternal snoring on fetal growth.

Methods: Women of singleton uncomplicated full-term pregnancies were recruited during labor. All participants together with their sleep partners completed a designated questionnaire that included information regarding BMI, age, smoking, medication use, pregnancy complications, snoring before and during the current pregnancy, sleep pauses and daytime sleepiness using the Epworth Sleepiness Scale. Subjects with frequent snoring (> 4 nights a week) were considered habitual snorers. Birth weights were obtained following delivery. Birth weights percentiles were calculated for gender and gestational age.

Results: Two hundreds and fifty women were recruited. 49% of women reported habitual snoring during pregnancy. Of those, 26% were chronic snorers (snored before pregnancy) and 74% were new-onset snorers (began to snore during the current pregnancy). There were no differences in maternal age (30.9±4.1 vs. 31.1±4.7 years), BMI at the beginning of the pregnancy (27.4±3.3 vs. 26.5±3.8 kg/m2) and maternal weight gain percentage (23.7±9.6 vs. 21.7±9.3%) between snorers and non snorers. No differences were found in gestational age (39.4±1.0 weeks vs. 39.3±1.1 weeks) between snorers and non snorers. No differences were found between neonates born to snorers and non-snorers in Apgar scores (Apgar 1: 8.9±0.4 vs. 9.0±0.5; Apgar 5: 9.9±0.3 vs. 9.9±0.4, respectively, p=NS) and in birth weight percentiles (59.2±24.6 vs. 60.3±25.2, respectively, p=NS).

Conclusion: In this prospective cohort maternal snoring did not affect fetal growth.

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0832

EFFECTS OF BREASTFEEDING ON SLEEP IN INFANTS AND MOTHERS

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Introduction: While many infants at 6 months sleep through the night, some infants continue to wake and disrupt their mothers' sleep. The purpose of this study was to examine the effect of breastfeeding on sleep in infants and mothers.

Methods: The study was a secondary analysis using data from the National Sleep Foundation's 2004 Sleep in America Poll. A nationwide, representative sample of infants (N = 107) was obtained using a telephone survey of caregivers (72% mothers). The survey contained questions on infant bedtime schedule, sleep duration, nighttime awakenings, and caregiver sleep.

Results: Infants ages 6 to 11 months were more frequently (54%) bottle-fed. There was no significant difference between breast and bottle-fed infants in sleep duration or bedtime. More than 25% of the infants slept < 8 hrs/night and almost half were put to sleep after 9 p.m. Infants who went to bed before 9 p.m. had significantly (p = .002) longer total sleep duration (M = 13.07 hrs, SD = 1.96) than infants who went to bed after 9 p.m. (M = 11.80 hrs, SD = 2.06). Mothers (N=77, M = 31 years, 92% married, 87% White) were the primary caregiver (90%) at night. Almost 40% of the mothers had ≤ 6 hours of sleep/night. There was no significant difference in sleep duration between mothers who breast-fed (M = 6.76 hrs, SD = 1.31) and mothers who bottle-fed (M = 6.42 hrs, SD = 1.18). Mothers who breast-fed were woken more frequently at night (p <.05). Binary logistic regression found maternal age, infant age/gender, other children in the household and breastfeeding status were non-significant in predicting mothers who received ≤ 6 hours sleep; however, infants' total sleep duration was significant (p=.024).

Conclusion: Although breastfeeding does not negatively affect sleep, inadequate sleep is common among both infants and their mothers. Improving infants' nighttime sleep may be associated with improvements in mother's obtaining adequate sleep duration.

0833

SLEEP AND SOCIO-EMOTIONAL DEVELOPMENT IN INFANTS

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Introduction: The aim of this study was to assess the impact of sleep on socio-emotional functioning in infants.

Methods: A longitudinal study was conducted of infants' sleep at 9-months (N=49) and 12-months (N=74). Parents completed the Brief Infant Sleep Questionnaire at 9- and 12-months, as well as the Infant-Toddler Social and Emotional Assessment (ITSEA) at 12-months of age. Subdomain scores for competence, internalizing, and externalizing, were examined.

Results: Bivariate correlations were first conducted, with significant variables then entered into linear regressions. Sleep variables significantly predicted competence and internalizing scores at 12-months, with 9-month sleep more highly predictive of future socio-emotional functioning (22-31% variance) than concurrent sleep (13-17% variance). Specifically for competence at 12 months, sleep onset latency, sleep consolidation, and parental perception of sleep at 9-months accounted for 31% of the variance. Concurrent sleep variables that predicted competence (17% variance) at 12 months included sleep consolidation and parental perception of sleep problems. Internalizing at 12-months was predicted by how often the infant had the same bedtime routine, total daytime sleep, and morning mood at 9 months (R2=.22) and bedtime and total sleep time at night concurrently (R2=.13). Sleep at 9-months was not related to externalizing scores and at 12 months concurrent sleep only accounted for 1% of the variance.

Conclusion: This study is one of the first studies to examine the relationship between sleep and socio-emotional functioning in infants. Interestingly, sleep at 9-months of age was more highly predictive of competence (e.g., compliance, attention, peer relations) and internalizing symptoms (e.g., anxiety, depression/withdrawal) at 12-months than concurrent sleep behaviors. On the other hand, sleep variables were not very predictive of externalizing behaviors (e.g., activity, aggression). These findings suggest that sleep may be more important to competence development and internalizing behaviors during infancy than externalizing behaviors. Furthermore, early sleep issues may be more predictive of future behavioral issues in infants than current sleep issues.

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0834

ARE THERE ASSOCIATIONS BETWEEN MOTHER-CHILD BEDSHARING AND COGNITIVE AND BEHAVIORAL OUTCOMES?

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Introduction: Little is known about the developmental consequences of bedsharing for toddlers and older children. Most prior studies have examined the effects of bedsharing on sleep problems rather than considering cognitive and behavioral development as outcomes. This study examines the predictors and consequences of mother-child bedsharing at 1, 2, 3 and 5 years of age in a racially/ethnically and geographically diverse sample of low-income families across the U.S.

Methods: This study uses data from The Early Head Start Research and Evaluation Study, an evaluation of the Early Head Start (EHS) program that began when the program was authorized in 1995. The study was conducted at 17 EHS programs across the country selected for their geographic and programmatic diversity. We analyze data from 958 low-income families who were assessed at 4 timepoints up to age 5. Bedsharing was assessed at the 1, 2, and 3 year home visits. The parenting and maternal depression variables in our analyses are from the 1st year home visit. Demographic variables were all collected at enrollment. Child cognitive and behavioral outcomes were collected at the age 5 home visit.

Results: Race and some parenting practices were the only characteristics significantly associated with higher odds of bedsharing. In the bivariate models, bedsharing was negatively associated with three out of the four outcomes studied (i.e. social skills, letter-word identification, and applied problems, but not hyperactivity). However, the association between bedsharing and behavioral and cognitive outcomes was rendered insignificant once we controlled for child and mother characteristics.

Conclusion: The negative association between bedsharing between the ages of 1 and 3 years and later behavioral and cognitive outcomes is probably not due to bedsharing itself, but rather to the sociodemographic characteristics of those who are more likely to bedshare.

0835

ASSOCIATION BETWEEN DELAYED BEDTIME AND SLEEP PROBLEMS AMONG COMMUNITY-DWELLING 2-YEAR-OLD CHILDREN IN JAPAN

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Introduction: Although delayed sleep timing has been revealed to be related to many socio/psycho/biological problems in adults including sleep loss, excessive daytime sleepiness, obesity, and impaired daytime neurocognitive performance, there are insufficient data showing the clinical significance of 'night owl life style' in early life. The aim of this study was to examine the association between habitual bedtime and sleep problems among community-dwelling 2-year-old children in Japan.

Methods: The study data were derived from attendants of the counseling program for 2-year-child-rearing from November 2008 to October 2009 in Nishi-Tokyo city, Japan. This study was a census survey and approximately 55% (868 / 1,570) of the community-dwelling mothers having raising 2-year-old child in the city joined the program. The participants were requested to answer a questionnaire consisted of thirty-one items to evaluate sleep habits and sleep problems of their children for the past one month.

Results: One hundred forty-nine children (20.2% of respondents) went to bed at 10 p.m. or later. Sleep habits varied greatly among children and sleep problems including insomnia, parasomnia, or sleep related breathing disorders were frequently observed and were regarded as problematic habits by their parents. Delayed bedtime was significantly correlated with irregular bedtime, delayed wake time, shorter total sleep time, and poor appetite. Although this relationship indicated the presence of sleep debt in children with delayed bedtime, the sleep onset latency did not differ between the children with earlier and delayed bedtime. Moreover, children with delayed bedtime showed high prevalence of bedtime resistance.

Conclusion: The present findings suggest that the severely delayed bedtime in a group of 2-year-old children could be fairly attribute to their circadian properties (intrinsic factors) rather than to their parent's life schedule (environmental factor), and these 'night owl type children' are vulnerable to various sleep and sleep-related problems.

0836

MATERNAL SENSITIVITY AND BEHAVIOR PROBLEMS IN TODDLERS: THE MODERATING ROLE OF INFANT SLEEP

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Introduction: The idea that children may vary in their susceptibility to rearing experiences due to certain biological factors refers to "differential susceptibility" (Belsky, 1997). As of today, temperamental and genetic characteristics have been found to modulate children's susceptibility to parenting influences. Sleep, as a core indicator of infants' psychophysiological regulation, may also play a modulating role in children's susceptibility to parenting, however this has yet to be investigated. The purpose of the current study was to examine the differential susceptibility hypothesis as it pertains to relations between infant sleep, maternal sensitivity and toddler behavior problems, in a prospective longitudinal design.

Methods: 39 infants (21 girls) took part in three visits, at 12, 18 and 25 months. Maternal sensitivity was rated by trained observers at T1 with the Maternal Behavior Q-Sort, based on direct observations performed throughout a 90-minute home visit. Infant sleep was assessed at T1 and

T2 using a sleep diary. The mean night-time sleep duration was derived separately at T1 and at T2 (r = .50). At T3, mothers completed the Child Behavior Checklist to assess children's internalizing and externalizing behavior problems.

Results: Results indicated that parenting quality interacted with infant sleep, at both 12 and 18 months, to predict toddlers' externalizing problems (β = - 0.32, p < .05; β = - 0.57, p < .05). These results were not found in regards to internalizing problems. The significant interactions were broken down, revealing in both cases that higher maternal sensitivity was related to lower levels of externalizing problems, however only for children who slept more at night.

Conclusion: The results of this study suggest that maternal sensitivity protects against externalizing problems when children get more nighttime sleep, and therefore perhaps that children who sleep less benefit to a lesser extent from quality parenting because they are more fatigued or irritable, and hence less receptive to external influences.

0837

ASSOCIATIONS BETWEEN NAP DURATION AND OBSERVED CHILDCARE QUALITY USING DATA FROM THE EARLY CHILDHOOD LONGITUDINAL STUDY-BIRTH COHORT

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Introduction: Most young children spend time being cared for in childcare programs, and most two-year-olds are still napping daily. Very little is known about napping and its potential relationship with characteristics of childcare programs. Previous exploratory research found that children in high quality child care slept less during the day compared to peers in low quality settings. This study examines whether the observed quality of childcare settings is associated with two-year-olds' nap duration in a national dataset: the Early Childhood Longitudinal Study - Birth Cohort (ECLS-B).

Methods: ECLS-B is a longitudinal, nationally representative study of children in the U.S. The analyses reported here use data from the two-year wave of data collection (approximately 1,000 two-year-olds). All analyses used SAS PROC SURVEY Taylor Series Linearization, which takes into account the complex sampling design. Childcare quality was measured by the Infant/Toddler Environmental Rating Scale (ITERS), an assessment of the quality of center-based childcare classrooms. Our analysis used both subscale scores and the global quality rating (ranging from 1 to 7; 7 = highest quality). Childcare providers reported on children's nap duration.

Results: Average nap duration for children in center-based care was 1.83 hours per day. After controlling for gender, ethnicity, hours in care, socioeconomic status, and bedtime characteristics, we found that the global ITERS rating is negatively related to nap duration (β = -0.03, p < .0001). All ITERS subscales also were significantly associated with nap duration (p value ranges from <.05 to <.0001).

Conclusion: There is growing recognition that sleep plays a critical role in development and there is clear evidence that high quality child care promotes better outcomes for children. Future research should examine specific characteristics and nap policies in high and low quality child care to further understand the negative association found between nap duration and childcare quality.

0838

SLEEP DURING EARLY DEVELOPMENT: A LONGITUDINAL STUDY OF THE NATURE, PREVALENCE, AND PERSISTENCE OF SLEEP PROBLEMS IN THE FIRST 3 YEARS OF LIFE

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Introduction: Sleep problems (SP) during childhood are prevalent and associated with morbidity. Unfortunately, there is a lack of attention to screening and treating SP in primary pediatric care settings. Additionally, little is known about what sleep behaviors are associated with parental endorsement of SP during early development. Clarifying how parents interpret their child's sleep behavior could critically inform sleep screening practices in primary care settings.

Methods: 359 mother-child dyads participated in a prospective birth cohort study. Subjects were assessed via sleep questionnaires when 6, 12, 24, and 36 months old. Sleep variables: 1) the presence/absence of SP and 2) eight scores characterizing sleep behavior (e.g., sleep onset latency, sleep maintenance, 24-hour sleep duration, snoring). Aims were to assess 1) nature and prevalence of SP, 2) stability of sleep behaviors, and 3) persistence of parent endorsed SP. Data analyses: descriptive statistics (prevalence estimates), point-biserial correlations (sleep behaviors associated with SP), Spearman correlations (stability of sleep behavior), odds ratios and associated Fisher's Exact tests (persistence of SP).

Results: Prevalence of SP approximated 10 percent of sample at each assessment. Prolonged sleep latency was associated with parent endorsed SP at each assessment. Nightwakings and lower sleep duration were associated with SP during early infancy and early toddlerhood while nightmares and restless sleep were associated with SP in later developmental periods. Napping, sleep location, and snoring were not associated with SP. Overall, sleep behavior remained stable across all developmental stages. Children with early onset SP were at greater risk for SP later.

Conclusion: SP are persistent in a significant minority of infants/toddlers. While sleep behavior is stable during early development, the nature of SP varies somewhat during the first three years of life. Parent reported SP may not include certain sleep behaviors associated with morbidity (e.g., snoring). Sleep screening should be ongoing, developmentally sensitive, symptom/behavior specific, and family-centered.

0839

SLEEP PROBLEMS, BEHAVIORAL FUNCTIONING, AND PARENTING STRESS: AN EXAMINATION OF FACTORS ASSOCIATED WITH PARENT FUNCTIONING IN CHILDREN REFERRED FOR BEHAVIORAL SLEEP MEDICINE EVALUATION

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Introduction: There is growing recognition of the need to understand pediatric sleep disturbances within a family context. Parenting stress (PS) is an aspect of parent functioning relevant in clinical settings as it may compromise treatment. Within the context of behavioral sleep medicine evaluation and treatment, the role of PS is not well understood.

Methods: Retrospective chart review of patients 18 months - 10 years old referred to Behavioral Sleep Medicine Clinic at CCHMC for insomnia evaluation from 6/2009 - 12/2010. Subjects were 181 primary caregiver-child dyads who completed the Child Sleep Habits Questionnaire (CSHQ), Child Behavior Checklist (CBCL), and Parenting Stress Index-Short Form (PSI-SF). Study aims: 1: Determine prevalence of clinically

significant PS; 2: Identify relevant child and parent correlates of PS. 3: Explore specific sleep related behaviors that play a role in PS. Data analytic procedures conducted to address study aims included descriptive statistics and regression analyses.

Results: 48.7% of primary caregivers had clinically significant PS. Externalizing behavioral problems (p<.0001) predicted PS over and above other independent variables (caregiver mental illness; caregiver sleep disturbance; child internalizing behavior problems; child sleep problems). When examining the relationship between sleep and PS, bedtime resistance (p=.04), nightwakings (p=.049) and daytime sleepiness (p<.0001) were statistically significant predictors of PS over and above all other CSHQ subscales. When all statistically significant predictors of PS were considered in a single regression equation, both externalizing behavior problems (p<.0001) and daytime sleepiness (p=0.00) independently explained considerable variability in PS (R2=.42).

Conclusion: Primary caregivers of children with insomnia have clinically significant PS. PS in caregivers is associated with both daytime behavioral dysfunction and sleep disturbance. Clinicians working with pediatric insomnia patients should carefully evaluate parental functioning and daytime functioning of patients as these variables will likely have an impact on service delivery and treatment outcomes.

0840

BEDTIMES, CAFFEINE USE AND SLEEPINESS IN MIDDLE SCHOOL STUDENTS: FINDINGS OF THE PILOT CAFFEINE LITERACY AND SLEEP STUDY (CLASS)

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Introduction: Adolescents report variable weekday-weekend bedtimes, daytime sleepiness and frequently use caffeinated beverages (CB). We report data from a survey of 7 and 8th grade students at a public school in Cleveland, OH, using (CLASS), and the recently validated Cleveland Adolescent Sleepiness Questionnaire (CASQ). CLASS is a 15 question pilot survey designed to evaluate children's recall of caffeinated beverage use, knowledge of caffeine content and recent concurrent sleep habits.

Methods: After prior passive parental consent and an in-class opt-out option for subjects, surveys were distributed and collected anonymously on the same day in school. We expected to find increased sleepiness reported by caffeine users and those reporting later bedtimes.

Results: Of 635 students, 80 (12.5%) opted-out. 555 surveys were analyzed (55% males, 57.5% 7th graders, median ages(yr) 12 [grade 7] and 13 [grade 8]). Overall 62% reported sleeping around or before 10 pm on weekdays but > 60% slept after midnight on weekends. Days napped per week were reported as none (48%), <2(20%), 3-5(13%), >5(4%), and unreported (15%). Sleep onset was described as hard (22.5%), easy (32%) or equivocal (45.5%) and 35% reported nocturnal awakenings (2.5%> 3 times per night). Only 14.3% reported no CB use. CASQ scores differed significantly between those drinking no caffeine vs any caffeine per day (30.5 ± 9.3 vs 36.1 ± 10.1; p< 0.0001), those sleeping before vs after midnight on weekends (30.1 ± 7.7 vs 38.1 ± 10.4; p < 0.0001) and those sleeping around or before 10pm vs later on weeknights (32.8 ± 9.6 vs 38.7 ± 10.3; p < 0.0001).

Conclusion: Students reported delayed sleep times on weekends, napping, nocturnal awakenings, difficulty with sleep onset and use of CB. Sleepiness scores were significantly greater among late sleepers and caffeine users. This resonates with available national data.

0841

AWARENESS OF CAFFEINE CONTENT OF COMMON BEVERAGES: COMPLETE FINDINGS OF THE CAFFEINE LITERACY AND SLEEP SURVEY (CLASS)

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Introduction: Assessing the effects of caffeine consumption on sleep in children may be hampered by inaccuracy in reporting intake due to lack of knowledge of caffeine content in common beverages. This study is a preliminary investigation of adolescent caffeine knowledge and intake at a Cleveland area middle school.

Methods: The Caffeine Literacy and Sleep study (CLASS) is a pilot instrument designed to assess caffeine knowledge and intake by type, quantity and timing as well as limited sleep habits. Awareness of the presence or absence of caffeine in 10 common beverages was assessed using a yes/no format. The Cleveland Adolescent Sleepiness Questionnaire (CASQ) is a validated survey measuring excessive daytime sleepiness in teenagers. After passive parental consent, and an opportunity for subjects to decline participation, both questionnaires were distributed in a Cleveland area middle school and collected anonymously in class on the same day.

Results: Of the 635 students attending 7th and 8th grade, 555 participated (55.5% male, 57.3% in 7th grade, median age in years 12 and 13 for 7th and 8th grade respectively). More 7th than 8th grade students were able to correctly identify the presence of caffeine in Arizona Green Tea (67% vs 47%, p<0.0001), and the absence of caffeine in bottle water (95% vs 88%, p<0.01). More boys were able to correctly identify the lack of caffeine in Sierra Mist (35.7% vs 24.5%, p<0.01). More girls were able to identify the lack of caffeine in water (95.5% vs 89.6%, p<0.0253). Fewer girls were correctly able to identify the lack of caffeine in 7up (16% vs 26.4%, p<0.0057).

Conclusion: Students were not consistently able to identify caffeine content or lack thereof in some common beverages. The results of this pilot study show that Caffeine literacy in adolescents warrants further investigation.

0842

THE PREVALENCE OF SLEEP INSUFFICIENCY IN ADOLESCENTS AND ITS IMPACT ON HIGH SCHOOL PERFORMANCE

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Introduction: A typical adolescent requires 9 hours of sleep each night. However, American high school bell schedules do not allow this. Studies showed that poor sleep quality, reduced total sleep time and excessive daytime sleepiness negatively impacted academic performance, behavior, and social competence in adolescents. The objective of this study is to determine how prevalent sleep inadequacy is among high school students and its impact on school performance.

Methods: An anonymous questionnaire on sleep quantity and quality, schedule, daytime sleep disorder symptoms, and self reported academic grades was utilized among high school students. The differences between weekday and weekend schedules were taken into account. The frequency of variables was tallied for statistical analysis.

Results: Of 1778 students completed the survey, 69% of them reported 7 hours or less of sleep on school nights. In comparison, on weekends, 66% reported more than 7 hours of sleep, and 36% reported more than 10 hours of sleep. Approximately 65% of students perceived insufficient sleep on school nights. Almost 82% of students reported sleepiness during school days. Insufficient sleep on school nights is reflected by the 78% of students using alarm clocks on school mornings, compared to

only 12% using alarm clocks on weekend mornings. Students (60%) reported either waking up earlier, going to bed later, or both, between 5thgrade and high school. There was significant association between night awakening and school performance with the night awakening being an unfavorable factor for school performance (p<0.0001). Likewise, less than 7 hours of sleep during the weekends was significantly associated with a poorer school performance (p=0.001).

Conclusion: This study suggests that the majority of high school students participated in the survey suffered from sleep inadequacy that might contribute in part to unfavorable academic performance in some of these students.

0843

ARE ADOLESCENT GIRLS LOSING SLEEP OVER PRESSURES TO LOOK THIN?

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Introduction: Social reinforcement of the thin-ideal in adolescent girls was found to be associated with the development of unhealthy behaviors, such as disordered eating. No study has attempted to discover if a similar link exists between pressure to be thin and sleep behavior. Decreased sleep has been linked to increased anxiety and depression. The present study assessed how perceived sociocultural pressures affect and predict sleep duration in a sample of ethnically/racially diverse adolescent girls.

Methods: Participants were 789 female middle school students from a suburban school district in Texas (U.S.). The mean age was 12.31 years (SD = .972). Race/ethnicity characteristics were: 59.9% White, 26.1% Hispanic/Latina, 10.5% African American. Less than 4% of participants were Asian American or Native American and were subsequently not included in analysis. Participants completed the Perceived Sociocultural Pressure Scale (PSPS), which assesses how much pressure an individual has felt in different areas (i.e., losing weight, exercising, being attractive, dieting) from different sources (i.e., girl friends, media), and the Pittsburg Sleep Quality Index (PSQI), which is the most commonly used measure of sleep in epidemiological literature.

Results: A linear regression was used to assess to what degree perceived sociocultural pressure predicts hours of sleep in adolescent girls. Results indicate that pressures to be skinny from girl friends and from the media significantly predict sleep duration and account for 4.5% of the variance in this variable, $F_{(2, 786)} = 18.442$, $p < .001$. Results of linear regressions divided by ethnicity indicate that pressures from girl friends and the media to be skinny continue to be significantly predictive of sleep duration for White/Caucasian girls, $F_{(2, 470)} = 14.965$, $p < .001$, but not for Hispanic/Latina, $F_{(2, 203)} = 1.737$, $p = .179$, or Black/African American, $F_{(2, 80)} = 1.670$, $p = .195$, adolescent girls. Together, these two predictors share 6% of the variance in hours of sleep, with the strongest predictor being pressures to be skinny from girl friends (beta = -.186), followed by pressures from the media (beta = -.092).

Conclusion: The current analyses revealed that increased pressure to be thin is a significant predictor of decreased sleep duration in adolescent females. A decrease in sleep has been correlated with an increase in anxiety and depression. These analyses indicate that Caucasian females are especially at risk for these consequences.

0844

EFFECT OF PART-TIME EMPLOYMENT ON SLEEP DEPRIVATION AMONG HIGH SCHOOL STUDENTS

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Introduction: Over 40% of American high school students work some number of hours during the school year. Although much research has been carried out to determine the psychological benefits and detriments of working while in high school, few if any studies have dealt with its impact on sleep deprivation. The purpose in conducting this study was to determine the association of the number of hours worked per week during a school year and its association with sleep deprivation.

Methods: Data were collected from 262 high school seniors attending a public high school in Mercer County, NJ. Participating students filled out a survey that included basic demographic information, the Epworth Sleepiness Scale (ESS), and hours worked per week during the school year. The relationship between the variables was assessed through frequencies and with their corresponding mean ESS.

Results: The mean age of students surveyed was 17.7 years. Of the 260 students, 36% (93 students) worked some amount of hours during the school year. Of the working students, 37% (34 students) worked fewer than 13 hours during the week. The average ESS score of this group of students was 9.1 indicating that they were not sleep deprived. The other 63% of the working students (59 students) worked more than 13 hours in the week with an average ESS score of 10.1 indicating Excessive Daytime Sleepiness (EDS). This group of students slept on average 18 minutes fewer on school nights and 16 minutes fewer on weekends than the students who worked fewer than 13 hours per week.

Conclusion: High school students who worked more than 13 hours per week during the school year were sleep deprived and slept fewer hours per week than the students who worked fewer than 13 hours. Additional studies are needed to confirm these results.

0845

HIGHER ALTITUDE SLEEP PARAMETERS IN CHILDREN

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Introduction: Little is known about normal sleep in children who live at higher elevations. Individuals who travel to higher elevations are noted to have increased arousals, elevated respiratory rates and lower CO2 levels during the initial days to weeks at higher elevations. At some point, the human body adapts to the lower oxygen tension and the respiratory rates normalize. A child's normal pulse oximetry level at these higher elevations is known to be lower than at sea level. There is a significant amount of information in regards to normal sleep parameters in children who live at or near sea level, but how the relative hypoxia at elevation plays into normal sleep in children is still unknown.

Methods: A prospective study of 3-5 year old, non-snoring children recruited from communities around Denver, CO was performed. Sleep studies using standard techniques were performed on 44 healthy, normal, non-snoring 3-5 year olds. All children were screened and required residence for greater than one year at an elevation around 1600 meters and no significant underlying medical conditions. Children were recruited via print and electronic advertisements in the Denver metro area. Normal sleep indices were obtained and compared to previously published normals in a similar aged population living near sea level.

Results: In children living at 1600 meters altitude, the mean central apnea index was noted to be 1.7±1.3 events/hr, and the mean apnea-hypopnea index was 2.2±1.7 events/hr. This compares to published normals of 0.8±0.7 and 0.9±0.8 events/hr respectively from sea level studies. Mean end tidal C02 levels were very similar (41.7±3.2 mm Hg at 1600 meters

and 40.6±4.6 mm Hg at sea level). The ≥3% desaturation index mean was 7.6±6.1 events/hr at altitude compared to the ≥4% desaturation index mean of 0.3±0.3 events/hr at sea level.

Conclusion: In comparison of altitude vs sea level sleep studies, there is a significant difference noted in central apnea index, apnea-hypopnea index and desaturation index (we currently report 3% desaturations on clinical reports, where published normals present 4%). The end tidal CO_2 does not seem to be significantly different.

0846

THE IMPACT OF SLEEP HEALTH ON PEDIATRIC SOCIAL BEHAVIOR

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Introduction: Child's disturbed sleep may lead to social difficulties which can impact family health and well being. This study investigates the relation between children's sleep behavior, and parents' and teachers' reports of the children's social adjustment.

Methods: Second grade students, 8-9 years old, were studied in Tartu City and County, Estonia. This study was approved by the University of Tartu Review Committee on Human Research; All data was coded. The Pediatric Sleep Questionnaire for Parents, the Rutter Behavior Scale A for Parents, and the Rutter Behavior Scale B for Teachers were distributed by post to the parents and teachers of 120 students; 97 complete sets were returned via mail. Fourteen variables were selected from the Questionnaire to form an Index of Sleep Health. Fourteen Rutter A variables were used to form an Index of Parental Assessment of Social Adjustment. 25 variables were used from Rutter B to generate an Index of Teacher Assessment of Social Adjustment. The instruments allow an assessment of the relation between sleep health and behavior. The Pearson Product Moment Correlation was used to assess the relation between the scales.

Results: The correlation between the sleep health index and teacher assessment of behavior is 0.29; Between sleep health index and parental assessment of behavior 0.18; Between teacher and parental behavioral assessments it is 0.40. The correlation between the twenty worse sleep health cases and teacher behavioral assessment is 0.31; For parental assessment of behavior it is -0.06.

Conclusion: The results suggest that teachers grasp the impact of sleep health on social behavior more than do the parents, especially in severe cases of poor sleep health. This may be explained by the fact that parents see their children less in social situations than do the teachers. The moderate correlation between teacher and parental behavioral assessments suggests this may be the case.

0847

ASSOCIATIONS BETWEEN SLEEP DURATION AND SEXUAL RISK-TAKING IN AFRICAN AMERICAN ADOLESCENT GIRLS

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Introduction: Recent research demonstrates substantial connections between inadequate sleep and risk-taking behavior in adolescents. However, little research has examined the association between sleep duration and risky sexual behavior. African American (AA) adolescent girls are disproportionately at risk for sexually transmitted infections (STIs); therefore, understanding factors related to sexual risk in this population is crucial. Previous work with this population has shown poor sleep hygiene is related to shorter sleep duration.

Methods: Participants are 150 AA mid to late adolescent girls (ages 14-22) from low-income neighborhoods in Chicago. Girls reported time to sleep on weekdays and weekends and average sleep duration on the Pittsburgh Sleep Quality Index (PSQI), and responded to a series of

questions about sleep hygiene. They also answered computer administered questions regarding sexual risk behavior.

Results: Preliminary analyses revealed that less hours of sleep reported in the past month was correlated with reporting more male partners in the past month (r=.28; p=.01), having oral sex without a condom (r=.26; p=.04), sex while under the influence of alcohol or drugs (r=.21; p=.02), and sex with a high-risk partner (r=.36; p=.001). Additional analyses will divide reported sleep into short (<6 hours), average (7-8 hours), and long duration (9+) and use analysis of variance to examine differences between the groups in sexual risk taking behavior.

Conclusion: It is well established that sleep duration can have detrimental effects on cognitive performance in adolescents, and a similar mechanism may be at work in sleep deprived adolescents who are presented with sexually-risky situations. Implications for prevention of STIs and affects on overall health risk and will be discussed.

0848

HOW MUCH DOES OUR MEDICAL STAFF KNOW ABOUT SLEEP HABITS IN CHILDREN?

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Introduction: Despite significant growth of Sleep Medicine, awareness amongst nonspecialists of normal and abnormal sleep physiology remains limited. As many sleep medicine problems are initially encountered in non-sleep clinics, we sought to measure the understanding of pediatric sleep habits amongst medical professionals from various specialties.

Methods: Grand Rounds attendees in the following departments were asked to anonymously answer ten questions regarding pediatric sleep habits: Neurology, Pediatrics, Family Medicine, and Psychiatry. Analysis was performed on each question by specialty and by learner category to explore correlations and common deficiencies in knowledge.

Results: To date, we have 107 completed surveys; 19 were completed by attending physicians, 25 by residents, 45 by medical students, and 18 by "other medical personnel." Results categories can be divided into 3 broad groups: those with a high percentage of disagreement, those with a high rate of agreement, and those in which many attendees professed no knowledge (i.e.: response was "no clue"). A high rate of disagreement was found regarding total nocturnal sleep requirement for 2-year olds, with 24% responding 8-10 hours, 38% 10-11 hours and 32% >11 hours. Disagreement for normal daytime nap needs in 3-year olds was also seen, with 46% responding "1 nap" and 34% "2 naps." A high lack of knowledge was found regarding whether snoring is considered "normal" in children, with 13% reporting "no clue." Conversely, a high rate of agreement was found for responses regarding infant sleep needs, with 82% responding ">12 hours". Responses were similar across learner categories.

Conclusion: There are high rates of disagreement among medical professionals of all levels of training regarding total sleep needs and napping among toddlers, and a significant knowledge deficit was identified regarding pediatric snoring. These findings may represent a lack of widely-accepted normative sleep data, or a need for more sleep-specific education among medical professionals.

0849

THE COLLEGE LIFESTYLE: MORE MEDIA, MORE STRESS, LESS SLEEP

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Introduction: College students' schedules are consumed with technology use (Rideout, et al., 2010), stimulants (McCabe et al., 2005), and

stress (Bertocci et al., 1992). Studies have suggested that environmental factors, especially stress and stimulant use, are associated with poor sleep quality (Lund et al., 2009). The aim of this study was to elucidate the associations between sleep, stress, and the caffeine-powered, technological environments of emerging adults.

Methods: A sample of 1st - 4th year students (N=194) from a New England college completed self-report questionnaires. Questions were adapted from prior measures of sleep, stress, caffeine, and media use (Cohen, et al., 1983; Ludden & Wolfson, 2010; Sharif & Sargent, 2006; Van Den Bluck, 2004; Wolfson & Carskadon, 1998).

Results: In the hour before "lights out," 46% of respondents reported watching television, 78% used a computer, 36% used an MP3 player, and 73% text messaged. Males had more delayed bed/wake times, yet females experienced greater daytime sleepiness and perceived stress (all p < .05). Students with at least 1 TV in their bedroom reported earlier class wake times and those with 2+ computers in their bedrooms experienced more irregular sleep (all p < .05). Those text messaging in the hour before "lights out" reported more daytime sleepiness, while students who played more video games had more delayed bed/ wake times. Finally, 65% reported using caffeine to stay awake.

Conclusion: This study provides a picture of sleep patterns and perceived stress in the context of college environments. Findings suggest that increasingly technological, caffeinated, and stressful environments might compromise sleep and daytime functioning. Future studies should investigate the complex relationships between screen use, stimulants, stress, and sleep in emerging adults' lives to develop solutions that improve sleeping habits and promote well-being during emerging adulthood.

0850
SLEEP PATTERNS ACROSS ADOLESCENCE AND SLEEPINESS DURING CLASS HOURS

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Introduction: Teenagers show a delay in their sleep-wake pattern resulting in later bedtimes (BT) and rise times (RT) as they get older. This contrasts with fixed schedules imposed by social and school demands and therefore has an influence on daytime functioning. This study examined the changes in sleep patterns throughout adolescence and its influence on daytime sleepiness.

Methods: 759 adolescents (47% boys, 53% girls, 13 to 19 years old, grade 9 to 11) completed a questionnaire on sleep habits and daytime sleepiness. Mean differences between age groups (13-14, 15-16, 17 and up) for BT, RT, total sleep time (TST) during school nights (SN) and weekend nights (WN), sleep disorders, sleep initiation difficulties, and sleepiness during class were assessed using one-way ANOVAs.

Results: Results show a significant interaction between age and BT on SN and WN (F(2,746) =20.02, p< 0.01; F(2,737)=13.13, p< 0.01), age and TST on SN and WN (F(2,733)=8.27, p< 0.01; F(2,719) = 5.42, p< 0.01) and age and sleepiness (F(2,738) =7.5, p< 0.01). Post-Hoc comparisons using Tukey's test revealed that as teenagers got older, BT were delayed, TST decreased, and sleepiness increased.

Conclusion: These results confirmed that adolescents tend to go to bed later on SN and WN as they get older (even later than the mean bedtimes observed in adult), but do not compensate by delaying their wake up time. As a result, they tend to get less sleep and to become sleepier as they get older. Our results also suggest that daytime sleepiness in teenagers is more related to changes in sleep patterns rather than to the manifestation of sleep disorders or sleep initiation difficulties.

0851
EFFECTS OF SLEEP-SMART PROGRAM ON YOUNG ADOLESCENTS' PERCEIVED SLEEP BEHAVIOR COMPETENCE

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Introduction: Although laboratory research has demonstrated that adolescents require 9.2 hours of sleep, self-report and actigraphy methods have documented that adolescents obtain insufficient sleep with adverse consequences. This study examined the impact of a social learning based, prevention for early adolescents, Sleep-Smart Pacesetter Program, that focused on sleep efficacy, hygiene, and sleep need. Studies (Martin, et al., 2009), have suggested a connection between perception of competence (ability to maintain consistent sleep patterns) and change (improved sleep).

Methods: Cluster sampling of 7th graders from 2 urban, public middle schools (SST = 8:37am) was used with health classes assigned to Sleep-Smart (SS = 70) or Comparison group (C = 73). During the 6-week program (8 sessions, M = 23 students/class), SS 7th graders learned to establish efficacious sleep patterns and hygiene. Pre- (T1) and Post-program (T2), SS and Comparison adolescents completed questionnaires (Health-Sleep Efficacy, Sleep Hygiene) and wore actigraphs to estimate their sleep patterns. Data were analyzed using repeated measures (controlling income, gender, pubertal, bmi status) and correlations between efficacy, hygiene and actigraphy variables.

Results: SS adolescents reported 8% improvement in sleep efficacy vs. Comparison's 6% decline (p < .05. Likewise, SS vs. Comparison reported greater improvement in overall Sleep Hygiene (Physiological, Emotional particularly, p's < .05). SS participants' increased Sleep Efficacy/ Hygiene were significantly correlated with increased sleep duration and later offset times (T1-T2) and improved T2 sleep patterns (r's = .21 - .30, p's < .05). Comparison adolescents' efficacy/hygiene weren't associated with their sleep patterns.

Conclusion: Results indicate that early adolescents who participated in the Sleep-Smart Program improved their sleep competence and associated actigraphically estimated sleep patterns, such as duration. Future analyses will assess the impact of SS Program on school performance and emotional/behavioral well being at T2, 6-month, and 1-year follow-ups.

0852
ADOLESCENT MOOD AFTER 5 NIGHTS OF SLEEP RESTRICTION

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Introduction: Adolescents often experience chronic sleep restriction on school nights, and there is correlational evidence that short sleep is associated with negative mood. However, it is difficult to establish the presence or direction of causation from correlational data. Here we examine mood after 5 nights of experimental sleep restriction, compared to more optimal sleep duration.

Methods: Data were pooled from two studies that enrolled healthy adolescents aged 14-16.9 years, all of whom completed a three-week experimental protocol that included a baseline week followed in counterbalanced order by a sleep-restricted week (SR; 6.5 hours in bed Monday-Friday nights) and an extended sleep week (ES; 10 hours Monday-Friday nights), with a two-night "washout" before each condition. Sleep duration was monitored by actigraphy. On the Saturday morning at the end of each condition, teens completed the Profile of Mood States

(POMS), inquiring about the past 3 days. Paired t-tests compared the 6 validated POMS subscales across SR versus ES.

Results: Of 43 subjects, one was nonadherent to the sleep regimen and one failed to complete the POMS. The remaining 41 averaged 6.2 hours of nightly sleep during SR and 8.6 hours during ES (p<.001). After SR, subjects rated themselves as less vigorous (p=.025), more fatigued (p<.001), and more confused (p=.036) than after ES. There were no cross-condition effects on the anxiety, depression, or anger subscales (p>.25).

Conclusion: Complementing prior correlational findings, current findings suggest that chronic sleep restriction can indeed cause changes in adolescents' subjective vigor, fatigue, and level of confusion, even after only a few days. We failed to find evidence that sleep restriction across several nights can induce anxiety, depression, or anger in teens, though it remains possible that such effects might be seen after longer-term sleep restriction, might develop in particularly vulnerable individuals, or might increase vulnerability to acute stress.

Support (If Any): National Institutes of Health (R01 HL092149, K23 HL075369, UL1 RR026314)

0853

CARBOHYDRATE CRAVING ASSOCIATED WITH SLEEP DEPRIVATION AND DEPRESSION IN HIGH SCHOOL STUDENTS

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Introduction: Previous studies have shown a link between sleep deprivation, hunger, and food intake in the adult population. There are no studies to date that have examined the relationship between carbohydrate craving and its association with sleep deprivation and depression in a high school population.

Methods: Data were collected from 262 high school seniors attending a public high school in Mercer County, NJ. Participating students completed a survey that included demographic information, the Epworth Sleepiness Scale (ESS), a 5-point Likert scale (one meaning high craving and five meaning no craving) to gauge carbohydrate craving, and a validated depression scale. The relationships between the variables were determined by odds ratios (OR) and 95 percent confidence intervals (CI).

Results: The mean age of students surveyed was 17.7 years. 12% of students surveyed answered 1 on the craving scale. 32% , 35%, 17%, and 3% answered 2, 3, 4 and 5 respectively on the craving scale. Their corresponding ESS scores were 12.4, 10.2, 9.2, 9.8, and 8.25 respectively. The odds of strong carbohydrate craving if sleep deprived was moderately high (OR: 1.5, 95CI:0.78 to 2.9), but not statistically significant due to the limited sample size. Of the 115 students who had a high craving for carbohydrates, 34% (39 students) were depressed. The average ESS of this group of students was 10.8. Out of the 52 students who had little or no craving, fewer than 22% (11 students) were depressed. The average ESS of this group of students was 9.6. The odds of strong carbohydrate craving if experiencing strong depression was high (OR: 2.9, 95CI:1.25 to 6.7226).

Conclusion: These data show an association between increased carbohydrate craving and sleep deprivation and depression among a high school population and therefore may be clinically important.

0854

SLEEP DURATION AFFECTS THE RELATIONSHIP OF ADIPOSITY WITH PULSE PRESSURE IN GUJARATI INDIAN ADOLESCENTS

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Introduction: Studies indicate that increase in adiposity tends to decrease the vascular distensibility of the adolescents predisposing them to the risk of hypertension. The current study was therefore undertaken to determine if sleep duration affects the relationship of adiposity with Pulse Pressure (PP), an indicator of Vascular Distensibility, amongst Gujarati Indian adolescents so as to develop preventive strategies for the local population.

Methods: A cross-sectional study was conducted on 353 Gujarati Indian adolescents of age group 16-19 years. Night sleep duration was reported by the participants as the number of hours they slept on most of the nights in a week over the last one year. Body Mass Index (BMI), Fat Mass Index (FMI) and Waist Circumference (WC) were assessed as indices of adiposity. Fat Mass was measured using bioelectrical impedance technology. Arterial blood pressure was measured by oscillometry using automatic blood pressure instrument. PP was calculated using the average value of Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP). Pearson's correlation coefficient, r was determined for studying the correlationship between adiposity and PP after grouping the participants into Night Sleep Duration 6 hr (NSD6), Night Sleep Duration 7 hr (NSD7) and Night Sleep Duration 8 hr (NSD8) groups.

Results: In boys, BMI and FMI showed significant (P<0.05) positive correlationship with PP in NSD 6 and NSD7 groups while WC showed significant (P<0.05) positive correlationship with PP in NSD 7 group. BMI, FMI and WC showed no significant correlationship with PP in NSD 8 group. In girls, WC showed positive correlationship with PP in NSD 6 group while no correlationship was found between adiposity and PP in NSD 7 and NSD 8 group.

Conclusion: Sleep duration of 8 hours at night tends to protect the vasculature of the Gujarati Indian adolescents from the adverse effects of increasing adiposity especially visceral adiposity.

0855

OBJECTIVE AND SUBJECTIVE SLEEP CHARACTERISTICS OF INSOMNIA IN A COMMUNITY SAMPLE OF YOUNG CHILDREN

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Introduction: Few population-based studies have examined the polysomnographic (PSG) and subjective sleep characteristics of insomnia in children.

Methods: A sample of 700 children (6-12 yr) from The Penn State Child Cohort underwent a 9-hour polysomnogram, physical examination and a parent completed sleep questionnaire. Insomnia was defined as parent-reported difficulty falling (DFA) and/or staying (DSA) asleep.

Results: Children with insomnia had significantly increased sleep latency and stage 2, and decreased slow wave sleep and REM latency, whereas no differences were found in subjective sleep latency, total sleep time or number of awakenings. Within insomniacs, those with DFA were the ones that showed the above mentioned PSG abnormalities, whereas those with DSA or DFA and DSA did not differ significantly from children without insomnia in terms of PSG characteristics. Children with DFA also had increased subjective sleep latency, whereas the other subtypes did not differ significantly in terms of any subjective sleep measure.

Conclusion: These data suggest that sleep onset insomnia in children is associated with prolonged objective sleep latency. Future studies should

examine whether sleep latency is a physiological marker of the severity of the disorder predicting its medical and psychiatric morbidity.

0856

A TEMPORAL RELATION BETWEEN PUBERTAL MATURATION AND THE ADOLESCENT DECLINE IN DELTA ELECTROENCEPHALOGRAM POWER

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Introduction: Electroencephalogram (EEG) power in the 1-4 Hz frequency band during NREM sleep is high across childhood and then declines steeply across adolescence. This reduction in slow wave activity (SWA) is thought to reflect an adolescent brain maturation driven by synaptic pruning. We previously reported that the SWA decline between age 12 and 14 years was related to chronologic age rather than the rate of pubertal maturation. However, we recognized that the timing of the SWA decline might be linked to the timing of pubertal maturation. We can now address this issue with longitudinal data covering ages 9 to 18 years.

Methods: Data are from 6 years of semiannual sleep EEG recordings from two cohorts: C9 (n=31), initially age 9, and C12 (n=38), initially age 12 years. SWA was measured as power in the 1-4 Hz band during first 5 hours of NREM sleep. Tanner stage scores of pubertal maturation were determined during a physician's exam. Non linear mixed effect analysis was used to fit a Gompertz curve to the sigmoidal SWA decline and a logistic curve to the Tanner stage increase. Both analyses indicate the age at which the curve is changing most rapidly.

Results: The age of most rapid SWA decline was related to the age of most rapid pubertal increase. The SWA decline occurred 0.72 years earlier (p<0.0001) for every year earlier that the Tanner stage increase occurred. This relation held with sex controlled.

Conclusion: We do not interpret the temporal relation between the Tanner stage increase and the SWA decline as indicating that pubertal maturation drives cortical maturation. As we will discuss, we believe that brain maturation involves a programmed sequence of events that includes cortical pruning and activation of the hypothalamic, pituitary, gonadal axis.

Support (If Any): This research was supported by United States Public Health Service grant R01MH62521.

0857

THE DECLINE IN TOTAL SLEEP TIME ACROSS ADOLESCENCE RESULTS FROM A SELECTIVE DECREASE IN NON-RAPID EYE MOVEMENT SLEEP DURATION

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Introduction: Many previous studies have shown that total sleep time decreases across adolescence. However these have been primarily questionnaire based experiments which cannot distinguish between non rapid eye movement (NREM) and REM sleep. Our longitudinal study of sleep and EEG changes between ages 9 and 18 years can address this issue.

Methods: All night sleep EEG was recorded in two cohorts for 6 years: C9 initially age ~9 years, n=31 and C12 initially age ~12 years, n=38, with overlap at ages 12-15 yrs. Recordings were performed semiannually at the subjects' homes on the subjects' habitual school-day sleep schedules. These schedules were allowed to change with age.

Results: Total sleep time declined significantly (p<0.0001) by 10.3 (+/- 0.8 s.e.) min/year. This decline was comprised entirely of a significant (p<0.0001) NREM sleep duration reduction of 12.0 (+/- 0.6) min/year. REM sleep duration actually increased 1.9 (+/- 0.4) min/year (p<0.0001).

Conclusion: The selective reduction of NREM sleep cannot be attributed to sleep deprivation caused by insufficient time in bed. Deprivation by acute or by chronic sleep restriction reduces both REM and NREM

sleep. Instead, we attribute the reduction of NREM sleep to adolescent changes in brain biology. Our longstanding model proposes that it is during NREM sleep that the brain recovers from plastic changes induced by waking neuronal activity. The amount of NREM recovery needed decreases across adolescence as synaptic elimination reduces the intensity of waking brain activity (as evidenced by declining brain metabolic rates). The relative absence of changes in REM sleep despite extensive brain reorganization adds to the enigma of its functional role.

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0858

DEVELOPMENTAL CHANGES IN THE SLEEP ELECTROENCEPHALOGRAM OF ADOLESCENT BOYS AND GIRLS

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Introduction: Sleep architecture undergoes major changes across the period of adolescence in a manner that is thought to reflect changes in brain. The study was designed to determine the relationship between age and sleep EEG changes at different derivations, in both NREM and REM sleep, in girls and boys.

Methods: 33 normal healthy adolescents (18 boys and 15 girls) aged 11-14 were studied using laboratory polysomnography on two occasions 6 to 8 months apart. EEG was sampled at F3-A2, F4-A1, C3-A2, C4-A1, O1-A2 and O2-A1. In addition to standard measures of sleep architecture, the EEG signals were subjected to power spectral and period amplitude analyses.

Results: Data from the first time point were analyzed for age and sex effects and revealed significantly smaller SWS percentage, delta power (NREM and REM), delta wave incidence (NREM) and delta wave amplitude (REM) with increasing age, with the slopes of each age relationship being steeper at occipital sites. Data from both time points were analyzed for longitudinal changes as a function of electrode site. NREM delta power, incidence, and amplitude were lower at follow-up, with a significant time x interaction effect for delta power showing that the effect was greatest at the occipital site. REM delta power and amplitude were lower at follow-up, again with the effect being greatest at the occipital site. No sex differences were apparent.

Conclusion: The results confirm the sensitivity of occipital delta EEG power to age related changes within early adolescence. This pattern was seen in both NREM and REM sleep, however the NREM effect was associated with reductions in both amplitude and incidence of delta waveforms, whereas the REM effect was only associated with decreases in delta wave amplitude.

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0859

NORMATIVE HEART RATE PARAMETERS OF ADOLESCENT HISPANIC AND CAUCASIAN ADOLESCENTS DURING SLEEP

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Introduction: While data of normative heart rates during sleep exist for school-aged children, little is known about adolescent normative heart rates during sleep. The purpose of this study was to describe adolescent

heart rate parameters during sleep and determine if age, sex, ethnicity, and obesity influenced adolescent heart rates during sleep.

Methods: Electrocardiogram (ECG) heart rate data was analyzed from 315 adolescent participants aged 10 to 17 years who underwent in-home polysomnography (PSG) in the Tucson Children's Assessment of Sleep Apnea (TuCASA) 2nd cohort. Participants (N=163) were 49.2% female; 35.6% Hispanic; mean age 13.3 years (SD = 1.7). The sample included only subjects who had a mild respiratory distress index (RDI) of less than 5 and were without any major medical conditions. Obesity was defined as a body mass index (BMI) ≥95th percentile for age. Analysis included descriptive characteristics, independent t-tests, and least square means analysis of variance.

Results: Females (mean ± SD) (68.5±9.5) had significantly faster average heart rates during sleep than males (63.8 ±10.4), p= .003, there were no significant differences observed between Hispanic and Caucasian adolescents or in those who were obese. Sleeping heart rate decreased significantly with age (F = 5.78, p < .001).

Conclusion: Consistent with sleeping heart rates in school-aged children, adolescents aged 10 to 17 years old had sleeping rates that decreased significantly as age increased. Compared to males, adolescent females had significantly faster heart rates during sleep. Contrary to other findings in the adult and pediatric literature, there were no significant differences found between sleeping heart rates in adolescents who were obese and those who were non-obese.

0860
ETIOLOGY OF OBSTRUCTIVE SLEEP APNEA IN INFANTS

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Introduction: Obstructive sleep apnea syndrome (OSAS) is a common cause of morbidity in children and adults. Adenotonsillar hypertrophy & craniofacial abnormalities are common causes of OSAS in children, whereas obesity is the major determinant in adults. In contrast, little data exists regarding the etiologies of OSAS in infants.

Methods: A retrospective chart review of sleep studies and clinical records of all infants, one year and under who underwent an overnight polysomnography (PSG) from December 2003- July 2010 was performed. Age at the time of the study, gender, severity of OSA, and etiologic risk factors were recorded.

Results: Ninety-two patients out of 281 patients who underwent PSG were identified with OSAS. The mean age was 5 ± 3.3 months; 62% were males. Forty-four-percent of the patients had mild OSAS (AHI 1.5 -5/hr), 18% had moderate (AHI 5-10/hr), and 38% had severe OSAS (AHI>10/hr). The mean nadir oxygen desaturation was 81.1%. Forty-percent had chromosomal abnormalities/genetic mutations, of which 89% had accompanying hypotonia. 21% of all infants had craniofacial abnormalities of syndromic/non-syndromic etiology. Other causes of OSAS included GERD (9.8%) and laryngomalacia (9.8%). Rare causes included isolated hypotonia of diverse etiology (4.3%), prematurity (4.3%), seizure disorder (4.3%), tracheomalacia (2%), vascular ring (1.1%), adenotonsillar hypertrophy (1.1%), and chest neuroblastoma (1.1%). Of note, 18% of all patients had GERD and 13% had laryngomalacia as accompanying co morbidity. No diagnosis was mentioned for 1.1% of the patients.

Conclusion: The etiology of OSAS in infancy is diverse, with a high proportion of genetic conditions characterized by neuromuscular weakness and craniofacial abnormalities. In addition, many infants with OSAS have GERD and laryngomalacia as isolated or co- morbidity. This is clearly different from traditional pediatric and adult-onset OSAS. A multidisciplinary approach is needed to evaluate and effectively manage these children.

0861
ARE HEAVY CHILDREN MORE SLEEPY?

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Introduction: A relationship between overweight and excessive daytime sleepiness (EDS) have been suggested in the adult population, and to a limited extent, in the pediatric population. Daytime sleepiness can interfere with various components of daytime function. In light of the increase in the rates of pediatric overweight and obesity, the aim of this study was to investigate the relationship between weight and excessive daytime sleepiness in a pediatric population.

Methods: A retrospective chart review of all patients, age 6-18, who were assessed for EDS using the multiple sleep latency test (MSLT) at the Youthdale Child and Adolescents Sleep Centre from October 2006 to May 2010 was performed. The relationship between the mean sleep latency (MSL) on the MSLT and body mass index (BMI) percentile was examined, after adjusting for age, gender and the presence of sleep apnea.

Results: 188 patients' charts were reviewed. Of these 100(53%) were in the normal weight range, 28(15%) were overweight and 60(32%) were obese. After adjusting for sleep apnea, BMI percentile was not significantly associated with MSL when data from entire population was grouped. While the main effect of gender was non-significant, age was found to have a significant effect on the association between BMI percentile and MSL. In children 6-13 years old, a greater BMI percentile was associated with a lower MSL (indicating EDS) even after adjusting for the presence of sleep apnea.

Conclusion: Our analysis suggests that in school age children under the age of 14 (pre/early adolescence) overweight/obesity is associated with greater EDS independent of the presence of sleep apnea.

0862
CHANGES IN HEART RATE VARIABILITY FOLLOWING SPONTANEOUS AROUSAL IN CHILDREN WITH PRIMARY SNORING

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Introduction: The impact of arousals on the autonomic function has not been well studied in children. Our aim was to evaluate heart rate variability (HRV) in children following spontaneous arousal. We hypothesized that spontaneous arousal is associated with predominant sympathetic activity leading to a higher heart rate (HR) and higher ratio of low frequency to high frequency power (LF/HF).

Methods: Electrocardiography data was extracted from polysomnography and analyzed in 2-minute epochs. Arousal was defined per AASM criteria. In addition, each arousal required 4-minutes of stable sleep (no respiratory event, arousal, or movement) before and after the event. Epoch 0 was defined as the 2 min prior to arousal; epochs 1 and 2 were defined as 0-2, and 2-4 min after arousal, respectively. 5 arousals (4-NREM, 1-REM) were analyzed per subject. Epochs 1 and 2 were compared to epoch 0 by paired t-test or Wilcoxon test. Data are presented as mean±SD. *P<0.05 was considered significant.

Results: We studied 5 children, 4 males, age 6.6-10.8 years. Following arousal, mean HR decreased from 79.3±7.3 to 77.1±5.9* (epoch 1) and 77.0±7.1* (epoch 2). LF power did not change significantly: 810±904 epoch 0, 1,296±1,763 epoch 1, 529±380 epoch 2. HF power increased transiently after the arousal from 1,774±2165 to 2,919±3,142* in epoch 1 (epoch 2: 2,220±2,916, not significant). The LF/HF ratio was 0.72±0.85 in epoch 0, 0.63±0.66 in epoch 1 and decreased to 0.43±0.38* in epoch 2.

Conclusion: Spontaneous arousal is associated with: a decrease in HR in the first 4-minutes after arousal, an immediate increase in HF, and a

decline in LF/HF- 2-minutes after arousal. These findings suggest an overall parasympathetic predominance in contrast with our expectation. Further analysis is needed to confirm these results and to assess the influence of other factors such as age, sex, BMI and respiratory events on HRV.

0863

CARDIOPULMONARY COUPLING MEASURES OF SLEEP STABILITY BUT NOT SLEEP QUALITY IMPROVE AFTER ADENOTONSILLECTOMY IN OVERWEIGHT AND OBESE CHILDREN WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Cardio Pulmonary Coupling (CPC) is a measure of sleep stability linking autonomic and respiratory data from an overnight polysonomgraphy. High Frequency coupling (HFc) and Low Frequency Coupling (LFc) along with their ratios give insight to sleep stability and quality. Children with obstructive sleep apnea (OSA) have disrupted sleep. The purpose of this study was to examine CPC values in overweight and obese children with known OSA before and after adenotonsillectomy

Methods: Overnight polysonomgraphy from of 10 children aged 8-18 with OSA were analyzed using RemLogic CPC 1.0 analysis software.

Results: Data from pre-and post-operative polysomnography obtained from 20 subjects (5 males); Mean age ±SD (13.2±3.3) BMIz score 2.2±0.6 ; pre-operative Apnea-Hypopnea Index(AHI) 24.1±20.3, post-operative AHI 3.8±2.4 were analyzed. LFc/HFc ratio (a measure of sleep instability) was statistically better post surgery (1.9±3.6 pre vs 0.67±0.47 post; p<0.5) but was still statistically higher than previously published normative cutoff value of 0.25 (p<0.05). There was no change in HFc/LFc ratio (measure of sleep quality) pre-operatively (2.2±1.8) compared to post-operatively (2.1±1.2, p=n.s.) but HFc/LFc ratio was statically lower than the normative average of >4 (p<0.05). Neither CPC measure of sleep stability (LFc/HFc) or sleep quality (HFc/LFc) correlated with either severity of OSA (as measured by AHI) or BMI z-score.

Conclusion: CPC measure of sleep stability improve following treatment of OSA with adenotonsillectomy whereas CPC measures of sleep quality did not. Further studies are needed to explore the relationships between CPC measures of sleep quality and stability and symptoms/sequelae associated with obstructive sleep apnea and the response to therapeutic intervention.

Support (If Any): CPC module supplied by EMBLA.

0864

SEVERITY OF OBSTRUCTIVE SLEEP APNEA PREDICTS AUTONOMIC AND METABOLIC DYSFUNCTION IN OBESE HISPANIC BOYS

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Introduction: In adults, obstructive sleep apnea (OSA) has been associated with both impaired glucose metabolism and autonomic dysfunction, independent of obesity. These relationships have been less studied in children.

Methods: We measured metabolic and autonomic function in 18 otherwise healthy obese Hispanic boys (age = 13.3 ± (SD) 2.0 years, BMI ≥ 95 percentile for age, gender) with snoring. Measurements included: (1) polysomnography; (2) frequently-sampled intravenous glucose tolerance test (FSIVGTT); (3) dual energy X-ray absorptiometry for assessing adiposity; and (4) respiration, heart rate, and noninvasive continuous blood pressure during supine and standing postures. Insulin sensitivity (SI) and other Bergman (Am J Physiol 236:E667-E677, 1979) minimal model parameters were derived from the FSIVGTT. Baroreflex gain (Gabr) and respiratory cardiac coupling gain (Grcc) were computed using a minimal model of cardiorespiratory control (Chaicharn et al., Sleep 32:927-938, 2009). Autonomic reactivity to orthostatic stress was defined as 1 - (Gain_standing/Gain_supine), for Gabr and Grcc. Correlations among the indices of metabolic, autonomic function, and polysomnographic measures were determined following adjustment for age and adiposity.

Results: Metabolic and sleep interactions: SI decreased with desaturation index (r=-0.50, p=0.047). Insulin resistance, as measured by fasting insulin levels (r=0.52, p=0.041) and HOMA index (homeostatic model assessment, r=0.51, p=0.043), increased with total arousal index (TAI). Autonomic and sleep interactions: Autonomic reactivity to orthostatic stress (both Grcc [r=-0.54, p=0.029] and Gabr [r=-0.52, p=0.039]) was negatively correlated with TAI. Autonomic and metabolic interactions: Gabr reactivity was negatively correlated with fasting glucose (r=-0.61, p=0.013). Baseline Gabr decreased with fasting glucose (r=-0.54, p=0.031).

Conclusion: We conclude that intermittent hypoxemia and sleep fragmentation in OSA contribute independently to metabolic and autonomic dysfunction in obese Hispanic boys. We speculate that autonomic dysfunction (via sympathetic overactivity) accentuates metabolic dysfunction by increasing fasting glucose.

0865

ASSOCIATION OF BMI AND AGE WITH NEUROPSYCHOLOGICAL AND BEHAVIORAL CHANGES AFTER ADENOTONSILLECTOMY IN CHILDREN

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Introduction: Cognitive and behavioral symptoms are associated with sleep-disordered breathing (SDB) in children but resolution after treatment by adenotonsillectomy (AT) is variable. Children's body mass index (BMI) and age could influence outcomes, but have not been extensively examined in this context.

Methods: Children (n=100, age 3-8 years) referred for AT, based on office visits only, were evaluated before and 6 months after surgery. Evaluations included: height, weight, nocturnal polysomnography, neuropsychological tests, and parent behavioral ratings. SDB was defined by a respiratory disturbance index (RDI)>1. Repeated Measures ANOVAs were computed to examine effects of Age (3-5, 5.1-8 years), BMI (>90th percentile="heavier"; <90th percentile="lighter") and Session (pre- and post-AT) on respiratory disturbance index (RDI), cognition, and behavior. Analyses included age-adjusted scores from the Stanford-

Binet: 5th-Edition Abbreviated IQ and NEPSY Memory and Attention/ Executive domains, and Conners' Oppositional and Hyperactivity subscales.

Results: A significant session effect for mean RDI, which showed that both heavier and lighter children's mean RDI improved at follow up (p < .0001; "Lighter" baseline RDI=7.35, Follow-up=1.78; "Heavier" baseline RDI=8.87, Follow-up=2.67). For executive functioning, younger children demonstrated more significant age-adjusted gains than did older children, regardless of BMI (p=.003). For IQ, there were no significant main effects or interactions. For memory, a significant BMI X Session interaction was observed. Although both BMI groups improved, heavier children demonstrated the largest improvement in memory scores (p=.002; lighter change=0.5 Standard Deviations, heavier change=1.0 SD). On behavioral measures, regardless of age or BMI, significant improvements emerged over time for oppositional (p=.002) and hyperactive (p=.01) ratings.

Conclusion: Age and BMI may influence cognitive, if not behavioral improvement following AT. Although the RDI improved for both heavier and lighter children, heavier children demonstrated more significant improvement in memory scores. Memory may be particularly sensitive to obesity-related factors in children with SDB.

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0866

EPIGENETIC DNA METHYLATION PROFILES IN CHILDREN WITH OSA AND EITHER HIGH OR LOW SERUM C-REACTIVE PROTEIN LEVELS

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Introduction: Obstructive sleep apnea (OSA) is common in children, and leads to multiple end-organ morbidities induced by the cumulative burden of oxidative stress and inflammation. However, not all children with OSA exhibit increased systemic inflammation, suggesting that genetic and environmental factors could play a role in determining the inflammatory phenotype among children with OSA. DNA methylation occurs mainly at CpG dinucleotides and involves the enzymatic addition of a methyl group to the cytosine residue without changing the primary DNA sequences. Such modifications at regulatory gene correlate with the transcriptional state of a gene. DNA methylation is an essential mechanism for normal cell development and for maintaining tissue specificity, and has been implicated in progression of various human diseases. We hypothesized that discrepant inflammatory responses in the context of pediatric OSA may be accounted for by different patterns of methylation in genes associated with inflammation.

Methods: 12 children with OSA (mean age: 7.8±2.4 years) were included. All participants underwent polysomnography and a fasting blood draw next morning. Children were divided into 2 groups based on the presence of high and low C-reactive protein level (high CRP levels >1.50 mg/dl). DNA methylation status of 24 inflammatory-related genes was examined using methyl-profiler DNA methylation quantitative PCR assay (SABiosciences Corp., Frederick, MD).

Results: Of 24 inflammatory associated genes methylation profiles, we found that forkhead box P3 (Foxp3) and interferon regulatory factor 1 (IRF1) genes were significantly hypermethylated in OSA children with high CRP levels compared to those children with low CRP levels (Foxp3: 41.4 ±30.4% vs. 12.9±1.3%, P<0.05; IRF1: 26.6 ±16.0% vs. 8.1±5.5%, P<0.05).

Conclusion: Foxp3 and IRF1 genes were highly hypermethylated in OSA children with increased inflammatory responses, suggesting that down-regulation of specific T-lymphocyte subpopulations may be an important determinant of inflammatory phenotype. These findings suggest that epigenetic changes may underlie differential susceptibility to OSA in children.

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0867

COMPARISON OF CONVENTIONAL METHOD AND MICRODEBRIDER TECHNIQUE IN THE ADENOTONSILLECTOMY IN INFANTS AND YOUNG CHILDREN WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Although adenotonsillectomy remains the gold standard treatment for pediatric obstructive sleep apnea syndrome (OSAS), the debate continues as to what surgical technique is most effective. Accordingly, the aim of this study is to evaluate the safety and efficacy of microdebrider adenoidectomy in treating OSAS in pediatric patients comparing a conventional method.

Methods: We retrospectively reviewed the medical records (sleep parameter, size of residual adenoids) of children who had undergone adenoidectomy/adenotonsillectomy for the treatment of OSAS. The study was designed to collect data in the course of standard treatment for OSAS, and was thus classified as an exempt by the local institutional review board. The microdebrider group (Group I) comprised of 17 Japanese OSAS patients (14 boys, 3 girls). In comparison, 27 children undergoing classical adenoidectomy (Group II) were selected from among 87 pediatric Japanese OSAS patients. Group II children were matched for age, sex and Kaup index with Group I.

Results: A significant improvement in postoperative apnea/hypopnea index (AHI) was found with less pre-operative AHI in Group I (p<0.05). Prevalence of AHI <1 was significantly higher in Group I than in Group II (p<0.05). Postoperative residual adenoid was significantly less in Group I (Grade 3 or 4 adenoid size in 1/17) than in Group II (9/27, p<0.05). Moreover, postoperative AHI was reduced in proportion with the smaller amount of residual adenoid.

Conclusion: The newly developed microdebrider adenoidectomy for pediatric OSAS patients with adenotonsillar hypertrophy is more accurate than standard adenoidectomy and therefore effective for ameliorating sleep apnea.

0868

ASSESSMENT OF SLEEP DISORDERED BREATHING IN CHILDREN WITH CLEFT PALATE REPAIR

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Introduction: Children with a history of cleft palate repair (CPR) may be at increased risk for sleep disordered breathing (SDB), but how to screen or assess for SDB among these patients has not been well studied. The study objective was to examine among children with CPR both the frequency of SDB and the effectiveness of a symptom-based questionnaire screen for SDB.

Methods: Children aged 5-16 years with CPR were recruited from a tertiary care university hospital craniofacial anomalies clinic. Parents completed a validated 22-item Pediatric Sleep Questionaire (PSQ) SDB scale. A score ≥0.33 (one-third of symptom-items endorsed) identifies increased risk for SDB in children with no history of CPR. Subjects underwent overnight PSG including esophageal pressure (Pes) monitor-

ing, and SDB was defined by an apnea-hypopnea index (AHI) >1 or a minimum Pes ≤ -20 cm H2O.

Results: Thus far, 31 children with CPR have been studied, with a mean age of 9.9 ±3.1 years, including 16 boys (52%). Among the 31 children, 17 (55%) screened positive for SDB on the PSQ-SDB scale. Of these 17 children, 13 (76%) had AHI>1, another 2 (12%) had a minimum Pes worse than -20 cm H2O, and the remaining 2 did not have SDB. However, among the 14 children who screened negative for SDB, 10 (71%) had SDB on PSG. In total, 25 of 31 children (81%) had PSG-defined SDB (n=23 [74%] with AHI>1). Sensitivity and specificity of the PSQ-SDB scale for PSG-defined SDB were 60 and 67%, respectively.

Conclusion: In this initial sample from a craniofacial anomalies clinic, the PSQ-SDB scale did not show good sensitivity or specificity for PSG-defined SDB. In this setting, different thresholds for the PSQ-SDB scale may show improved utility, but evaluation by PSG should be considered for all patients because more than 80% may have some level of SDB.

0869

EFFECT OF SOFT TISSUE SURGICAL INTERVENTION ON SLEEP APNEA AND SLEEP ARCHITECTURE IN CHILDREN WITH DOWN SYNDROME

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Introduction: Down syndrome (DS) children have multifactorial risks for sleep disordered breathing (SDB) including craniofacial abnormalities, relative macroglossia, obesity and hypotonia. We sought to evaluate the impact of soft tissue surgeries (lingual tonsillectomy, midline posterior glossectomy and genioglossus advancement among others) on polysomnography (PSG) parameters in these children.

Methods: A Retrospective review of data before and after surgery on DS children from 1/2003-6/2010 was conducted. Only children with a PSG before and after surgery were included. Patients receiving hypnotic medications, requiring tracheostomy or ventilatory support, and those with insufficient data were excluded. Date and type of surgeries performed was collected.

Results: 52 patients (29 male; 23 female) met inclusion criteria with mean age 10.3 years (SD 5.5 years). Comparing the pre- and post-surgery PSG, there was decrease in AHI (15.8±16.6/hr [pre] vs 11.4±16.9/hr [post], P=NS) and obstructive index (14.8±16.8/hr [pre] vs 10.5±17.0/hr [post], P=NS) after surgery, however this was not statistically significant. Additionally, there was a significant increase in average oxygen desaturation associated with obstructive respiratory events (88±4% [pre] vs 90±4% [post], P<0.05). Analysis of sleep architecture revealed a significant decrease in sleep onset latency (58.5±41.1 min [pre] vs 45.3±42.3 min [post], P<0.05), decrease in NREM 2 (56±10% [pre] vs 51±12% [post], P<0.01) and a corresponding increase in NREM 3 (24±8% [pre] vs 25±9% [post], P<0.01) after surgery.

Conclusion: Soft tissue surgeries for SDB in DS children lead to significant improvement in sleep architecture as evidenced by a decrease in sleep latency and an increase in percentage of slow wave sleep. In addition, there is a lesser degree of hypoxia associated with apneic events after surgery. This may explain subjective reports of clinical improvement in sleep quality and daytime functioning despite a lack of significant improvement in overall apnea index.

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0870

OUTCOME OF MANDIBULAR LENGTHENING FOR INFANTS WITH PIERRE-ROBIN SEQUENCE AND UPPER AIRWAY OBSTRUCTION

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Introduction: Severe upper airway obstruction(UAO) is seen in 10% of infants with Pierre-Robin Sequence (PRS) and micrognathia. The purpose of our study is to identify objective measures of success in regard to relief of UAO in these infants after mandibular lengthening by distraction osteogenesis (MLDO).

Methods: Retrospective study of 13 infants from November 2004 to March 2010 with the diagnosis of PRS who underwent MLDO. Data collected to assess for independent variables that may affect outcome: patient demographics, pre- and post-operative polysomnography (PSG) results, bronch and airway CT data, and operative data.

Results: Thirteen infants (7♂) diagnosed with PRS with mean gestational age 38 weeks, and mean age 44 days at time of surgery. Most infants did not require pre-operative respiratory support (e.g., HFNC or CPAP). Pre-operative physical exam revealed all infants had a vertical tongue position with positive tongue thrust; there was significant maxillomandibular discrepancy indicating severe micrognathia. Post-operative exam revealed a horizontal tongue position and resolved vertical tongue thrust; the average maxillomandibular relationship improved to 0 mm. Pre-operative bronch data showed all infants had tongue base obstruction;majority had relief of obstruction with jaw lift. Tongue base obstruction was not seen post-operatively. Five infants had mild laryngomalacia; no other significant airway anomalies were seen. Using CT scans, the airway volume (1.5 cc versus 3.6 cc) and bone mandible volume (7.6 cc versus 20.2 cc) were significantly larger post-operatively. (p=.003) There was significant improvement in post-operative PSG results compared to pre-operative results (p<0.05 for all values): Pre-operative AHI=31.0 vs post-operative AHI=4.2, obstructive AHI=29.2 vs 3.8, supine AHI=37.6 vs 3.7, active sleep AHI=53.6 vs 7.5, SpO2min=66.4% vs 82.8%, %TST SpO2<90%=6.3% vs 0.6%, and ETCO2max=59.7 mmHg vs 50.1 mmHg. Infants did not have frequent central apneas. There were no significant correlations between PSG indices and maxillomandibular discrepancy.

Conclusion: Severe UAO is seen in a subset of infants with PRS and micrognathia. Etiology is related to tongue base obstruction. Mandibular lengthening significantly improves airway size and UAO in these very young infants. Ventilation improves as represented by increased SpO2 and decreased ETCO2. This has important implications given the concern for neurocognitive deficits in infants and children with sleep-disordered breathing.

0871

OBSTRUCTIVE SLEEP APNEA IN ADOLESCENTS EVALUATED FOR LAPAROSCOPIC ADJUSTABLE GASTRIC BANDING

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Introduction: Severe obesity is a risk factor for obstructive sleep apnea (OSA). Adult bariatric patients have a high prevalence of OSA (45% to 98%), whereas data for severely obese adolescents are limited. We aimed to determine the prevalence of OSA in a racially and ethnically diverse population of adolescents referred for laparoscopic adjustable gastric banding (LAGB).

Methods: All subjects underwent overnight polysomnography (PSG). A retrospective review of records and sleep questionnaires was conducted. Subjects with Medicaid insurance were classified as low socioeconomic status (SES). OSA was diagnosed if Respiratory Disturbance Index (RDI) was ≥ 5 events/hr.

Results: Of 72 subjects (mean age 17.3 ± 1.3 yrs, mean BMI 45.6 ± 6.0 kg/m2) 24% were African Americans, 25% Hispanics and 51% Caucasians. 24% of subjects were of low SES. The prevalence of OSA was 24%. Subjects with OSA had a mean RDI of 12.1± 11.4 events/hr. By questionnaire, only snoring incidence was higher (94% vs. 66%, p =.03) in OSA vs. non OSA group by Fischer's Exact Test. The logistic model showed both BMI and gender are significant predictors of OSA in adolescents with high BMI at higher risk for OSA (OR=1.2; p=0.0024) and females at lower risk (OR=0.09; p=0.0007). Fasting serum insulin levels were higher in the OSA group (21.9 ± 8.9 vs. 13.9 ± 12.3 uI/ml p = .02) based on Two-sample t-test but there were no differences in fasting glucose levels suggesting insulin resistance is associated with OSA in the absence of alteration in glucose tolerance. Controlling for BMI, covariates including ethnicity and SES were marginally significant predictors of OSA while diabetes, hypertension, metabolic syndrome were not.

Conclusion: The prevalence of OSA in adolescents undergoing evaluation for LAGB, although lower than reported in adults, is high. OSA was poorly predicted by clinical parameters.

0872

PREVALENCE OF RESTLESS LEG SYNDROME AMONG ADOLESCENT CHILDREN IN THE TUCSON CHILDREN'S ASSESSMENT OF SLEEP APNEA STUDY (TUCASA)

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Introduction: Restless Leg Syndrome (RLS) and it's association with sleep problems in a general population of adolescents has been understudied. This analysis aims to describe the prevalence of RLS, and its association with sleep problems, in the adolescent age group.

Methods: The TuCASA study is a prospective, cohort study that initially enrolled Hispanic and Caucasian children between the ages of 6 and 11 years and subsequently re-studied them about 5 years later at approximately 10-18 years of age. At the time of the 2nd examination, in-home polysomnography as well as a comprehensive sleep habits survey including questions pertaining to RLS were completed. RLS was present if the subject met 4 essential adult RLS criteria described by Allen et al (2003). Habitual snoring (SN), excessive daytime sleepiness (EDS), difficulty initiating or maintaining sleep (DIMS), and learning problems (LP) were present if symptoms were endorsed frequently or almost always. Enuresis (EN), sleep terrors (TR), sleep walking (SW) and sleep talking (ST) were also assessed.

Results: Assessments were obtained in 348 children (49% girls; 36% Hispanic). The prevalence of RLS was 4.3%. RLS was associated with the presence of EDS (p< 0.006), DIMS (p< 0.013), and SN (p< 0.029). Although the prevalence of RLS was higher in girls than boys (5.3% vs 3.4%), this did not achieve statistical significance. There was no association between RLS and ethnicity, LP, EN, SW, or ST.

Conclusion: The prevalence of RLS in a community based sample of adolescents is approximately 4.3%. RLS in adolescents is associated with EDS, DIMS, and habitual snoring.

Support (If Any): HL 62373

0873

EFFECT OF AGE, GENDER AND IRON DOSING ON SYMPTOMATOLOGY AND FERRITIN LEVELS IN CHILDREN WITH RESTLESS LEG SYNDROME

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Introduction: Serum ferritin level< 50ng/mL, indicative of low iron bio-availability, is associated with the presence of symptoms of restless leg syndrome (RLS). Treatment with iron to increase serum ferritin above 50ng/mL reduces these symptoms. The purpose of this study was to assess response to oral iron in children with low ferritin levels and symptoms of RLS.

Methods: Retrospective chart review of 238 patients with serum ferritin level obtained at a large regional pediatric sleep lab from 6/28/2007-3/30/2010. Symptomatology and ferritin levels were analyzed for changes before and after treatment with oral iron (n=64) as was data from polysomnography (n=201).

Results: There was a correlation between age and initial ferritin level (r= -0.295, p<0.0001) and LM Index (r= -0.200, p=0.005) such that younger children had lower ferritin levels and move more during sleep. Boys (LM Index=14.9±12.2) move more during sleep vs. girls (LM Index=10.9±7.3, p=0.008). Duration of therapy was a positive predictor of the absolute increase in ferritin level whereas mg/kg daily dosing was not. Interestingly, children dosed with liquid iron received higher average daily doses (2.4±0.8 mg/kg/day) compared to children treated with tablets (1.7±0.9 mg/kg/day, p<0.005) Significant differences before and after treatment in complaints of discomforts that delay sleep onset (33.9% before, 20.3% after treatment, p=0.018), discomforts relieved with movement (20.3% before, 11.9% after treatment, p=0.002), and discomforts that are worse when still (16.9% before, 10.2% after treatment, p=0.0001) were found. These differences correspond to a significantly higher mean ferritin level after treatment (24.7±14.0 pretreatment, 45.0±23.3 post-treatment, p=0.02).

Conclusion: Our data demonstrate that younger age and male gender are important predictors of frequency of limb movements recorded during polysonography. Iron treatment improves symptoms of RLS although most patients continued to have ferritin levels below threshold values of 50ng/mL. Dosing regimen and duration are important therapeutic considerations that warrant further investigation.

0874

ESTIMATED RATES OF RESTLESS LEGS SYNDROME (RLS) AND PERIODIC LIMB MOVEMENTS IN SLEEP (PLMS) IN A CLINICAL SAMPLE OF CHILDREN WITH TOURETTE SYNDROME (TS)

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Introduction: Tourette Syndrome (TS) and Restless Legs Syndrome (RLS) share clinical, pathophysiologic, and treatment-related features in childhood. Periodic Limb Movements in Sleep (PLMS) is a physiologic diagnosis based on polysomnographic data. Survey data can estimate RLS and PLMS, with an estimated rate for RLS of 2.0% in the general population. However, little is known about RLS in children with TS, despite shared features. Thus, the aims of this study were to estimate rates of RLS and/or PLMS in childhood TS and identify pharmacologic treatments that might be contributing to an association of TS with RLS and/or PLMS.

Methods: Children were identified via the Children's Hospital of Pittsburgh Tourette Syndrome Clinic and its Child Neurology Research Registry. Based on parental mail-in surveys, rates of RLS and PLMS were

estimated using 2003 NIH workshop criteria for RLS in children and the Pediatric Sleep Questionnaire.

Results: Fifty-six of 102 surveys were returned, 48 of which were evaluable. Eleven respondents (23%) had probable or definite RLS. Nineteen (40%) had survey answers consistent with PLMS. All subjects who met criteria for RLS also had responses consistent with PLMS. Five of 11 respondents with RLS (46%) reported using medication for TS (SSRI's/SNRI's, stimulants, or alpha-2 agonists), with 3/ 11 (27%) reporting polypharmacy. Thirteen of 19 respondents with probable PLMS (68%) reported using medication (SSRI's/SNRI's, stimulants, neuroleptics, alpha-2 agonists, benzodiazepines), with 10/ 19 (53%) reporting polypharmacy.

Conclusion: Based upon this cohort, it appears that children with TS have higher rates of both RLS (23%) and PLMS (40%) than the general population (2.0%). Although this association is made ambiguous by concurrent medication use, even after removing patients with current medication exposure, an estimated 12.5% (6/48) of TS patients endorsed RLS/PLMS. Future studies examining RLS and PLMS in larger groups are needed to clarify the relationship of TS and RLS/PLMS and its neuropharmacology.

0875

HEART RATE RESPONSES TO SPONTANEOUS AROUSALS FROM SLEEP IN CHILDREN WITH CHROMOSOME 15Q11-13 DUPLICATION SYNDROME: HYPOAROUSAL AS A CONTRIBUTOR TO SUDDEN DEATH?

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Introduction: Chromosome 15q11-13 contains imprinted genes essential for normal mammalian neurodevelopment. Over-expression of maternally expressed imprinted genes is associated with a neurodevelopmental disorder with autistic features. There is an increased risk of sudden unexpected death during sleep among children and adults with chromosome 15q duplication syndrome, estimated at 1% per year. The etiology of the sudden death has not been established, even after autopsy. We tested the hypothesis that hypoarousal may be present in children with 15q duplication syndrome as evidenced by a reduced heart rate (HR) response to spontaneous arousal from sleep.

Methods: Five children with chromosome 15q11-13 duplication who had overnight polysomnograms (PSGs) for suspicion of sleep-disordered breathing were compared to 5 age/gender matched healthy controls with normal PSGs. A total of 30 spontaneous arousals were identified during NREM sleep based on guidelines of the ASDA criteria (an abrupt shift in EEG frequency lasting >3 seconds). The arousal length, baseline heart rate, and heart rate response to arousal were compared using an unpaired t-test with statistical significance at p<0.05 level.

Results: One subject with iso-dicentric 15q mutation had frequent seizure activity resulting in central apneas. Otherwise, no OSA or cardiac arrhythmias were detected in either group. The baseline HR and spontaneous arousal length did not differ between the subjects. The peak HR relative to baseline (100%) in NREM sleep was 117.4 +/- 14.63% in 15q11-13 duplication subjects and 135.6 +/- 12.78% in controls (P =0.001121).

Conclusion: Children with 15q11-13 duplication syndrome have a reduced HR response to spontaneous arousals compared to normal children during NREM sleep. These findings suggest that the 15q11-13 duplication maybe associated with a decreased arousal response from sleep that may act with other genetic and environmental risk factors to contribute to reports of sudden unexplained death in sleep in this population.

0876

SLEEP DISTURBANCE AMONG DISADVANTAGED MINORITY TEENS

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Introduction: Sleeplessness in teens is associated with problems such as impaired mood regulation, depression, poor academic performance, substance use, somatic health problems and accidents/injuries. What is not known is the relationship between insufficient or disrupted sleep, violence, and risk behaviors among adolescents who live in high poverty neighborhoods where sleeping conditions are much less than optimal and where youth violence is a common feature.

Methods: A subsample of the Mobile Youth Survey (MYS) (N=149, ages 14-15 years: 73%-age 14; 46%-female) completed extensive interviews in summer 2010 that addressed sleep quality, sleep hygiene, sleep/wake quality, nightmare symptoms, self-rated health, and household crowding. The MYS is a longitudinal study of impoverished inner-city African-American adolescents in Mobile, Alabama.

Results: Good sleep quality was negatively associated with substance abuse (-.37), externalized anger (-.23), callousness (-.28), having been drunk/high within 30 days (-.22), injury (-.26), nightmare symptoms (-.23), and crowding (-.17). Sleep hygiene practices were negatively associated with having been drunk/high within 30 days (-.22) and nightmare symptoms (-.21) while positively associated with self worth (.22). Sleep/wake quality, where higher scores represented reports of better sleep or waking symptoms, was inversely associated with substance abuse (-.17), eternalized anger (-.23), getting drunk/high within 30 days (-.18), nightmare symptoms (-.19), and hopelessness (-.26). Nightmare symptoms were negatively associated with self-rated health (-.22), general self-worth (-.21), sleep/wake quality (-.19), sleep hygiene (-.21), and sleep quality (-.23) while positively associated with externalized anger (-.18).

Conclusion: Even without the time constraints of school or work, teens in these low income neighborhoods reported a variety of sleep problems and poor sleep hygiene practices associated with risk behaviors, emotional or social problems. These findings suggest further research into sleep problems and sleep hygiene among teens in minority homes.

0877

STABILITY OF OVERNIGHT POLYSOMNOGRAPHY (PSG) AMONG CHILDREN WITH SICKLE CELL DISEASE (SCD)

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Introduction: OSA has been linked to pain crises, pulmonary hypertension, and strokes in children with SCD. Snoring and sleepiness may be particularly poor predictors of OSA in children with SCD. Because of the severe morbidity associated with OSA, an argument could be made to do routine second PSGs in the absence of progression of symptoms or abnormalities on the first PSG.

Methods: Two PSG were performed on 63 clinically stable children 4 to 18 years old with Hgb SS or HgbS βThal[0], as part of SAC protocol. Exclusion criteria for this analysis (18 of 63) were adenotonsillectomy or beginning hydroxyurea or transfusions between the PSGs, or pain crisis/acute chest within 3 months of the 2nd PSG. OSA was diagnosed using 2 thresholds: ≥ 2 or ≥ 5 obstructive events per hour. Events were either an apnea, or hypopnea with 3% desaturation.

Results: Age 12.3 yrs $\pm$ 4.0, BMI 18.2 $\pm$ 3.2. Interval between studies 581 $\pm$ 119 days. Ten of 45 changed from $\geq$ 2 events per hr to < 2; 3 of 45 from < 2 to $\geq$ 2; 7 of 45 had $\geq$ 2 on both nights. Six of 45 changed from $\geq$ 5 to < 5, 2 of 45 from < 5 to $\geq$ 5, and 1 had $\geq$ 5 on both nights.

Conclusion: Among children with SCD, in the absence of progression of SCD severity, overnight PSG remains quite stable over a 12 to 30 month period. By either threshold, only 6.7% or fewer had a new diagnosis of OSA on follow-up PSG; most who changed diagnosis were improved. Future studies should analyze PSG stability among children with SCD who have worse snoring or sleepiness.

Support (If Any): NHLBI, HL079937, SAC: Sleep and Asthma Cohort Study

0878

SLEEP PROBLEMS IN INFANTS WITH PRENATAL ALCOHOL EXPOSURE

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Introduction: Sleep problems are common among school-aged children with significant prenatal alcohol exposure (PAE), yet little is known about sleep in this high-risk population during the crucial developmental window of infancy, when sleep patterns initially consolidate. We aimed to describe sleep in infants with PAE compared to matched non-exposed controls.

Methods: Infants from 6-15 months of age with moderate to heavy PAE assessed through standardized report and non-exposed control subjects underwent overnight polysomnography using standard pediatric techniques. Parents completed questionnaires assessing infant sleep habits and psychosocial risk. Appropriate statistical analysis will be performed on the final sample (10 per group). Initial results are reported as mean $\pm$ SD per group.

Results: Data for seven infants with PAE (age 10.6 $\pm$ 1.3 months, 43% female) and five control infants (age 10.5 $\pm$ 1.2 months, 60% female) are available now. Infants with PAE had slightly decreased % sleep efficiency (81.7 $\pm$ 8.8 vs 85.6 $\pm$ 2.4), increased %N1 sleep (14.4 $\pm$ 5.9 vs. 9.6 $\pm$ 3.0) and slightly increased % wake after sleep onset (13.6 $\pm$ 8.0 vs. 11.6 $\pm$ 3.3). Respiratory analysis revealed that infants with PAE had higher apnea-hypopnea indices (7.8 $\pm$ 3.7 vs 6.2 $\pm$ 1.7). Oxygen desaturation indices were markedly higher in exposed infants compared to controls (11.5 $\pm$ 12.2 vs 2.6 $\pm$ 2.0), with most desaturations occurring in REM sleep for both groups (REM desaturation indices 23.4 $\pm$ 9.6 vs. 10.5 $\pm$ 5.2). On questionnaires, parents of infants with PAE reported more difficulty putting baby down for sleep, more nighttime awakenings, and fewer daytime naps compared to controls.

Conclusion: Infants with PAE have more difficulty maintaining sleep, with increased sleep disordered breathing and more frequent oxygen desaturations particularly in REM sleep. These differences may provide direction to early diagnostic and therapeutic interventions in this prevalent clinical population.

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0879

SLEEP QUALITY AND DISTURBANCE IN PARENTAL CAREGIVERS OF CHILDREN IN THE MAINTENANCE PHASE OF ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

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Introduction: Parental caregivers of children with chronic illnesses have reported sleep disturbance and poor quality, possibly due to nighttime caregiving, frequent monitoring, child sleep disturbance, and emotional distress. Among chronic illnesses, ALL is the most common pediatric cancer and the maintenance phase is the third and longest phase of treatment. However, despite the prevalence of ALL, few studies have examined the rates of sleep disturbance and quality among this specific population of caregivers. The aim of this study was to describe subjective sleep quality and disturbance in a pilot study of caregivers of children in the maintenance phase of ALL.

Methods: Participants included a preliminary sample of 23 ALL caregivers of children ages 3 to 12 receiving care at The Children's Hospital of Philadelphia (M child age=5.22 $\pm$ 1.75). Caregivers completed measures at a single visit where the child was receiving monthly corticosteroid treatment. The Pittsburgh Sleep Quality Index (PSQI) assessed sleep quality and disturbance, while the Child Sleep Habits Questionnaire (CSHQ) assessed child sleep disturbance.

Results: Participants were 19 biological mothers and 4 biological fathers (87% married, 87% Caucasian, 8.7% Hispanic). All but 3 had at least one other child living at home (range= 1 month to 17 years). Time since the child started maintenance therapy ranged from 3 months to 2.89 years (M= 1.48 $\pm$ 0.87). Interestingly, the sample was nearly evenly divided between good and poor sleepers: 43.5% scored >5 on the PSQI. Mean sleep efficiency was 85.29 $\pm$ 13.74. However, almost all caregivers reported sleep disturbances within the past month, with 14 (60.9%) reporting $\leq$ 9 and 30.4% experiencing 10 to 18 disturbances on the PSQI. Additionally, the majority (87%) reported a CSHQ total child sleep disturbance score $\geq$ the proposed clinical cut-off of 41.

Conclusion: Although this sample of ALL caregivers reported slightly above-average sleep efficiency compared to other caregiver population norms, nearly all reported experiencing sleep disturbances, both from their own sleep and child's sleep. The findings provide insight into the frequency of sleep disturbance in this distinct caregiver population and highlight the need for further research and support of caregivers and families of children with pediatric illnesses, particularly sleep patterns, quality, and sources of sleep disturbance over time.

0880

MOTHER-CHILD SLEEP PATTERNS DURING MAINTENANCE THERAPY FOR ACUTE LYMPHOCYTIC LEUKEMIA (ALL)

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Introduction: Pediatric cancer in general and ALL in particular disrupts sleep in the child and family. Sleep disruption and deprivation in caregivers of children with ALL is common and distressing, owing to the level of attention and nocturnal care required. Evidence suggests that caregiver sleep deprivation is associated with increased stress, irritability, and reduced work performance. Few qualitative studies have investigated the relationships among childhood ALL and caregiver sleep.

Methods: To elicit an understanding of mother-child sleep patterns during ALL maintenance chemotherapy, a qualitative descriptive approach was chosen. This approach allows for the discovery of themes that are not identified in the literature, or may not be revealed through quantitative methods. The sample, obtained through The Children's Hospital Denver (TCH) hematology practice included 23 dyads of mothers and children with ALL. The typical maternal participants were mid-thirties, married (76.9%), white (65%), 42% had a college education or higher, and 35% were employed. To the extent possible, patients from diverse cultural and socioeconomic backgrounds were included to provide broad perspectives. Participants shared audio recorded narratives (30-60 minutes) pertaining to their sleep (e.g., quality, quantity) relative to their child's ALL diagnosis.

Results: Interviews were transcribed and independently analyzed by co-PIs and compared. Themes emerging from the data included:" A Whole New Cancer World" and "I don't remember what it is like to sleep." Facets of the sleep theme included "sick at night," "coping with exhaustion," and "moving toward sleep." Participants described the best and worst nights, and shared a wide variety of strategies to improve sleep.

Conclusion: Even during maintenance chemotherapy, the quality and quantity of the child's sleep had a major negative impact on maternal sleep and family sleeping arrangements. This study has implications for clinicians in assessing and implementing interventions for impaired sleep in parents, and children with ALL.

Support (If Any): UC Denver Colorado Clinical Translational Science Institute (CCTSI) Pilot Award (1UL1RR014780)

0881

THE PREVALENCE AND PATTERNS OF SLEEP DISORDERS AND CIRCADIAN RHYTHM DISRUPTIONS IN CHILDREN WITH FETAL ALCOHOL SPECTRUMS DISORDERS (FASD)

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Introduction: Sleep disorders have been poorly described in children and adolescents diagnosed with FASD. The objective of this study is to describe the sleep and circadian rhythm characteristics of children with FASD using 2 nights of overnight polysomnography, sleep questionnaires, and the Dim Light Melatonin Onset (DLMO) test. To our knowledge, no comprehensive study of this nature has been conducted.

Methods: Children aged 5-18 years diagnosed with Fetal Alcohol Spectrum Disorder (FASD) were recruited from various FASD clinics to the Youthdale Child and Adolescent Sleep Centre in Toronto. After a medical consultation, each participant had 2 nights of overnight polysomnography, as well as an additional night of DLMO. Participants completed various sleep, alertness, and mood questionnaires. To date, objective sleep parameters, subjective questionnaire data were analyzed using SPSS for 9 study patients.

Results: Descriptive pilot data shows the mean percentage values for stage 4 slow wave sleep (SWS) were slightly elevated compared to the normative values. The mean percentage values of REM sleep was slightly decreased. Mean percentage values of wakefulness were also increased, suggesting increased sleep fragmentation during the night. The DLMO results obtained to date in this group are all abnormal.

Conclusion: Polysomnographic analysis supports disrupted sleep patterns in children with FASD including increased night awakenings, increased sleep fragmentation, and decreased REM sleep. The increased prevalence of sleep and circadian disturbances in this population suggests the need for a more proactive approach to sleep.

0882

POLYSOMNOGRAPHY AND ACTIGRAPHY CONCORDANCE IN JUVENILE IDIOPATHIC ARTHRITIS AND ASTHMA COMPARED TO HEALTHY CHILDREN

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Introduction: Agreement between actigraphy and polysomnography (PSG) have been reported in healthy school-age children < 9 years old, but to our knowledge studies have not been reported in children with chronic illnesses such as arthritis or asthma. The purpose of this study was to evaluate sensitivity, specificity, and accuracy with an epoch-by-epoch comparison between PSG and actigraphy, and to compare PSG derived sleep parameters to those derived from actigraphy in 9-to-11 year-old children with juvenile idiopathic arthritis (JIA), asthma, and healthy children.

Methods: Seventy-one children 9-11 years of age. Two consecutive nights of PSG and actigraphy were recorded and sensitivity, specificity, and accuracy were evaluated in an epoch-by-epoch comparison of PSG and actigraphy.

Results: Overall, mean sensitivity and accuracy were higher than specificity but sensitivity was significantly higher for JIA on night 1, while specificity was significantly lower for JIA compared to asthma and controls for both nights at all three activity count thresholds evaluated. Total sleep time (TST), wake after sleep onset (WASO), and sleep efficiency (SE) derived from PSG were not different among the 3 groups, but TST and SE were higher and WASO was lower in JIA. Based on the Bland-Altman technique, actigraphy was more accurate in estimating TST and WASO at the medium sensitivity threshold.

Conclusion: Compared to PSG, actigraphy was reasonably accurate in identifying sleep from wake in 9 to 11 year old children with JIA and asthma. However, actigraphy was less accurate in the identification of nocturnal wakefulness at all activity count thresholds tested in JIA. It is important for clinicians and researchers to understand the strengths and limitations of the various actigraphy devices, as actigraphy is not as sensitive for measuring nocturnal wakefulness in children with certain chronic illnesses.

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0883

SLEEP DISCREPANCY, SLEEP COMPLAINT, AND POOR SLEEP AMONG OLDER ADULTS

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Introduction: Discrepancy between sleep diary and actigraphic measured sleep has been documented among those with insomnia. While aspects of this difference may reflect measurement error, considerable portions of sleep discrepancy (SD) may be meaningful.

Methods: The current study explored SD in four groups of community dwelling older adults: good sleeping complainers, poor sleeping complainers, good sleeping non-complainers and poor sleeping non-complainers. Participants (N = 153, Mean age = 71.6) were screened for comorbid sleep disorders, completed demographic questions, BDI-II, and 14 consecutive nights of sleep diaries and actigraphy.

Results: A MANCOVA [$F(12,331.01) = 8.876$, $p < 0.001$] controlling for gender, medical conditions, medications, and depression symptoms showed significant group differences on relative amounts of SOL [$F(3,128) = 11.566$, $p < 0.001$] and WASO [$F(3,128) = 13.928$, $p < 0.001$] SD and frequency of SOL [$F(3,128) = 8.883$, $p < 0.001$] and WASO SD [$F(3,128) = 28.102$, $p < 0.001$]. Greater amount and frequency of WASO SD (p's < 0.01) best separated poor sleeping complainers from the other groups. Among those with poor sleep (regardless of complaint), there was little difference in SOL SD (quantity or frequency). A multiple regression analysis predicting depressive symptoms showed an association between the quantity of SOL ($\beta = 0.39$) and WASO ($\beta = 0.323$) SD beyond medical and demographic factors [$F(8,127) = 6.52$, $p < 0.001$, $r2 = 0.291$].

Conclusion: These results suggest that older adults with poor sleep have heightened awareness of idle time in bed and that this impact is more pronounced in the middle of the night among individuals with a sleep complaint. Furthermore, these results suggest that the degree to which participants' self report of SOL and WASO exceeded actigraphy was associated with more depressive symptoms. The concurrent patterns of sleep discrepancy and depressive symptoms may be linked through the effects of cognitive hyperarousal, which has been independently suggested as an explanation for depression, sleep discrepancy and insomnia.

Support (If Any): This project was supported by a grant from the National Institute of Health/National Institute of Aging (1 R21 AG024459-01 Christina S. McCrae, PhD, PI).

0884

SELF-REPORTED SLEEP DURATION IN ADULTS: CHANGE AND CORRELATES OF CHANGING DURATION OVER 20 YEARS OF FOLLOW-UP IN THE WISCONSIN SLEEP COHORT STUDY

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Introduction: Short and long usual sleep durations are associated with health decrements and increased mortality. Reports of repeated cross-sectional evaluations of sleep duration have suggested a pattern of decreasing mean duration in recent decades; however, there have been almost no studies examining longitudinal trends in US adults. We use >20 years of self-reported sleep duration data from the Wisconsin Sleep Cohort Study to characterize within-subject trends in sleep duration.

Methods: 1686 Wisconsin Sleep Cohort Study subjects (58% female, 30-61 years old in 1988) provided 7825 (from 3 up to 9 per subject) survey and interview-based self-reports of usual sleep duration between 1988 and 2010. We fit individual-level sleep duration slopes (change in duration over time) by linear regression and examined the association of subjects' slopes with sex, baseline age (<40, 40-49, and ≥50 years), and morbidity status (e.g., cardiovascular disease).

Results: Mean (SD) sleep duration in 1988 was 7.4 (0.9) hours. Mean (SE) duration slope was 0.014 (0.002) hours/year (i.e., mean sleep duration increased 8.2 minutes/day per 10 years). Subjects ≥50 years at baseline increased sleep duration the most (14.4 minutes/day per 10 years; 95% confidence interval (CI): 9.0, 19.8) compared to subjects in their 40s (10.8 minutes/day per 10 years; 95% CI: 7.3, 14.3) and subjects <40 years (1.2 minute/day per 10 years; 95% CI: -2.4, 4.8) (p-value for difference in slopes among age categories <0.001). Slopes were similar for men and women. Morbidity status was associated with decreasing slopes in sleep duration (-11.4 minutes/day per 10 years; 95% CI: -11.7, -11.1). While population-average sleep durations were relatively stable, individual subjects showed high variability: the mean within-subject standard deviation of sleep durations reported over follow-up was 33 minutes.

Conclusion: In a large population-based adult cohort, sleep duration has been slightly, but significantly, increasing over time, especially in older subjects.

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0885

SLEEP DISTURBANCES AND INCIDENT FRAILTY STATUS IN OLDER MEN

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Introduction: Sleep complaints and frailty are common with aging. A prior cross-sectional study reported that sleep disturbances were associated with greater prevalent frailty status, but longitudinal associations between sleep disturbances among non-frail older adults at baseline and risk of incident frailty are uncertain.

Methods: Subjective (questionnaire, PSQI and ESS) and objective sleep parameters (actigraphy, mean 5.2 nights; in-home overnight polysomnography) were measured at baseline among 2,505 non-frail men aged ≥67 years. Repeat frailty status assessment was performed an average of 3.4 years later. Sleep parameters were expressed as dichotomized predictors using clinical cut-points. Frailty status at follow-up was classified as robust, intermediate stage, frail, or dead (died in interim). Three separate logistic regression models were performed dichotomizing the outcome as intermediate/frail/dead (vs. robust), frail/dead (vs. robust/intermediate) and dead (vs. robust/intermediate/frail).

Results: Of the 2505 non-frail men (mean age 75.7 years) at baseline, status at the follow-up exam (an average of 3.4 years later) was robust in 701 (28.0%), intermediate stage in 1264 (50.5%), frail in 360 (14.4%), and died in interim period in 180 (7.2%). After adjustment for multiple potential confounders, neither subjective nor objective sleep disturbances were associated with the odds of being intermediate/frail/dead at follow-up. Poor subjective sleep quality, greater nighttime wakefulness, and greater nocturnal hypoxemia at baseline were associated with a 1.2 to 1.3-fold higher odds of frailty/ death at follow-up. Excessive daytime sleepiness, reduced sleep efficiency, greater nighttime wakefulness, severe sleep apnea, and greater nocturnal hypoxemia were associated with a 1.5 to 2.1-fold higher odds of mortality. Short sleep duration and prolonged sleep latency were not associated with incident frailty status.

Conclusion: Self-reported and objectively measured sleep disturbances at baseline in older non-frail men were independently associated with a higher risk of frailty or death at follow-up.

0886

DIFFICULTY MAINTAINING SLEEP AND EARLY WAKE-UP TIMES ARE ASSOCIATED WITH VASCULAR DYSFUNCTION IN JAPANESE HEALTHY INDIVIDUALS

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Introduction: Introduction: Previous investigations have shown sleep loss causes hypertension and atherosclerosis. Sleep fragmentation and earlier wake-up times characterize sleep patterns of older adults. Taken together, vascular dysfunction with aging could be associated with the age- related changes of sleep-wake patterns in forms of difficulty maintaining sleep and waking-up early . In the present study, we have cross-sectionally investigated whether self- reported difficulty sleep maintaining and habitual wake-up times are associated with higher blood pressure and vascular dysfunction.

Methods: The current study included 2062 apparently healthy individuals (mean aged 57.2±10.1, 1074 male)who underwent general health screening test in a general hospital. Habitual patterns concerning sleep (bed times, wake-up times, and symptoms of difficulty initiating or maintaining sleep) on weekdays were recorded from answers on the questionnaire. Vascular condition was assessed by blood pressure and brachial-ankle pulse-wave velocity (PWV) value. *Hypertension* was defined as blood pressure ≥130/85 mmHg,and *atherosclerosis* was determined as the highest tertile of baPWV values. Multivariate logistic regression model, adjusted for variables including gender, age, sex, body mass index, blood pressure, sleep duration were applied.

Results: Difficulty maintaining sleep was associated with increased prevalence of *hypertension* with adjusted odds ratio of 1.23(1.01-1.50). Wake-up times before 5:00 a.m. were associated with increased prevalence of *hypertension* and *atherosclerosis* with an adjusted odds ratio of 1.48(1.06-2.07) and 1.83(1.12-2.99), respectively, compared to wake-up times after 5:00 a.m. Adjusting for sleep duration did not contribute to the association between difficulty maintaining, early waking, and vascular condition.

Conclusion: Difficulty maintaining sleep and early wake-up times were strongly associated with vascular dysfunction. Age- associated sleep forms might influence vascular condition.

0887

MILD COGNITIVE IMPAIRMENT IN OLDER ADULTS IS NOT ASSOCIATED WITH SIGNIFICANT SUBJECTIVE SLEEP DISTURBANCE

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Introduction: The disturbed sleep of Alzheimer's disease (AD) patients has been well characterized even in early stages of the disease. Mild Cognitive Impairment (MCI) in older adults has recently been recognized as a pro-dromal phase of AD, opening the question of whether the sleep disturbances that characterize early stage AD might be present in MCI patients. To address this question we compared the subjective sleep quality of a group of amnestic MCI (aMCI) patients with a control group of healthy normal older adults.

Methods: Fifty-seven aMCI patients (age 70.5 + 1.1 years (mean + SEM); 22 men and 35 women) and 69 Controls (age 66.3 + 0.9 years; 30 men and 39 women) completed the Pittsburgh Sleep Quality Index (PSQI) as part of the baseline assessment of an ongoing randomized controlled trial. Groups were carefully screened to exclude major medi-

cal conditions and primary sleep disorders and had similar levels of education and comparable body mass indices.

Results: aMCIs did not report more subjective sleep disturbance than Controls for either PSQI total (5.7 + 0.4 versus 5.4 + 0.4, respectively) or subscale scores. Women tended to have higher PSQI scores than men, regardless of diagnosis, although such differences were also non-significant.

Conclusion: Older adults with aMCI do not report significantly impaired subjective sleep quality relative to healthy older controls; despite the older age of the aMCIs potentially biasing in favor of more impaired sleep quality in that group. These findings indicate that, while MCI may be a pro-dromal phase of AD, either the changes in cognitive function, particularly memory, which are the hallmark of AD, occur sooner than changes in sleep quality, or that objective changes in sleep patterns, not measured in the current study, are not of sufficient magnitude to be reliably perceived by aMCI patients.

0888

DIFFERENCE IN LIPID PEROXIDATION CONCENTRATIONS IN ADULTS AND ELDERLY PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS)

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Introduction: The aging process and intermittent hypoxia observed in obstructive sleep apnea syndrome (OSAS) may lead to an increase in the generation of reactive oxygen species and to an increase in malondialdehyde (MDA) plasma concentrations. Studies that compare lipidic peroxidation in elderly and adult people with OSAS are scarce. Our aim was to evaluate the effect of age upon lipid peroxidation concentrations in adult and elderly men with OSAS.

Methods: Male volunteers with ages between 25 and 75 years old were selected. Their body mass index (BMI) was under 40 kg/m2, and they had a clinic and polysomnographic diagnosis of OSAS. Each OSAS group had its own control group. They underwent blood analysis for lipid peroxidation evaluation.

Results: Participants were divided into four groups: 13 adults with OSAS, 12 adult controls, 30 elderly OSAS and 27 elderly controls. According to apnea-hypopnea index (AHI), as expected, there were significant intra-group differences both in the adult group [controls: 5.7 (95% 3.1-14.4) vs. OSAS=40.6 (95% 30.4-50.8)], and in the elderly group [controls:1.8 (95% 8-11.6) vs. OSAS=36.5 (95% 27.4-45.5)]. The elderly group with apnea had a higher mean MDA in relation to the elderly control group [2.9 nmol MDA/mL (95% 2.2-3.6) vs. 1.5 nmol MDA/mL (95% 0.9-2.2) respectively] and the adult apnea group [2.9 nmol MDA/mL (95% 2.2-3.6) vs. 1.5 nmol MDA/mL (95% 0.8-2.2) respectively]. There were no differences between the elderly apnea and the adult control groups [2.9 nmol MDA/mL (95% 2.2-3.6) vs. 2.1 nmol MDA/mL (95%1.4-2.8), respectively].

Conclusion: In our study we observed that in comparison with adults and controls, the elderly group with OSAS was influenced by two additive effects of oxidative stress, aging and OSAS, as suggested by the increase of lipid peroxidation.

0889

PREVALENCE AND CORRELATES FOR SLEEP COMPLAINTS IN OLDER ADULTS IN LOW AND MIDDLE INCOME COUNTRIES: A 10/66 DEMENTIA RESEARCH GROUP STUDY

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Introduction: Although it is well recognized that the prevalence of sleep complaints increases in older ages, estimations of this parameter in developing countries are still unknown. The present study aims to describe the prevalence and estimate prevalence ratios of sleep complaints' correlates in a large population of older adults from low and middle income countries (LAMIC).

Methods: A cross-sectional survey was performed in 16,680 65 year-old or older residents in catchment areas of eight LAMIC (Cuba, Dominican Republic, Peru, Venezuela, Mexico, China, India and Puerto Rico) as part of the 10/66 Dementia Research Group research program. Information about socio-demographic factors, lifestyle and health status as well as questions regarding sleep complaints was obtained. The prevalence of sleep complaints was estimated based on the question: "Have you had trouble sleeping recently?". The results (with robust 95% confidence intervals) were standardized by age group, sex, household clustering and residence site (urban or rural), for each studied country. Prevalence ratios were derived from Poisson regression models for each country and fixed or random effects meta-analyses was used to combine them.

Results: Standardized prevalence of sleep complaints varied from 9.1% (China) to 37.7% (India). Overall, after correction for all other variables, the meta-analysis showed that female gender, urban residence, low educational level, low physical activity status, high scores in pain score, poor health condition, higher memory impairment score, presence of DSMIV major depression, mild cognitive impairment and high number of co-morbidities were associated with the presence of sleep complaints (p<0.05).

Conclusion: This is the first study to robustly characterize the prevalence of sleep complaints in large samples of elders in LAMIC, especially from Latin America, as well as to identify potential risk factors that may be specific for these populations. This approach can help to direct efforts in health-care related to sleep disturbances in these countries.

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0890

RESTLESS LEG SYNDROME AND OBJECTIVE AND SUBJECTIVE SLEEP CHARACTERISTICS AMONG THE OLDEST OLD

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Introduction: Limited information is available regarding the prevalence and consequences of restless leg syndrome (RLS) in the very old.

Methods: As part of the Sleep and Cognition Ancillary Study of the Study of Osteoporotic Fractures (SOF), 795 women (mean age 87.5 years; SD 3.2) had measurements of self-reported sleep [questionnaire regarding symptoms of RLS; Pittsburgh Sleep Quality Index (PSQI); Epworth Sleepiness Scale (ESS)] and completed wrist actigraphy (mean 4.2 days). Other measurements included questionnaires regarding demographics, comorbidities, health status, physical functioning, mood [Geriatric Depression Scale (GDS, range 0-15) and Goldberg Anxiety Scale (GAS, range 0-9)], and medication use. Women were categorized

as having RLS if they answered positively to four questions based on criteria established by the International Restless Leg Syndrome Study Group.

Results: 149 (18.7%) of participants were identified as having RLS. Women with RLS had slightly higher levels of depressive symptoms (GDS 2.7 vs. 2.3, p=0.03) and anxiety (GAS 2.8 vs. 1.9, p<0.001). Women with and without RLS had similar rates of antidepressant medication use, including SSRI use, and performed similarly on physical function measures. In age-adjusted and multivariable models controlling for multiple potential confounders, presence of RLS was independently associated with a higher scores on the PSQI and ESS (MV models: PSQI > 5: OR 1.58, 95% CI 1.04, 2.39; ESS>10: OR 1.98, 95% CI 1.35, 2.92) In age-adjusted models, the presence of RLS was associated with a higher likelihood of nighttime wakefulness >1.5 hours (OR 1.65, 95% CI 1.13, 2.40) and frequent awakenings (>8 episodes) of 5 min or more (OR 1.53, 95% CI 1.04, 2.25). In multivariable models, these associations were attenuated and were of borderline significance.

Conclusion: RLS is common in very elderly women and is associated with increased subjective sleep complaints and, to a lesser degree, with increased objectively measured sleep fragmentation.

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0891

PREDICTORS OF BRIGHT LIGHT EXPOSURE IN OLDER POST-ACUTE REHABILITATION PATIENTS

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Introduction: Fragmented sleep is common among older patients undergoing inpatient post-acute rehabilitation (PAR). Prior research has demonstrated that most institutionalized older adults are never exposed to bright light (> 1,000 lux), and that bright light therapy consolidates sleep and improves rest/activity rhythms. We aimed to describe levels and predictors of bright light exposure in the PAR setting.

Methods: We examined light data from wrist actigraphs for 1 week by 262 PAR patients (aged > 65 years) at 1 community and 1 Veterans Administration (VA) site. We assessed bivariate relationships between bright light exposure and frequency of naps, as well as minutes of daytime sleep. Using logistic regression, we modeled the relationship between bright light exposure (mean daily minutes > 1000 vs. < 1000 lux) and demographics (gender, age, race, marital status), rehabilitation factors (bed near window, reason for admission, facility, admission functional status, Cumulative Illness Rating Scale-Geriatrics, Geriatric Depression Scale, Geriatric Pain Measure, Mini-Mental Status Exam, and Lubben Social Network Scale.

Results: Twenty-six percent of patients had no bright light exposure. On average, patients were exposed to 15.7 (SD 24.6) minutes of light > 1000 lux/day and were exposed to no light > 1000 lux on 52.8% (SD 36.1) of recorded days. The average maximum duration of bright light exposure on any one day was 44.4 minutes (SD 57.6). In regression analyses predicting bright light exposure, there was no association with daytime sleep (P>.05) or other measured variables. Patients at the VA site were exposed to less bright light (adjusted OR= 0.23, p<.001) than those at the community facility.

Conclusion: Patients had minimal exposure to bright light in the PAR setting. There were differences between facilities. Studies assessing fa-

cility-level predictors of bright light and interventions to increase bright light exposure in a variety of settings, including PAR, are needed.

Support (If Any): VA HSR&D (Project # IIR 04-321) and NIH/NIA K23 AG028452

0892

MINIMAL COGNITIVE IMPAIRMENT IN THE ELDERLY WITH SLEEP APNEA SYNDROME

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Introduction: Cognitive functions are known to be impaired in the middle-aged with sleep apnea syndrome (SAS), but the relation between cognitive dysfunction and SAS in the elderly has yet to be decided. The aim of the current study was to investigate whether SAS may result in cognitive decline in elderly subjects.

Methods: Sixty five elderly subjects (29 women, 36 men; mean age, 68±4.7 years) participated in the study. None of the subjects had been diagnosed or treated for SAS. All the subjects underwent polysomnography and comprehensive cognitive function test. Subjects without SAS (AHI<15, n=23), with mild to moderate (AHI=15-30, n=21) SAS and severe (AHI>30, n=21) SAS were compared for the attention, memory and executive function.

Results: No difference was observed among three groups in all the measures of attention, memory and executive function except delayed recall. Daytime sleepiness was not different across the groups, either. There was no correlation between cognitive functions, and polysomographic variables or daytime sleepiness. Delayed recall was impaired in subjects with severe SAS, followed by subject with mild to moderate SAS compared to subjects without SAS (p=.016). The time of trail making test A tended to be different among three groups (p=.072) with being longest in severe SAS.

Conclusion: In the present study, we found that SAS had minimal impact on cognitive function in the elderly population. The sequela of hypoxia and respiratory disturbances in SAS might be less prominent in the elderly than in middle-aged population. The findings need to be corroborated with larger samples.

0893

LONGITUDINAL STUDY ON MENTAL HEALTH AND AGING: THE EVOLUTION OF SLEEP QUALITY

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Introduction: Sleep quality tends to decrease as we age, mainly due to typical sleep architecture modifications, sometimes complicated by other physiological conditions, like primary insomnia. The incidence of depression and/or anxiety disorder is also high in this population. The goal of this study was to establish if the presence of a mental health condition could influence the evolution of sleep quality during a one-year period in elderly subjects.

Methods: Participants were 2182 adults (M age=74.8, SD=6.01 years) (40.9 % men, 59.1% women) selected from a probabilistic sample composed of aging individuals living at home in three different areas of the province of Québec. They participated in a longitudinal study held from 2005 to 2008. The inclusion criteria's were: being older than 65 years old, understanding and speaking French and having no diagnostic of cognitive disorders. The interview was held at the residence of the par-

ticipants and had an average length of 90 minutes. The DIS (Diagnostic Interview Schedule) was used to evaluate the presence of depression or anxiety symptoms in the last 12 months, whereas the PSQI (Pittsburg Sleep Quality Index)was used to measure sleep quality (Buysse, 1989). Data were collected twice, with an interval of one year.

Results: The mental health status examination revealed that 3.8% of the participants met the diagnosis for anxiety disorder and 5.6% met the diagnosis for depression. Of these, 37% reported taking a sleep medication more than 3 times a week compared to 16.9% of those having no mental health problem. Forty-nine percent of the subjects had a score higher than 5 on the PSQI at time 1. Of participants initially having no sleep issues, 32.1% reported a decrease in sleep quality after one year. Paradoxically, for subjects initially reporting sleep issues and having at least one mental health condition, an increase in sleep quality was observed for 38.8% of them, while only 8.3% did continue to deteriorate. A multiple regression revealed that the factors related to mood state, anxiety, use of hypnotics, sex and age contributed to explain 33.6% of the variance.

Conclusion: The presence of insomnia symptoms is often associated with a certain psychological distress. The consequence is a significant decrease of subjective sleep quality. However, while aging and mental health problems are associated to a decrease in sleep quality, the co-occurrence of both is not to be readily interpreted as having a long lasting synergistic effect.

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0894

METABOLIC SYNDROME AND RISK OF OBSTRUCTIVE SLEEP APNEA (OSA) IN THE ELDERLY

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Introduction: Metabolic syndrome (MetSyn) is the clustering of central obesity, insulin resistance, hypertension, and dyslipidemia. Important consequences include increased risk of cardiovascular disease and type 2 diabetes (T2DM) (AHA Circulation 2004). Obstructive sleep apnea (OSA) may contribute to development of MetSyn and subsequently to T2DM through inflammation exacerbated by chronic intermittent hypoxia and sleep fragmentation associated with OSA. However, this complex relationship remains to be elucidated (Tasali et al. Am Thorac Soc 2008, Vol.5). Thus, we examined influences of OSA risk in the elderly relative to constituent biomarkers of MetSyn.

Methods: Subjects were 328 free-living individuals from the Stanford AAA STOP study (Abdominal Aortic Aneurysm: Simple Treatment or Prevention). Each completed the Berlin Questionnaire to classify for OSA risk (Low-risk, n=158; High-risk, n=170). Clinical tests were administered to assess status on biomarkers of MetSyn, including central obesity, insulin resistance, glucose intolerance, dyslipidemia and elevated blood pressure (AHA Circulation 2004).

Results: Findings on a substantial subset of these subjects (n=113) suggest that up to 96% were receiving anti-lipemic and/or anti-hypertensive medications; approximately 8% also had a diagnosis of T2DM. Low- vs. High-OSA risk groups were similar for gender (86% vs. 83% male) but differed on age (Mean±SD=74.8±8.5 vs. 72.0±8.4 yr; p<0.01). Upon adjusting the analyses for age, we determined that the Low- vs. High-OSA risk groups differed on the following MetSyn biomarkers: waist circumference (97.4±13.6 vs. 103.6±14.7 cm; p<0.01), fasting serum triglycerides (104.7±57.9 vs. 127.5±68.5 mg/dL; p<0.01), and fasting insulin (11.1±10.6 vs. 14.8±12.5 uU/ml; p<0.05). The groups did not differ on the MetSyn biomarkers of blood pressure, fasting serum glucose, or serum HDL cholesterol.

Conclusion: Risk for OSA increases biomarkers of MetSyn in older adults. Undiagnosed and untreated OSA in the elderly may exacerbate

development of MetSyn and potentially contribute to excess CV morbidity and mortality.

0895

PILOT STUDY OF CYCLIC ALTERNATING PATTERN (CAP) NREM SLEEP MICROARCHITECTURE IN PATIENTS WITH CLINICALLY DIAGNOSED LEWY BODY DEMENTIA AND ALZHEIMER DISEASE

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Introduction: Cortical brain arousal may be indexed by NREM cyclic alternating pattern (CAP) sleep microarchitecture, which is thought to reflect cerebral cortical infraslow oscillatory activity. Slow cortical oscillations have recently been shown to correlate with cognition, specifically learning and memory. We aimed to determine whether CAP sleep rates differed between two subgroups of patients with clinically diagnosed neurodegenerative disorders: Lewy body dementia (LBD) and Alzheimer disease (AD).

Methods: Full night diagnostic polysomnographic data of 4 (2 LBD and 2 AD) patients were manually analyzed using Hypnolab CAP scoring software (ATES Medica Labs, Verona, Italy). CAP sleep index during diagnostic polysomnography was obtained. All patients have apnea/hypopnea index <5 by standard AASM scoring criteria. Functional status was assessed by Global Deterioration Scale, excessive daytime sleepiness by Epworth sleepiness score.

Results: The patients' age range from 60 to 71, with LBD patients on average 3 years younger than AD. LBD patients are all male, and AD are female. GDS of the patients are comparable, with AD being 3 and 5, and LBD 3 (one patient has no available GDS but MMSE was 22). CAP rate was higher in DLBD vs. AD patients (24.8 vs. 15.1). CAP subtype percentages in DLBD vs. AD patients were: A1=19.1 vs. 16%, A2=75.2 vs.68.5%, A3=5.75 vs. 15.5%. Higher CAP rate was also associated with a higher ESS score.

Conclusion: LBD patients had a higher CAP rate than AD patients in this pilot study. Further analysis of larger numbers of LBD and AD patients may further clarify differences in cortical arousal potential between these patient groups, and enable correlation with clinical outcomes of daytime sleepiness and cognitive performance.

0896

SLEEPINESS AND WORD PAIR LEARNING AND MEMORY IN OLDER ADULTS

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Introduction: Learning and memory deficits are a hallmark of aging. Sleep disturbances and daytime sleepiness are common in older adults and have been associated with cognitive impairment. This study sought to examine the relationship between measures of sleepiness and impaired learning and memory on a word pairs association task (WPAT) in older adults.

Methods: Fifty-five older adults (mean age: 73y/o SD: 4.29; 5 females) were evaluated in a 2 day study. Each participant had an overnight polysomnogram on both nights. The following day (on day 2), participants had 5 multiple sleep latency tests (MSLT) at 2 hourly intervals starting 2 hours after awakening. Participants were given the WPAT 45 minutes after awakening. They learned 34 words immediately followed by a recall task. After the initial recall, they were shown the words a 2nd time. Eight hours after the 2nd learning period, they were asked to recall the words again. The number of correct answers was tallied for the 1st 2 recall points along with a value of the sum of improvement of words recalled 8 hours after the 2nd learning period. Performance measures were compared with sleep latency (SL) (average of 5 MSLTs) and the number of total minutes slept (stage 1 + stage 2) using Pearson's partial correlations controlling for age and education, and with independent t-tests between groups: group 1 mean SL > 7 minutes; group 2 mean SL > 7 minutes.

Results: There was a significant positive correlation for WPAT correct answers and mean SL ($r = .413$, $p = .012$) after initial learning. There was a negative trend for an improvement in the number of words recalled 8 hours later and mean SL($r= -.345$, $p= 0.072$). In addition, there was a significant negative correlation for total minutes of sleep and initial learning ($r= -.575$, $p=0.000$) and a positive trend for total minutes of sleep and remembering more words at the delayed recall ($r=.287$, $p=0.065$).Those with an average SL > 7 minutes showed a significantly higher recall after the initial learning ($p=0.033$) and significantly lower improvement in delayed recall 8 hours later ($p=0.049$) than those with an average SL <7 minutes.

Conclusion: Together, these findings indicate that sleepiness impairs overall immediate recall (perhaps via attentional impairment), and that short sleep latency and more total minutes of sleep during the day is beneficial to delayed word recall, perhaps similar to the positive learning effects of napping in older adults.

0897

SEX DIFFERENCE IN INTRINSIC CIRCADIAN PERIOD IN HUMANS

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Introduction: Circadian period is shorter in female rodents than in males, and exposure to exogenous estrogen shortens period. In humans, there are sex differences in SCN structure, but conflicting reports of whether there are sex differences in period. We recently reported that women have an earlier entrained circadian phase than men, consistent with either a shorter period or altered light sensitivity in women.

Methods: We conducted a series of forced desynchrony (FD) studies on 157 healthy participants (52 women, 105 men; mean ± SD age 33.13 ± 17.37 years), studied for a total of >4,000 days. In FD, the light-dark/activity-rest cycle ("T cycle") is scheduled to be shorter or longer than 24 hours, with low light levels during scheduled wakefulness, resulting in photic and non-photic influences being distributed across all circadian phases. Under such conditions, it is possible to estimate the intrinsic period of the circadian pacemaker with precision. The FD segments lasted at least two weeks (range 14-43 days), and T-cycles were 11 (n=1), 20 (n=26), 28 (n=114), or 42.85 (n=16) hours. Core body temperature and blood samples assayed for melatonin were analyzed for determination of circadian period using non-orthogonal spectral analysis, a method that accounts for the imposed activity-rest cycle and searches for unknown periodicity in the circadian range. Sex differences were analyzed with mixed model ANOVA and Student's t-tests.

Results: A significant influence of sex on circadian period was observed for temperature [$F(1,155)=8.54$, $p<0.01$] and melatonin [$F(1,127)=7.76$, $p<0.01$] data. Circadian period was significantly shorter in women than men for temperature [women (n=52): 24.09 ± 0.2 h vs. men (n=105): 24.19 ± 0.19 h; $p<0.01$] and melatonin [women (n=43): 24.08 ± 0.19 h vs. men (n=86): 24.18 ± 0.19 h; $p<0.01$] data.

Conclusion: We found that circadian period is significantly shorter in women than in men, consistent with reports from animals. This finding helps to resolve inconsistencies from earlier reports in humans, derived from studies using uncontrolled or unevenly distributed light exposure The shorter period in women may have implications for understanding sex differences in the pathophysiology of circadian rhythm sleep disorders, and sex differences in habitual sleep duration and insomnia prevalence.

0898

SLEEP DURATION IN EARLY GESTATION IS ASSOCIATED WITH INCREASED MARKERS OF INFLAMMATION IN WOMEN WITH A HISTORY OF PREECLAMPSIA

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Introduction: Sleep duration is recognized as a potential contributor to adverse health conditions. While there is a growing literature describing a relationship between short sleep duration and morbidity, the evidence regarding the consequences of long sleep duration on health outcomes is limited. The data are even further limited when evaluating the relationship in pregnant women, since they are excluded from most studies. We sought to evaluate whether sleep duration in early gestation (15 weeks) is associated with increased circulating concentrations of inflammatory cytokines across pregnancy.

Methods: Participants were 85 pregnant women with a history of preeclampsia enrolled into an exercise intervention study at ~15 weeks gestation. Self-reported sleep duration and blood samples were obtained concurrently at 15, 24 and 36 weeks gestation. Plasma samples were assayed for the inflammatory cytokines IL-2, -6, -8, IFNγ, TNFα, GM-CSF and anti-inflammatory cytokines IL-4, -5, and -10 using Luminex technology. A ratio of pro-to-anti-inflammatory cytokines was calculated using multiples of the median (MOMs) for each relevant cytokine type to normalize the data for comparison. Data were analyzed using repeated measures mixed models.

Results: Women with long sleep (> 8 hours) at 15 weeks gestation, had higher IL-6 concentrations throughout gestation than women who were average sleepers, however this was only significant in early gestation ($p < .01$). No other cytokine or the ratio of pro-to-inflammatory cytokines differed between groups. No interaction of group by time were significant.

Conclusion: The tendency to sleep for more than 8 hours in early pregnancy may contribute to increased low-grade inflammation as evidenced by higher circulating concentrations of IL-6. This may initiate the pathophysiological changes associated with adverse pregnancy outcomes. While our data are only speculative at this time, further investigation is warranted to determine whether this association increases risk for adverse pregnancy outcomes.

0899

GENDER DIFFERENCES IN COLLEGE STUDENT SLEEP: EMERGENT PATTERNS OF STRESS AND MOOD SLEEP DISRUPTIONS IN WOMEN

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Introduction: Although gender specific changes in sleep have been widely examined during periods of significant hormonal change, such as puberty, pregnancy, and menopause, there is less known about gender differences in sleep quality that emerge during late adolescence, a tumultuous period of profound biopsychosocial change.

Methods: 1125 students ages 18 - 24 from an urban Midwestern university completed an extensive online survey that included the Pittsburgh Sleep Quality Index, the Epworth Sleepiness Scale, the Profile of Mood States, and other questions about health and behavior. Gender differences were compared with t-tests, and stepwise regression analyses to predict sleep quality were conducted separately for males and females.

Results: Although there were no significant differences between genders in total sleep time or self-rated sleep quality, female students had higher levels of daytime sleepiness and fatigue, and reported more sleep disturbances due to nightmares, early morning awakening, and stress

(for all cases, t = <-2.5, p < .01). In males, tension and morningness-eveningness were significant predictors of sleep quality, accounting for 25% of the variance in the PSQI score. In contrast, in females depression was the primary predictor of sleep quality, accounting for 21.5% of the variance in PSQI score, with the variables tension, morningness-eveningness, anger, and sleep schedule accounting for another 7%. Exercise, caffeine and alcohol use were not significant predictors of sleep quality in either sex.

Conclusion: In general, college women show more stress and mood induced sleep disturbances than men do. Because insufficient and poor quality sleep exacerbate vulnerabilities in mood, anxiety and substance abuse disorders, all of which show gender differences in diagnoses, health care providers should work toward managing the psychological factors that disrupt sleep in young women.

0900

INSOMNIA WITH SHORT SLEEP DURATION AND CARDIOVASCULAR DISEASE MORTALITY IN THE WOMEN'S HEALTH INITIATIVE

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Introduction: Heart disease is the leading cause of death for American women. Insomnia may contribute to cardiovascular outcomes through over-activating the hypothalamic pituitary adrenal axis and autonomic nervous system. This association may depend on insomnia severity, indicated by concurrent short sleep duration, and co-existing conditions. We tested the hypothesis that insomnia with short sleep duration (< 6 hours) is related to increased cardiovascular mortality and that diabetes or hypertension may increase the risk.

Methods: A total of 90,682 women aged 50 years and over in the Women's Health Initiative observational and clinical trials were followed for up to 15.5 years. At baseline women reported typical sleep duration and completed the Women's Health Initiative Insomnia Scale (score 0 - 20), with a score of ≥ 9 indicating insomnia. Subjects also reported potential confounding variables at baseline and during follow-up. We used Cox proportional hazards models to examine the relationship between insomnia with short sleep duration and cardiovascular mortality. We examined these associations accounting for prevalent and incident diabetes and hypertension. We performed analyses for follow up ≤ 12.3 years and > 12.3 years because of violation of the proportional hazards assumption.

Results: Insomnia with short sleep duration was associated with increased cardiovascular mortality (adjusted HR: 1.38 (95% CI 1.18, 1.63)) within 12.3 years of follow-up. However, this association was similar in magnitude to that of sleep duration < 6 hours alone (1.37(1.09, 1.73)). Baseline diabetes increased the risk for cardiovascular disease associated with insomnia with short sleep duration. The association between insomnia with short sleep duration did not vary by incident hypertension or diabetes status. Insomnia with short sleep duration was not related to cardiovascular mortality beyond 12.3 years of follow-up.

Conclusion: Short sleep duration may drive the relationship between insomnia with short sleep duration and increased cardiovascular mortality in women.

0901

PREVALENCE OF ALVEOLAR HYPOVENTILATION IN MENOPAUSAL WOMEN PRESENTING FOR EVALUATION OF A SLEEP COMPLAINT

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Introduction: In a group of menopausal women ages 40-65 presenting for sleep evaluation with PSG, an effort is made to examine prevalence of alveolar hypoventilation syndrome (AH) and review demographics as well as sleepiness. Epworth Sleepiness Scale (ESS) is a validated tool measuring excessive daytime sleepiness (EDS).

Methods: Records of 21362 women undergoing baseline PSGs from 2009-2010 at SleepMed were reviewed. ESS was administered prior to each study. Oxygen desaturation index (ODI) was measured at equal to or greater than the 4% level during the total sleep time as well as saturation index time less than 90%. Patients were selected with low RDI but sustained desaturation. Comparison was made with patients RDI >15 without regard to ODI.

Results: Of 21362 women that were studied, 12063 (56%) women were 40-65. Of the 12063 women, 5447(45%) were identified to have sleep disordered breathing (AH+OSA=SDB). AH group accounted for 686/12063 (6%) of the total and 686/5447 SDB (13%) of women ages 40-65. AH was characterized by RDI< 10, nadir oxygen less than 85%, time below 90% > 10 minutes, ODI <10/hour . Women with AH ages 40-65 were characterized by a mean age of 55(7); BMI 36(9); ESS 10.6 (6); RDI 6(3); nadir O2 sat 80(5); time<90% minutes 104(103); ODI 4(2). OSA accounted for 4761/12063 (39%) of the total and 4761/5447 SDB (87%) of women ages 40-65. OSA group was characterized by an RDI>15. Demographics of this group were: mean age of 54(7); BMI 37(9); ESS 10.5 (5); RDI 32 (21); nadir O2 Sat 79.5(8); ODI 22(20); time<90% minutes 80(8).

Conclusion: 6% of women age 40-65 met criteria for alveolar hypoventilation or nocturnal hypoxemia. This represented 13% women in the sleep disordered breathing group presenting with a sleep complaint. As a group menopausal women with SDB often experience excessive sleepiness as measured by ESS. The prevalence of AH, OSA in this group should be contrasted with premenopausal women and men of comparable age.

0902

THE PHYSICAL PHENOTYPE AND MALLAMPATI SCORE ASSOCIATED WITH SLEEP DISORDERED BREATHING IN A PREGNANT OBESE COHORT

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Introduction: Studies have indicated that symptom-based screening questionnaires have functioned poorly in identifying pregnant women at risk for sleep disordered breathing (SDB). We sought to investigate the

role of physical measurements, including the Mallampati score-a measure of airway crowding, in improving SDB identification in an obese pregnant population.

Methods: Participants in an observational cohort of obese pregnant women (BMI >30 kg/m²) underwent overnight sleep studies for SDB using a portable home monitor (ARES Unicoder; Carlsbad, CA), recording nasal pressure, oxygen saturation, snoring, and head movement, and measurement of body composition using air displacement plethysmography (Pod Bod). Physical morphometric measurements, Mallampati scoring and sleep assessment took place at the gestational ages 13-20 weeks of gestation. Data were analyzed utilizing chi square, t-test, Mann Whitney U test and multinomial logistic regression.

Results: The sample consisted of 110 women. Nine had an apnea hypopnea index (AHI) > 5. Those with and without SDB had similar race distributions (African American race 56 vs. 60 %, p=0.8), prevalence of diabetes (24 vs. 29%, p=0.9) and hypertension (62 vs. 42, p=0.3). The SDB group was older (33±7 vs. 28±6 years, p=0.04), had a higher BMI (45 vs. 39 kg/m2, p=0.03), and a wider neck (41 vs. 37 cm, p=0.002), but a similar waist to hip ratio (0.96±0.07 vs. 0.97± 0.13, p=0.4) and percent body fat (44±6 vs. 45±7%, p=0.9). The SDB group had a higher median Mallampati score:(2[2-3] vs. 1[1-2], p=0.02). After controlling for BMI, increasing neck circumference, per centimeter increase (OR 1.8 [1.1-3.3]), but not a Mallampati score of 3 (OR 0.9 [0.07-13]) was predictive of SDB.

Conclusion: Among obese pregnant women, even after adjusting for BMI, SDB is associated with an increased neck circumference. SDB was also associated with upper airway crowding as shown by the elevated Mallampati score. The latter, however was associated with BMI. Thus, adiposity that results in a larger neck circumference is associated with SDB in pregnancy, perhaps through effects on airway patency. Further research on the utility of neck and airway measurements in the screening for SDB in pregnancy may lead to fruitful approaches for identifying this disorder.

0903

GENDER DIFFERENCES IN ADHERENCE TO POSITIVE AIRWAY PRESSURE TREATMENT IN OBSTRUCTIVE SLEEP APNEA

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Introduction: The data regarding how men and women with obstructive sleep apnea (OSA) approach positive airway pressure (PAP) treatment are sparse, and a few studies have reported conflicting results of gender differences in PAP adherence. This study further examined this question by comparing PAP use and the motivation underlying its use in men and women over a 1-year period.

Methods: We analyzed data from 172 men and 93 women with OSA participating in a longitudinal study testing efficacy of behavioral interventions to improve PAP adherence. Daily use of PAP was objectively monitored over 1 year. Psychological constructs of behavior-change were examined at baseline, 1-week, 2-week, and 3-, 6-, 12-month, and clinical manifestations were evaluated at baseline, 3-, 6-, and 12-month after treatment initiation.

Results: During the first week of treatment, women showed a higher nightly use (4.7±2.5 vs. 3.9±2.5, p=0.027) and a higher percentage of active nights using PAP (86.3% vs.79.5%, p=0.051) than men. Similar gender differences of PAP use were observed during the first 2 weeks (p=0.041) but this difference disappeared after week 2. Comparing to men, women showed a higher confidence (self-efficacy) of using PAP at week 1 (p=0.036) and week 2 (p=0.001). Although women had a lower

income, higher body mass index, higher apnea hypopnea index, more daytime sleepiness, poorer overall functional status, and more depressed mood than men at baseline, only poor functional status (r=-0.153, p=0.025) and depressed mood (r=0.167, p=0.023) were correlated with their greater CPAP use during the first 2 weeks. A significantly higher percentage of men had a bed partner (81.2% vs. 63.0%, p=0.001), but the presence of a bed partner did not predict adherence outcomes. The changes of self-efficacy from baseline to 3 months [median (interquartile-range): 1.0 (4.0) vs.0.0 (5.0), p=0.34] and from baseline to 6 months [1.0 (6.0) vs. 0.0 (5.8), p=0.36] after treatment initiation significantly differed between participants with and without a bed partner.

Conclusion: We observed that women had a higher nightly PAP use than men in the initial 2 weeks of treatment, which is consistent with their higher confidence of using PAP during this time. A greater functional impairment in women before treatment may contribute to their higher motivation of PAP use when treatment starts. Additional research is needed to examine the important role bed partners may have on motivation of PAP use in men and women.

0904

HYPOTHALAMIC-PITUITARY-ADRENAL AXIS IN POSTMENOPAUSAL APNEIC WOMEN: EFFECT OF CPAP TREATMENT

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Introduction: Previous studies in obese and non obese men with Sleep Apnea (OSAS) have shown that OSAS is associated with HPA axis hyperactivity consisting of elevated night cortisol levels which decrease after CPAP treatment. However there is paucity of studies focusing on apneic women. The goal of this study was to examine HPA axis activity in postmenopausal women with apnea and assess the effects of CPAP treatment.

Methods: Seventeen non-emotionally distressed postmenopausal women with obstructive sleep apnea, and twenty postmenopausal age-matched controls were monitored in the sleep laboratory for four nights and 24h blood sampling was performed during the fourth day. Groups did not differ in terms of anxiety or depression. Apneic women were then assigned on a 2X2 crossover design, with half of the subjects randomized to the sham-CPAP/CPAP sequence and the other half to the CPAP/sham-CPAP sequence. Subjects were reassessed at the sleep laboratory 2 months following the use of CPAP and 2 months following the use of sham- CPAP.

Results: There were no significant differences in 24h cortisol levels between apneics and controls. However, women with OSAS had significantly higher nocturnal cortisol levels compared to controls, even after controlling for BMI and age (p= 0.01). The use of CPAP for two months resulted in a significant decrease of early morning cortisol levels and a non significant decrease of nocturnal cortisol levels compared to baseline. There were no significant differences in 24h or nocturnal cortisol levels between baseline and sham-CPAP.

Conclusion: HPA axis appears to be activated in post-menopausal women with sleep apnea and the use of CPAP treatment may decrease cortisol levels in these women. CPAP use may be beneficial for the adverse cardiometabolic effects associated with chronic hypercortisolemia.

0905

SLEEP PATTERN IN WOMEN WITH MENSTRUAL PAIN

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Introduction: Menstrual pain is a common problem in reproductive-age women and often impairs working ability and well-being. As painful conditions frequently affect sleep, we investigated the impact of this menstrual disorder on sleep pattern in a large population-based survey. Additionally, we examined whether medication used to alleviate menstrual pain promoted changes in sleep.

Methods: Women of reproductive age (n=328) were classified into different phases of the menstrual cycle according to their hormone profiles and menstrual histories. Only women who were in their menstruation period on the day of the polysomnography (PSG) recording were included in this study (n=36). The presence of menstrual pain and the use of medication were self-reported via questionnaire.

Results: Menstrual pain was reported by 58.3% of the women on the night of the PSG. No marked effects were observed on the sleep pattern of these subjects. The group of women exhibiting pain was younger than the women who were pain-free. The use of medication did not promote significant changes on sleep pattern.

Conclusion: The presence of menstrual pain or the use of medication to alleviate menstrual pain did not significantly alter sleep pattern. Thus, it appears that menstrual pain does not affect sleep pattern with the same magnitude as other acute or chronic pain conditions.

0906

UPPER AIRWAY COLLAPSIBILITY IN AFRICAN-AMERICAN AND CAUCASIAN MIDLIFE WOMEN AND RELATIONSHIP WITH APNEA-HYPOPNEA INDEX

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Introduction: Upper airway (UA) collapsibility measurements using pharyngeal critical closing pressure (PCRIT) have demonstrated that UAs of individuals with OSA are more prone to collapse than normals. Given increased risk of SDB imposed by menopause, postmenopausal women may have more collapsible UAs than pre/perimenopausal women. We compared UA collapsibility between pre/perimenopausal (PRE/PERI) and postmenopausal (POST) women and examined the relationship between PCRIT and AHI.

Methods: African-American and Caucasian women were classified as pre/perimenopausal (n=51) or postmenopausal (n=28) using bleeding patterns. They underwent a) home PSG to determine AHI and b) lab studies to determine PCRIT while wearing a tight-fitting nasal mask. We measured passive PCRIT, reflecting mechanical UA properties. PCRIT was calculated through linear predictive modeling of maximum inspiratory volume against NP, with PCRIT defined as extrapolated pressure at zero volume. At least 3 NP levels and 2 flow-limited breaths per level were required. PCRIT values < -25 were excluded from analysis. AHI and PCRIT were compared between groups using Wilcoxon Rank Sum. PCRIT relationships with AHI were modeled using multiple linear regression adjusting for age, BMI, and menopausal status.

Results: Data from 86 of 109 subjects met quality standards. AHI did not differ between menopausal status groups (mean 22.8, SD 19.4).

PCRIT was higher among PRE/PERI (-5.3±4.7) compared to POST (-3.6±4.9 cm of water), but was not statistically significant (p=0.13). PCRIT was significantly related to AHI, so that a 1 cm PCRIT increase was associated with a 9% AHI increase (p<0.001). We observed a significant interaction between race and PCRIT (p=0.03); this relationship was stronger for African-Americans (p<0.01).

Conclusion: The UA tended to be more collapsible among POST than PRE/PERI women, though this difference was not statistically significant. Higher PCRIT values in midlife women were associated with more severe SDB. This relationship between PCRIT and AHI was stronger among African-Americans than Caucasians in this sample.

0907

OBJECTIVE AND SUBJECTIVE SLEEP QUALITY MEASURES IN WOMEN WITH AND WITHOUT NOCTURNAL HOT FLASHES

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Introduction: Hot flashes (HF) are a common menopausal symptom that are often reported to disrupt sleep. However, studies of the relationship between HF and objective measures of sleep are limited and contradictory. We compared subjective and objective measures of sleep quality among midlife women with and without hot flashes during sleep.

Methods: Overnight polysomnography and sternal skin conductance recordings (Biolog 3991, UFI Morro Bay, CA) were collected from 98 women. Two recordings were excluded due to poor signal quality. HF were scored by a trained technician using criteria of ≥2.0 uMho increase in skin conductance over a 30 second period.

Results: Data were collected from 96 African-American and Caucasian women in midlife (age 51.5 ± 4.1 years). 45% had objective HF during sleep, which were significantly more common among postmenopausal (60% had HF, p=0.04) than premenopausal (20%) or perimenopausal (44%) women. The proportion of African-American and Caucasian women with HF was similar (49% and 42%, respectively). When objective and subjective sleep measures were compared between groups with and without HF, there were no differences in total minutes of sleep, sleep efficiency, arousal index, WASO, AHI, percentage of REM or delta sleep and PSQI and Epworth Sleepiness Scale scores (p=0.21-0.99). When interactions with race were examined, Caucasian women with HF reported higher ESS and PSQI Daytime Fatigue scores than Caucasians without HF (p=0.01). There were no differences in these measures between African-Americans with and without HF.

Conclusion: We did not observe significant differences in sleep architecture and other objective sleep measures between women with and without HF. Subjective sleep quality generally did not differ between groups, except that Caucasian women with HF reported more sleepiness and fatigue than Caucasians without HF. These findings suggest that vasomotor symptoms may not be a primary reason for complaints of poor sleep among midlife women.

0908

ACUTE AND PERSISTENT SLEEP DISTURBANCES IN MID-LIFE WOMEN: RACE MATTERS

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Introduction: Sleep disturbances are common in mid-life women and, if persistent, may contribute to the increased morbidity associated with menopause and aging. Cross-sectional data suggest that these effects may be compounded in ethnic/racial minorities, especially African American women. Yet, there are no published longitudinal studies of sleep and race in mid-life women.

Methods: We evaluated the prevalence of acute and persistent sleep disturbances in a community sample of African American and Caucasian women (n=309, 44.7% African American, mean age 52 +/- 2.1 yrs). The PSQI and in-home PSG were assessed at two timepoints (1.21-5.63 years apart). Clinically-significant sleep disturbances were defined as: poor sleep quality (PSQI >5), short sleep duration (time spent asleep <6 hrs), fragmented sleep (sleep efficiency <85%) and sleep disordered breathing (AHI >15). For each outcome, sleep disturbances were characterized as "acute" or "persistent" if participants met criteria at 1 or both timepoints, respectively.

Results: Compared to Caucasians, African American women were 3 times more likely to exhibit persistent sleep disturbances including poor sleep quality (OR 3.33, 95% CI 1.32-7.88), short sleep duration (OR 3.95, 95% CI 1.58-9.87) and fragmented sleep (OR 3.36, 95% CI 1.42-8.00). Less consistent race effects were observed for acute sleep disturbances. Compared to Caucasians, African American women were more likely to report poor sleep quality (OR 2.19, 95% CI 1.02-4.70) and less likely to exhibit sleep disordered breathing (OR 0.27, 95% CI 0.10-0.77). These effects were observed after adjusting for age, BMI, vasomotor symptoms, health complaints, medications that affect sleep, depression and financial strain.

Conclusion: These results suggest that race is a significant moderator of sleep disturbance profiles in mid-life women. Future studies are needed to examine the extent to which persistent sleep disturbances in mid-life women contribute to racial disparities in morbidity and mortality.

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0909

POOR SUBJECTIVE SLEEP QUALITY IS ASSOCIATED WITH ANXIETY AND NOT WITH POLYSOMNOGRAPHIC SLEEP DISTURBANCES IN WOMEN WITH SEVERE PREMENSTRUAL SYNDROME

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Introduction: Women with severe premenstrual syndrome (PMS) report sleep disturbances as one of their symptoms in the premenstrual phase of the menstrual cycle. We investigated whether there are underlying disturbances in polysomnographic (PSG) sleep patterns in association with their subjective sleep complaints.

Methods: 18 women with severe PMS, 12 of whom met criteria for a DSM-IV diagnosis of premenstrual dysphoric disorder, and 18 symptom-free controls (age range: 18-43 years) participated. Following an adaptation night, participants had laboratory-based PSG recordings and completed questionnaires about mood and sleep in the follicular phase (6-10 days after onset of bleeding) and in the late-luteal phase (1-6 days before onset of bleeding).

Results: Women with severe PMS reported a poorer subjective sleep quality in the late-luteal phase compared with their follicular phase and compared with controls (p < 0.05). However, sleep PSG measures were similar between groups apart from percentage slow wave sleep, which was lower, and percentage Stage 1 sleep, which was higher, in controls than women with PMS in both menstrual phases. Regression analysis revealed that subjective sleep quality in the follicular phase was predicted by subjectively estimated sleep onset latency in controls (R[2] = 0.28, p = 0.01) and minutes of Stage 1 sleep in PMS women (R[2] = 0.23, p = 0.025). In contrast, sleep quality in the late-luteal phase was predicted by state anxiety in PMS women (R[2] = 0.41, p = 0.005) and perceived stress and subjective number of awakenings in controls (R[2] = 0.55, p = 0.004).

Conclusion: Women with severe PMS perceive their sleep quality to be poorer in association with higher levels of state-anxiety in the symptomatic late-luteal phase in the absence of PSG-defined sleep disturbance. This uncoupling of subjective and objective measures of sleep, which is common in depression, is also a factor in severe PMS.

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0910

DIFFERENCES OF POLYSOMNOGRAPHIC FINDINGS BETWEEN SALARIED MEN AND HOUSEWIVES

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Introduction: Salaried men and housewives have many stresses in each company and home. Their stressful conditions can affect the sleep quality and somewhat have different effects on salaried men and housewives. We hypothesized that salaried men have more obstructive sleep apnea syndrome(OSAS) and housewives more psychophysiologic insomnia(PPI). To prove our hypothesis and compare the differences of their sleep quality between salaried men and housewives, we studied the polysomnographic data and the sleep questionnaire.

Methods: One hundred twelve patients between 35 and 60 years of age consecutively underwent the polysomnography in the tertiary center from December 1, 2008 to December 1, 2009. All patients completed the overnight PSG and the Sleep Questionnaire included Beck Depression Inventory (BDI), Epworth Sleepiness Score (ESS), and Stanford Sleepiness Score (SSS). We compared and analyzed the polysomnographic data and the sleep questionnaire.

Results: The mean age was 49.4±6.8yrs and sixty-nine patients(61.6%) were salaried men. The mean body mass index(BMI) was 24.8±3.3kg/m2. Fifty-nine patients(52.7%) underwent the polysomnography because of sleep apnea and 29 patients(25.9%) were because of insomnia. Majority of the final diagnosis was OSAS(56.3%) and the second diagnosis was periodic limb movement syndrome(PLMS, 14.3%). 4 patients had normal polysomnographic findings. Salaried men were more obese than housewives(p<0.001). Salaried men enjoyed more alcohol drinking and smoking(p<0.01). Housewives had more insomnia symptoms and salaried man had more sleep apnea and snoring(p<0.001). Usual time to fall asleep was longer in housewives(p=0.001), but the polysomnographic sleep latency had no significant difference between salaried men and housewives. Housewives had higher periodic limb movement index(20.3 vs 8.7, p=0.05) and salaried men had more PPI(15.9% vs 9.3%), but no significant difference between two groups. Also, Other polysomnographic findings did not show statistically significant difference.

Conclusion: Most salaried men and housewives have sleep disorders including OSAS, PLMS, and PPI. Although OSAS is major sleep problem in all salaried men and housewives, PLMS is more in housewives and PPI is more in salaried men.

0911

THE RELATIONSHIP BETWEEN RESTLESS LEGS SYNDROME AND HYPERTENSION IN MIDDLE-AGED WOMEN

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Introduction: Limited research suggests a relationship between Restless Legs Syndrome (RLS) and hypertension but no direct association has been established. We, therefore, assessed the relationship between RLS and hypertension among middle-aged women.

Methods: This is a cross-sectional observational study including 65,544 women (aged 41-58 years) participating in Nurses Health Study II. The participants with diabetes and arthritis were excluded as these conditions can mimic RLS. RLS was assessed by a self-administered questionnaire based on the International Restless Legs Study Group criteria. Information on diagnosis of hypertension and blood pressure values were collected via questionnaires. Multivariable logistic regression models were used to analyze the relation between RLS and hypertension, with adjustment for age, race, body mass index (BMI), physical activity, menopausal status, smoking, use of analgesics, oral contraceptive pills, alcohol, caffeine, folate, and iron along with a score of dietary approaches to stop hypertension (DASH).

Results: Women with RLS symptoms had higher prevalence of having hypertension compared to those without symptoms (OR=1.43, 95% CI: 1.33-1.53; P<0.0001), after adjusting for age, BMI, and other potential confounders. We observed a clear relation between severity of RLS symptoms, as assessed by the frequency of the symptoms, and prevalence of having hypertension. The adjusted OR for women who reported RLS symptoms 5-14 times/month was 1.06 (95% CI 0.94-1.18) and for those with RLS symptoms ≥15 times/month, the OR was 1.41 (95% CI 1.24-1.61) compared to those without RLS (P trend <0.0001). Greater frequency of RLS symptoms were associated with higher concurrent systolic and diastolic blood pressures (P trend<0.0001 for both).

Conclusion: We conclude that women with RLS symptoms have a higher prevalence of hypertension, and this prevalence increases with more frequent RLS symptoms.

0912

GENDER DIFFERENCES AND THE IMPACT OF STATE RELATED STRESS ON SLEEP AND FUNCTIONING

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Introduction: Those with high trait stress often report poorer sleep quality and daytime functioning. Transient stress can also result in differential effects on sleep, such as sleep loss or improved sleep depending on an individual's coping strategies. The goal of the present study was to assess the impact of state related stress, by gender, on sleep and daytime functioning utilizing a large database of patients presenting for diagnostic sleep evaluation.

Methods: A total of 1,120 patients who presented to a Midwestern metropolitan sleep center for diagnostic PSG completed a brief estimate of their state stress. In addition, patients completed subjective sleep measures including the Epworth Sleepiness Scale (ESS), Fatigue Severity Scale (FSS), and the Pittsburgh Sleep Quality Index (PSQI). Inclusion

criteria were ages 18-79, no shift work, no prior sleep disorder diagnosis, and no split-night studies.

Results: The sample was divided into low and high state groups by gender (LstM, LstF, HstM, HstF) using a split median analysis (range 0-100). There was a significant difference among the groups according to the PSQI (p<.001), ESS (p< .001), and FSS (p< .001), with significantly poorer scores in the HstF group according to post-hoc analysis. There was also a significant difference among groups in PSG variables of sleep efficiency (p< .001), WASO (p< .001), and Stage 3% (p< .001), with females generally having less WASO and more Stage 3%. However, the HstF group had significantly less WASO and higher sleep efficiency than all other groups (p< .01). Both male groups had significantly higher AHI than the female group (p< .001). However, there was still a significant effect for stage 3% and WASO by stress groups after controlling for the effect of AHI differences (both p< .001).

Conclusion: In general, stress can have impact on our perceptions of sleep and how well we actually sleep. This study concluded that the HstF reported the poorest sleep quality and most significant daytime functioning impairments among the groups. Interestingly, measures impacting their actual sleep during PSG, such as WASO, sleep efficiency, and stage 3% were suggestive of better consolidated sleep in comparison to the other groups, even when controlling for sleep disturbed breathing. Although higher stressed females appear to respond with improved sleep consolidation, further work is needed to explain gender and stress level differences on sleep continuity.

0913

SLEEP DISTURBANCES AND DEPRESSIVE SYMPTOMS IN HEALTHY POSTPARTUM WOMEN

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Introduction: Studies have consistently demonstrated maternal sleep deprivation and fragmentation and its association with postpartum depression. However, sleep regularity has been addressed in only a limited number of maternal sleep studies. The purpose of this study was to examine the relation between sleep disturbances and depressive symptoms in healthy postpartum women.

Methods: This was a prospective, intensive within-subject design exploratory study of healthy first-time mothers recruited < three months postpartum. Participants wore wrist actigraphy monitors for seven continuous days and completed the following validated questionnaires: the General Sleep Disturbance Scale (GSDS) and the Edinburgh Postnatal Depression Scale (EPDS). Pearson correlations were used to examine the relation between objective actigraphic and subjective self-reported sleep characteristics and depressive symptoms.

Results: Twenty-six women were recruited; however, two were unable to participate due to scheduling difficulties and two did not provide consistent sleep data, resulting in a final sample of 22. Data collection was performed at 49.8 ± 17.1 days after delivery. The mean EPDS total score was 3.73 ± 2.96, and none of the women experienced clinically-significant postpartum depression. Nineteen (86.36%) of the women experienced poor sleep quality, as defined by a GSDS total score ≥ 43 or at least one GSDS subscale score ≥ 3. The actigraphy recordings showed that the mean night-time sleep duration was only 5.52 ± 0.92 hrs, with none of the women experiencing a night-time sleep of > 7 hrs. A variable duration of night-time sleep from night to night (r = 0.53, P = 0.01) and reported awakening too early (r = 0.51, P = 0.01) were significantly correlated with increased depressive symptoms.

Conclusion: Our results suggest the negative effects of episodic disruption of sleep on maternal depressive symptoms. First-time mothers who complain of irregular night-time sleep and waking-up too early should be evaluated for potential postpartum depression.

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0914

SEX EFFECTS ON NREM SPECTRAL POWER WITH GABAERGIC DRUGS

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Introduction: Tiagabine, a selective GABA reuptake inhibitor, and gaboxadol, a selective extrasynaptic $GABA_A$ agonist, are two SWS-enhancing drugs that produce larger increases in NREM slow wave activity (SWA; 0.75-4.5Hz) and theta (4.5-8Hz) power for females than males. The current analysis explores the spectral profile of males and females in response to sodium oxybate, a ligand of both GHB and $GABA_B$ receptors.

Methods: Fifty-five healthy individuals (21M, 34F; age 27.04±9.05) underwent a baseline PSG (2200-0700), followed by two days/nights of sleep deprivation, each with a subsequent 3-hour nap (0800-1100) with placebo (n=26) or 3.5mg sodium oxybate (n=29). Spectral analysis was conducted on NREM epochs from the first three hours of baseline and nap PSGs. Absolute power in quarter-Hz bins from central EEG was summed into SWA, theta, alpha, sigma, and beta bands.

Results: Absolute SWA and theta power were increased after sleep deprivation during the placebo naps, compared to baseline (p≤0.03); no sex differences were found. Compared to placebo, sodium oxybate increased relative-to-baseline SWA and theta (p≤0.001). Furthermore, this increase in relative-to-baseline power was greater for females (SWA=2.070; theta =2.484) than males (SWA=1.549; theta =1.934; p≤0.022 for all). Increases above baseline in absolute SWA and theta, respectively, were: 15.2% and 7.1% (female-placebo), 36.5% and 21.7% (male-placebo), 107.0% and 148.4% (female-sodium-oxybate), 54.9% and 93.4% (male-sodium-oxybate).

Conclusion: The greater SWA and theta power in females with sodium oxybate is similar to that observed previously with the GABAergic drugs tiagabine and gaboxadol. This contrasts with the $5\text{-}HT_{2A}$ antagonist eplivanserin, which was previously shown to enhance SWA without sex differences. The receptors for gaboxadol (delta-containing $GABA_A$) and sodium oxybate ($GABA_B$) are located extrasynaptically, and tiagabine-induced increases in GABA likely spill out of the synapse to extrasynaptic receptors. The sex difference observed may be associated with interaction of neurosteroids with these extrasynaptic GABA inhibitory processes.

0915

SLEEP APNEA IN POSTMENOPAUSAL WOMEN: ASSOCIATION WITH VISCERAL ADIPOSITY

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Introduction: Visceral adiposity is associated with sleep apnea (OSAS) in men, but very few studies have examined the association between OSAS and visceral adiposity in women. It is known that both the prevalence of OSAS and visceral adiposity increase in postmenopausal women. Therefore, this study aimed to examine the association between sleep apnea and visceral adiposity in postmenopausal women and to compare the patterns of this association between postmenopausal women and similar-aged men.

Methods: This study evaluated forty-two postmenopausal women, of whom twenty-one had OSAS and twenty-one were normal controls. The male sample consisted of twenty-two OSAS cases and twenty normal controls. All subjects were monitored in the sleep laboratory for 4 consecutive nights. The abdominal fat distribution wa measured with computed tomography scans at five mid-lumbar levels (L1 - L5). Sex and OSAS-status specific linear regression was used to assess the association between AHI and visceral adipose tissue measures, adjusting for age, BMI, and physical activity simultaneously.

Results: In both apneic women and apneic men, AHI was significantly associated with the L1 - L5 overall visceral adipose tissue, with β=0.60 and 0.56 for women and men, respectively (both p < 0.05). Moreover, there was a progressive decline of the magnitude of association from L1 to L5 in women, with β=0.67, p=0.02 at L1 and β=0.19, p=0.51 at L5, respectively. In contrast, in men this association remained relatively constant across all five levels.

Conclusion: These preliminary data suggest a similar association between the severity of sleep apnea and visceral adiposity in women and in men. The progressive decline of the magnitude of such association across lumbar levels seen in women, in contrast to the constant magnitude across all lumbar levels in men, may suggest different metabolic processes in visceral adiposity in postmenopausal apneic women versus men.

0916

COMPENSATORY SLEEP EFFORT IS ASSOCIATED WITH INSOMNIA SYMPTOMS IN WOMEN WITH AND WITHOUT BREAST CANCER

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Introduction: Chronic insomnia is prevalent in breast cancer patients both during and following chemotherapy. Psychophysiological models of insomnia suggest that compensatory sleep effort and pre-sleep cognitive activity may be both a precipitating and perpetuating factor. However, this has not been studied in cancer patients. This study examined this question in a sample of recently-diagnosed breast cancer patients and demographically-similar women without breast cancer.

Methods: 21 women (M_{age}=53.6 yrs, SE=2.9, range=38-81) diagnosed with stage I-III breast cancer and 19 yoked, demographically-similar healthy controls (M_{age}=53.6 yrs, SE=1.7, range=36-64) were studied before (BL) and after 4 cycles of chemotherapy (C4). The Glasgow Sleep Effort Scale (GSES), the Glasgow Content of Thoughts Inventory (GCTI) and the Insomnia Severity Index (ISI) were evaluated. Data are presented from both a linear and logistic regression analysis (α=0.05) on C4 follow-up data only.

Results: There was no significant difference at C4 in mean GSES, GCTI or ISI scores between cases and controls. A restricted linear regression model explained a significant proportion of variance in ISI (R^2=0.43, $F_{3,31}$=7.69, p=0.001), with GSES significantly predicting ISI ($β$=1.21, t=2.64, p=0.01) in both groups. The addition of age and case-control group and interaction terms between GSES, GCTI and group did not significantly increase the variance explained in ISI (ΔR^2=0.03). In an exploratory logistic regression model, the continuous ISI variable was dichotomized based on clinical cut-off for mild insomnia (ISI ≥8; Insomnia n=15, No Insomnia n=22); in this model, GSES significantly predicted insomnia status ($β$=1.20, p=0.01, OR=3.31).

Conclusion: Preliminary results suggest that independent of age or breast cancer diagnosis, women with increased compensatory sleep effort may experience more insomnia symptoms. Future analyses will investigate this relationship longitudinally (pre- and post-treatment) in a larger sample.

0917

DOES MENOPAUSE INFLUENCE NOCTURNAL AWAKENING WITH HEADACHE?

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Introduction: Our previous study presented a high prevalence of complaints of nocturnal awakening with headache (NAH) in women, 50-59 years old, in the population of São Paulo city (Brazil). Sleep disturbances are very frequent in menopausal transition and postmenopause. Headache is also a common symptom in women in this period. Therefore, our aim was to evaluate the influence of the menopausal status in the complaint of NAH and the association with sleep disorders in the female population of this city.

Methods: We used a population-based survey with a representative 3-stage cluster sample. All participants (N=1042) answered a sleep questionnaire and underwent polysomnographic recording. The women (N=576) had hormonal measures taken. They also filled out a gynecologic questionnaire in order to be classified in premenopause, perimenopause or postmenopause period. Perimenopausal (N=15) and pregnant (N=2) women were excluded from the sample.

Results: The presence of NAH at least once a week in the population studied was 8.4%. Among the women evaluated (55.3% of the total sample), 12.9% (N=75) had NAH [OR (CI 95%): 4.5 (2.9-7.4) as compared to men]. Premenopausal women represented 63% of the female sample and 34% were in postmenopause. We found no significant difference in the prevalence of NAH in premenopausal or postmenopausal women (12.4% vs. 11.7%, respectively). Moreover, we found no complaint of NAH in postmenopausal women under hormone therapy or using isoflavone. Insomnia and nightmares were highly frequent in women with NAH, but the association with restless legs syndrome (RLS) was only observed in the premenopausal women who presented NAH.

Conclusion: The frequent complaint of waking up during the night with headache in the population of São Paulo had a great predominance in women (four times higher) and was associated with insomnia, nightmares and RLS. We found no influence of the menopausal status, but interestingly no women in postmenopause under treatment complained about NAH.

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0918

INSULIN RESISTANCE AND INFLAMMATION IN POSTMENOPAUSAL WOMEN WITH SLEEP APNEA: EFFECTS OF CPAP

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Introduction: Sleep apnea is associated with increased inflammation and insulin resistance. However, the study of the association of the effects of inflammatory and metabolic biomarkers, as well as continuous positive airway pressure (CPAP) in women has been limited. The aim of this study was to determine whether CPAP reverses hypercytokinemia and insulin resistance in a sample of postmenopausal women with sleep apnea.

Methods: Seventeen postmenopausal women with obstructive sleep apnea, and twenty postmenopausal controls were monitored in the sleep laboratory for four nights. 24h blood sampling was performed during the fourth day for the assessment of inflammatory (IL-6, TNFR1, CRP) and insulin resistance markers (leptin, adiponectin, fasting glucose and insulin). The study design included two 2-month treatment periods of either CPAP or sham/CPAP in a counterbalanced order. Prior to and following each 2-month treatment period a 4-night PSG with a 24-hour cortisol sample on night 4 was completed.

Results: There were not significant differences between controls and apneics in terms of insulin resistance, and mean 24h values of leptin, adiponectin, TNR1 and IL-6. After controlling for BMI and age, early morning IL-6 levels were higher in the sleep apneic group compared to controls [at 5.00 am, 6.00 am, 7.00 am (all p<0.05) and at 8.00 am and 9.00 am (both p<0.1)]. CRP levels were significantly higher in the apneics compared to controls, even after controlling for age, BMI, smoking status, and systolic blood pressure (p<0.05). CPAP treatment did not improve insulin resistance, leptin, adiponectin, TNR1, IL-6 or CRP levels as compared to baseline.

Conclusion: Postmenopausal women compared to men with Sleep Apnea, have a lesser degree of inflammation/ metabolic abnormalities and CPAP treatment does not improve inflammatory or metabolic indices in these women.

0919

INSOMNIA AMONG WOMEN VETERANS: RESULTS OF A POSTAL SURVEY

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Introduction: In the general population, 15-20% of women report insomnia. Rates of insomnia documented in medical records of active duty servicewomen are higher (180 per 10,000) than rates for active duty servicemen (129 per 10,000). There is increasing emphasis on sleep complaints among active duty military, yet insomnia among women Veterans who receive VA healthcare has not been studied. Our objective was to estimate rates of insomnia among women receiving care within one VA healthcare system and to describe women Veterans with insomnia.

Methods: A postal survey addressing all ICSD insomnia diagnostic criteria was sent to a random sample of 333 women veterans (mean age=49.4 years; range=23-95 years) who had received care at one VA medical center within the past 24 months. Women meeting diagnostic criteria for insomnia were compared to those who did not meet criteria on potentially important predictors of sleep disturbance.

Results: 124 surveys (37%) were returned. Responders had more recent clinic visits (p=.003), but were similar in age (p=.94) vs. non-responders. 79% of responders reported difficulty with sleep quality (ICSD Criterion A); 86% reported adequate circumstances for sleep (ICSD Criterion B); 86% endorsed daytime consequences of poor sleep (ICSD Criterion C); 65% reported sleep problems lasting >3 months. 54% of respondents (20% of the total survey sample) met all diagnostic criteria for insomnia. Women with insomnia were more likely to take prescription and over-the counter medications for sleep (p's<.02), and were more likely to report sleep difficulties related to pain, menopausal symptoms, stress, and nightmares (p's<.03). There were no differences in age, time since last healthcare visit, shift work or pregnancy (p>.20) between those with vs. without insomnia.

Conclusion: We found high rates of insomnia among women Veterans which appears unrelated to age, but may be related to comorbid psychiatric and medical issues including PTSD and pain. Further research is needed to establish national prevalence estimates and to identify effective treatments for women Veterans with insomnia.

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0920

OBJECTIVE SLEEP PRIOR TO CHEMOTHERAPY FOR BREAST CANCER PREDICTS CHANGES IN INFLAMMATION PRE-TO-POST-CHEMOTHERAPY

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Introduction: Sleep disturbances are common and distressing in women with breast cancer, particularly during chemotherapy. Chemotherapy may increase peripheral inflammation and inflammation is also related to disturbed sleep. We examined the relationship between objective sleep variables and circulating levels of inflammatory markers in women with breast cancer before and after chemotherapy.

Methods: 20 women (mean age=52, SD=7.6 years, range=34-67) diagnosed with stage I-IIIA breast cancer and receiving anthracycline-based chemotherapy were studied. Each woman wore an actigraph for 72 hours before the start of and at the end of cycle 4 chemotherapy. Blood was collected at the same time points. A canonical correlation analysis was performed to examine the overall associations between the changes in inflammatory markers (e.g., Interferon gamma [IFN-γ] C-reactive protein, Interleukin-6; assayed via ELISA) from pre-to-post-chemotherapy, and the set of pre-chemotherapy actigraphic sleep measures (e.g., number of daytime naps, nighttime total wake time). Rejection of the omnibus multivariate test prompted further analyses of the association between pre-chemotherapy sleep and changes in pre-to-post-chemotherapy inflammatory markers with Pearson product correlations. Sleep variables that were significantly associated with inflammatory markers were entered into multiple linear regression models predicting change in inflammatory markers from pre-to-post-chemotherapy. We report only the final significant model.

Results: Changes in inflammatory markers from pre-to-post-chemotherapy were correlated with pre-chemotherapy sleep (omnibus multivariate Hotelling's $F_{(42,14)}=2.69$, p=0.024). Multiple linear regression analysis revealed that fewer daytime naps (t=-2.81, standardized beta=-0.489, p=0.02) and more time spent awake during the night (t=2.73, standardized beta=0.476, p=0.014) pre-chemotherapy were associated with larger changes in IFN-γ pre-to-post-chemotherapy (model $F_{(2,17)}=8.02$, p=0.004, Adjusted R2=0.43).

Conclusion: Less sleep (i.e., fewer naps and more wake time at night) before chemotherapy was correlated with larger changes in IFN-γ, an inflammatory marker involved in aging, metabolic syndrome and mental illness. Replication studies with larger samples are warranted.

0921

SOCIAL ROLES AND SLEEP: TOO MANY OR TOO FEW SOCIAL ROLES ARE LINKED WITH SLEEP DISTURBANCE IN COMMUNITY ADULTS

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Introduction: Previous research suggests that social isolation and loneliness are risk factors for sleep disturbance, suggesting the importance of the social environment for sleep. On the other hand, having too many social roles may also contribute to sleep disturbance via increased demands and stress. The present study examined the association between social roles and sleep, as measured subjectively and objectively, using in-home polysomnography (PSG).

Methods: Participants were 221 men and women (43% African American; 49% women; M age = 59.9 years) drawn from a community sample.

PSG outcomes derived from 2 nights of in-home sleep studies with standard montage included: total sleep time (TST), sleep efficiency (SE), and the percentage of Stage 3+4 and rapid eye movement sleep (REM), as these measures have most consistently been linked with aspects of the social environment. Number of social roles were characterized using a questionnaire which assesses frequent engagement in a variety of different types of social roles (e.g., spouse, parent, church member) and categorized into tertiles (high, medium, or low). Analyses examined the relationship between level of social roles and sleep, after statistically adjusting for age, sex, race, body mass index, and depressive symptoms. We also examined whether associations differed according to race/ethnicity or gender, by including the respective interaction terms.

Results: There was a significant main effect of social roles on the percentage of Stage 3+4 sleep (F= 5.4, p=.005). Individuals with fewer social roles had higher levels of Stage 3 + 4 sleep. There were also significant race or gender interactions for SE, TST, and PSQI. Specifically, both high and low levels of social roles were associated with poorer SE and shorter sleep duration for blacks, but not for whites (F=3.0, p =.05). Similarly, high and low levels of social roles were associated with poorer sleep quality for women, but not for men (F=4.1, p<.05).

Conclusion: These findings suggest a complex relationship between sleep and social roles, moderated by race and gender. For some, having too few or too many social roles may negatively impact sleep

0922

SLEEPLESS NIGHTS AND MARITAL STRIFE? EXAMINING THE BIDIRECTIONAL LINKS BETWEEN NIGHTLY SLEEP AND DAILY MARITAL INTERACTIONS

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Introduction: The majority of adults sleep with a partner. For many, sleep problems and relationship problems co-occur. However, sleep researchers have tended to view sleep at the level of the individual. The current study considers the dyadic nature of sleep by examining the bidirectional links between nightly sleep duration and continuity and daily marital interactions.

Methods: Participants were 35 healthy, married couples (Mean age = 32 years; 73% Non-Hispanic Caucasian) who were screened to be free of clinically relevant significant sleep, psychiatric, or medical disorders. Sleep latency (SL), wakefulness after sleep onset (WASO), and total sleep time (TST) were measured using 10-nights of actigraphy. The quality of marital interactions was assessed daily using electronic diaries, with 4 items that assessed Positive Marital Interactions (e.g., felt supported or valued by spouse) and 4 items that assessed Negative Marital Interactions (e.g., felt criticized or ignored by spouse). Dyadic, time-series analyses were used to examine the degree to which nightly sleep predicted next day's marital interactions, and vice versa, how daily marital interactions predicted subsequent sleep.

Results: Wives' greater SL predicted wives' report of more negative and less positive interactions the next day (B = .19, p =.02 and B = -.27, p=.001, respectively). In addition, wives' greater SL predicted husbands' report of less positive marital interaction ratings the next day (B = -.21, p =.01). Husbands' sleep did not affect his own or his spouse's report of next day's marital interactions. However, for husbands, his report of higher levels of positive marital interactions predicted his own shorter sleep duration the next night (B= -1.04, p =.003). These significant results persisted with adjustment for depressive symptoms.

Conclusion: Overall, we found stronger evidence linking sleep to next day's marital interactions rather than the reverse direction. In particular, findings suggest that wives' prolonged sleep latency predicts her own and her husband's next day's marital interactions, and the effects are in-

dependent of depressive symptoms. These findings have important clinical implications inasmuch as they highlight the potential interpersonal consequences of sleep disorders, such as insomnia.

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0923

COGNITIVE DEFICITS: RELATIONSHIP TO SLEEP AND FATIGUE IN BREAST CANCER PATIENTS

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Introduction: Patients treated with chemotherapy complain of decreased cognitive functioning before and during chemotherapy. This has been termed "chemobrain." Understanding the cause of chemobrain is critical as these patients require increased care, experience impaired decision making ability, experience decreased quality of life and express concern about their ability to maintain employment. This study examined whether the cognitive impairment associated with chemotherapy might be secondary to fatigue and sleep.

Methods: Data from 71 women (Mean age=51.8 years; SD=9.7) are presented. All were diagnosed with stage I-III breast cancer and were undergoing chemotherapy. As a comparison, 53 age and education-matched women (Mean age=51.4 years; SD=9.6) with no history of cancer were studied. Measures of subjective and objective cognitive function, questionnaires on fatigue, sleep, mood, , and quality of life (QOL) were administered the start (baseline) and after the cycle 4 (C4) of chemotherapy. An actigraph was also worn at both points. Naps and total sleep time were based on actigraphy.

Results: Compared to controls, patients napped significantly more, slept less at night, and had worse depressive symptoms, fatigue, and worse QOL at baseline and at C4 (all p<0.05). There were no baseline group differences in cognitive function, but at C4 controls improved whereas there were no significant cognitive changes in patients. Patients self-reports indicated deterioration in language and overall cognition at C4. Approximately 20% of the variance in cognitive function deterioration is explained by each of sleep (R2=0.21; Beta=/-SE=-0.0215+/-0.0098; p=0.032), fatigue (R2=0.19; Beta+/-SE=-0.0037+/-0.002; p=0.076) and depression (R2=0.19; Beta+/-SE=-0.0070+/-0.0039; p=0.074).

Conclusion: Results suggest chemotherapy is in fact associated with subtle deterioration in at least some aspects of objective and subjective cognitive function. The possibility that these cognitive changes are mediated by sleep, fatigue, and depression should be considered as part of treatment planning.

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0924

PREVALENCE OF ALVEOLAR HYPOVENTILATION IN MEN AGE 40-65 PRESENTING FOR EVALUATION OF A SLEEP COMPLAINT

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Introduction: In a group of men ages 40-65 presenting for sleep evaluation with PSG, an effort is made to examine prevalence of alveolar hypoventilation syndrome (AH) and review demographics as well as sleepiness. Epworth Sleepiness Scale (ESS) is a validated tool measuring excessive daytime sleepiness (EDS).

Methods: Records of 22151 men undergoing baseline PSGs from 2009-2010 at SleepMed were reviewed. ESS was administered prior to each study. Oxygen desaturation index (ODI) was measured at equal to or greater than the 4% level during the total sleep time as well as saturation index time less than 90%. Patients were selected with low RDI but sustained desaturation. Comparison was made with patients RDI >15 without regard to ODI.

Results: Of 22151 men studied 12149(55%) men were 40-65 years. Of the 12149 men, 7500(62%) were identified to have sleep disordered breathing (AH+OSA=SDB). AH group accounted for 367/12149 (3%) of the total and 367/7500 SDB (5%) of men ages 40-65. AH was characterized by RDI< 10, nadir oxygen less than 85%, time below 90% > 10 minutes, ODI <10/hour . Men with AH ages 40-65 were characterized by a mean age of 54(7); BMI 32(6); ESS 9(5); RDI 7(3); nadir O2 sat 80(4); time<90% minutes 100(98); ODI 4(2). OSA accounted for 7133/12149 (59%) of the total and 7133/7500 SDB (95%) of men ages 40-65. OSA group was characterized by an RDI>15. Demographics of this group were: mean age of 53(7); BMI 33(14); ESS 10(5); RDI 38 (23); nadir O2 Sat 80(8); ODI 26(21); time<90% minutes 42(62).

Conclusion: 3% of men age 40-65 studied met criteria for alveolar hypoventilation or nocturnal hypoxemia. This represented 5% of men in the sleep disordered breathing group presenting with a sleep complaint. As a group men with SDB often experience excessive sleepiness as measured by ESS. However, men with AH appeared to be less sleepy than men with OSA. The prevalence of AH, OSA in this group should be contrasted with women of comparable age.

0925

ASSOCIATION BETWEEN SLEEP DURATION AND MATERNAL MENTAL WELL BEING DURING PREGNANCY: A POPULATION BASED STUDY

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Introduction: Sleep durations of more or less than 7-8 h in a 24-h period are associated with depression in the general population. Antepartum depression is associated with negative fetal/obstetrical and neonatal outcomes. However, little is known between sleep duration during pregnancy and antepartum depression. This study aimed to examine sleep duration during pregnancy and its effects on maternal mental well-being.

Methods: This cross-sectional study was based on data from the 2009 Behavioral Risk Factor Surveillance System. The study sample included pregnant women from states where optional modules of inadequate sleep was surveyed (n=214). The exposure was the self reported average sleep/24 hours. The outcome, maternal mental well-being, was the number of days women reported having poor mental health including depression during the past 30 days (0 days, < 10 days, ≥10 days). A logistic regression model was used to estimate odds ratios (OR) and 95% confidence intervals (95% CI).

Results: Out study included pregnant women who were mostly White, married, college graduates with normal weight and a mean age of 31. The average sleep time pregnant women reported was 7.5 (SD=1.80) hours per 24 hours. In our study sample, the average days of reported poor mental health in the past 30 days was 2.5 days with 9% of women reported having 10 or more days of poor mental health in the past 30 days. Using sleep as a continuous measure, one hour increase in sleep/24 hours reduced the likelihood of having ≥10 days of poor mental health during pregnancy by 29% (OR: 0.71, 95% CI: 0.53, 0.96) after controlling for maternal age, BMI, and income level.

Conclusion: Sleep duration during pregnancy may be associated with maternal mental health, even though the direction of effect is unclear. This finding could have clinical implications for intervention and prevention antepartum depression.

0926

SLEEP DURATION DURING PREGNANCY AND MATERNAL AND FETAL OUTCOMES: A PILOT STUDY USING ACTIGRAPHY

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Introduction: Pregnant women are at risk for short sleep duration because of the physical changes of pregnancy. Few research has examined the correlates of short sleep duration during pregnancy and its effects on maternal and fetal outcomes. The purpose of the present study examined the role sleep duration during pregnancy plays in maternal and fetal outcomes.

Methods: In a prospective cohort pilot study (n=31), women aged 14 to 40 years old at 6 to 14 weeks of gestation were recruited from the obstetrics clinic at the Barnes Jewish Hospital in St. Louis. Sleep duration was measured with actigraphy as follows for 7 consecutive days at each interval: 1) 5 to 20 weeks; 2) 21 to 28 weeks; 3)30 to 36 weeks. Sociodemographic information and birth outcomes were collected through survey questionnaires and medical record abstraction. The exposure was sleep duration per 24 hours during pregnancy. Outcomes of interest included preterm delivery, small for gestational age (SGA), preeclampsia, and gestational weight gain. Binary Logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (95% CI).

Results: Being African American, higher BMI, self-perceived poor coping, and lack of social support increased the odds of short sleep duration during pregnancy. Using sleep as a continuous measure, each additional hour of sleep per 24 hours in late pregnancy decreased the odds of SGA (OR: 0.57, 95% CI: 0.40, 0.81) whereas one hour increase in sleep in mid pregnancy decreased the odds of preeclampsia (OR: 0.86, 95% CI: 0.77, 0.97). Each hour increase in sleep per 24 hrs in early pregnancy was also associated with less gestational weight gain (OR: 0.83, 95% CI: 0.87, 0.99).

Conclusion: Sleep duration during pregnancy may be associated with maternal and fetal outcomes. More studies with larger sample size are needed to confirm the study findings.

0927

FEATURES OF POST-PREGNANCY RLS IN WOMEN WHOSE RLS WORSENED DURING PREGNANCY

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Introduction: Pregnancy is a risk factor for the development or worsening of RLS symptoms. Clinical characteristics of women whose RLS worsens during pregnancy are not fully known.

Methods: An RLS symptom questionnaire was given to a convenience sample of 61 mothers diagnosed with RLS but not currently on treatment. Questions covered the effect of past pregnancies on RLS, demographics, and characteristics of current symptoms. Serum ferritin levels were obtained at the time of questionnaire completion. Nineteen percent of women had one child, 45% two children, and 36% three or more children. 74% were Caucasian and 25% African-American. 41% had a first degree relative with RLS. Mean age was 53.5 years (SD = 16.5).

Results: Eighteen percent experienced worsening of RLS during pregnancy. Comparing these women to those whose RLS was unchanged by pregnancy, women who worsened were more likely to experience current RLS symptoms as painful (Fisher's exact test, p = 0.0497), to experience symptoms alternating from one leg to the other (rather than occurring simultaneously in both legs, p = 0.022), and to experience worsening of symptoms with exercise (p = 0.031). Serum ferritin was significantly lower in those women whose RLS had worsened during pregnancy (30.7 vs 63.6, p = 0.036). There were no differences in age, race, family history, frequency of symptoms, number of pregnancies, presence of leg cramps or a history of "growing pains" between women whose RLS worsened or remained unchanged during pregnancy.

Conclusion: This preliminary, cross-sectional evaluation of the relationships between RLS during and after pregnancy suggests that those women whose RLS worsens during pregnancy are more likely to experience post-pregnancy RLS as painful, alternating between legs, and worsening with exercise, and are more likely to have iron-deficiency. Further study of the factors causing pregnancy-related RLS and its long term consequences is needed.

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0928

HOW SHOULD WE SCREEN FOR SLEEP APNEA IN PREGNANCY?

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Introduction: The Berlin Questionnaire (BQ) and Epworth Sleepiness Scale (ESS) are commonly used to screen for sleep apnea (SA). While these screening tests have a high sensitivity and specificity in non-pregnant individuals, these tools may not be as accurate during pregnancy. The objective of this study was to evaluate the performance of the BQ and ESS in screening for SA during pregnancy, and to determine whether a simpler screening method would be more accurate.

Methods: High-risk women (women with chronic hypertension, pregestational diabetes, obesity, and/or a prior history of preeclampsia) were recruited to complete a sleep survey, comprised of the BQ and ESS, and to participate in an overnight sleep evaluation with the WatchPAT100 (WP100), a wrist-mounted, ambulatory device designed to diagnose SA. The presence of SA was defined as an apnea hypopnea index (AHI) of ≥5. In addition to evaluating the BQ and ESS, we assessed the performance of a 2 question approach in which patients were considered to be screen positive if their pre-pregnancy BMI was ≥25 and they reported snoring. The performance of the BQ, ESS, and a two-question approach (BMI and snoring) were assessed through the use of receiver operating characteristic (ROC) curves.

Results: Complete sleep survey and WP100 data was available for 86 women. Area under the curve (AUC) data from the ROC for the BQ, BQ+ESS and the two-question approach are shown in the Table. The two-question approach performed better than the BQ, the BQ+ESS combined, and performed better than the null hypothesis (AUC=0.5). The sensitivity and specificity of the BQ were 35% (95% CI 17%, 57%) and 69% (95% CI 55%, 79%), respectively. The two-question approach had a much better sensitivity 74% (95% CI 51%, 89%) without sacrificing much specificity 59% (95% CI 46%, 71%).

Conclusion: Standard screening tools for SA are not adequate in pregnancy. A simpler approach, using pre-pregnancy BMI and self-reported snoring, yields better results. Further studies are needed to design and test the most appropriate screening tool for SA in pregnant women.

0929

THE EFFECTS OF SUBTLE BREATHING ABNORMALITIES DURING SLEEP IN PREGNANCY

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Introduction: Sleep disordered breathing is known to cause an increase in both nocturnal and daytime systemic blood pressure. Prior studies have shown snoring and flow limitation during pregnancy may be associated with blood pressure elevations. However, relatively little is known about the effects of sleep disordered breathing and more subtle breathing abnormalities during pregnancy. Inspiratory flow limitation is commonly observed in pregnancy. In addition, saturation values above 95% are typically recommended although the data underlying this recommendation are somewhat unclear. We hypothesized that pregnant women with subtle breathing abnormalities would have higher nocturnal blood pressure.

Methods: Twenty-five women admitted into our hospital in their third trimester of pregnancy participated in a sleep study using an unattended portable monitoring device. Following informed consent, participants were given subjective sleep questionnaires. Blood Pressure was acquired upon admission and during the night as part of usual care by nursing staff. Subjects' sleep was recorded for roughly 10 hours. We then scored the sleep recordings using modified Chicago criteria(2 and 3 percent desaturation); an automated flow limitation marker was also used and verified visually(Embla Software).

Results: To date, we have enrolled 25 women with ages ranging from 18-48 years, with pre-pregnancy BMI 17-45 kg/m2 and 8 having pre-eclampsia and 17 pregnant controls. We observed minimal sleep apnea using either a 2 or 3 percent desaturation criterion(RDI ranging from 0-6/h). Using a Spearman Correlation test, we found that flow limited breathing was a predictor of raised blood pressure as measured during the middle of the night. Among women without pre-eclampsia, we observed that an increase in the flow limitation index(from 1- 27%) predicted an increase in blood pressure with a mean nocturnal blood pressure of $104\pm13/63\pm10$. We further observed that borderline hypoxemia during the middle of the night(saturations below 95%) were predictive of blood pressure as measured during the night(p value .04).

Conclusion: Pregnant women had relatively subtle breathing abnormalities as manifest by flow limitation and saturations below 95%. Based on nocturnal blood pressure measurements, we observed some predictive value of flow limitation as well as sub-clinical hypoxemia. These data suggest that subtle breathing abnormalities may be important in pregnant women. Further research is clearly required.

0930

SDB RISK, GESTATIONAL HYPERTENSION AND RACIAL BACKGROUND IN PREGNANT WOMEN

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Introduction: Sleep-disordered breathing (SDB) may be associated with gestational hypertension (GHTN), a leading cause of maternal morbidity. Both GHTN and SDB are more common in African-American women than Caucasians. Therefore, we hypothesized that an excess frequency of SDB in African-Americans may explain the higher prevalence of GHTN in this population.

Methods: Third-trimester pregnant women were recruited from obstetric clinics and invited to complete several sleep questionnaires. Women who were normotensive at study entry were enrolled and high risk for

SDB was defined as habitual snoring ≥ 3 nights/week. Diagnoses of GHTN/pre-eclampsia were obtained from medical records.

Results: Among 1171 participants (mean age 29.6±5.6 years, mean BMI 26.1±8.6kg/m2), 194 (17%) were African-American, 241 (21%) had GHTN, and 403 (34%) had high SDB risk. The prevalence of GHTN was similar in African-Americans and Caucasians (23% vs. 20%, p=0.42), as was SDB risk (37.5% vs. 35.5%, p=0.14). SDB was more common in women with GHTN than in those without (48% vs. 34%, p<0.001). The prevalence of GHTN was greater in women with high SDB risk than in those without high risk (27% vs. 17%), and the odds ratio (OR) for GHTN and high SDB risk was 1.8. The OR for GHTN and SDB risk was higher in Caucasians than African-Americans (OR 1.9, vs. OR 1.4). In a logistic regression model including race, body mass index (BMI), age, and parity, SDB status was independently associated with GHTN (OR=1.3, 95%CI 1.01-1.75). Race was not independently associated with GHTN.

Conclusion: A significant proportion of pregnant women are at risk for SDB regardless of racial background, and SDB risk is associated with GHTN. Nearly half of women with GHTN had high risk for SDB. Neither SDB risk nor GHTN were more common in African-Americans. These findings require confirmation by objective measures, but suggest that all pregnant women should be screened for SDB, especially in the setting of GHTN.

0931

RELIABILITY AND VALIDITY OF MULTIVARIABLE APNEA PREDICTION QUESTIONNAIRE TO MEASURE SLEEP DISTURBANCES IN PREGNANCY

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Introduction: Sleep disturbances during pregnancy are common and associated with adverse maternal and fetal outcomes. However, few studies have validated sleep questionnaires for use during pregnancy. Therefore, we aimed to assess the validity and reliability of Multivariable Apnea Prediction questionnaire (MAP), including four subscales (MAP1: apnea symptoms, MAP2: difficulty sleeping, MAP3: daytime sleepiness, MAP4: narcolepsy symptoms) for use during pregnancy.

Methods: In first trimester 195 women and in third trimester 105 women completed MAP, Pittsburgh Sleep Quality Index (PSQI) which was previously validated in pregnancy (its subscales; PSQI1: sleep quality, PSQI2: sleep latency, PSQI3: sleep duration, PSQI4: sleep efficiency, PSQI5: sleep disturbance, PSQI6: daytime dysfunction) and Epworth Scale (ESS) and underwent full polysomnography. Concurrent validity of MAP was assessed with subjective and objective sleep measures, using a random-effects regression model, adjusted for trimesters. Cronbach's alpha was used to assess internal reliability.

Results: The overall questionnaire had an acceptable internal consistency as measured by Cronbach's alpha reliability (0.70 in first and 0.77 in third trimester). MAP1 showed significant correlations with total-PSQI (β=0.55(SE=0.27); p=0.04), PSQI5 (β=0.27(0.05); p=0.001), apnea-hypopnea index (β=1.30(0.2); p=0.03) and borderline significance with ESS (β=0.65(0.4); p=0.07). MAP2 was significantly correlated with ESS (β=1.08(0.3); p=0.001), total-PSQI (β=1.41(0.2); p=0.001) and all PSQI subscales (β=0.1(0.05) to (β=0.3(0.04); all p≤0.01). MAP3 was significantly correlated with ESS (β=3.02(0.3), p=0.001), total-PSQI (β=0.71(0.3), p=0.001), PSQI5 (β=0.12(0.05); p=0.001), PSQI6 (β=0.40(0.06); p=0.001) and apnea-hypopnea index (β=10.01(3.6); p=0.001). MAP4 was significantly correlated with ESS (β=0.93(0.3); p=0.02), total-PSQI (β=1.11(0.4); p=0.001) and all PSQI subscales except for PSQI4 (β=0.19(0.09) to β=0.21(0.09); all p<0.04).

Conclusion: The results showed moderate concurrent validity and internal consistency indicating that MAP is reasonably valid and reliable to measure sleep disturbances frequency during pregnancy. Further evaluation of the MAP, including factor analysis, is warranted.

0932

AN OPEN PILOT OF COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA IN WOMEN WITH POSTPARTUM DEPRESSION

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Introduction: Postpartum depression (PPD) is experienced by up to 20% of women. Sleep difficulties are common in PPD and its treatment may improve both sleep and mood disturbances for childbearing women. In an open label pilot study, we evaluated the effects of cognitive-behavioral therapy for insomnia adapted for postpartum women (CBTI-PP) on sleep and mood.

Methods: Six women with PDD (age = 27 ± 5, mean infant age = 33 ± 16 weeks) who also reported chronic insomnia participated in 5 weekly sessions of CBTI-PP. Three women received concurrent treatment for MDD (medication plus psychotherapy). Modifications to CBTI-PP, based on feedback obtained from focus groups of women with PPD, included: education regarding sleep and mood; addressing circadian factors related to caring for the infant; tips to help the infant sleep better; flexibility with sleep restriction; and ways to enlist support of their partner.

Results: All participants completed 5 sessions of treatment. Paired-sample t-tests were used to evaluate pre- and post-treatment changes. Sleep diaries showed improvements in sleep efficiency (75 ± 9 to 91 ± 4, p = .004) and total wake time (98 ± 38 minutes to 37 ± 18 minutes, p = .008). Insomnia Severity Index score decreased from 18 ± 5 to 7 ± 3 (p = .008). Clinician-rated depression severity (Hamilton Rating Scale for Depression, excluding sleep items) declined from 17 ± 3 to 9 ± 4 (p = .03), and self-reported depression severity (Edinburgh Postnatal Depression Scale, excluding sleep items) declined from 13 ± 3 to 8 ± 4 (p = .048).

Conclusion: In this small, open pilot intervention for insomnia in women with PPD, CBTI-PP was associated with improvements in subjective reports of sleep, insomnia severity, and mood. We are continuing to refine this treatment in anticipation of a larger, randomized controlled trial.

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0933

THE ROLE OF SLEEP IN STRESS AND WELLBEING AMONG POSTPARTUM WOMEN WITH A LOW BIRTH WEIGHT INFANT

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Introduction: Mothers with low birth weight (LBW) infants hospitalized in the intensive care unit (ICU) are vulnerable to sleep deprivation, and at high risk for adverse health outcomes due to the stress associated with their infants' medical conditions. This study aimed to examine the role of sleep quantity and quality in the direct and indirect associations of stress to depressive symptoms, fatigue, and health-related quality of life (H-QOL) among mothers with a LBW infant in the ICU during early postpartum period.

Methods: Fifty-five first-time mothers filled out a battery of questionnaires, including the Perceived Stress Scale, Impact of Event Scale, General Sleep Disturbance Scale, Lee's Fatigue Scale, Edinburgh Postnatal Depression Scale, and Medical Outcomes Short Form-36. Wrist actigraphy method was used to collect quantitative sleep data.

Results: Poor sleep quality as reported by mothers, but not sleep quantity as indexed by objective actigraphic measures, was significantly associated with greater stress, greater depression, and poorer H-QOL. A path model with maternal sleep mediating the link of stress to health-related wellbeing was tested. Greater stress contributed to poor sleep quality reported by mothers, which was associated with greater fatigue, which in turn, contributed to poorer physical and mental health aspects of QOL.

Conclusion: Sleep quality mediates stress and health-related wellbeing among mothers of LBW infants hospitalized in ICU. As a gateway in regulating the effect of stress on health, maternal sleep may be a target for intervention. Better quality of sleep is expected to mitigate the negative effect of stress on health. Further research is needed to explore the underlying mechanisms that regulate sleep (e.g., circadian rhythms, serotonin) and other psychosocial factors linking stress to health outcomes. The role of sleep in the effect of stress on maternal parenting and infant attachment also needs to be explored.

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0934

SLEEP QUALITY AND DEPRESSION SYMPTOMS IN DISADVANTAGED POSTPARTUM WOMEN

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Introduction: Depression affects 13% of women after childbirth. Poor sleep quality is a diagnostic feature of depression and common after childbirth, yet rarely studied in disadvantaged women. Interventions are working to address depression symptoms by improving postpartum sleep; however, whether objective or subjective sleep quality is the better measure of intervention effectiveness is unknown. The aims of this study were to: 1) Describe objective and subjective sleep quality, and 2) Compare the association of objective versus subjective sleep quality to depression symptoms in multiparous disadvantaged women.

Methods: Medicaid recipients (n = 119) from a Midwestern urban city completed 72 hour actigraphy and the Pittsburgh Sleep Quality Index at 8 weeks postpartum, and the Edinburgh Postpartum Depression Scale at 12 weeks. Sample characteristics were: age 26 (5.1) years, 12(1.8) years education, 3(1.7) children (range 2-9), African American (72%), Caucasian (14%), and partnered (79%). Analysis used multiple regression controlling for hematocrit (a priori alpha 0.05).

Results: Mean sleep quality at 8 weeks postpartum was 7.7 (3.13) with 71% of the sample having poor sleep quality (PSQI score > 5). Subjective sleep quality at 8 weeks was predictive of 12-week depression symptoms with a 0.5 point increase in depression score for every 1 point worsening of sleep quality (F (2, 105) = 6.2, p = .003), accounting for 8.9% of the variability. Further analysis of objective sleep quality and its comparison to subjective sleep quality and depression measures will be presented.

Conclusion: The high percent of women having poor sleep quality has significant clinical implications, because sleep quality in this group of healthy, yet economically disadvantaged women should have been improving by 8 weeks. Interventions to improve sleep quality should examine intervention effects in relation to both physical and mental health outcomes, and compare whether subjective or objective sleep improvements best improve health.

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0935

PREGNANCY-RELATED SLEEP DISTURBANCES: A COMPARISON OF PREGNANT WOMEN WITH AND WITHOUT INSOMNIA DISORDER

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Introduction: Nearly 50% of women report sleep disturbances during pregnancy. The present study sought to determine whether pregnancy-specific sleep disturbances differentiate those who meet DSM-IV criteria for Insomnia Disorder from those who do not.

Methods: Sixty-three women at different stages of pregnancy completed the Duke Interview for Sleep Disorders, the Insomnia Severity Index, and demographic information. Forty-seven of these women also completed questions about pregnancy-related symptoms interfering with sleep (e.g. hip pain). A series of t-tests and Chi-square analyses compared participants with and without insomnia disorder on a variety of demographic information and endorsement of pregnancy-specific sleep disruptions.

Results: Fifty-four percent of the sample met criteria for current Insomnia Disorder, with a mean Insomnia Severity Index score of 14.3 (sd = 3.5), statistically larger than the score of the women without Insomnia Disorder (4.6; sd=3.4). While hip pain and sleeping position were more likely to disrupt sleep in those with Insomnia Disorder (p's < .08), baby movements, breast tenderness, contractions, breathing difficulties, hot flashes, hunger, indigestion, restless or cramping legs, nausea, pelvic pain, and urination, and worry did not. Groups did not differ in the number of previous episodes of insomnia either during or outside of pregnancy.

Conclusion: Reliance on the presence of pregnancy-related sleep disruptions alone is insufficient for determining whether a given pregnant woman is suffering from a sleep disorder. Screening insomnia in pregnant women requires the use of reliable screening measures, such as the Insomnia Severity Index (cut-off score of 11 or higher in pregnant women), followed by a clinical interview.

0936

ASSOCIATIONS BETWEEN HABITUAL SNORING AND PSG-DEFINED SDB IN PREGNANT WOMEN

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Introduction: Sleep-disordered breathing (SDB) is associated with adverse pregnancy outcomes, but methods to screen large numbers of pregnant women for SDB risk have not been studied adequately. A history of snoring is robustly associated with objectively assessed SDB in non-pregnant adults. We examined the extent to which this association can be demonstrated in pregnant women.

Methods: Women were recruited from obstetric clinics during their last trimester of pregnancy to complete several sleep questionnaires. Habitual snoring (HS) was defined as snoring ≥3 nights/week. Participants also underwent full overnight home polysomnography using the MediPalm system. Polysomnograms were scored by an experienced technologist using AASM 2007 criteria. SDB was considered present if the apnea/hypopnea index (AHI) was ≥5.

Results: Thus far 27 pregnant women have been studied, 11 with HS and 16 controls without HS. Mean age was 29.8±6.0 years and mean BMI was 30.8±7.2 kg/m2. Total recorded sleep time was 341.3±91.5 mins and 347.6±107.0 mins in HS and controls respectively (p=0.87). The mean AHI in women with HS compared to those without was 10.3±12.1

vs. 3.6±3.6 (p<0.05) and nadir SpO2 was 89.5±3.9 vs. 91.5±2.7 (p=0.1). In total, 8 of 11 women (73%) with HS were found to have objective evidence of SDB, compared to 3 of 16 (19%) without HS (Chi square p=0.015). The sensitivity and specificity of the screening question (HS) for SDB was 0.73 and 0.81 respectively

Conclusion: Our preliminary findings suggest that self-reported HS during pregnancy helps to predict the presence of objectively-defined SDB. This simple screening tool may be useful in research and, perhaps with a less stringent and more sensitive criterion for habitual snoring, in obstetric practices.

0937

EFFECTS OF A BEHAVIORAL SLEEP INTERVENTION ON POSTPARTUM SLEEP

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Introduction: Emerging research shows that postpartum sleep can be improved with behavioral interventions. We hypothesize that we can improve sleep duration and sleep consolidation of postpartum women with a history of smoking as a potential strategy for improving their daytime capacity to stay smoke-free after the birth of their babies. This study documents the preliminary sleep outcomes following 5 weeks of behavioral sleep intervention.

Methods: Ten postpartum mothers (mean age 23.1 years [SD = 2.85], 40% minority, 100% low SES, 70% unmarried, 80% with other children at home) were enrolled in the hospital after the birth of their babies prior to discharge. Baseline sleep data was collected using wrist actigraphy (Octoganol Basic, AMI) and sleep diaries. These measures yielded values of Longest Sleep Bout (LB), Nocturnal Total Sleep Time (NTST), and 24 Hour Total Sleep Time (24TST), which we used to compare the intervention group to the control group on sleep duration and consolidation. Post-treatment sleep data was collected around week 7.

Results: Independent t-tests revealed no significant baseline differences on any of the 3 sleep outcomes (intervention and control group respectively): LB (M = 106.06 [SD = 35.51] minutes vs. 110.74 [23.35]); NTST (314.34 [101.94] vs. 298.79 [62.87]); 24TST (359.28 [129.866] vs. 324.29 [2.77]). The intervention group had significantly longer LBs post-treatment (M = 153.36 [31.42] mins) than the control group (M = 97.036 [17.62]): t (8) = 2.372, p = .045.

Conclusion: Our behavioral sleep intervention significantly consolidated the sleep of new mothers during the first 7 weeks postpartum when compared with controls. These results will be updated based on a larger sample size available by the meeting date. Helping postpartum women decrease their sleep fragmentation may make them feel better and perform better during the day, which is particularly important for new mothers seeking to remain smoke-free.

0938

POSTPARTUM MOTHERS' FATIGUE, SLEEP CHARACTERISTICS AND THE IMPACT ON EMOTIONAL STATUS

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Introduction: Postpartum sleep disturbance and fatigue are prevalent and can negatively impact maternal emotional status and, potentially, parenting behaviors. Maternal sleep disturbances may persist after the initial postpartum period, beyond the age when infants typically consolidate sleep. In a non-clinical sample of first-time mothers of infants ages

4-7 months, we hypothesized that significant levels of sleep disturbance and fatigue would exist and that sleep disturbance and fatigue would be positively associated with two measures of emotional status: depression and parenting hassles.

Methods: Twenty-three mothers (M age=31.18 ± 3.86 years) of infants (M age=5.22 ± .86 months) completed self-report measures assessing fatigue (IFS), depressive symptoms (CES-D) and parenting hassles (Parenting Daily Hassles Scale; PDH). Additionally, participants recorded their sleep for one week using actigraphy and sleep diaries. Non-parametric correlations were calculated to test associations between variables.

Results: Average total nightly sleep time was 6 hours, 57 minutes and average wake after sleep onset was 49 minutes; 61% reported clinically significant symptoms of fatigue (IFS>30). Non-parametric correlations revealed that fatigue was associated with depressive symptoms (.622, p=.002). Less 24-hour total sleep time was associated with greater parenting hassles (-.414, p=.055). Actigraph-derived sleep characteristics and fatigue were not associated with frequency of infant night-time waking (crying) or infant sleep onset latency.

Conclusion: High levels of maternal fatigue persist after the newborn phase; fatigue is also a robust indicator of depressive symptoms. As both depression and parenting hassles are related to sleep measures and can impair mother-infant relationship quality, assessment of maternal sleep and fatigue beyond the newborn period is warranted. From a public health perspective, these findings are particularly relevant as this age-range captures the stage when mothers are returning to work, requiring adaptation within the mother-infant relationship while also creating changes in sleep schedules and routines.

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COMPARISON OF LABORATORY POLYSOMNOGRAPHY AND AN AMBULATORY SLEEP APNEA MONITOR FOR DETECTING OBSTRUCTIVE SLEEP APNEA IN PREGNANT WOMEN

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Introduction: The purpose of this study was to validate a portable recorder, the Apnea Risk Evaluation System (ARES) Unicorder (Watermark Medical, FL), with polysomnography (PSG) for detecting obstructive sleep apnea (OSA) in pregnancy. The ARES is validated in non-pregnant adults, but we hypothesized that facial edema during pregnancy could affect ARES oximetry and change performance of the device in pregnant women

Methods: We recruited pregnant patients referred for a sleep study for clinical suspicion of OSA. PSG was scored using standard criteria to determine PSG apnea/hypopnea index (AHI). ARES data were processed using ARES software, which applies automated algorithms to identify SaO2 changes, pulse rate, head movements, and snoring and combines these factors to calculate an ARES AHI. We examined ARES AHI determined with 4% and 3% desaturations. We used AHI≥5 events/hour as the cutoff for OSA diagnosis for all methods. We computed sensitivity, specificity, and Kappa coefficients to assess diagnostic consistency between PSG and ARES.

Results: Fifteen women (mean age±SD = 29.6+5.5 years; mean gestational age = 29.1±6.3 weeks, range= 17 to 38 weeks; mean BMI 44.8±7.3 kg/m², range=30.3 to 61.2 kg/m²) had concurrent data collection with the ARES Unicorder and laboratory PSG. Eight women had OSA diagnosed with PSG: AHI range=6.8 to 113 events/hour. The ARES AHI 4% algorithm had sensitivity=0.63, specificity=1.0, and Kappa=0.61, p=.01. The

ARES AHI 3% algorithm had sensitivity=0.75, specificity=0.71, and Kappa=.46, p=.07. Two patients with PSG AHIs of 8.4 and 8.9 events/hour were not identified with either ARES algorithm.

Conclusion: The ARES Unicorder demonstrated reasonable consistency with PSG in this small, heterogeneous sample of pregnant women. The ARES algorithm with higher sensitivity (ARES AHI 3%) should be utilized in pregnancy because of potential adverse maternal and neonatal outcomes associated with untreated sleep-disordered breathing.

Support (If Any): ARES Unicorders provided to GB by Advanced Brain Monitoring, Inc.

0940

SLEEP TIMING DURING POSTPARTUM WEEKS 1 AND 7

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Introduction: Prior research has linked postpartum sleep duration and fragmentation to poor daytime outcomes. In the general population, sleep schedule variability and circadian shifting have also been linked to poor daytime functioning, but have not been investigated in postpartum women. This study investigates how postpartum women's sleep schedules vary, if women are more likely to extend their total sleep time by advancing their bedtime or delaying their final morning wake time, and if these behaviors increase total sleep time.

Methods: Participants included 10 postpartum mothers (M = 23.1 years; 70% unmarried; 80% multiparous; 100% low SES) with a history of smoking who were participating in an intervention to remain smoke-free. Actigraphic data corroborated by sleep diaries from postpartum weeks 1 and 7 were used to measure sleep onset/offset and nocturnal total sleep time. Standard deviations were used to measure variability of sleep start and end times.

Results: Variability of sleep start time was negatively correlated with nocturnal total sleep time: (r = -.511, p = .025). Women were more likely to extend their total sleep time by waking after 8 am (53.3%) than by going to sleep before 11 pm (19.7%). Participants significantly increased their sleep duration by either going to sleep before 11 pm or waking after 8 am (M = 367.67 min, SD = 107.14) or by doing both (M = 520 min, SD = 82.45) as compared to women who did neither (M = 299.23 min, SD = 80.83): F (121) = 28.1, p < .001.

Conclusion: This study documents late bedtimes (M = 12:02 am) and wake times (M = 8:17 am) for mothers in the first seven weeks postpartum, which may represent a shift from pre-pregnancy sleep schedules. Future studies should investigate a possible early postpartum circadian shift and whether poor daytime outcomes result from such a shift.

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0941

SDB IS ASSOCIATED WITH AN INCREASED RISK OF ADVERSE PREGNANCY OUTCOMES

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Introduction: The term sleep-disordered breathing (SDB) describes a group of disorders characterized by abnormal respiratory patterns or quality of ventilation during sleep, resulting in hypoxia and nocturnal arousals. In non-pregnant populations SDB has been associated with cardiovascular and metabolic morbidities and mortality. Few studies have examined the relationship between SBD in pregnancy and adverse obstetrical outcomes. The objective of this study was to examine the association between SDB and adverse pregnancy outcomes (APO).

Methods: This was a retrospective cohort study. Using ICD-9 codes, we queried our medical records database to find women who had a delivery as well as an in-laboratory polysomnogram (PSG) done at our institution between January 2000 and June 2009. Charts of identified patients were reviewed and data regarding patient demographics, sleep study results, and pregnancy outcomes were abstracted. The first pregnancy with outcome information was selected for those with more than one pregnancy. The primary outcome was an APO composite compromised of: pregnancy induced hypertension (PIH), gestational diabetes (GDM), and early preterm birth (ePTB, ≤34 week). Absence of SBD was defined as an apnea hypopnea index (AHI) of <5, mild to moderate SDB as an AHI of 5-14.9, and severe SDB as an AHI ≥15. Chi-square test for trend was used to assess the associations between SBD and APO.

Results: 150 women who had undergone a PSG as well as a delivery were identified. 61% (91/150) were nulliparous at the time of their first documented delivery at our institution. 72% (108/152) had undergone PSG within 3 years of their delivery. 86.7% of the cohort was overweight or obese (BMI≥25) at delivery. APO by SDB category are presented in the table. SDB was associated with an increased risk of APO. Women with severe SDB had the highest incidence of APO. The increased prevalence of APO seen in women with SDB was principally driven by an increased incidence of GDM and ePTB.

Conclusion: Pregnancies complicated by SDB are at increased risk for APO. Further prospective studies are needed to assess the independent impact of SDB on maternal and neonatal health.

0942

THE IMPACT OF BLUE LIGHT ON ACUTE MELATONIN SUPPRESSION: IRRADIANCE AND DURATION RELATIONSHIP

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Introduction: The spectral sensitivity of melatonin suppression peaks close to 450 nm. A model of human circadian phototransduction was developed based on the neuroanatomy and neurophysiology of the human retina. This model has been used to successfully predict acute melatonin suppression of polychromatic light sources. The present study is aimed at providing a further, a priori test of the model using a previously described personal light delivery device. In addition, a more accurate estimate of threshold for human circadian phototransduction is provided.

Methods: Each of 11 healthy adults (age 50 or older) experienced seven lighting conditions (dark, 0.7, 2, 7, 11, 20 and 65 microwatts/cm2) of 470-nm light. Blood and saliva samples were collected for 110 minutes. The first two samples were collected 10 minutes apart while subjects remained in the dark, after which the 470-nm light goggles were energized. During the first 30 minutes after lights were turned on, blood samples were collected every 10 minutes and saliva sample collection was interleafed five minutes after each blood sample collection.

Results: Melatonin concentrations from both fluids were normalized and a 2 x 2 ANOVA (7 lighting conditions x 14 sample times) were performed. Results were consistent with model predictions. Threshold for melatonin suppression was between 0.7 and 2 microwatts/cm2 and significant suppression was observed only after 15 minutes of exposure to the highest irradiance.

Conclusion: A priori predictions of acute melatonin suppression can be made using the model of human circadian phototransduction. Much lower levels of 470-nm light can suppress nocturnal melatonin. Implications for clinical applications include more confortable, less bright, and flexible light treatment delivery device.

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0943

NEW TOOLS TO MEASURE LIGHT EXPOSURE, ACTIVITY AND CIRCADIAN DISRUPTION IN OLDER ADULTS

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Introduction: Sleep disturbances in older adults may result from lack of entrainment to the 24-hr day-night cycle due to low circadian light stimulus experienced by older adults. Clinicians will not embrace light treatment, such as blue light, until the relationships between sleep disturbances, circadian disruption and light exposures are established in the field. Several practical measurement problems exist for obtaining human circadian light-exposure data as they might relate to quantifying circadian disruption in older adults.

Methods: Each of 18 healthy older adults (age 65 or older) wore a Daysimeter, three Dime-simeters and a commercially available wrist actigraph for seven consecutive days; all devices measured activity as well as light. Saliva samples were collected every 4 hrs. The Daysimeter is a head-worn device that places a calibrated red-green-blue (RGB) sensor package near the plane of the person's cornea. The Dime-simeter also contains a calibrated RGB sensor package, but is dime-sized and can be worn as a pin, a pendant, attached to glasses, and on the wrist.

Results: Phasor analysis was applied to the light and activity data from each device to quantify circadian entrainment. Like healthy young adults, but in contrast to persons with Alzheimer's disease, healthy older adults have high phasor magnitudes, suggesting a good circadian entrainment. The phasors obtained with the different devices were cor-related despite the significant differences in the absolute levels of light recorded by the different devices.

Conclusion: The Daysimeter and Dime-simeter are tools that can be used to accurately measure light exposures as they affect the circadian system and can quantify circadian entrainment in older adults. The next step will be to deploy these devices among people with and without sleep disorders to determine if measured circadian disruption is related to sleep disturbances in older adults.

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0944

COMPARISON OF AN AMBULATORY SLEEP-STAGE RECORDER WITH OUTPATIENT ACTIGRAPHY AND SLEEP LOGS ACROSS A WIDE RANGE OF SLEEP PHENOTYPES

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Introduction: Wrist actigraphy (ACT) and sleep logs (SL) are validated techniques for estimating habitual sleep timing outside the laboratory. In 2009, Fabregas et al demonstrated reasonable agreement between a commercially available wireless sleep-stage recorder ("Zeo") and both inpatient polysomnography and inpatient ACT in 10 healthy participants. Here we report the results of a 10-day outpatient protocol using this wireless system (WS), ACT, and SL in participants with a wide range of sleep phenotypes.

Methods: Seventeen participants (11 female; ages 25-75; mean=51) completed the protocol. Sleep phenotypes were determined by CRJ using questionnaires and structured telephone interviews: Delayed Sleep Phase Syndrome (n=1); Sighted Non-24-Hour Sleep-Wake Syndrome (n=1); Narcolepsy (n=1); Advanced Sleep Phase Syndrome (n=2); Conventional Sleepers (n=5); Short Sleeper Syndrome (n=7). ACT data were collected using the Phillips Respironics Actiwatch-L (n=10) and Ambulatory Monitoring Inc. MicroMini-Motionlogger. Total sleep time (TST), initial sleep onset (ISON) and final sleep offset (FSOFF) were scored automatically using Actiware-Sleep 3.4 and Action-W 2.0 software. TST, ISON and FSOFF were scored automatically by the WS using an artificial neural network. Participants estimated daily ISON and FSOFF by SL. Correlation coefficients (r) between the WS and both ACT and SL for TST, ISON, and FSOFF were calculated across all 134 participant-nights.

Results: There was a wide range of average TST, ISON, and FSOFF across all six sleep phenotypes by conventional, well-validated ACT: TST=287-484 min; ISON=15:26-03:58; FSOFF=04:32-18:44. The WS correlated well with ACT and SL: WS/ACT TST r=0.75; WS/SL TST r=0.74; WS/ACT ISON r=0.99; WS/SL ISON r=0.92; WS/ACT FSOFF r=1.00; WS/SL FSOFF r=0.93. Over all 134 participant-nights, WS estimated a lower TST relative to both ACT and SL: WS average TST=369 min; ACT average TST=396 min; SL average TST=425 min.

Conclusion: Ambulatory WS TST was moderately correlated with TST from conventional, well-validated ACT and SL measures across both genders and a wide range of ages and sleep phenotypes. Further research is needed to determine whether the lower WS TST relative to ACT and SL is a measure of its ability to detect wakefulness during sleep.

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0945

DURABILITY, SAFETY, EASE OF USE AND RELIABILITY OF A TYPE 3 PORTABLE MONITOR AND A SHEET-STYLE TYPE 4 PORTABLE MONITOR

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Introduction: To examine durability, safety, ease of use and reliability to monitor obstructive sleep apnea syndrome with a type 3 (cardio-respiratory) and a sheet-style type 4 portable monitors (PMs) in unattended home settings.

Methods: A cross-sectional survey was conducted to male employees of a wholesale company in Osaka, Japan (n=139, 44.4 ± 8.36 years). Participants used either of the two PM on the second and third nights and both of the PMs on the fourth nights. Ease of use was conducted by a self-administered questionnaire. Results from the type 3 PM were manually scored; while those form the type 4 PM were automatically scored.

Results: No safety problems were reported. A few repayments were needed only for the type 3 PMs. The type 4 PM was more inconvenient to bring home (type 3: 15.1%; type 4: 68.3%). The type 3 PM was more inconvenient to use (type 3: 71.2%; type 4: 0.7%) and more uncomfortable to use (type 3: 81.3%; type 4: 9.4%). Data from 107 and 133 out of 139 participants were comprehensible for both of two recorded nights with the type 3 and the type 4 PMs, respectively. Blant- Altman plot and scattered plot revealed high night-to-night reliability of these PMs

Conclusion: The type 3 and the type 4 PMs were durable, safe, easy to use and reliable. Both the PMs can be used to monitor OSA in unattended home settings.

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0946

EVALUATING A NOVEL SLEEP DIAGNOSTIC SYSTEM

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Introduction: Huneo is developing a novel sleep diagnostic system that can be used both at home and in lab. The system consists of quarter-sized wireless sensor units that contain both internal and external sensors and a base station. The base station receives encrypted data wirelessly from the sensor units and transmits it to a cloud-based data center via Wifi or 3G/4G network. Sensor units are designed to be modular so that patients can wear as many of them as desired (e.g., head unit measuring EEG, EMG, EOG, and airflow, and chest unit measuring EKG, chest movement and position). Users with appropriate security credentials can view the data and score within a web browser at anytime (real-time or afterwards) anywhere on computers or mobile devices. This study's main objective is to evaluate validity and reliability, compared to the standard in-lab PSG.

Methods: Twelve sleep-lab patients undergoing PSG simultaneously wore a sensor unit with the following sensors: microphone (snore), position, movement, airflow, and pulse oximeter. Direct visual comparison of the raw signals from the PSG and the novel system, along with independent manual respiratory score comparisons were performed, or are in progress.

Results: Visual comparison of the raw signals between PSG and the new system revealed equivalent signal quality in all instances. AHI scores (according to AASM guidelines) from the first 5 PSG studies are tabulated below. (Results of the subsequent 7 PSGs are pending.) Study/AHI (PSG)/AHI (new system) 1/34.7/33.4 2/2.0/2.0 3/4.8/3.8 4/53.4/49.4 5/112.5/103.1

Conclusion: We introduce a novel sleep data collection system with real-time data viewing, transmitting and analysis capacity. The results of a limited number of sleep studies from an on-going trial suggest that data collected from this new system are equivalent to those from the sleep-lab PSG.

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VALIDATION OF A NOVEL SLEEP EEG SLOW WAVE AUTOMATED DETECTION ALGORITHM

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Introduction: EEG slow waves (SW) are key components of deep NREM sleep. A previous method to detect SW during sleep stages 3 and 4 has been proposed by Massimini et al. Here we propose a novel algorithm to detect SW regardless of sleep/wake stages.

Methods: We first detected SW in filtered EEG signals (0.2-4Hz) with criteria similar to previous methods using the PRANA biosignal processing environment (PhiTools, France). Next, we introduced an additional processing stage of the unfiltered signal to discard false positives. We used a central EEG channel from a total of 191 PSG recordings collected in young and middle-aged adults using portable or laboratory systems. Sleep stages were visually score in 20-30s epochs as follows: 29357 wake, 11810 stage 1, 104357 stage 2, 13552 stage 3, 14909 stage 4 and 97164 REM. Non-parametric statistics were performed on the SW temporal density to assess differences between algorithms, sleep stages and recording equipments.

Results: Our algorithm detected a total of 230981 SW, as compared to a total of 302000 using the Massimini method. Ninety-seven percent of SW were detected in NREM sleep (2.79, 9.78 and 21.39 SW per min for stages 2, 3 and 4, respectively), with a significant difference between stages (chi2=602.46, p<0.0001). No significant difference were found between recording equipments, independently of sleep stages. Our method rejected 81% of SW that were detected by Massimini algorithm in wake, sleep stage 1 and REM.

Conclusion: This novel method, compared to former approach, can accurately detect SW independently of visual sleep stage scoring. Future clinical implications of this method include automatic analysis in patients with sleep disorders.

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0948

EEG FREQUENCY-BASED AUTOMATED SLEEP STATE DETECTIONS BY SINGLE EEG DERIVATION IN HEALTHY HUMAN SUBJECTS

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Introduction: In clinical settings, sleep stages are visually determined based on polysomnograms by a human scorer. The scoring is time consuming, and a large inconsistency may exist among scorers. There have been an increasing number of applications to determine human sleep stages by automated computer systems. However, most applications aim to imitate human scorers' decisions, such as by EEG pattern recognitions, and validations of these scoring methods are still limited. By comparison of three EEG frequency based analyses, we developed a new

automated scoring method based on probability analysis from a single EEG derivation.

Methods: Polysomnograms (F, C and O) spanning a whole night were recorded from ten healthy subjects and rated by two human scorers every 30 seconds. Discrete Fourier Transform (DFT) was performed on every second of all the derivations. On every DFT frequency bin (f), probability distribution (P(s,i,f)) was calculated on each stage (s) of each subject (i). The contribution rate (C(i,f)) was then calculated on every derivation of all the subjects. Each pair of probability distribution and contribution rate of the subject (P(s,i,f) x C(i,f)) was chosen as a classifier, and sleep stages were estimated every second. The most frequent estimation within every 30-seconds was selected and compared with the human scorers' ratings. We also applied two-dimensional and cluster analyses on the same signals, and compared the efficacy of the classifiers.

Results: Among the three analyses, we obtained the best results from the probability analysis. In the probability analysis, the best classifier worked at more than 80% accuracy on all the polysomnogram derivations. Although the detection rate of NREM stage exceeded 95% on most derivations, the rate on Wake and REM stages remained in a lower range (50-85%). The accuracy and the detection rate of the classifiers were influenced by many parameters, such as epoch length, frequency ranges and the contribution function.

Conclusion: Our multi-dimension probability evaluations on human sleep EEG worked as well as other automated scoring systems. This simple classifier based on statistical data does not simulate complex decisions by human scorers, but it can eliminate arbitrary errors. Since this method does not depend on specific frequencies or wave forms, it can be easily applied to other biological signals. Using our classifier parameters, it may also be possible to estimate the EEG features that affect human scorers' decisions.

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CHARACTERIZATION OF SLEEP MICROSTATES

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Introduction: Nonlinear analysis of EEG signals using the RQA method quantifies deterministic (nonrandom) changes in brain states of arbitrary length. RQA has been used to study cognitive processing in normality and disease, but not to characterize sleep microstates. We sought evidence indicating RQA's usefulness for this purpose.

Methods: Polysomnograms scored based on the ASSM manual were analyzed using published computational procedures (implementing LabView code available). Employing the RQA variable %R, which measures amount of law-governed activity whether or not visually perceivable, we quantified EEGs from frontal, central, and occipital electrodes, resulting in approximately 25,000 sequential values in successive 1-s intervals (time series). Additionally, phasic events (EEG arousals, K complexes, spindles, delta bursts) were analyzed by calculating %R for 100-ms intervals using a step of 2 ms (500 values of %R per sec). Additional calculations were performed using the RQA variable %D (independent measure of determinism). Spectral power analysis was employed as a control procedure.

Results: In each case (6 patients x 6 electrodes), the %R time series consisted of 3 relative maxima with periods of 200-400 min; as expected, for each patient, the patterns for all derivations were essentially identical. The patterns were not detected using power analyses. Visible phasic events consistently resulted in localized increases in %R; similar changes occurred in the absence of visually-scored phasic EEG events. Averaged over 30-s epochs, increased %R correlated strongly with increased sleep-state depth as assessed by standard scoring (80-90% agreement); the extent of the agreement was increased when %D was included in the RQA sleep-stage classification.

Conclusion: Nonlinear EEG analysis reliably permitted quantification of brain states lasting 0.1-1 s and reproduced the scoring of gold-standard-scored PSGs, suggesting the possibility of an integrated approach to the study of brain dynamical changes that includes both background signals and superimposed phasic changes.

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DIGITIZED FEATURES OF PHASIC ACTIVITY OF SURFACE ANTERIOR TIBIALIS ELECTROMYOGRAPHY (EMG): VALIDATION BY CONSENSUS PANEL

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Introduction: Phasic EMG activity has been shown to occur at high rates in synucleinopathic conditions and may also reflect medication effects. Its quantification using visual analyses is time-intensive. We describe here an automated approach to such measurement.

Methods: Five scorers evaluated independently 16,200 seconds of low-noise AT EMG from a PSG containing a moderate amount of phasic activity, encompassing NREM and REM sleep. Overall X rate of phasic activity across scorers (% of 1-sec intervals with activity) was 9.3% (range 7.67-12.7%). Signal processing features included: high freq spectral power (HF), Spectral Edge, Skew, Variance, Kurtosis, Simple Entropy, Mobility, 75th % Amplitude, Complexity, Absolute Amplitude, Curve Length (CL), Energy, Zero Crossing (ZC), Non-Linear Energy (NLE) and Spectral Entropy (SENTRO). Signals were digitized at 200 Hz and were acquired with Embla N7000 PSG.

Results: Consensus agreement among 5 scorers for presence or absence of phasic activity within 1-sec segments was very high (% agreement = 93.52%; Kappa = .818, p < .0001). All examined digitized features differentiated phasic present vs absent (nearly all p's < .0001) seconds. We also compared expert consensus agreement (binary) versus continuous, Gaussian distributions of each feature using binary classification models derived from MATLAB. Data showed wide divergence for features, with highest True Positive/True Negative Rates for SENTRO, NLE, CL and Variance (all > 88%), lowest for HF (65%), and ZC (71%) and other features intermediate. Among consensually agreed upon seconds with phasic activity (N = 1090), coefficients of variation were highest for SENTRO and NLE, approximating a 100-fold difference from the poorest functioning features.

Conclusion: Experts can agree on the presence or absence of phasic EMG events in sleep at rates far exceeding chance. Parametric analyses suggest nearly all digitized features make this discrimination well, but classification optimization may favor novel non-linear approaches.

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0951

TOP-DOWN INTEGRATED SLEEP-STATE BIOMARKERS IN PEDIATRIC BRAIN DISORDERS

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Introduction: During non-rapid eye movement (NREM) sleep, the scalp electroencephalogram (EEG) in the 0.5 to 4 Hz (delta) range reflects dynamic changes within cortical activity. The sleep spectrogram is an EEG-independent, electrocardiogram (ECG) - derived method to map the coupling of heart rate variability and respiration-driven ECG-QRS amplitude fluctuations. High frequency coupling (HFC), a proposed cardiopulmonary (CPC) spectrogram biomarker of "effective" sleep, correlates with slow wave power across the night, providing a new metric (Cortico-CPC, a correlation metric) of cortical modulation

of cardiorespiratory coupling. We assessed Cortico-CPC in Down's syndrome, Pervasive Development Disorder, and 15q deletion syndromes, free of sleep apnea.

Methods: Instantaneous delta power (from the C4-A1 EEG) and HFC power (from the polysomnogram ECG) were correlated in 2.1 minute epochs from polysomnograms performed in the target population, at the Children's Hospital, Boston. Age matched control data was available. We analyzed 19, 13 and 6 children with Down's syndrome, PDD and 15q deletion syndrome, aged 6.1 ± 3.8, 8.3 ± 2.3 and 6.4 ± 5.7, respectively.

Results: Normative data shows a clear developmental profile of Cortico-CPC (lowest at birth and peaking at 10-12 years, decreasing to an adult plateau in the 20's); all three conditions had a reduction relative to age-matched subjects. Cortico-CPC was found to be 0.442±0.140 and 0.519±0.128 for healthy children ages 5-6 (n=217) and 10-12 (n=44) respectively, compared with 0.172±0.309 and 0.185±0.225 in Down's syndrome ages 5-6 (n=10) and 8-12 (n=9), 0.279±0.274 and 0.449±0.139 in children with PDD ages 5-6 (n=6) and 8-12 (n=7), and 0.138±0.243 in 2-14 year old children with 15q deletion syndromes (n=6).

Conclusion: Cortico-CPC may be a biomarker of brain health. Poorly integrated cortical and subcortical activity may provide clues to brain development, and the risk of sudden death (in the 15q syndrome).

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0952

RELATIONSHIP BETWEEN THE HIGHER ORDER STATISTICAL FEATURES OF SNORING SOUNDS AND ANTHROPOMETRIC FACTORS OF SNORERS

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Introduction: Snoring sounds have been shown to have non-linear behavior. Higher order statistical (HOS) techniques can reveal non-linear properties of snoring sound (SS) segments. While there are few studies investigating the effect of anthropometric factors on spectral behavior of snoring sounds, there was no study to investigate the effect of anthropometric factors such as age, height, weight, BMI on the non-linear properties of snoring sounds, which is the focus of this study.

Methods: The respiratory sound signals were collected from 30 patients with different levels of airway obstruction by a microphone placed over the subjects' trachea simultaneously with full-night Polysomnography during sleep. The SS segments were identified automatically from respiratory sounds using our recent method. HOS features including skewness, kurtosis, and Mean Peak Frequency (MPF) were estimated from the 15-minute randomly selected SS segments of all subjects. The subjects were also divided into different groups based on their height (G1: <169cm, G2: >179 cm), weight (G1: <85kg, G2: 85~100kg, G3 >100kg), BMI (G1: <30, G2: 30~35, G3: >35), and age (G1: <48, G2:48~53, G3: >53). The effect of anthropometric factors on HOS features was investigated using statistical Analysis of Variance (ANOVA).

Results: Kurtosis and skewness showed significant differences (p<0.05) in different age groups: the higher the age, the smaller kurtosis and the larger skewness. On the other hand, the MPF change was also significant due to height, weight and BMI parameters (p<0.05): the higher of these parameters, the smaller MPF.

Conclusion: It is known that the anatomy of the trachea determines the characteristic features of tracheal sounds. This study confirms the change in HOS features of SS segments due to tracheal anatomy. These results are preliminary and have to be investigated in a larger population for statistical validation. However, the results are encouraging in better understanding the different behavior of airway walls oscillation in different snorers, and are helpful for modeling the snoring sound generation.

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0953

UTILITY OF A RAPID SLEEP SCREENING QUESTIONNAIRE FOR PREDICTION OF OBSTRUCTIVE SLEEP APNEA DIAGNOSED BY POLYSOMNOGRAPHY

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Introduction: The Glidewell Rapid Sleep Screen (GRSS) is a brief questionnaire developed to enable quick, reliable detection of sleep disorders in the primary care setting. Our aim is to determine the utility of the GRSS as a clinical screening tool for Obstructive Sleep Apnea (OSA) by comparing the GRSS impression for OSA to the gold standard of OSA diagnosed using polysomnography (PSG).

Methods: 165 patients presenting to a private diagnostic testing facility completed the GRSS prior to overnight polysomnography for evaluation of suspected OSA. Two diagnostic thresholds were evaluated: Cutoff #1 (AHI ≥5 or RDI ≥15; N=145 OSA, N=20 Non-OSA) and Cutoff #2 (AHI ≥10 or RDI ≥20; N=133 OSA, N=32 Non-OSA). A 3-Item rule composed of snoring, daytime sleepiness, and restful/restorative sleep was used to generate GRSS diagnostic impressions for OSA. Classification statistics were computed with PSG diagnosis as the criterion.

Results: The sample was 72% male with a mean age was 43.5 years old and BMI of 31.1. The mean AHI and RDI were 26.2 and 39.8 respectively. Using cutoff #1, the GRSS correctly classified 76% of cases (Kappa = .180, P = .013) with a sensitivity of .80 and specificity of .45. Positive predictive value (PPV) is .91 and negative predictive value is .24. Using cutoff #2, the GRSS correctly classified 73% of cases (Kappa = .194, P = .013) with a sensitivity of .81 and specificity of .39. Positive predictive value (PPV) is .84 and negative predictive value is .34.

Conclusion: 1) High positive predictive value of the GRSS makes it a useful tool in the primary care setting for selection of cases which may be appropriate for immediate autoPAP trial. 2) However, poor negative predictive value suggests that OSA cannot be ruled out on the basis of the GRSS result and polysomnography may be indicated.

0954

UNOBTRUSIVE MONITORING OF SLEEP APNEA

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Introduction: Sleep apnea occurs in 9 to 24% of the population and is associated with several diseases. Polysomnography (PSG) is performed over a single night in a laboratory and cannot efficiently monitor patients over extended periods of time. We are investigating the use of load cells placed under the supports of a bed to unobtrusively monitor patient respiration and automatically detect sleep apnea unobtrusively in the home.

Methods: We fitted load cells under the supports of one bed in the Oregon Health & Science University Sleep Lab and collected load cell data simultaneously with overnight diagnostic PSG for 15 patients (mean AHI 52.3; range 3.0-155.8). Patient's PSG data were scored in accordance with AASM standards. All episodes of disordered breathing (DB: central apneas, obstructive apneas, hypopneas) and 20 periods of normal breathing (20sec in duration) were identified from the PSG for each patient; corresponding periods were segmented out of the load cell data. A computer algorithm was developed to classify the load cell data segments as normal breathing or DB.

Results: Classifying data from all patients collectively resulted in a sensitivity and specificity for detecting DB of 0.75 and 0.82. However, classification using the normal and DB segments for each subject separately showed improved ability to discriminate normal breathing and DB. The sensitivity and specificity of these subject-specific models were 0.86 and 0.79 on average. Analysis of variance revealed no effects of age, sex,

BMI, weight, or AHI severity on the sensitivity or specificity of the classifications.

Conclusion: Load cells are capable of differentiating disordered breathing events from normal respiration without direct patient contact. Further work is needed to detect events within a continuous collection. This technology could ultimately provide low cost, contact free monitoring for respiratory events over many nights in the comfort of a patient's own bed.

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0955

RELATIONSHIPS BETWEEN HOME POLYSOMNOGRAPHY AND WATCH-PAT MEASURES OF SLEEP DISORDERED BREATHING IN PREGNANCY

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Introduction: Sleep-disordered breathing (SDB) during pregnancy is associated with adverse pregnancy outcomes. However, full overnight polysomnographic (PSG) studies are labor-intensive and challenging to perform in pregnant women, particularly in late gestation. The Watch-PAT device is a simple, wrist-worn device approved for diagnosis of SDB. We examined levels of agreement between key variables obtained from full ambulatory PSG and Watch-PAT in pregnant women.

Methods: Women in their third trimester were recruited from obstetric clinics to undergo full overnight PSG at home using the MediPalm system as well as the Watch-PAT200 device. PSGs from the MediPalm were scored by an experienced technologist using AASM 2007 criteria; the Watch-PAT was scored automatically with its proprietary software.

Results: A total of 17 pregnant women have been studied. Mean age was 30.6±6.5 years and mean BMI was 31.0±7.2 kg/m2. Good correlations were found between the two devices for total sleep time (r=0.91, p<0.001), AHI (r=0.95, p<0.001), respiratory disturbance index (RDI; r=0.92, p<0.001), mean SpO2 (r=0.70, p=0.002), and SpO2 nadir (r=0.79, p<0.001). Paired t-tests showed no significant differences between the MediPalm and Watch-PAT for mean AHI (7.8 vs. 10.6), mean SpO2 (95.8% vs. 95.5%), or SpO2 nadir (90.6% vs. 90.9%). However, total sleep time was longer (342.6 mins vs. 370.1 mins; p=0.01) and RDI higher (8.6 vs. 14.7; p=0.008) when measured by the Watch-PAT. Six of 7 women with a MediPalm AHI>5 had a Watch-PAT AHI>5. However, 7 of 10 women with a MediPalm AHI<5 were found to have a Watch-PAT AHI>5.

Conclusion: These preliminary results suggest that results from the Watch-PAT and full home PSG are similar for key SDB-variables in pregnancy. However, the Watch-PAT may be more sensitive to, or exaggerate, respiratory disturbances.

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0956

ACCURACY OF CPAP-MEASURED APNEA AND HYPOPNEAS

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Introduction: Few studies have specifically examined the accuracy of the apnea-hypopnea index (AHI) as measured by the CPAP unit in the home environment. Given the improved CPAP data transmission technologies and resultant increased use of this data, we sought to investigate the accuracy of the CPAP-measured AHI. We had the opportunity to conduct "CPAP efficacy" studies in which participants wore CPAP simultaneously with Type III cardiopulmonary recording equipment.

Methods: Embletta (Embla, Inc, Broomfield, CO) was directly connected to the ResMed AutoSet S8 (ResMed, Inc., San Diego, CA) via a specialized cable that allowed for the direct recording S8 data. RemLogic software was used for manual respiratory scoring, using the standard AASM criteria for apneas while hypopneas were scored according to the alternative AASM definition (>50% drop in airflow from baseline and >3% desaturation). AutoSet respiratory events were autoscored by the device and summary statistics were provided within RemLogic. Participants from a larger trial of CPAP adherence who had a clinical indication for performing an efficacy study (i.e., either high residual CPAP-measured AHI or subjective report that was inconsistent with CPAP data) were included.

Results: Mean CPAP-scored AHI was 15.1±12 (3.9 - 46.3) and mean manual-scored AHI was 9.9±10.5 (1.2 - 39.3). The main finding was that CPAP-scored HI was 2.55 times higher on average than the manual-scored HI. Further, the CPAP-scored AI was 1.2 times higher and the overall CPAP-scored AHI was 1.9 times higher on average than the manually scored AI and AHI, respectively.

Conclusion: In this sample, CPAP-scored HI was on average more than double the manual-scored HI. Given the importance of CPAP efficacy data in tracking treatment progress, it is important to recognize the possible bias of CPAP in overreporting hypopneas. The most likely cause of this discrepancy is the use of desaturations in manual hypopnea scoring.

0957

A NON-ACOUSTIC MODEL OF SLEEP FRAGMENTATION

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Introduction: Sleep disordered breathing (SDB) causes recurrent partial or total airway occlusion, cyclical hypoxia, and sleep fragmentation. Sleep fragmentation also occurs in insomnia, chronic pain, congestive heart failure, fibromyalgia, rheumatoid arthritis, depression, malignancy, and circadian rhythm disturbances. In humans, acoustic or combined acoustic and sensory stimulation have been used to fragment sleep, models that are labor intensive and pose potential risks (e.g., auditory injury) to subjects. We tested a non-acoustic model of sleep fragmentation to assess efficacy, reproducibility, habituation effects, and autonomic effects.

Methods: A stepwise approach tested the effectiveness of standard non-invasive blood pressure cuffs (inflating at intervals of 1.5-5 minutes to determine the most effective interval) as a method of fragmenting sleep in normal healthy subjects. N = 4 subjects underwent baseline polysomnography (PSG), followed by 3 nights of non-acoustic fragmentation with PSG monitoring for protocol optimization. N = 1 completed psychomotor vigilance testing (PVT) and multiple sleep latency testing (MSLT) before and after fragmentation (3 nights). N = 2 underwent muscle sympathetic nerve activity (MSNA), progressive isocapnic hypoxia (HVR), and measurement of serum catecholamine and cortisol levels pre- and post-fragmentation (3 nights).

Results: In all subjects, our model consistently produced delta EEG bursts, suggesting reproducibility without habituation. EEG bursts correlated with blood pressure cuff inflation, as well as autonomic effects with increased heart rate and absence of nocturnal blood pressure dipping. The degree and length of fragmentation in our study population did not impact vigilance or result in daytime sleepiness (MSLT).

Conclusion: Our sleep fragmentation model may be a practical, reliable, and reproducible method to study the effects of sleep fragmentation. We propose that adaptive mechanisms which prevent effects on vigilance and daytime hypersomnia lead to changes in sympathetic activity, resulting in reversal of nocturnal blood pressure dipping profiles in normal healthy subjects. Longer durations need testing.

0958

COMPARISON OF COMMONLY USED VISUAL ANALOGUE SCALE FORMATS FOR ASSESSING CHANGE IN SLEEP QUALITY

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Introduction: There is no consistent way of assessing sleep quality. It can be estimated from measured variables such as sleep efficiency, from a composite measure such as the LSEQ or rated in its own right. The LSEQ has the advantage of negating the need for a baseline week, as it requires participants to rate their own change from baseline.

Methods: Fifty-four poor sleepers took part in a 3-week placebo controlled dietary intervention study that included a baseline week. Sleep diaries included ratings in different formats; 'How would you rate the quality of your sleep last night?' and 'How would you rate the quality of your sleep last night after using the supplement compared with your usual sleep without the supplement?' (more restless/restful, awake more/less than usual). Paired t-tests and correlations were made between the different question formats averaged over each week.

Results: There was no significant difference between the single rating and the LSEQ composite measure of sleep quality, and correlations were significant at .63 and .73 in week 1 and week 2 respectively. However, when change scores were calculated (week one minus baseline) and compared with the LSEQ composite measure, significant differences were found at week one ($p < .03$) and correlations were somewhat weaker ($r = .54$ and .63 respectively). For a more direct comparison of format, analyses were also performed on single ratings of 'refreshed' and although well correlated ($r = .51$ and .75), scores were significantly different ($p < .003$).

Conclusion: It is suggested that the use of a baseline week would be more suitable for assessing change when participants' baseline sleep is highly variable, as is often the case in those with poor sleep. Participants with poor sleep are likely to find the task of making comparisons to 'usual' sleep difficult as they have more variable sleep than good sleepers.

0959

A WEB-BASED MORNING SLEEP DIARY SYSTEM

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Introduction: Widespread availability of and familiarity with computers and web browsers has enabled collection of data directly from outpatients participating in clinical trials. We describe an interactive, graphical morning sleep diary system with which patients interacted on a daily basis for several weeks in the multicenter Phase 2 clinical trial I2K-MC-ZZAD(b).

Methods: Multiple exemplars of sleep diaries used in past studies were reviewed, and data elements to be collected were chosen. An interactive display of a noon-to-noon timeline was developed, such that as a patient would report on his/her times of study drug ingestion, lights off, sleep onset, final awakening, lights on, alarm set time, and nap start/stop times, the timeline would dynamically update a graphical representation of these events and of when and for how long at time the patient was asleep. Unusual values provided were immediately challenged. Patients indicated their overall sleep quality on a visual analog scale, and answered a Yes/No question, "Did you sleep well last night?" Patients also answered multiple choice questions about their difficulty getting to sleep and returning to sleep after awakenings, their sleep experience, and their feeling upon awakening. Patients were provided with laptops with built-in wireless wide area network connectivity which automatically launched a web browser and connected to the study's web server when powered on, to minimize difficulty for patients with little computer experience. All entries were timestamped.

Results: Compliance with morning diaries was very high. Diary entries were completed quickly by patients, and there was very little missing data. System downtime was minimal. Patients questioned about the morning diary system indicated a high level of comfort and satisfaction with it.

Conclusion: Daily, contemporaneous collection directly from patients of high quality and highly detailed information about sleep was successfully accomplished by a web-based system.

0960

VALIDATION OF AN EXCESSIVE SLEEPINESS DIARY (ESD)

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Introduction: Excessive Sleepiness (ES) is a symptom associated with sleep disorders (e.g. narcolepsy, obstructive sleep apnea), non-sleep disorders (e.g., multiple sclerosis, cancer, depression), and certain occupations. The aim of this study was to characterize measurement properties of a newly developed daily diary designed to assess sleepiness and its impact among patients experiencing ES.

Methods: The Excessive Sleepiness Diary (ESD) is a 16-question, paper-and-pencil self-administered daily diary completed in the evening before going to bed. The ESD assesses experiences related to sleepiness including difficulty staying awake, difficulty concentrating, feeling tired or sleepy, taking naps, and motor vehicle or other accidents or near-accidents. The ESD also collects information on factors that may impact ES, including consumption of caffeinated and alcoholic beverages and cigarettes. The ESD was included in a randomized, double-blind, double-dummy, placebo and active controlled (modafinil 200 mg), 3-period crossover study with 2-week treatment periods to treat ES in patients with obstructive sleep apnea/hypopnea syndrome (OSA/HS), appropriately using nCPAP therapy. Improvement on the Maintenance of Wakefulness Test (MWT) was the primary efficacy endpoint. The Epworth Sleepiness Scale (ESS), SF36, Clinical Global Impression scales (CGI), and Functional Outcomes of Sleep Questionnaire (FOSQ) were included. The data from this study were used to assess the psychometric properties of the ESD.

Results: 125 patients were enrolled. Factor analysis of the ESD items supported combining the items into a total ES score. Test-retest reliability (ICC) coefficients of the single items and total score ranged from 0.4 to 0.7. Cross-sectional and longitudinal construct validity of the ESD was supported by moderate correlations ($r > 0.5$) with other measures included in the study. The ESD was able to distinguish severity groups by level of ES as measured by ESS and CGI ($p<0.05$).

Conclusion: Results support the reliability and construct validity of the ESD.

0961

VALIDATION OF THE SLEEP DISORDERS SCREENING QUESTIONNAIRE

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Introduction: According to the National Sleep Foundation, 11-14% of Americans are at risk for insomnia, restless legs syndrome and/or obstructive sleep apnea; yet sleep disorders are widely under diagnosed. To address this problem, a Sleep Disorders Questionnaire (SDQ) was developed for use in primary care practice.

Methods: To test the psychometric properties of the SDQ, 413 subjects underwent overnight polysomnography (PSG) for diagnostic purposes after filling out the Sleep Disorders Screening Questionnaire (SDQ), the Multidimensional Fatigue Inventory (MFI) or the Fatigue Severity Scale and the Epworth Sleepiness Scale (ESS). Sleep diagnoses were derived from clinical interview and PSG findings using AASM diagnosis criteria for insomnia, obstructive sleep apnea, central sleep apnea, restless legs syndrome and narcolepsy. The SDQ was evaluated using Principal Component Factor Analysis with Varimax rotation, Pearson's correlations using SPSS (version 18). SDQ subscales were extracted, assessed for face validity, and then correlated with categorical outcomes representing specific sleep diagnoses.

Results: 413 subjects (47% female), ages 18-83 (M 49), BMI 18-72 (M 35), ESS 0-24 (M11), MFI subscales General Fatigue M15.5, Physical Fatigue M12.4, Reduced Activity M10.6, Reduced Motivation 10.3, Mental Fatigue 11.7. Sleep Diagnosis: OSA (n=357), CSA (n=3), RLS (n=28), Insomnia (n=81), Narcolepsy (n=5). Principle Component Analysis extracted five subscales that accounted for 57.66% of variance. Pearson correlation between SDQ subscales and diagnosis categories is as follows: Subscale 1 - Insomnia (r = .379, p. = .000); Subscale 2 - Narcolepsy (r = .112, p. = .02); Subscale 3 - OSA (r = .105, p. = .03); Subscale 4 - RLS (r = .367, p. = .000).

Conclusion: The Sleep Disorders Screening Questionnaire shows some preliminary promise as a screening tool for the major sleep disorders. Subscales are correlated with matching diagnosis. Further work is ongoing to establish other psychometric properties of the SDQ.

0962

INCLUSIVE MULTIPLE IMPUTATION FOR MISSING DATA IN A VA LONGITUDINAL TRIAL ASSESSING COGNITIVE BEHAVIORAL THERAPY IN PATIENTS WITH SLEEP DISORDERS

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Introduction: We describe and implement an inclusive multiple imputation (MI) strategy for handling missing data in a randomized trial examining sleep outcomes. This strategy is compared with last observation carried forward (LOCF), a commonly used, single imputation strategy.

Methods: Eighty-one veterans with chronic primary or comorbid insomnia were randomized to receive cognitive behavioral therapy (CBT) or sleep hygiene (SH). Sleep measures, including the Pittsburgh Sleep Quality Index (PSQI) and Dysfunctional Attitudes and Beliefs About Sleep Scale (DBAS), were assessed at baseline, post-treatment, and follow-up. Markov chain Monte Carlo methods were used to create multiply-imputed datasets of the sleep measures at all time points. Auxiliary variables predicting dropout were included in the imputation model. General linear models were fit to analyze the treatment effect of CBT compared to SH over time.

Results: Approximately 19% (n=15) of the sample was lost to attrition with most dropout occurring before post-treatment. Dropout predictors included insomnia type, therapist, medication use, comorbidities, age, and full-time employment. Model-based standard errors (SE) with LOCF were smaller than MI for all outcomes. Subjects randomized to CBT had greater PSQI improvement at post-treatment compared to SH using LOCF (-1.6, 95% CI:-3.1, -0.1; p=0.04); in contrast, MI results were not statistically significant (-1.3; 95% CI:-2.8, 0.2; p=0.09). However, CBT subjects had greater DBAS baseline to post-treatment improvement compared to SH when using MI (-10.3; 95% CI:-20.2, -0.4; p=0.04); LOCF results were not statistically significant (-6.8, 95% CI:-15.0, 1.4; p=0.10).

Conclusion: Methodologies for accommodating missing data can produce different results with regard to both direction and strength of treatment effects. LOCF typically underestimates SE by not accounting for the uncertainty attributable to missing data. MI provides a framework to incorporate information from auxiliary variables predicting dropout while preserving a parsimonious main treatment effect model, as well as appropriately estimating SE.

0963

SLEEP DISORDERED BREATHING IN INSOMNIA PATIENTS RECOGNIZED BY ECG ANALYSIS

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Introduction: Baseline recordings in insomnia patients in a sleep laboratory are conducted in order to quantify the extend of insomnia in terms of sleep efficiency and sleep onset latency. In addition the sleep study is used to exclude other sleep disorders which may occur together with primary insomnia.

Methods: We investigated 64 patients with insomnia with cardiorespiratory polysomnography in our sleep center. Sleep stages, arousal and respiratory events were scored according to AASM criteria by an experienced sleep technician. Recorded ECG was analyzed by a software (Hypnocore) which could provide a sleep evaluation and a respiratory event score by a new automated analysis (denoted as ECG). All patients were analyzed first. A second analysis was performed on 54 patients after removing subjects with bad signal quality, arrhythmias and a total sleep time below 3 hours.

Results: The analysis of respiratory events based on ECG in the group of 64 subjects resulted in 52 subjects (48 true negative, 4 false negative) with an RDI≤5/h. 12 subjects (10 true positive, 2 false positive) were scored with an RDI>5/h. Agreement was 0.91. For the second analysis agreement remained the same. Sleep stages in the second analysis were scored surprisingly good: 48.9% (ECG) vs. 48.7% (PSG) for light sleep, 15.7% (ECG) vs. 15.8% (PSG) for slow wave sleep, 14.0% (ECG) vs. 23.4% (PSG) for wake, and 19.9% (ECG) vs. 12.2% (PSG) for REM sleep. Sleep efficiency was 84% (ECG) vs. 77% (PSG).

Conclusion: Not too many respiratory events occur in insomnia patients. These events are detected with a sufficient accuracy. Agreement for classification of subjects is adequate. Sleep stage analysis based on ECG reveals the very good ability to distinguish light sleep, slow wave sleep, and wake / REM sleep. To distinguish wake and REM sleep by ECG alone is possible moderately. The biggest effect of this uncertainty is apparent in sleep efficiency. To distinuish wake and REM cannot be perfect due to high sympathetic activity in both states.

0964
ACTIGRAPHY RELIABILITY
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Introduction: Actigraphy has gained popularity as an objective method for measuring sleep in a home setting. We evaluated whether missing data affects the utility of actigraphy for the measurement of sleep parameters in normal sleepers.

Methods: We evaluated actigraphy data from 60 normal sleepers who participated in a study of setting changes effects on sleep. The sample was composed of 26 males and 34 females ranging in age from 35 to 65 years with a mean age of 47.7 . Participants were asked to wear a Mini Mitter Actiwatch actigraph for 35 days and to use event markers to record bedtime and arising time. Participants also completed sleep diaries during this assessment period. Counts of nights on which participants failed to supply actigraphy data were computed using the following criteria: missing nights, missing bedtime markers, missing arising time markers, and multiple markers supplied at bedtime or arising time. A night on which any of these problems occurred was counted as unscorable.

Results: We evaluated a total of 2100 nights. We deemed 559 (27%) nights unscorable due to missing data. Missing markers at bedtime (206) and arising time (172) accounted for the majority of missing data. Trends over the five weeks indicated that incidence of missing data increased over the assessment period. During the first week 20% of nights were unscorable, whereas 37% of nights during the fifth week were unscorable. Additionally, we evaluated nights deemed unscorable on sleep diaries as a benchmark comparison for the actigraphy data.

Conclusion: We found that missing data was a significant problem for long-term assessment of sleep using actigraphy. These findings highlight the importance of using adjunctive measures of bedtime and arising times, such as sleep diaries, to avoid data loss when using actigraphy.

0965
ACTIGRAPHY AS INPUT TO A CIRCADIAN LIGHT MODEL PREDICTS RELATIVE IMPACT OF BRIGHT LIGHT AND SLEEP SCHEDULE ON CIRCADIAN PHASE DURING A SIMULATED SHIFT-WORK PROTOCOL
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Introduction: Estimating circadian misalignment during shift-work is of interest for both workers and managers for predicting times of poor performance/alertness and the need for countermeasures, but measuring circadian markers can be invasive. We tested the ability to predict the effect of simulated shift-work and scheduled light interventions on circadian phase when using actigraphy recordings as input to a model of the effect of light on circadian phase.

Methods: Actigraphy data were collected from 42 subjects divided into four treatment groups created by crossing Bright Light (~ 2500 lux for 6 hours) vs. Room Light (150 lux) and Fixed vs. Free sleep factors (Horowitz et al Am.J.Physiol. 2001). We estimated endogenous circadian phase for each subject using actigraphy (activity and light levels measured at the wrist) validated with sleep wake logs as an input to a mathematical model of the effects of light on the circadian pacemaker [Jewett et al J Biol. Rhythms 1999). Data were analyzed with a 2x2 ANOVA.

Results: The light levels recorded at the wrist during the Bright light condition were much less than the target light levels recorded at eye level. Using actigraphy data, the average (± standard deviation) predicted phase shifts for the Bright-Fixed, Bright-Free, Room-Fixed, and Room-Free groups were 2.3 (±1.0), 1.5(± 1.4), 0.6(± 0.3), and 0.1 (± 1.0) hours, respectively. Both Bright light (1.6 hours [$F_{(1,42)} = 26.461$, $P < 0.0001$]) and a Fixed sleep schedule (0.6 hours [$F_{(1,42)} = 4.231$, $P < 0.05$]) conditions had statistically significant phase delays. There was no interaction [$F_{(1,42)} < 1$] between the factors. While the magnitudes of predicted phase shifts were smaller than in the published data, the overall pattern in predicted phase shifts across groups was the same as what was observed experimentally.

Conclusion: Estimating circadian phase in a shift-work protocol using actigraphy and a mathematical model provides group estimates of circadian phase that can be used to compare schedules as well as to select lighting interventions. Our results suggest that our methods could be used to estimate the relative effect of interventions in field studies and operational setting.

0966
COMPARISON OF AMBULATORY ACTIGRAPHY AND SLEEP/WAKE DIARY INPUT TO A CIRCADIAN-LIGHT MODEL FOR PREDICTING CIRCADIAN PHASE
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Introduction: Assessment of endogenous circadian phase is important for predicting performance and alertness and for the timing of countermeasures, including light and pharmaceuticals. Actigraphy data collected in operational settings have not been regularly used to estimate circadian phase. We investigated the ability to estimate circadian phase from actigraphy data input to Circadian Performance Simulation Software (CPSS), which is based on a published model of the effect of light on circadian phase [Jewett et al. J Biol. Rhythms 1999].

Methods: Actigraphy (activity and light) data were collected from the non-dominant wrist of 62 healthy subjects while they maintained a regular schedule and kept a sleep diary at home for one week immediately prior to admission to our research facility. The output of the Respironics Actiware Software ver. 5 on these actigraphy data and the subjective sleep/wake logs were separately input to CPSS to estimate circadian phase. Circadian phase was assessed using the dim light melatonin onset (10 pg/mL crossing) on the first admission day.

Results: There were statistically significant linear relationships between CPSS predictions from actigraphy and sleep/wake logs (independent variables) and melatonin phase (dependent variable), with slopes of 0.76 hr/hr and 0.83 hr/hr, respectively. The R^2 values from the linear regressions were 0.46 and 0.52. The CPSS predictions were within ±1.5 hour of the melatonin phase 77% and 76% of the time.

Conclusion: We conclude that (1) circadian phase in healthy, entrained adults can be estimated using outpatient actigraphy data as an input to CPSS; (2) outpatient actigraphy and sleep/wake logs from healthy, entrained adults may be equally reliable inputs; and (3) actigraphy may provide an approach to automating the estimation of circadian phase in operational settings. Further investigation is needed to determine if accuracy of phase estimation may be enhanced by using additional subject-specific inputs to complement actigraphy data.

0967

THE ROLE OF ACTIGRAPHY AND A SLEEP DIARY IN CPAP ADHERENCE

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Introduction: The topic of CPAP adherence is of continual clinical relevance. Various studies have tried to assess variables that may predict or influence adherence with CPAP therapy. Actigraphy and sleep diaries are common tools used to gather ambulatory sleep patterns, but limited data have been presented on the benefits of these tools in reporting adherence patterns. The goal of the present study was to assess the relationship between CPAP usage patterns and actigraphy/sleep diary data.

Methods: Data was used from a prior study assessing adherence with various treatment modalities. As part of that study, actigraphy, sleep diary, and treatment adherence was measured daily. Each day with matching and complete variables was used as a data point for analysis.

Results: A total of 333 days with complete data sets were used for analysis. CPAP adherence significantly correlated with actigraphy variables of TIB (p< .001), TST (p< .001), WASO (p< .05), and Fragmentation Index (p< .001). However, only the Fragmentation Index was significantly correlated to diary estimates of CPAP use (p< .001). Using actigraphy and diary variables as predictors for CPAP adherence, the variables of diary TST and actigraphy TST entered the predictive model and accounted for 12% of the variance (F= 20.691, p< .001). Comparing compliant vs. non-compliant CPAP users (> 240 min/nt), the non-compliant users drastically overestimate usage (diary: 305.2 min vs. actual 87.1 min) whereas the compliant users more accurately estimate their usage (diary: 374.1 min vs. actual 375.1 min). Actigraphy may also be a beneficial tool for assessing treatment adherence, as non-compliant users had a significantly higher WASO and Fragmentation Index and lower TST than the compliant users (all p< .05).

Conclusion: There are a variety of factors involved in CPAP adherence, and it can be challenging to clinicians to fully assess and understand adherence patterns. Actigraphy and sleep diary collection while on CPAP may be a beneficial tool to understanding this process. Specifically, the fragmentation index may give insight to either non-use or unresolved sleep disruptions that may be factors tied to treatment use.

0968

DIRECT ACTIVITY MEASURES ARE USEFUL ACTIGRAPHY ENDPOINTS FOR DETECTING DIFFERENCES IN SLEEP AND DAYTIME ACTIVITY AMONG DIFFERENT PATIENT POPULATIONS

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Introduction: Actigraphy helps diagnose sleep problems in patients, but clinical studies require objective endpoints that quantify sleep and daytime activity. An algorithm is typically used to identify "sleep" vs. "awake" periods allowing endpoints such as total sleep time (aTST) and sleep efficiency (aEff) to be derived. Alternatively, activity counts can be used to calculate direct activity endpoints. This study assessed direct activity and derived endpoints in different populations.

Methods: A Bodymedia Armband was worn day and night (3-21 days) by 38 healthy volunteers (HV), 66 fibromyalgia (FM) patients, and 15 obese subjects. 24 patients with Restless Leg Syndrome (RLS) wore the armband for 2-5 nights. All patient data are from the placebo-arm of clinical trials. A program calculated derived (aTST [mins], aEff [%]) and direct activity endpoints (mean, 75th, 90th percentiles during sleep, and mean, 10th, 25th percentiles during daytime). Percentiles were based on patient's distribution of recorded activity (counts/min). Data are mean±s.e.

Results: Compared with HV (415.0±10.4), aTST (mins) was unchanged in FM (419.2±10.3), increased in obese (477.0±17.9;P<0.04), and decreased in RLS (348.9±18.2;P<0.04) patients. aEff (%) was decreased in all patient groups (FM: 90.7±0.4; obese: 90.4±0.7; RLS: 88.7±1.1) vs. HV (92.3±0.4;all P<0.04). Mean sleep activity was higher in patients (FM: 16.4±1.2; obese: 16.1±1.3; RLS: 18.5±1.9) vs. HV (12.2±0.7;all P<0.04). 75th percentile sleep activity was elevated in obese (11.8±2.0) and RLS (16.2±2.2) vs. HV (7.4±0.7;both P<0.04); 90th percentile was elevated in all patient groups (FM: 43.3±3.5; obese: 40.6±3.9; RLS: 47.9±6.9) vs. HV (29.3±2.2;all P<0.04). All daytime activity endpoints were lower in FM and obese cohorts vs. HV.

Conclusion: Direct activity and derived endpoints were significantly different in patient populations compared with healthy subjects. This finding, along with the advantages associated with direct activity endpoints, may promote use and acceptance of actigraphy in clinical investigations.

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0969

FUNCTIONAL DATA ANALYSIS OF ACTIGRAPHY REVEALS SUBJECTIVE SLEEPINESS DOES NOT CORRELATE WITH REDUCED ACTIVITY

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Introduction: : Daytime sleepiness and fatigue are frequent complaints that bring many patients to the attention of sleep physicians. The Epworth Sleepiness Scale (ESS) is a commonly used tool to assess the patient's subjective sleepiness. Actigraphy is an inexpensive but sensitive and accurate method to evaluate circadian patterns of activity and behavior. Here, we examine the relationship between subjective sleepiness and objective activity levels as measured by actigraphy. We use the actigraphy data, not simply to determine if the patients are awake or asleep, but to evaluate the level of activity on a continuous basis.

Methods: Patients were invited to participate in an actigraphy study at the initial consultation visit. There were over 160 participants that volunteered to complete a variety of sleep related questionnaires and to undergo actigraphy recording. In addition, most underwent an overnight polysomnogram. Actigraphy data was collected on average for 7 days recording data at 15 second intervals and analyzed using Functional Linear Models Analysis (functional LM).

Results: Surprisingly, increased values of sleepiness from the ESS do not correlate with reduced activity as measured by actigraphy. In fact, there is a clear trend toward increased activity with increased sleepiness in a dose-dependent manner, though this does not reach statistical significance.

Conclusion: The relationship between subjective sleepiness and activity is not straightforward. Perhaps patients are more active to combat sleepiness or perhaps increased activity leads to increased sleepiness. Functional data analysis is a new useful tool for analyzing and extracting more information from actigraphy data. Further research is warranted utilizing this novel statistical method for actigraphy analysis of circadian activity and subjective sleepiness.

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0970

FUNCTIONAL DATA ANALYSIS OF ACTIGRAPHY REVEALS THAT AHI AND BMI IMPACT CIRCADIAN ACTIVITY

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Introduction: Actigraphy is used extensively in sleep medicine to record movements and assess sleep/wake patterns. Analysis of this data often reduces this time series data to a single summary statistic (eg, total sleep time) and comparing those values across groups. We introduce more powerful functional data analysis (FDA) methods for analyzing circadian activity patterns of patients categorized according to apnea-hypopnea index (AHI) and body mass index (BMI), age and gender.

Methods: 138 patients having PSG volunteered to undergo 7 days of actigraphy recording. Actigraphy data was collected at 15 second intervals and converted to functional data activity profiles over time. Functional Linear Models, a subset of FDA, was used to correlate circadian activity patterns with AHI, BMI, age and gender.

Results: Circadian activity pattern differences are seen across high and low AHI and BMI patient subgroups, and showed statistically significant different throughout different times of the day. When analyzed jointly in combination with age and gender, high AHI results in low activity from 10 am - 6 pm, independent of BMI, and high BMI results in low activity between midnight and 10 am, independent of AHI.

Conclusion: Functional data analysis is a new statistical tool for analyzing and extracting more information from actigraphy data than is currently extracted with data reduction techniques. Unexpected patterns of actigraphy across clinically important subgroups were discovered. Further research and application of FDA statistical approaches for actigraphy analysis could have important consequences for understanding how sleep disturbances impact activity, fatigue, and treatment response.

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0971

FUNCTIONAL DATA ANALYSIS OF ACTIGRAPHY SHOWS PERIODIC LIMB MOVEMENTS IMPACT DAYTIME ACTIVITY LEVELS

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Introduction: Periodic limb movements of sleep (PLMS) can disrupt sleep leading to daytime fatigue. It is unknown whether PLMS, or associated arousals, objectively affect daytime function. We used functional data analysis (FDA), a recently-developed statistical method for actigraphy, to assess the effect of PLMS on 24-hour activity.

Methods: Subjects from the Washington University Sleep Center underwent wrist actigraphy for 7 days. PLMS index (PLMI) and PLMS arousal index (PLMAI) were scored during an overnight polysomnogram. Subjects were grouped into those with PLMI of 0, and the rest into quintiles; PLMAI groups were assigned identically. FDA was used to derive functions describing the activity level of each group. Age, gender, apnea-hypopnea index, and body mass index were added into FDA.

Results: Of 155 subjects (female 52.6%, median age 52.5), 63.2% had PLMI 0, and the rest had PLMI quintiles 0.3-3.1, 3.1-6.8, 6.8-16.1, 16.1-

38.5, and 38.5-120.4. With each quintile increase in PLMI, morning activity increased, and afternoon-evening activity decreased (statistically significant ~6:30-7pm). PLMAI was 0 in 68.4%, and similar analysis showed each PLMAI quintile increase was associated with increased activity in the morning and decreased activity at all other times (statistically significant 6am-12pm, 1pm-3am). Younger (<52.5years) and female groups had robustly-increased activity compared to older and male groups. However, in all age and gender groups, increasing PLMI and PLMAI was associated with decreased evening activity in a "dose-dependent" manner. Neither PLMI nor PLMAI were significantly correlated with apnea-hypopnea index (Pearson r -0.113, -0.117).

Conclusion: PLMS are associated with decreased activity in the evening in a "dose-dependent" fashion. FDA of actigraphy offers an objective method of assessing the effect of PLMS on daytime function, and may be helpful in defining a normal range for PLMI and PLMAI for use in clinical practice.

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0972

FUNCTIONAL DATA ANALYSIS OF ACTIGRAPHY REVEALS THAT SSI AND ISI IMPACT NIGHT ACTIVITY

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Introduction: We reported that insomnia is associated with suicidal ideation during clinical trials. We are testing the hypothesis that suicidal ideation in depressed patients with insomnia is associated with increased motor activity during nighttime compared to patients with no suicidal ideation. Actigraphy is used to record movements and assess sleep/wake patterns and can allow us to test this hypothesis. Functional data analysis methods for analyzing night activity patterns have provided support for this hypothesis.

Methods: 58 participants with depression and insomnia were recruited for an 8 week randomized trial for treatment of insomnia. As part of this study, subjects wore actigraphs for 8 weeks and completed Beck Scale for Suicide Ideation (SSI) and Insomnia Severity Index (ISI) surveys at their first visit. Actigraphy data was collected at 30 second intervals and converted to functional data activity profiles over time. Functional Principle Component Analysis (FPCA), a subset of FDA, was used to correlate week 1 night activity patterns with week 1 SSI and ISI scores.

Results: Night activity pattern differences are seen across different groups. Larger variability for low SSI group (SSI <1) occurred from 10 pm to 2 am, but for the high suicidal ideation group (SSI >=1), larger variability and higher activity values occurred from midnight to 2 am. Overall, higher variability and activity were seen in the patients with increased suicidal ideation. Variability for the moderate insomnia group (ISI 15-21) happened from 10 pm to 4 am, but severe insomnia group (ISI 22-28) has greater variability and higher activity values from 2 am to 6 am.

Conclusion: Different nighttime activity patterns in depressed insomnia patients with high suicidal ideation were discovered using functional data analysis. These results suggest the hypothesis of increased nighttime activity in high suicidal ideation patients may be real. Further analysis will be conducted.

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0973

FUNCTIONAL DATA ANALYSIS OF ACTIGRAPHY REVEALS THAT DEPRESSIVE SYMPTOMS IMPACT CIRCADIAN ACTIVITY

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Introduction: Depression is commonly seen in individuals with insomnia, obstructive sleep apnea, restless legs syndrome, and hypersomnia. Studies suggest that treatment of the sleep disorder leads to a decrease in depressive symptoms. In this study, we will examine the interaction between depression and activity levels.

Methods: Patients were invited to participate in an actigraphy study at the initial consultation visit. There were 163 participants that volunteered to complete a variety of sleep related questionnaires and to undergo 7 days of actigraphy recording. Participants completed the Patient Health Questionnaire (PHQ-9) to assess depressive symptoms. Actigraphy data was collected at 15 second intervals and analyzed using Functional Linear Models Analysis (functional LM).

Results: Participants scores on the PHQ-9 were categorized into 5 groups: normal (0-4), minimal (5-9), moderate (15-19), and severe (20-27). The depression scores were distributed as follows: 34% normal, 31% minimal, 19% mild, 11% moderate, and 4% severe. Actigraphy analysis reveals that PHQ-9 scores have a significant effect on nighttime circadian activity.

Conclusion: Actigraphy is a useful tool for detecting circadian variations between depressed and non-depressed patients. Functional data analysis is a new useful tool for analyzing and extracting more information from actigraphy data. Further research is warranted utilizing this novel statistical method for actigraphy analysis of circadian activity and depressive symptom correlates.

0974

COMPARISON BETWEEN ACTIGRAPHY, POLYSOMNOGRAPHY AND SLEEP DIARY IN INDIVIDUALS WITH BIPOLAR DISORDER AND HEALTHY CONTROLS

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Introduction: Bipolar disorder is an illness characterized by sleep and circadian disturbance, with changes in sleep often preceding a mood episode. Actigraphy may be an important clinical and research tool for monitoring sleep changes in this population, but has not yet been systematically validated against polysomnography or sleep diary. The present study compares actigraphy, polysomnography and sleep diary estimates of sleep onset latency, wake after sleep onset, number of awakenings, total sleep time and sleep efficiency across two nights of assessment.

Methods: Twenty-seven individuals who met diagnostic criteria for bipolar disorder type I or II and were currently between mood episodes, along with 27 matched controls with no history of psychopathology or sleep disturbance, underwent two nights of laboratory monitoring via polysomnography, actigraphy (Actiwatch AW-64), and sleep diary. The total sample included 108 comparison nights.

Results: Sleep parameter estimates from actigraphy and polysomnography did not differ between the two groups or across the two nights for sleep onset latency, wake after sleep onset, number of awakenings, total sleep time or sleep efficiency percentage. Parameter estimates were highly correlated ($.49 \leq r \leq .92$) with the exception of a modest cor-

relation observed for SOL ($r = .33$). Estimates between actigraphy and sleep diary were more variable, with actigraphy underestimating sleep onset latency ($p < .001$) and overestimating number of awakenings ($p < .001$) when compared to sleep diaries. Bland-Altman plots of all sleep parameters suggested the medium wake threshold algorithm in the actigraphy software was the most concordant with polysomnography and diaries across the five sleep parameters. Concordance between actigraphy, polysomnography and sleep diary was unrelated to insomnia presence or medication use.

Conclusion: Actigraphy is a valid tool for measuring sleep length and fragmentation in bipolar disorder, and demonstrates particularly favorable concordance with polysomnography in this population.

0975

PATIENTS WITH SLEEP COMPLAINTS UTILIZE MORE HEALTHCARE: AN ANALYSIS OF NHANES

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Introduction: The relationship between sleep complaints and healthcare utilization has not been rigorously evaluated. We explore this relationship within a nationally-representative sample.

Methods: Multivariate analysis of randomly-selected US adult residents (n=2183) participating in the National Health and Nutrition Examination Survey (NHANES; 2005-2006).

Results: 99% of US adults report at least one sleep-related complaint occurring five or more times per month including nonrestorative sleep (56%), not enough sleep (54%), snoring (46%), daytime sleepiness (45%), waking too early (44%) and trouble falling asleep (37%). On average, most respondents reported four or more concomitant complaints (mean 4.2), but only 24% had told a healthcare provider they had trouble sleeping. All assessed medical non-sleep comorbidities (e.g. diabetes) and complaints (e.g. arthritis pain) were associated with having reported trouble sleeping. Although 37% of respondents were at risk for insomnia and 33% for sleep apnea, few had a prior diagnosis (1% and 5% respectively). In univariate analysis, most sleep complaints and disorders were associated with increased healthcare utilization. In multivariate risk adjusted models, subjects who reported trouble sleeping had higher healthcare utilization and work absenteeism including number of healthcare visits (OR 3.1, p<0.001), overnight hospitalizations (OR 2.8, p=0.004), evaluations by a mental health provider (OR 4.9, p<0.001) and missing ≥6 days of work due to illness (OR 2.4, p<0.001). This association remained significant for most measures when controlling for number of hours slept or the presence of sleep apnea or insomnia.

Conclusion: Sleep complaints are highly prevalent and are associated with increased healthcare utilization. However, sleep disorders such as insomnia and sleep apnea appear to be highly under-diagnosed. Healthcare providers should routinely assess for the presence and etiology of sleep complaints and disorders in their patients and asking, "Do you have trouble sleeping?" may be a time efficient screening tool to target more extensive evaluations.

0976

SCREENING APPLICANTS FOR PROFESSIONAL DRIVING LICENSE FOR SLEEP DISORDERED BREATHING

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Introduction: Patients suffering from sleep disordered breathing (SDB) have a substantial risk of being involved in motor vehicle accidents. In Israel applicants for professional driving license, usually 20-30 years old, undergo a detailed medical examination but are not screened for SDB. The present study aimed at developing and validating a screening questionnaire to suspect SDB in healthy applicants for a professional driving license.

Methods: 301 applicants for a professional driving license were approached to participate and 204 completed the study (Mean Age: 7 ± 28.8; BMI 25.4 :± 4.1; 38% Jewish and 62% Arab). They filled out the 10 item mini sleep questionnaire (MSQ), ESS, PSQI, and sleep habits / demographic questionnaires, and their sleep was investigated for one night in the home utilizing the WatchPAT (WP) (Itamar-medical LTD, Caesarea, Israel). Statistical analysis included: Classification and Re-

gression Trees (CART) and Multiple Logistic Analysis (MLA) which were used to select the items that predict clinically significant SDB.

Results: Based on the respiratory disturbance index (RDI) from the WP participants were divided in 2 groups: clinically significant SDB (RDI≥15) 25%, and no SDB (RDI<15) 75%. The CART and MLA analyses identified the following items as significant predictors of clinically significant SDB: age, BMI, the total sum of the MSQ-questionnaire, smoking, a snoring father, taking an afternoon rest, and a report on falling asleep while traveling (not driving). Using these variables 70% of the applicants with clinically significant SDB were successfully identified in comparison with 17% misclassification of healthy participants.

Conclusion: Age, BMI, total score of the MSQ, smoking, family history and taking afternoon nap predict objective SDB in young professional driving license candidates. The WatchPAT ambulatory diagnostic device is a convenient tool to diagnose SDB in this group, diagnosing 25% with SDB in the current cohort.

0977

HEALTH AND SAFETY ON NIGHT SHIFT: A CANADIAN NATIONAL SURVEY OF CRITICAL CARE NURSES

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Introduction: Critical care is a demanding environment requiring nurses to attend to seriously ill patients and engage in rapid decision-making around the clock. Nurses working night shifts experience sleep deprivation, sleep disturbance, and fatigue contributing to patient safety issues and impaired health and injury for nurses. The magnitude of this occupational health and safety concern is gaining recognition. This report provides national data from critical care nurses' perspectives on nurse health and nurse and patient safety related to working night shift.

Methods: Following ethical and access approval, a national, web-based survey of staff nurse/charge nurse members of the Canadian Association of Critical Care Nurses was conducted. The 62-item survey contained closed and open-ended questions on nurses' perceptions of symptoms experienced during night shift, sleep health (work/non-work days), napping practices and impact, nurse and patient safety during night shift, and nurse safety on the drive home.

Results: Respondents included 536 staff/charge critical care nurses (88% female; mean age 42 years ± 9.8), from 11/13 provinces and territories. Most nurses were experienced in critical care (66% ≥ 6 years), and worked full-time (75%) in a tertiary hospital (65%). Symptoms on night shift included fatigue, irritability, forgetfulness, stress, chills, nausea, and eye strain. Nurses slept fairly or poorly during the work day (66%) for ≤ 6 hours (72%). Sixty-six percent usually napped during break; 30% reported their care was safer post-nap. Nurses reported fatigue-related personal work injuries/near injuries (26%), patient safety incidents (16%), and accidents/near accidents on the drive home (20%).

Conclusion: Night shift work is a challenging reality for nurses caring for critically ill patients. This national survey identified a number of health and safety concerns for critical care nurses and their patients. The findings will help target effective national occupational health strategies and make their implementation a priority.

0978

IMPACT OF EXTENDED-DURATION SHIFTS ON MOTOR VEHICLE CRASHES, MEDICAL ERRORS AND ADVERSE EVENTS IN PGY 2-7 RESIDENT PHYSICIANS

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Introduction: The Harvard Work Hours, Health and Safety Group has established that extended-duration (greater than or equal to 24 hours) work shifts, which have been a hallmark of medical education, are associated with higher risks of motor vehicle crashes, medical errors and adverse events among resident physicians in postgraduate year one (PGY-1). Here we report these safety outcomes in resident physicians in postgraduate years 2-7 (PGY 2-7).

Methods: We conducted a nationwide web-based survey over 5 years and gathered 13,737 person-months of data from PGY 2-7 resident physicians. 94% of these data were collected following the introduction of work-hour guidelines established by the Accreditation Council for Graduate Medical Education (ACGME) in July, 2003.

Results: In 46% of person-months, PGY 2-7 physicians reported their longest work shift was greater than or equal to 24 hours. The risk of a reported motor vehicle crash and near-miss incident was significantly increased after an extended duration work shift as compared with a shift that was not of extended duration (OR: 1.72; 95% CI: 1.01-2.90 and OR: 5.13; 95% CI: 4.40-5.96, respectively). The risk of reporting a fatigue-related error was significantly increased in months including 1-4 extended shifts (OR: 1.77, 95% CI: 1.27-2.47) or 5 or more extended shifts (OR: 5.2; 95% CI: 3.79-7.1), as compared to months including no extended shifts. Risk of reporting a fatigue-related adverse events in which a patient was injured was significantly increased in months including 1-4 extended shifts (OR: 2.53; 95% CI: 1.02-6.25) or 5 or more extended shifts (OR: 3.36; 95% CI: 1.52-7.41), as compared to months including no extended shifts.

Conclusion: Extended duration work shifts are a major risk factor for PGY 2-7 resident physicians and their patients. These data suggest that the ACGME should consider extending its recently-announced 16-hour work-hour limit for PGY1 resident physicians to PGY2-7 resident physicians as well.

0979

THEORY OF PLANNED BEHAVIOR AS A PREDICTOR OF SLEEP HYGIENE AND SLEEP QUALITY

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Introduction: The theory of planned behavior (TPB) suggests the importance of three independent considerations: attitude or value regarding the importance of sleep, perceptions of subjective norms or social support, and perceived behavioral control or self-efficacy. These considerations may be factors related to sleep hygiene behaviors and sleep quality. The objective of the present study was to examine associations among sleep hygiene and quality with public attitudes regarding the importance of sleep, perceived social support, and levels of health self-efficacy.

Methods: Men and women primarily from a Midwest metropolitan area and between the ages of 18-65 years completed an online survey. The survey included demographics, sleep hygiene (SH) measure, Pittsburgh Sleep Quality Index (PSQI), Health Associations Scale (HAS), Value on Health Scale (VHS), Social Support Scale, and the Perceived Health Competence Scale (PHCS). The HAS assesses health attitude by associating health indicators with outcomes. Measures related to the components of TPB were regressed on sleep hygiene and quality measures.

Results: A total of 232 surveys were completed. Of the eight health indicators on the HAS, poor sleep was on average the fourth most significant (rank 1-8, mean rank = 4.26), behind stress, diet, and exercise. The health outcome of insomnia ranked sixth of nine outcomes (rank 1-9, mean rank = 6.15), suggesting poor sleep does not rank high according to personal importance of health outcomes. Using a stepwise regression, the VHS (F= 21.25, p< .001), the PHCS (F= 15.08, p< .001), and the HAS Sleep item (F= 11.74, p< .001) all entered the model to predict sleep hygiene and accounted for 14% of the variance. For sleep quality, only the PHCS entered the model (F= 18.83, p< .001) and accounted for 8% of the variance.

Conclusion: As measured by the HAS, attitudes about health indicators and outcomes generally undervalue sleep as a leading cause of negative health outcomes. Lower value placed on one's health and lower health competency are predictive factors of poor sleep behaviors. Whereas individuals with higher perceived health competence predict better sleep quality. Applying the TPB may be a useful tool in designing interventions to promote better sleep habits and quality.

0980

AN INTERNET BASED EDUCATION PROGRAM IMPROVES SLEEP LITERACY IN COLLEGE PSYCHOLOGY STUDENTS

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Introduction: Knowledge regarding the importance of sleep in health and performance, and good sleep hygiene practices is low, especially among adolescents and young adults. Introductory psychology is one of the most highly enrolled courses at colleges and universities. This study tested the impact of an internet-based learning module on improving sleep literacy in this venue.

Methods: An internet-based learning module containing sleep physiology and hygiene information was developed using content from the Harvard Medical School sleep educational website http://www.understandingsleep.org. Access to the module was provided as an extra credit activity for 2 of 4 sections (Experimental, N=889) of an introductory college psychology course during their standard instruction on sleep and dreaming. The remaining 2 sections (Control, N=878) were encouraged to visit only the website. Level of knowledge was assessed before and after access to the module or website, and just before the final examination.

Results: 354 in the Experimental and 253 in the Control groups participated in the extra credit activity. Pretesting showed equivalency in sleep knowledge between the 2 groups (Experimental: 17.7 +/- 3.9 [sd]; Control: 18.1 +/- 3.1, p=ns). At the end of standard instruction, the Experimental group improved their sleep knowledge while the Control group's scores did not change (23.9 +/- 4.3 vs. 18.4 +/- 3.9, p<.001). Greater improvement in Experimental versus the Control was still evident ~ 2 months later (20.8 +/-3.6 vs. 19.9 +/- 3.6, p=.007). 55.9% of the Experimental vs. 45.1% of the Controls indicated that they made changes in their sleep habits after participation in the activity.

Conclusion: Use of an Internet-based learning module has the potential to enhance sleep literacy and change behavior among students enrolled in a college introductory Psychology course.

Support (If Any): American Sleep Medicine Foundation

0981

INCORPORATING SLEEP RESEARCH INTO UNDERGRADUATE PSYCHOLOGY AND BIOLOGY COURSES: BLENDING STUDENT INTEREST WITH PROBLEM-BASED LEARNING

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Introduction: Most psychology and biology undergraduate textbooks allocate only a chapter or half-chapter to sleep, yet sleep is one of the most interesting and important topics to undergraduate students. Total sleep time and sleep quality are particularly disturbed in late adolescence, so the subject of sleep research has high personal relevance to most students. This presentation details five years of successful integration of sleep research into undergraduate courses, and highlights numerous laboratory experiments, readings, writing assignments, and active learning exercises that can be modified to fit almost any course budget, time restriction, or background knowledge level.
Methods: Sleep research was integrated into four separate psychology and neuroscience courses at two different colleges; two of these courses were lecture only (a freshman/sophomore level survey course "Brain & Human Behavior" and a junior/senior level topics course "Sleep and Dreaming") and two were laboratory courses (a short term course "Introduction to Sleep Research" and a senior capstone course "Physiological Psychology"). Students in these courses analyzed self-assessments of sleep quality and schedule, measured biological rhythms of several physiological markers, observed polysomnography at sleep clinics, and kept detailed sleep diaries.
Results: Course evaluations indicate that for the sleep-specific courses, students substantially increased their knowledge of and interest in the subject and rated the overall courses very highly (all values > 4.25/5). For the full term laboratory course, the sleep units were rated the highest of all labs for measures of student interest, engagement, and successful learning outcomes.
Conclusion: Because of the wealth of experimental approaches used to quantify sleep, the sleep research makes for an outstanding stand-alone course or as an add-on unit for laboratories, problem-based learning activities, and discussions within psychology or biology courses.

0982

SLEEP/WAKE MEDICINE AMONG SELF-IDENTIFIED SLEEP SPECIALISTS AND PRIMARY CARE PROVIDERS: GAPS IN KNOWLEDGE AND THE EFFECTIVENESS OF CONTINUING EDUCATION

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Introduction: This study evaluated baseline knowledge and the effectiveness of continuing education (CE) in sleep/wake medicine for self-identified sleep specialists (SSs) and primary care providers (PCPs). Educational gaps and knowledge gains were compared between practitioner groups. Additionally, follow-up questionnaires evaluated incorporation of the new educational information into practice and consequent improvements in patient outcomes.
Methods: Stage 1 comprised a series of live CE programs on best practices in sleep/wake disorder assessment and management, tailored to either SSs or PCPs. Knowledge and practice behaviors related to sleep/wake disorders were assessed pre- and post-activity via 10 Likert statements. Pre- and post-activity responses were compared. Results were also analyzed to identify intergroup differences in baseline knowledge and educational effectiveness. In Stage 2, participants self-reported on their integration of the education into their practices and effects on patient outcomes.
Results: During Stage 1, 201 and 942 clinicians participated in CE activities at sleep and primary care meetings, respectively. Significant pre- to post-activity improvements were observed for 9/10 and 8/10 educational content-specific Likert statements directed at SSs and PCPs, respectively. Surprisingly, knowledge- and practice-based statements presented to both cohorts revealed similar baseline deficits. For example, contrary to American Academy of Sleep Medicine guidelines, 43.3% of clinicians in each group believed that sleep histories/sleep logs are not usually sufficient to diagnose circadian rhythm disorders. Further, 65.5% of sleep meeting attendees and 60.7% of the primary care audience incorrectly indicated that subjective self-reports of sleepiness generally reflect objective measures of sleepiness. Finally, Stage-2 evaluations suggested that the CE changed practice behaviors and improved patient outcomes.
Conclusion: The CE programs effectively narrowed knowledge gaps in the assessment and treatment of sleep/wake disorders. Comprehensive CE programs for both SSs and PCPs are needed to address educational deficits and improve clinical decision making.
Support (If Any): This educational outcomes study was made possible by an independent educational grant from Cephalon, Inc.

0983

SLEEP MEDICINE ELECTIVE ROTATION AMONG ADULT AND CHILD NEUROLOGY RESIDENTS: AN INTERNET BASED SURVEY OF PROGRAM DIRECTORS

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Introduction: There is limited evidence regarding participation of adult and child-neurology residents in sleep-medicine training. We therefore surveyed adult and child-neurology residency program-directors regarding trainee participation in sleep-medicine in the form of elective and/or fellowship-training.
Methods: Online web-based survey emailed to all program-directors (PDs) of ACGME accredited adult-neurology (AN) and child-neurology (CN) programs in the United States.
Results: A total of 22% complete responses (41/183) were obtained; 50% of PD respondents were CN-based. The vast majority of respondents (93%) lead university-based programs accepting between 1-3 residents per year (52%). Residents typically underwent 1 month elective rotations (74%). Sleep-medicine training was not a prerequisite during residency in the overwhelming majority of programs (95%), despite majority of neurology departments employing a sleep-neurologist and/or operating a sleep-lab. Less than 1/4th of residents typically undertook sleep-medicine electives in 57% of institutions surveyed and almost all these residents undertook these electives at the home institution (73%). The majority of PDs believed that sleep-medicine elective trainings improved the ability of neurology residents to obtain sleep-fellowships (73%) and also improved residents' abilities to care for patients with sleep-disorders in neurological practice (90%). PDs did not feel that compulsory sleep training during residency would make it more likely for neurology residents to become sleep specialists (54%). DMore CN-PDs and PDs for dual training programs, than AN-PDs (59% vs 20%) believed that sleep-medicine training helped residents identify and treat sleep-disorders more appropriately (p=0.04).
Conclusion: While only a minority of residency programs had recommended sleep medicine electives, the majority of PDs believed that sleep-medicine training in residency would benefit residents by allowing them to better manage patients with co-morbid sleep-disorders.

0984

EFFECTS OF A ONE-TIME SLEEP SPECIALTY CONSULTATION ON SLEEP PROBLEM MANAGEMENT IN PRIMARY CARE

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Introduction: Previous research suggests sleep disorders often are not adequately addressed in the primary care setting. The current study was conducted to determine the effects of a one-time consultation with a sleep specialist on sleep management patterns and outcomes in a primary care setting.

Methods: The study design was a prospective, randomized, clinical intervention trial. The participants were 137 veterans (Mage=55.4years; 29 women) enrolled in the Primary Care Clinics of the Durham VA Medical Center. Eligible study participants had a sleep complaint > 1 month duration, ≥ 6 on the Pittsburgh Sleep Quality Index-PSQI, ≥ 24 on the Folstein MMSE, no unstable medical or psychiatric disorders, and no previous sleep specialist treatment. Participants were randomized to an intervention (INT; N=68) or wait-list control (WLC; N=69). INT consisted of one meeting with a sleep specialist who administered structured interviews assessing sleep and psychiatric disorders, and then provided manualized treatment recommendations to patients and their respective primary care providers. Providers' referral patterns and patient outcomes were then monitored for a subsequent 10-month period.

Results: Provider-initiated sleep-focused interventions were significantly more frequent in the INT group compared to the WLC group including PSG referrals (p<.0001), mental health clinic referrals (p<.05), and medication for restless legs (p<.05). The INT group showed somewhat greater improvements in their PSQI total scores than did the WLC group (P < .08; Effect Size = .26) at 10-month follow-up. Moreover, 56.14 % of the INT group had Epworth Sleepiness Scale scores < 10 at the 10-month follow-up, whereas only 43. 3% of the WLC group fell below this cutoff for clinically significant sleepiness.

Conclusion: A one-time sleep consultation significantly increased primary care providers' attention to sleep problems among their patients and resulted in some modest benefits to patient's sleep/wake symptoms.

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0985

AN INPATIENT SLEEP MEDICINE CONSULTATION SERVICE: POLYSOMNOGRAPHY, THERAPY AND OUTCOMES

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Introduction: Earlier reports show inpatient polysomnography (PSG) is feasible and useful. Acute stroke, heart failure, atrial fibrillation, coronary artery disease, and respiratory disease, common in the inpatient setting, are associated with sleep apnea. 80% of patients with sleep apnea remain undiagnosed and at risk of cardiovascular and cerebrovascular sequelae. The inpatient setting offers a unique opportunity to identify and treat patients with the goal of preventing future complications.

Methods: This study is a retrospective chart review of all inpatient sleep medicine consults over a three month period (December 2009 - February 2010) at a tertiary care facility, resulting in the formal evaluation of 123 hospitalized patients by the sleep medicine consult service. The majority of the consultations were prompted because of nocturnal hypoxia, risk factors for obstructive sleep apnea (OSA), or history of OSA. Information obtained included medical history, admitting diagnosis, airway class, and STOP-BANG questionnaire. Therapy was based upon comprehensive PSGs conducted bedside via wireless area network and virtual desktop.

Results: Of the 123 sleep medicine consults requested, 81 (66%) had inpatient PSG studies. The mean AHI was 29/hr with low SpO2 of 79%. An additional 5 patients had follow up outpatient studies, thus increasing total percentage of patients receiving PSGs to 70%. 22 patients refused PSG studies. CVA was the most common admitting diagnosis (33%). 47 patients were discharged on oxygen alone, often as interim therapy pending further study. 21 patients were discharged without therapy, 19 of which had outpatient PSGs recommended. The remaining patients were discharged on CPAP (43), bi-level (9) or ASV (3), with or without oxygen.

Conclusion: Sleep medicine consultation should be an integral component of inpatient care, especially in high risk patients. Neurology and cardiology specialists recognize the importance of this service as indicated by the number of sleep consult requests. A majority of inpatients consulted received PSG testing, appropriate therapy, or therapy recommendations, many of whom would not have had sleep specialist evaluation otherwise. With improved technology and process models, sleep medicine is no longer exclusively an outpatient service.

0986

ORIGINAL RESEARCH: COMPARING SLEEP HYGIENE EDUCATION PROVIDED BY SLEEP DISORDERS CLINIC VERSUS PRIMARY CARE CLINIC

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Introduction: Sleep is an essential physiological need; it is an active state that is critical for our physical, mental and emotional well-being. Sleep is also important for optimal cognitive functioning, especially in this technologically advanced era. Sleep disruption results in functional impairment. Lack of knowledge about the importance of adequate sleep further complicates our stressful existence and causes several deleterious health consequences. Sleep disruption not only affects productivity during the day but also affects physical, mental and emotional well-being. Providing sleep hygiene education can be a vital tool for patients complaining of insufficient sleep. Author was interested in comparing sleep hygiene education provided by sleep disorders clinic versus primary care clinic.

Methods: Retrospective chart review in which author studied 184 electronic medical records at VAMC, Milwaukee from Oct to Dec 2007. 57 charts were excluded due to lack of follow up or their providers were out of VA system. 10 charts were excluded due to death in follow up period. 117 charts were included in this study. Statistical analysis was performed in SAS (Cary, NC).

Results: Fisher's exact test was used to compare sleep hygiene education provided by sleep disorders clinic versus primary care clinic. It was significant (p<0.0001). Patients seen by primary care clinic providers were much less likely to have had sleep hygiene education compared to those seen by sleep disorders clinic providers.

Conclusion: Author concluded that patients seen by sleep disorders clinic services more commonly receive sleep hygiene education than those seen by primary care clinic providers. This can be due to a variety of factors.

0987

UNDERSTANDING SLEEP PATTERNS IN BRAZILIAN IMMIGRANTS IN LOWELL, MA: PERSPECTIVES FROM COMMUNITY HEALTH WORKERS AND HEALTHCARE CONSUMERS

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Introduction: The purpose of this study is to collect pilot data on the sleep and medical/psychiatric health of immigrants from the Brazilian community in Lowell, Massachusetts. Studies on Brazilian immigrants are rare in the United States. Factions of the immigrant community in Lowell are at great risk for medical comorbidity due to sleep dysregulation from a number of causes including the need for multiple jobs with irregular scheduling. Brazilian immigrants in the United States are especially at risk for physical and mental health issues due to loss of familiar surroundings and lack of social, financial and emotional support in the community where they live after immigration.

Methods: The first objective is to seek information related to sleep, sleep dysregulation and medical/psychiatric health from consumers of healthcare from the Brazilian immigrant community. The second objective is to seek information from Brazilian community lay health workers (Promotoras) regarding their impressions of factors related to sleep dysregulation with members of the Brazilian immigrant community in Lowell. Both groups participated in focus groups. In addition, the immigrant healthcare consumers completed a Health Questionnaire, the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale.

Results: Data analysis is currently in progress. Initial results reveal that sleep dysregulation is common in the sample (n=28) and that the causes are multifaceted and complex.

Conclusion: Brazilian immigrants may be at significant risk for comorbidities related to sleep dysregulation. This immigrant group is poorly studied in the United States and appears to be at great risk for health disparities related to sleep deprivation and dysregulation.

Support (If Any): University of Massachusetts Lowell, School of Health & Environment

0988

FACTORS ASSOCIATED WITH REFERRALS FOR OSA EVALUATION AMONG COMMUNITY PHYSICIANS

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Introduction: This study assessed knowledge and attitude towards Obstructive Sleep Apnea (OSA) among community physicians and explored factors that are associated with referrals for OSA evaluation.

Methods: RRespondents were 105 community physicians in SUNY Downstate Medical Center's catchment area. Average age was 48±14 years, 68% was male, 70% black, 24% white, and 6% other. Specialties included: Internal Medicine 28%, Family Medicine 22%, Psychiatry 16%, Anesthesiology 12%, Pediatrics 8%, OB 7%, and other 7%; 90% provided care to black patients. Medical students/residents visited community-based primary-care clinics collecting data using the Obstructive Sleep Apnea Knowledge and Attitudes (OSAKA) questionnaire. OSA-KA is a self-administered questionnaire eliciting responses in two domains: knowledge of OSA epidemiology, pathophysiology, symptoms, diagnosis, and treatment (18 true/false statements) and attitudes (5 state-

ments on importance of OSA and ability to identify/manage OSA patients using a 5-point Likert scale, from 1 strongly disagree to 5 strongly agree; sociodemographic data was collected.

Results: OSA referral rate was 75%; 68% of patients inquired about OSA. Knowledge and attitude scores ranged from 5 to 18 (mean=14±2) and from 7 to 20 (mean=13±3), respectively. Greater OSA knowledge was associated with white race/ethnicity [rp=0.26, p<0.05], years in practice [rp=-0.38, p<0.01], patients inquiring about OSA [rp=0.31, p<0.01], and referrals for OSA evaluation [rp=0.30, p<0.01]; positive attitude was associated with patients inquiring about OSA [rp=0.20, p<0.05]. Age, race/ethnicity, gender, or specialty was not significantly associated with greater referral rates. Logistic regressions adjusting for effects of OSA knowledge and attitudes showed physicians indicating that patients inquired about OSA were 10 times more likely to make a referral for OSA evaluation [OR=9.38, 95%CI:2.33-38.01, p<0.01].

Conclusion: Independent of physicians' knowledge and attitudes toward OSA, the likelihood of making a referral for OSA evaluation was influenced by whether patients inquired about OSA. Physicians reporting longer years in practice were less likely to refer for OSA evaluations.

Support (If Any): This research was supported by funding from the NIH (R01MD004113, R25HL105444 and P20MD005092).

0989

EVALUATION THE NEED OF HEALTH CARE UTILIZATION FOR THE DIAGNOSIS OF OBSTRUCTIVE SLEEP APNEA AMONG U.S. HYPERTENSIVE ADULTS

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Introduction: American Academy of Sleep Medicine (AASM) expert-based guidelines recommend that patients with Hypertension (HTN) undergo evaluation and testing for Obstructive Sleep Apnea (OSA) (HTN-OSA) when presenting with nocturnal symptoms (disturbed sleep, nocturnal dyspnea, or snoring), or if they remain hypertensive despite optimal medical management (resistant HTN). Study hypotheses are: 1. Age adjusted population prevalence rates of HTN-OSA are significantly higher in men compared to women. 2. African-Americans(AA) with HTN (HTN-OSA) have higher odds of currently undiagnosed OSA, independent of other social determinants of health vulnerability, overweight/obesity, lifestyle factors, self-reported health status, and depression.

Methods: Cross-sectional analysis of a stratified multistage probability adult sample (N=10,526) enrolled in the National Health and Nutrition Examination Survey (NHANES) between 2005 -2008 was obtained. Age-adjusted US population prevalence rates of HTN-OSA and adjusted odd ratios of undiagnosed OSA in the HTN-OSA population were calculated using weighted analysis.

Results: Age-adjusted US population prevalence rates of HTN-OSA is high in the general US population: 20.7% of U.S. men and 18.2% of U.S. women (p=0.01). Logistic regression models unadjusted and adjusted for socio-economic characteristics, health insurance, behavioral risk factors, health status and depression, found the odds of undiagnosed OSA in HTN qualifying for OSA screening as modest, but significantly higher in AA [OR=1.2, 95%CI (1.1-1.4)], individuals with depression [OR=1.4, 95%CI (1.1-1.9)], overweight/obese [OR=2.2, 95%CI (1.9-2.5)], lower education (OR=1.2, 95%CI (1.0-1.3) and self-reporting poor health status [OR=2.3, 95%CI (2.0-2.6)].

Conclusion: The high age-adjusted population prevalence of individuals with HTN qualifying for OSA screening suggest the need of further capacity planning for health-related resource allocation related to the diagnosis and treatment of OSA in the U.S. Modest, but significantly higher risk of untreated OSA may exist in HTN AA qualifying for OSA screening, independent of other risk factors for health disparities.

0990

VALIDATION OF PROCEDURE AND DIAGNOSIS CODES FOR SLEEP APNEA IN THE NATIONAL VA DATABASE

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Introduction: The National VA Outpatient Dataset (OPC) provides fertile ground for research in veterans but is limited to use of procedure and diagnosis codes. Sleep Apnea(SA) is of particular relevance to veterans, affecting nearly 1 in 5 US adults and, in particular, older men. We validated CPT and ICD-9 codes for SA diagnosis in the OPS as a stepping stone to SA-related health outcomes among veterans.

Methods: We identified all individuals in the OPC FY2000-2003 who were part of the NF/SGVHS and had at least one CPT code for polysomnography(PSG). Of these, a random sample of 100 veterans was selected. We then determined which individuals had a subsequent ICD-9 for SA within a year of the ICD-9 code. Finally, we reviewed the VA computerized medical record (CPRS) to confirm PSG and diagnosis of SA by ICD-9 and clinic note.

Results: Mean age was 56±11 y; 95% were male; 62% were white, 10% black. Average BMI was 36± 8. Of NF/SGVHS veterans with CPT for PSG in the OPC, 95% had CPT95811(PSG with CPAP titration); the remainder had CPT95806-10(varying levels of PSG). Of those with CPT for PSG in OPC, 99% had a subsequent diagnosis of SA by ICD-9 within a year of original CPT; 49% had ICD-9 780.53(Hypersomnia with SA), 49% had ICD-9 780.57(Unspecified SA) and 780.53, and 1% had 780.57(SA NOS). CPRS review revealed sensitivity of 92%, specificity of 12.5% for this algorithm; PPV of this algorithm was 92%, NPV was 100%.

Conclusion: An algorithm using CPT and subsequent ICD-9 coding from OPC is a sensitive method for identifying individuals with SA diagnosed by PSG. However, this algorithm may not identify individuals referred for PSG but without SA. Therefore, future studies utilizing codes in OPC may require selection of a control group from the general pool of veterans to capture individuals without disease.

0991

CHANGES IN HEALTH SERVICES UTILIZATION IN PATIENTS DIAGNOSED WITH OBSTRUCTIVE SLEEP APNEA AND TREATED WITH CONTINUOUS POSITIVE AIRWAY PRESSURE IN A COUNTY HOSPITAL SETTING

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Introduction: Obstructive sleep apnea (OSA) has been associated with an increase in co morbidities. Health care utilization (i.e. hospitalizations, emergence room visits and clinic visits) may be higher as a result. Whether there is a decrease in health care utilization after Continuous Positive Airway Pressure (CPAP) treatment is questionable.

Methods: We performed a retrospective review of patients diagnosed with OSA (AHI >5) that were studied at our county hospital. Currently patients purchase their own CPAP machines (only 18% of patients actually obtain CPAP). We looked at healthcare utilization (as defined above) 1 year prior to and after the diagnosis of OSA and compared patients who obtained a CPAP machine to those who did not.

Results: We compared 54 patients that had received CPAP with 120 patients that had not received treatment (controls). There was a pre-

dominance of African Americans and Latin Americans in each group (70% in the CPAP group and 84% in the control group). The age (mean 49.2 years, SD +/-10.1, p=0.78), BMI (mean 40.9, SD +/-14, p=0.24) and AHI (mean 49.3, SD +/-25, p=0.83) were not statistically different between the two groups. The mean number of medical diagnoses was high in both groups (7 in the CPAP group and 6 in the controls). When comparing the average number of admissions prior to the diagnosis of OSA between the two groups, it was not statistically different (mean 0.32, p=0.31), as neither were the pre diagnosis clinic visits (mean 8.5, p=0.38) or emergency room visits (mean 0.5, p=0.12). At a 1 year follow up, these hospital encounters were again not statistically different between the two groups (mean hospital admissions 0.37 with p=0.21, mean clinic visits 8.8 with p=0.08, mean emergency room visits 0.45 with p=0.23). When we analyzed the CPAP group comparing hospital admissions prior to and after being diagnosed with OSA, there again was no statistical difference (p=0.85).

Conclusion: We did not see any difference in health care utilization in patients that received CPAP. This may be a true effect (perhaps a longer follow up is needed to see a decrease in health care utilization). This may alternatively be a consequence of the population type we were studying i.e. lower socio economic groups with multiple existing co morbidities. The other variable that we were unable to determine was CPAP compliance, which may also be lower in this population. Further long term studies with compliance data are needed to clearly evaluate for any differences.

0992

IS CPAP ALWAYS THE ANSWER? A COST-EFFECTIVENESS ANALYSIS OF SURGICAL TREATMENT MODALITIES FOR OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA) is a prevalent disorder associated with increased cardiovascular morbidity and mortality. Conventional OSA therapy necessitates indefinite continuous positive airway pressure (CPAP). Although CPAP is an effective treatment modality, up to 50% of OSA patients are intolerant of and ultimately reject CPAP. We explore whether surgical modalities developed for those intolerant of CPAP (i.e. uvulopalatopharyngoplasty (UPPP), multi-level surgery (MLS), maxillomandibular advancement (MMA)) are cost-effective.

Methods: We construct a lifetime semi-Markov model of OSA that accounts for observed increased risks of stroke, cardiovascular disease and motor vehicle collisions in those with untreated OSA. Using this model, we compare the cost effectiveness of (1) no treatment, (2) CPAP only and (3) CPAP followed by surgery (either UPPP, MLS or MMA) for those intolerant to CPAP.

Results: CPAP therapy is cost-effective over no therapy at an incremental cost-effectiveness ratio (ICER) of $396 per quality-adjusted life year (QALY) for a 30-year old male with severe OSA. Compared with the CPAP only strategy, CPAP followed by surgery for those intolerant is cost effective with an ICER of $9,636/QALY to $29,079/QALY for the various surgical options (i.e. UPPP, MLS, MMA). The CPAP-UPPP strategy adds 0.28 QALYs for an increase of $2,726 (discounted 2010 dollars) over the CPAP only strategy for an ICER of $9,636/QALY. The CPAP-MMA strategy is most effective, and adds a further 0.70 QALYs for $11,211 (ICER: $16,084/QALY) more compared to CPAP-UPPP. The CPAP-MLS protocol is dominated by the CPAP-UPPP and CPAP-MMA protocols. In older OSA patients, surgery remains cost-effective (ICERs of $5,888/QALY for the CPAP-UPPP and $10,344/QALY for the CPAP-MMA protocols compared with CPAP alone).

Conclusion: CPAP therapy for OSA is highly cost-effective. Amongst surgical options, UPPP and MMA are cost-effective in CPAP intolerant

individuals. Despite high upfront costs, surgery should be offered for CPAP intolerant individuals.

0993

EXPEDITED EVALUATION AND TREATMENT OF COMMERICAL DRIVERS

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Introduction: Occupational health programs are referring commercial drivers thought at risk for OSA based upon elevated neck circumference and BMI. Drivers (most of whom do not regard themselves as patients) want expedited evaluations to permit them to drive. Demands for low cost timely evaluation and treatment are challenging already overloaded sleep centers.

Methods: We retrospectively reviewed results of 29 drivers referred to our sleep center to evaluate them for OSA. Our goal was to complete the evaluation process with six weeks using level 3 home sleep testing (HST), APAP, and/or level 1 PSG.

Results: 29 commercial drivers (mean age 40 years, 95% male) were referred to our sleep center over a 12-month period in 2010. Only 20 (69%) arrived for the initial visit. All 20 who came for their initial appointment had a level 3 HST. HST was interpretable in only 14 (70%): 6 were thought not to have significant OSA and cleared to drive; a level 1 PSG or APAP (depending upon availability) was recommended for 8 but only 3 proceeded with further testing. Only 8 (27%) of 29 drivers initially referred completed the process: 6 were cleared to drive and 2 who had OSA were treated with good CPAP compliance. Twenty-one (73%) of the initial 29 referred did not complete the process. The average duration of the process was 43 days for those who did not have OSA and 191 days for those with OSA who completed the entire process and demonstrated CPAP compliance. Further cost effectiveness data analysis will be presented.

Conclusion: Be advised that providing low cost expedited care to commercial drivers is difficult.

0994

RECOGNITION AND DIAGNOSIS OF EXCESSIVE SLEEPINESS ASSOCIATED WITH SHIFT WORK DISORDER: RESULTS FROM SHIFT WORKERS, PATIENTS WITH SHIFT WORK DISORDER AND HEALTHCARE PROFESSIONALS PARTICIPATING IN AN INTERNET SURVEY

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Introduction: To understand how shift work disorder (SWD) was diagnosed from the perspective of healthcare professionals (HCPs) and shift workers (SWs).

Methods: Two separate market research online surveys were administered to 2 groups: (1) SWs with/out a self-reported diagnosis of SWD and (2) HCPs. Participation in the SWs survey required ≥21 hours per week working shifts in the previous 2 weeks, a diagnosis of SWD or ≥10 score on the Epworth Sleepiness Scale (ESS), and ≥5 score on any of the subscales of the Sheehan Disability Scale (SDS). Participation in the HCP survey required ≥3 years in Primary Care, Psychiatry, Neurology, Sleep Medicine, Pulmonology, Occupational Medicine, Gynecology, Registered Nurse, or be a Physician's Assistant, or Nurse Practitioner, and that each respondent spend at least 75% of their time in patient care.

Results: 260 respondents completed the SWs survey and 673 the HCP survey. Of those SWs without a diagnosis (n=157), 23% did not believe they suffered from excessive sleepiness despite scoring ≥10 on the ESS and having functional impairment (SDS). For those SWs who discussed their excessive sleepiness with their HCPs, SWs initiated this conversation 82% of the time (vs. 13% HCP-initiated). HCPs believe that 67% of total SWD is never suspected by physicians. HCPs also believed that

50% of SWD is undiagnosed because SWD is often masked by other conditions (depression and obstructive sleep apnea [OSA]) and is misdiagnosed as depression (30%), non-SWD insomnia (27%), chronic fatigue syndrome (22%) and OSA (20%).

Conclusion: SWs do not always recognize their own symptoms of SWD and are more likely to initiate a discussion of those symptoms than HCPs. HCPs believe that SWD is missed 67% of the time, often because SWD is masked by other comorbidities or misdiagnosed.

Support (If Any): This research was sponsored by and conducted in collaboration with Cephalon, Inc., Frazer, PA.

0995

LOWER DAILY AVERAGE CONSUMPTION AND GREATER PRESCRIPTION COST SAVINGS OF ARMODAFINIL COMPARED WITH MODAFINIL: A 12-MONTH RETROSPECTIVE DATABASE ANALYSIS

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Introduction: Armodafinil and modafinil are indicated to improve wakefulness in patients with excessive sleepiness associated with treated obstructive sleep apnea, shift work disorder, and narcolepsy. Because both medications are approved for once-daily dosing with different tablet strengths, their real-world utilization may differ. This analysis examined utilization of armodafinil and modafinil based on daily average consumption (DACON) and determined the impact of armodafinil and modafinil on pharmacy budgets using an economic modeling technique.

Methods: DACON was examined in a retrospective database analysis of Wolters Kluwer Source LX pharmacy analytic data collected from March 1, 2009 to May 31, 2010. DACON was calculated by dividing the total tablets dispensed by the total days supplied. An economic model will be used to evaluate the financial impact of changes in prescription share from modafinil to armodafinil.

Results: The DACON for armodafinil and modafinil were 1.03 (70,976 prescriptions) and 1.40 (453,216 prescriptions), respectively. Among patients with 2 to 8 prescription fills for armodafinil, the DACON remained between 1.03 and 1.05. A total of 6,069 modafinil patients taking modafinil switched to armodafinil. Their DACON of modafinil was 1.46 before switching and was 1.05 after switching to armodafinil.

Conclusion: By using pharmaceutical claims data in tandem with well-designed economic models, payers can better estimate current and future pharmaceutical spending. Based on this DACON analysis, the utilization of armodafinil has a real-world advantage over modafinil that can significantly affect pharmacy budgets.

Support (If Any): This research was sponsored by and conducted in collaboration with Cephalon, Inc., Frazer, PA.

0996

HEALTHCARE RESOURCE UTILIZATION BEFORE AND AFTER INITIATION OF ARMODAFINIL TREATMENT FOR WAKEFULNESS

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Introduction: Once-daily armodafinil significantly improves wakefulness in patients with excessive sleepiness due to shift work disorder (SWD), treated obstructive sleep apnea (OSA), or narcolepsy. The objective of the current analysis was to examine resource utilization by patients who received armodafinil for these FDA-approved indications.

Methods: Data were collected from the IMS LifeLink Database (December 2008 to March 2010) and contained longitudinal patient data from medical claims (diagnostic/therapeutic services), pharmacy claims (prescriptions), and eligibility files (demographics and enrollment). Patients were identified and healthcare utilization data were collected for

6 months before and up to 10 months after their first armodafinil pharmacy claim. Healthcare costs and visits before and after initiation of armodafinil were statistically analyzed using paired t-tests.

Results: 1,282 patients were included (4.5% SWD; 85.9% OSA; 20.4% narcolepsy). The mean monthly healthcare cost for patients prior to taking armodafinil was $1,562.99 (pharmacy $432.26; medical $1,130.73). After armodafinil initiation, overall monthly cost decreased to $1,438.11 (p=0.0588). Armodafinil significantly increased prescription costs by $138.53/month (p<0.0001) but decreased medical costs by $263.41/month (p<0.0001). Medical costs were decreased by $133.23 for physician costs (p<0.0001) and $75.62 for outpatient costs (p=0.00039). Emergency room costs were lower by $3.99/month (p=0.0039), and inpatient costs were lower by $7.51/month (NS). The number of inpatient visits were reduced by 0.21/year (p=0.0307), physician visits by 4.91/year (p<0.0001), and outpatient visits by 0.89/year (p<0.0001).

Conclusion: After armodafinil treatment, reductions were seen in healthcare utilization and costs compared to the pre-armodafinil period. As expected, total prescription costs were greater following initiation of armodafinil therapy; however, lower total monthly costs were observed with armodafinil because use of medical resource decreased. This significant reduction in medical resource utilization appeared to be driven predominantly by fewer physician visits and lower outpatient costs.

Support (If Any): This research was sponsored by and conducted in collaboration with Cephalon, Inc., Frazer, PA.

0997

ASSOCIATION BETWEEN SLEEP DISORDERS AND DEMAND FOR MEDICAL SERVICES IN THE SAO PAULO EPIDEMIOLOGIC SLEEP STUDY COHORT

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Introduction: The aim of this study was to investigate if obstructive sleep apnea (OSA) and insomnia were predictors of hospitalizations or emergency service visits after a two year follow-up of the Sao Paulo Epidemiologic Sleep Study (EPISONO) cohort.

Methods: All participants (n=1101) of EPISONO, who had a basal evaluation from July to December 2007, were contacted (Dec 2009) either by e-mail, telephone, or were home visited when contact was not achieved. Interviews included a questionnaire on weight variation, number of hospitalizations and visits to any emergency service.

Results: We were unable to reach 3.2% (n=35) of the participants and other 7 had died. Hospitalizations were reported by 116 (10.5%) and emergency services visits by 136 (12.4%). The average body mass index (BMI) did not varied significantly from first to second assessment [26.7 (CI95% 26.3-27.1) kg/m2 vs. 26.9 (26.5-27.4)]. Multiple logistic model found female gender [OR=1.5 (CI95%:1.1-2.1); p=0.01)], age ≥50 years [2.2(1.5-3,0); p<0.001)], apnea-hypopnea index (AHI) 15-30 [1.8(1.1-3.0); p=0.02], AHI>30 [1.9(1.1-3.5); p=0.03], insomnia symptoms [1.5(1.1-2.1); p=0.01] and insomnia diagnosed according to the DSM-IV criteria [1.8 (1.1-2.8); p=0.01] as predictors of hospitalizations and/or demand for emergency services, after adjusting for confounders.

Conclusion: Our study shows that, after a short period of follow up in a cohort from Sao Paulo, OSA and insomnia were associated with health impairment. Considering the high prevalence and public health burden of sleep disorders, the consequences of untreated disease for the individual and society are undeniable and should be addressed.

Support (If Any): AFIP, FAPESP, CNPq

0998

CHANGES IN SLEEP-RELATED COMPLAINTS FROM JULY/AUGUST 2001 TO SEPTEMBER/OCTOBER 2001: RESULTS FROM A NATIONALLY REPRESENTATIVE SAMPLE OF PATIENT VISITS TO PHYSICIANS' OFFICES, HOSPITAL OUTPATIENT AND EMERGENCY DEPARTMENTS IN THE US

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Introduction: The terrorist attacks in New York City against the US on September 11, 2001(9/11) were catastrophic events; sleep-related complaints are often one of the first signs of psycholgical stress. We examined the frequency of sleep-related complaints presenting to medical facilities during the 2 months pre- 9/11 and for the immediate 2 months post- 9/11. We further examined regional differences in the frequency of sleep complaints. The data presented are from an epidemiologically representative sample of patient visits to doctors offices and hospitals during July to October 2001. To our knowledge there are no studies of such naturalistic data obtained pre- and post- 9/11, from a nationally representative sample.

Methods: Data collected by the National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Care Survey (NHAMCS), which are nationally representative samples of health care visits in the USA, were studied. Patient visits from July to October 2001, with the following sleep-related complaints - 'Disturbance of Sleep', 'Insomnia', 'Tiredness/Sleepiness', and 'Nightmares'- were studied.

Results: Pre- to Post- 9/11 only the following sleep complaint had changed significantly: 'Disturbance of Sleep': OR=5.29 (95% CI 1.31-21.43). OR for sleep complaints pre- and post-9/11 in the Northeast region versus all other regions of the US revealed the following: 'Disturbance of Sleep': 1.19 (95% CI 0.16- 8.89) versus 5.52 (95% CI 1.29-23.58); 'Insomnia': 0.40 (95% CI 0.17- 0.92) versus 4.15 (95% CI 1.71- 10.08); 'Tiredness/Sleepiness': 0.64 (95% CI 0.17- 0.92) versus 3.64 (95% CI 1.94- 6.84; and 'Nightmares': 2.88 (95% CI 0.25- 33.20) versus novisits in the Northeast.

Conclusion: Pre- to Post- 9/11 there were significantly more patient visits with complaints of 'Disturbance of Sleep', suggesting a dsyregulation of sleep-wake patterns overall. Examination of regional differences however revealed a significant increase in all sleep-related complaints except nightmares.

0999

ADDING A DEPRESSION MEASURE TO AN ASSESSMENT OF SLEEPINESS IMPROVES PREDICTION OF RESIDENCY EXPERIENCE

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Introduction: Evidence suggests that reducing work hours does indeed increase sleep hours, but a number of other factors along with sleep are important for defining the residency experience. We report here on how the combined effects of sleepiness and depression affect residents' reports of their experiences.

Methods: In late 2009, we surveyed residents about their first and second years of residency training in internal medicine, surgery, pediatrics, and ob/gyn, in 36 residency programs. The overall response rate was 83.37% (N = 634). Sleepiness was assessed by means of the Epworth Sleepiness Scale (EPSS) and Depression was assessed by the CES-D-10. Data from our 1999 survey served as a baseline for the study.

Results: For these specialties, average work hours declined from of 84.33 (SD = 17.9) in 1999 to 75.15 (SD = 9.3) in 2009, while average sleep hours increased from 40.04 (SD = 6.5) to 44.00 (SD = 6.2). In 2009, the average score for EPSS was 11.09 (SD = 5.1) and the average for CES-D-10 was 8.59 (SD = 4.9). Correlation between EPSS and

CES-D-10 was + 0.36 (p < 0.001). Both scales were dichotomized into high and low groups with low < 10 and high ≥ 10. This yielded four groups: high depression, high sleepiness (N = 180); high depression, low sleepiness (N = 60); low depression, high sleepiness (N = 204); low depression, low sleepiness (N = 167). Analyses of variance show a significant linear trend across these groups, with the highest indices of behavioral changes, conflict with others, working while ill or impaired, reports of problems during residency, and reports of five types of medical errors occurring in the high depression, high sleepiness group.

Conclusion: Sleepiness and Depression together predict residency experience better than either sleep hours or sleepiness by themselves.

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VARIATIONS IN SLEEP HOURS AND EPWORTH SLEEPINESS SCORES IN 36 RESIDENCY PROGRAMS

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Introduction: Neurobehavioral sleep research has identified genetic polymorphisms determining individual variations in vulnerability to sleep loss. Yet, most discussions about sleep deprivation during residency training are based on the "average resident." Averages obscure the empirical variation in individual sleep experiences found under real-life conditions.

Methods: In late 2009, we surveyed residents about their first and second years of residency training in internal medicine, surgery, pediatrics, and ob/gyn, in 36 residency programs at 15 hospitals to record the variability of individual sleep and work experiences within programs. The overall response rate was 83.37% (N = 634).

Results: Wide variations in sleep were found within as well as between programs. Within-program sleep hours had standard deviations ranging from 3.26 hours to 9.68 hours. Using ± 2 standard deviations, 95% of the residents in the program with the lowest variation reported sleep times within a 13.04 hour range, while in the program with the highest variation, the range was 38.72 hours. Within-program standard deviations for Epworth Sleepiness scores ranged from a low of 1.89 to a high of 6.94. Using ± 2 standard deviations, 95% of the residents in the program with the lowest variation had scores in a range of 7.56, while in the program with the highest variation, 95% reported scores in a range of 27.76. Pearson correlation between reported sleep hours and Epworth scores was -0.33 (p < 0.001). Specialty accounted for 6% and 7% of the variation in reported sleep hours and Epworth scores respectively, while program accounted for 13% and 14% respectively. Within-program standard deviations in work hours are not significantly related to within-program standard deviations for sleep hours or Epworth scores.

Conclusion: Reports from residents in real-work settings show substantial variations in both sleep time and Epworth scores within the same residency programs.

1001

SLEEP DEPRIVATION IN MEDICAL RESIDENTS: EFFECTS ON SUBJECTIVE AND OBJECTIVE MEASURES OF ATTENTION AND ALERTNESS

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Introduction: The impact of sleep deprivation (SD) on human cognitive functioning has received considerable research attention. The impact of SD on residents' neurocognitive functions such as vigilance, attention, and memory is extremely important for their and their patients' well being. We evaluate the effect of bedtime and total sleep time on several tests of attention, including the ZZ-Test (designed by our team and validated in previous study), Digit Span, Trail Making Tests, Stroop Color-Word Test and compare them with subjective measures of sleepiness.

Methods: A prospective study evaluating healthy consenting medical residents from two institutions. We administered above tests in randomized orders to residents and evaluated their reported sleep schedules for the night and the week before the evaluation. Reported sleep schedules, subjective sleepiness and tests' results were compared using T-Test and paired correlations. Statistical analyses were performed using the SPSS statistical software

Results: We included 28 (14 females and 14 males) subjects from two different institutions. Mean age was 34.32/3.73, mean sleep time/24h was 5.96/ 0.96 for the previous night and 6.89/1.17 for the previous week. Later bedtime (after midnight) correlated significantly with lower scores on ZZT (6.17/1.08 v.s 8.27/1.88, P= 0.05), TMT and SCW, but not with ESS scores (7.33/4.13 v.s 6.45/2.824, p= 0.64). Mean sleep time/24h in the previous week before evaluation correlated significantly with ZZT (r=0.541, p= 0.003), TMT (r= -0.471, p= 0.011) and SCW but again not with ESS (r=0.061, p= 0.757).

Conclusion: In medical residents, shorter sleep time and later bedtime correlated with lower attention and vigilance measured by multiple objective cognitive tests, but not with subjective sleepiness scales. This may reflect underestimation of subjective sleepiness in professionals. Limitations include no objective measures of sleep schedule (Actigraphy) and lower N at this time.

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SIMULATIONS OF ROTATION SCHEDULES FOR TEAMS OF RESIDENT-PHYSICIANS CAN IDENTIFY POTENTIAL AREAS OF LOW PERFORMANCE AND GUIDE RESIDENCY SCHEDULE DESIGN

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Introduction: The Accreditation Council for Graduate Medical Education (ACGME) will require residency training programs to limit PGY1 resident-physicians (interns) to 16 hour shifts beginning July 2011. We used a mathematical model of circadian rhythms and performance [Jewett et al. J Biol. Rhythms 1999] to evaluate predicted intern performance on alternate schedules designed in response to these guidelines.

Methods: Two daytime interns (A,B), with six "cross-cover" night float interns (X1-6) were assigned to cover a month-long rotation. The residency leadership wished for Interns A and B to work 5 days "on" (7:00 to 17:30) followed by two days "off". Two potential schedules were simulated for cross-cover night-float interns: 5 fourteen-hour shifts between 17:00 and 07:00 (contiguous) plus 2 days off vs. two blocks of 3 on-1 off-2 on-1 off (2-block) at the same hours. Based on prior research, sleep was estimated to be 6.6 hours per night for daytime interns and 5.5 hours for night-float interns. Their proposed sleep-wake schedules were simulated with the mathematical model and the quartiles of predicted performance for each work shift were compared.

Results: Over the entire month, the predicted performance (25%, 50%, and 75% quartiles) during the work-shift for daytime interns was 90.9%, 91.8%, and 94.1% of maximum performance. When the two possible night-float schedules were simulated, the quartiles of predicted performance for the contiguous night-float interns were 63.2%, 85.2%, and 94.2% and for the two-block night-float interns were 54.4%, 82.7%, and 93.8%, respectively. For model simulations, a value of ~50% corresponds to > 24 hours of wakefulness, which has been associated with increased medical errors and occupational injuries [Barger, New England J. Med 2005].

Conclusion: The revised schedule resulted in good predicted performance for daytime interns but identified periods of low performance for the night-float interns. Contiguous scheduling of night-float is better

than 2-block scheduling based on the lowest quartile of performance. Mathematical modeling is an effective tool for evaluating residency schedules. The residency program studied plans to implement the contiguous night-float schedule and educate residents on sleep deprivation, sleep hygiene, and the importance of napping before night shifts.

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1003

CANADIAN NATIONAL SURVEY OF CRITICAL CARE NURSES: PRACTICES AND PERCEPTIONS OF NAPPING ON NIGHT SHIFT

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Introduction: The critical care environment requires nurses to care for seriously ill patients and engage in rapid decision-making around the clock. Evidence supports that nurses working night shifts experience sleep deprivation, sleep disturbance, and fatigue with implications for nurses' health and care delivery. Napping during a work break is known to reduce fatigue and improve performance in shift environments outside of health care but is not well supported in nursing. Increased knowledge of nurses' practices and perceptions of napping on breaks on night shift is needed to better inform and direct effective fatigue reduction strategies.

Methods: Following ethical and access approval, a national, web-based survey of staff nurse/charge nurse members of the Canadian Association of Critical Care Nurses was conducted. The 62-item survey contained closed and open-ended questions on nurses' napping practices and perceptions, the impact of napping/not napping, and factors associated with napping or not napping.

Results: Respondents were 536 staff/charge nurses (88% female; mean age 42 years ± 9.8), from 11/13 provinces and territories. Most nurses were experienced in critical care (66% ≥ 6 years), and worked full-time (75%) in a tertiary hospital (65%). Many nurses (66%) usually napped during their break; 80% identified napping benefits; 46% recognized drawbacks. Nurses reported no awareness of (53%) or no napping policy (41%); 84% felt there should be a nap room; 17% had a designated nap room. Barriers to napping included patient care issues, resource deficits, and a lack of administrative support.

Conclusion: The survey findings offer insight into critical care nurses' practices and perceptions of napping on night shifts. While napping can be beneficial, the issue is complex. Solutions require innovation and adaptation at the individual, unit, and organizational level and a balancing of needs of patients, the organization, and the nurses working in critical care to effect positive change.

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