Sleep and Neuropsychiatric Disorders

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Social burden and management of sleep disorders

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Sleep disorders, such as insomnias, obstructive sleep apnoea, and central hypersomnias (narcolepsy, idiopathic hypersomnia), short sleep or sleep loss, and restless leg syndrome, are common disorders or complaints with a significant healthcare burden with consequences for healthcare contacts, medication use, education, employment and the risk of traffic accidents. There is now compelling evidence that the health-related (direct) and social (indirect) costs are significant, and comparable to those of other major disease areas. Thus, in order to care properly for patients presenting with sleep-related morbidity, and to reduce the consequential economic burden, accurate screening efforts and effective, cost-effective treatments need to be developed and employed.

Disclosure: Nothing to disclose.

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Psychiatric risk genotypes and sleep in a prospective population-representative study

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Sleep disturbancies often precede the onset of psychiatric illnesses, and hence effects of risk genotypes on psychiatric disorders and mental health may be mediated by alterations in neurochemical systems that contribute to shaping the sleep patterns. This presentation will examine the associations of two psychiatric 'risk genotypes' with measures of sleep, relying in particular on data collected in a longitudinally observed population-representative sample, the Estonian Children Personality Behaviour and Health Study. The serotonin transporter promoter polymorphism (5-HTTLPR) that is associated with enhanced sensitivity of amygdala to stimuli with negative emotional valence and, in response to environmental adversities, with anxiety and affective disorders, had a complex relationship with sleep and psychiatric morbidity in this sample. We also studied the neuropeptide S receptor gene (*NPSR1*) A/T polymorphism ($Asn^{107}Ile$), previously also associated with the development of anxiety and affective disorders in this sample (Laas *et al., Int J Neuropsychopharmacol* 2014, 17: 541–552). In animal experiments, higher NPS-ergic tone reduces sleep time. The human A/T exchange in *NPSR1* affects receptor function so that the receptor encoded by the T-allele is more efficient in signal transduction. AA homozygotes, previously found to have higher prevalence of anxiety disorders, had higher frequency of sleep disturbances, especially if exposed to adverse family environment. No *NPSR1* main effect on sleep duration was present; however, G × E interaction revealed that homozygotes (both AA and TT) slept less in adulthood if they had experienced adverse environment in adolescence. Conclusively, in this population-representative sample, genotype-related sleep problems precede genotype-related psychiatric disorders.

Disclosure: Nothing to disclose.

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Screening sleep disorders by mattress movement sensor

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The mattress sensors provide unobtrusive means to diagnose sleep disorders. In Finland the big static charge sensitive bed (SCSB) has been replaced by smaller Emfit mattress in many laboratories. The Emfit sensor has been proven to produce similar signal as SCSB. Emfit sensor is suitable in detecting sleep apnea and periodic movements. In addition we have observed that increased negative intrathoracic pressure induces respiratory-related spikes to the Emfit signal. In some patients the respiratory induced spikes appear in sustained form, lasting up to several minutes, sometimes half an hour. In our sleep laboratory 10% of the patients were found to suffer from sustained Emfit spiking (increased respiratory resistance, IRR). We have shown that during IRR there is a sustained negative increase in the intrathoracic pressure and partial pressure of transcutaneus carbon dioxide presents a cumulative increase but arousals and apneas/hypopneas are sparse. However, the ESS scores between the OSA patients and the IRR patients did not differ and the GHQ-12 score of the IRR-patients was high as compared to OSA patients indicating more depressive mood. Previously IRR has been found to be more common among women than among men. We suggest that Emfit mattress provides an easy and patient friendly tool for diagnosing sleep apnea and some movement disorders. In addition it provides unobtrusive means to assess increased respiratory effort and thus adds information to full polysomnography, too.

Disclosure: Nothing to disclose.

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Effects of insomnia CBT-oriented group therapy in adults in Estonia

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Cognitive -behavioural treatment for insomnia should be approachable for large number of patients, considering the large prevalence of insomnia and the proven efficacy of CBT for insomnia in research settings. We developed a group training protocol in the footsteps of the Glasgow University manualized training program, consisting of 5 weekly 90 min sessions. Emotional state questionnaires, including Emotional State Questionnaire (EST-Q; Aluoja, Shlik) and sleep dysfunctional attitudes scales- Sleep Disturbance Questionnaire (SDQ) and Glasgow Content of Thoughts Inventory (GCTI), both by Glasgow University, and a locally developed sleep disorders questionnaire are filled on the 1st and 5th session. From January 2009 to 2014 29 training groups with 153 patients have finished training. The group therapy is applied by 2 mental health nurses, trained in sleep disorders, having preliminary CBT training, also performing independent outpatient visits, CPAP therapy, polysomnography hookup and scoring, leading insomnia training courses for nurses. The centre also offers insomnia CBT courses for MD s and psychologists and teaches insomnia CBT for undergraduates.

We shall review the results of the following study. Subjects: 94 consequtive participants from all groups, who have filled in the tests on both 1 and 5 th session. We aimed to evaluate if there is a significant change from 1st to 5th session in the parameters of the performed tests. Independent samples t-test was performed.

Results: EST-Q depression (2-tailed significance 0.002), generalized anxiety (0.00) and insomnia (0.00) subsets scores,several SDQ and GCTI scores, and several local sleep disorders questionnaire questions scores dropped significantly.
Disclosure: Nothing to disclose.

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Treatment of DSPD with light and melatonin

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Objectives: Delayed sleep phase disorder (DSPD) is a circadian rhythm sleep disorder. Patients with DSPD have problems initiating sleep if they go to bed at a conventional time and they have serious problems waking up at desired times. The disorder is most common among adolescents. Many of the patients struggle with school attendance, and school grades deteriorate. Furthermore, studies show that DSPD is associated with smoking, alcohol usage, anxiety and depression. The recommended treatment options are bright light and exogenous melatonin. It is important to time these treatments appropriately according to the patient's endogenous circadian rhythm, in order to advance the sleep phase. Inappropriately timed light and/or melatonin may worsen the condition. Thus, knowledge of basic sleep regulatory mechanisms is important, for correct treatment of circadian rhythm sleep disorders (1).

I will in the symposium present results from a study investigating short- and long term effects of timed bright light and exogenous melatonin treatment alongside gradually advanced rise times in adolescents/young adults with DSPD in a randomized controlled 2-week trial with an open label 3-month follow-up study. The study shows that light and melatonin are effective measures in maintaining an advanced circadian rhythm among these patients. Both sleep and daytime function were improved by such treatment modalities (2, 3).

References:

1. Bjorvatn B, Pallesen S. Sleep Medicine Reviews 2009; 13: 47–60.
2. Wilhelmsen-Langeland A et al. Journal of Biological Rhythms 2013; 28: 306–321.
3. Saxvig IW et al. Chronobiology International 2014; 31: 72–86.

Disclosure

Nothing to disclose.

Sleep Disordered Breathing: Dilemmas and Cardiac Function

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Snoring and adverse health effects: a general population study in Iceland

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Objectives: To assess the relationship between habitual snoring and adverse health effects by comparing nonapneic snorers and nonsnorers in a general population cohort.

Methods: A random population sample 40–65 years was invited for a home sleep study, included sound recording of snoring (T3, Nox Medical, Reykjavik, Iceland). The psychomotor vigilance test (PVT) and questionnaires were administered and body mass index (BMI) and blood pressure measured.

Results: Among 400 participants, not previously diagnosed with OSA, altogether 164 (41.0%) had undiagnosed OSA (Apnea-hypopnea index [AHI] $\geq$5). Additionally, 101 subjects (25.3%) were nonapneic snorers (snored objectively $\geq$5% of the night and AHI <5). The nonapneic snorers were compared to the 135 (33.8%) nonsnorers for this analysis. Nonapneic snorers were more obese than nonsnorers (mean $\pm$ standard deviation, BMI 28.4 $\pm$ 4.9 vs. 25.9 $\pm$ 3.9 kg/m^{2,} $P < 0.0001$) and older (54 $\pm$ 7 vs. 52 $\pm$ 7 years, $P = 0.01$) but gender differences were not found. Nonapneic snorers had significantly higher blood pressure than nonsnorers, both diastolic (80 $\pm$ 10 vs. 77 $\pm$ 10 mmHg, $P = 0.02$) and systolic (129 $\pm$ 17 vs. 124 $\pm$ 15 mmHg, $P = 0.008$). Also, nonapneic snorers had a longer PVT mean reaction time than nonsnorers (255 $\pm$ 30 vs. 247 $\pm$ 32 ms, $P < 0.05$). However, the Epworth Sleepiness Scale showed no differences in subjective sleepiness. Finally, nonapneic snorers were more likely to report morning headaches $\geq$3 times a week (8.5% vs. 1.5% $P = 0.01$). This difference was still highly significant after adjustment for BMI, age and gender, but the mean reaction time ($P = 0.14$) and blood pressure differences ($P < 0.1$) were not.

Conclusion: A possible relationship between nonapneic snoring and adverse health effects was found.

Disclosure: Nothing to disclose.

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Management of obstructive sleep apnea among drivers in Estonia

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Untreated sleep apnea increases risk of falling sleep at the wheel and up 7 times the risk of accidents due to sleepiness. The prevalence of sleep related accidents in Estonia (2.7%) is the highest in Europe. The excessive daytime sleepiness is the main symptom of sleep apnea, which correlates with BMI and hypertension. Severety of sleep apnea correlates with neck circumference from previous studies. For early diagnosis we recommend add 3(+1) questions to the Health Declaration. STOP Bang Scoring Model. But driver could give to the questions false negative answers by several reasons and most of sleep apnea symptoms can affect every person in some cases.

Recommended questions:

1. Do you have high blood pressure or are you being treated for hypertension?
2. You are female with neck circumference over 40 cm? You are male with neck circumference over 43 cm?
3. BMI over 35 kg/m^2? Additional question: Did you felt repeated sleepiness and decrease of attention at the wheel?

Yes to 1 or more questions, driver needs further investigations and treatment in sleep lab. Evidence of blood pressure and treatment of hypertension are documented in Estonian Medical Databases. BMI and neck circumference are objective and repeated measurements. The most effective treatment is CPAP. Driver with sleep apnea needs regular control of treatment (Estonian e-Health Service). Other treatments: weight loss, ENT and maxillofacial surgey, oral appliances. The screening and treatment of sleep apnea in drivers, especially professionals, could significantly reduce the number of accidents caused by sleepiness at the wheel.

Disclosure: Nothing to disclose.

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Sleep time breathing disorders in Estonian paediatric patients

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Introduction: The aim of this study was to investigate sleep disorders in a sample of Estonian second grade children. The overall description of sleep time breathing disorders in northern region of Europe will be discussed as well in this presentation.

Methods: A retrospective questionnaire based survey was used to analyze factors influencing sleep, parasomnias, daytime sleepiness, and sleep disordered breathing (SDB). 1065 Pediatric Sleep Questionnaire (PSQ) packets were distributed by post to randomly selected parents of second grade students; 703 (66%) subjects were included in the study group; each parent/guardian participant had one second grade child. Descriptive statistics were used to compare characteristics of SDB symptomatic and healthy children. We used logistic regression to analyze factors influencing sleep and parasomnias in relation to SDB severity. Odds ratios (OR) and 95% CI were used to estimate relative risk.

Results: Parents of children with SDB complaints seem to pay attention to sleep disorders especially when a child is suffering from excessive day time sleepiness. Parasomnias are present simultaneously with SDB and tend to worsen in relation to more severe SDB complaints. Many underweight children have SDB symptoms after adenotonsillectomy.

Conclusion: SDB symptoms are found in both overweight and underweight children. Both groups should be observed, especially in terms of the current focus on overweight children. Careful follow up after SDB treatment is necessary in case of under and overweight children. Parental suspicions regarding SDB are noticeably higher in cases of excessive daytime sleepiness in their children.

Disclosure: Nothing to disclose.

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Sleep disordered breathing in women

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Most knowledge on consequences of sleep disordered breathing (SDB) is still based on studies performed solely on men. In addition, some studies have reported an association between SDB and morbidity or mortality in men while the power has been too low to ascertain such relationships in women.

As the prevalence of sleep disordered breathing is high also in women, there is an urgent need to verify the health consequences. During this session, data will be presented on how sleep disordered breathing is interact with markers of cardiac dysfunction and inflammation as well as glucose intolerance and parameters of the metabolic syndrome in women. The long term health effects of this will be discussed.

Disclosure: Nothing to disclose.

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Myocardial electric instability in patients with various degree of sleep apnea

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Myocardial electrical instability, i.e. predisposition to potentially life-threatening ventricular arrhythmias, can be indirectly assessed by parameters, reflecting ventricular repolarization prolongation and inhomogeneity. Various models used for QT interval variability (QTV) estimation, which is defined as a proportion between the absolute beat-to-beat changes of the QT interval durations and the RR interval variability, have demonstrated their utility for high-risk patient identification. Although these methods have been recognized as powerful predictors of arrhythmias and cardiac mortality in heart disease population generally, only few studies have examined QT interval properties in obstructive sleep apnea (OSA) patients. The QT interval analysis may also provide a useful marker of autonomic effects in patients with OSA.

Disclosure: Nothing to disclose.

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Sleep apnea as the main reason of sudden cardiac death at night

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Obstructive sleep apnea (OSA) is associated with significant increase in cardiovascular morbidity and mortality, including sudden cardiac death (SD). Certain circadian patterns for SD are connected to the 24-hour dynamicity of main physiological parameters-blood pressure, heart rate, plasma adrenaline and noradrenaline concentrations, etc. Among the general population, the risk of SD is highest between 6 AM and noon and lowest from midnight until 6 AM. On the contrary, in patients with OSA the SD risk is highest during sleeping hours between midnight and 6 AM — the time of lowest risk for those without OSA. Apneic episodes result in hypoxemia, hypercapnia, abrupt activation of sympathetic nervous system and RAA-system, increase in blood pressure, and cardiac wall stress — all of which run counter to the physiology of normal sleep. Along with other risk factors, this exacerbates the endothelial dysfunction and triggers the well-known pathogenic chain often bringing along a potentially life threatening arrhythmias.

Although changes in certain non-invasive markers of ventricular repolarization prolongation and inhomogeneity, mainly QT interval variability, have been recognized as powerful predictors of arrhythmias and cardiac mortality in heart disease population generally, only few studies have examined QT interval properties in OSA patients. Several novel data- processing programs applied for repolarisation changes, that occur in patients with OSA prior to, during and after apnoe episodes, have demonstrated their utility for high-risk patient identification.

Disclosure: Nothing to disclose.

Young Scientists Symposium

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Region-specific response to sleep restriction in children: associations with performance and myelination

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Objectives: Although slow-wave activity (SWA, 1–4.5 Hz) in the sleep EEG changes across childhood, the effects of increased sleep pressure on SWA during development remain understudied. We examined SWA-topography following sleep restriction, associations with myelination and reaction time in children.

Methods: High-density EEG was recorded in 13 healthy children (5–12 years, 7 m) during habitual sleep (HS) and restricted sleep (RS, 50% of HS, delayed bedtime). A topographic analysis of SWA was performed (first 60 min NREM sleep). Myelin-water-fraction (MWF) maps were determined (mcDESPOT-MRI, normalization to custom pediatric templates, Gaussian kernel smoothing). Before and after sleep, reaction time was measured in an auditory oddball task.

Results: RS led to an overall SWA increase, which was most pronounced in 3 regions (2 prefrontal, PF; 1 parieto-occipital, PO). The SWA increase in PO was negatively associated with MWF in the optic radiation (partial $r = -0.57$, $P < 0.05$). Moreover, the SWA increase in PF correlated with an overnight reaction time decrease (HS, $r = -0.79$ $P < 0.05$; partial $r = -0.81$ $P < 0.05$).

Conclusions: Unlike the adult-typical frontal SWA increase after sleep deprivation, parieto-occipital and prefrontal SWA was enhanced in children, which may be driven by anatomical substrates. Moreover, overnight performance changes may benefit from a more 'frontalized' SWA-response to RS. Similar to recent animal studies, our results suggest that maturing brain circuits in children are vulnerable to sleep loss. Chronic inadequate sleep throughout childhood may be a risk factor for the development of mental health disorders.

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Upper airway collapsibility is sleep state-dependent

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Objectives: An anatomically narrow or highly collapsible upper airway is a key cause of obstructive sleep apnea (OSA). The gold standard for measuring upper-airway collapsibility (or functional anatomy) during sleep is via the 'passive' critical closing pressure (Pcrit) technique. Upper-airway muscle activity and OSA severity are state-dependent. However, prior Pcrit studies involving a small number of participants, suggest that Pcrit does not vary with sleep state. This study aimed to determine the effect of sleep state on Pcrit and genioglossus muscle activity in a larger cohort than tested previously.

Methods: 75 men and women with and without OSA were studied on nasal CPAP. Transient CPAP reductions were applied during stable N2, N3 and REM sleep to induce varying degrees of upper-airway collapse for measurement of Pcrit (estimated mask pressure where airflow ceases). Peak genioglossus activity was measured via intramuscular electrodes on therapeutic CPAP immediately prior to CPAP reductions.

Results: Genioglossus activity on therapeutic CPAP was state-dependent (N2 = 2.3 $\pm$ 0.5, N3 = 2.8 $\pm$ 0.6, REM = 1.1% $\pm$ 0.2% of maximum, $P < 0.01$). Similarly, Pcrit was state-dependent ($P < 0.01$). The upper airway was 1.5 $\pm$ 0.7 cmH_2O and 2.3 cmH_2O more collapsible during N2 vs. N3 and during REM vs. non-REM sleep, respectively.

Conclusions: Contrary to previous findings, these data indicate that upper airway collapsibility measured via the Pcrit technique varies with sleep state. Even when upper-airway muscle activity is relatively low on therapeutic CPAP, state-dependent changes may contribute to alterations in airway collapsibility. These findings should be taken into account when performing and interpreting 'passive' Pcrit measures.

Disclosure: A modified CPAP device on loan from Philips Respironics was used to perform these upper airway physiology measures

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Investigating the role of microRNAs in sleep homeostasis

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Objectives: microRNAs (miRNAs) are key regulators of gene expression and have been involved in almost every cellular processes investigated thus far. However, their role in sleep, in particular in the homeostatic aspect of sleep control has received little attention and is the aim of our study.

Methods: First, miRNA expression was analyzed through miRNA microarray on the whole brain, the cerebral cortex and the hippocampus of sleep deprived (SD) and control C57BL/6J mice. In a second, transgenic approach, neuron-specific conditional *Dicer* knock-out (cKO) mice's sleep was recorded through EEG/EMG during 48 h of baseline, a 6 h SD starting at light onset, followed by 42 h of recovery.

Results: SD significantly affected the expression of several miRNAs in the mouse brain, with miR-709 being affected the most in the whole brain especially in the cerebral cortex. In situ hybridization confirmed an increase in *miR-709* expression in the cortex after SD, suggesting a role for this activity-induced miRNA in processes associated with SD. Region-specific changes in miRNA expression were observed, 45% of the miRNAs being significantly over-expressed in the hippocampus and 55% in the cortex, suggesting differential roles of miRNAs in regulating the processes activated by SD. EEG/EMG recording of *Dicer* cKO mice revealed an altered homeostatic sleep phenotype (i.e., higher increase in EEG delta power after 6 h SD, and lower REM sleep rebound during recovery sleep), but an intact sleep/wake distribution.

Conclusion: Through two different investigation techniques, the current study supports an important role for miRNAs in various aspects of sleep homeostasis.
Disclosure: Nothing to disclose.

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The impact of sleep on three-ball cascade juggling

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Objectives: Concerning fine-motor skills there is profound knowledge that sleep contributes to the consolidation of motor-learning. However, data on complex motor tasks are still rare. We here examine sleep effects on 3-ball cascade juggling.
Methods: 32 subjects (16 males; 19–29 years) were trained on 2 tasks in a randomized order on 2 different days: juggling (complex motor-learning) and throwing (simple motor-learning). 16 subjects were trained in the evening (sleep-group), 16 subjects in the morning (wake-group). After an 8 h retention-interval motor performance was tested again. Performance in both tasks was assessed by the number of ball-catches. The sleep-group spent 3 nights in the lab:
i) baseline-night (without prior motor learning)
ii) control-night (after simple motor learning) and
iii) experimental-night (after complex motor learning).
Results: A 2-factor ANOVA revealed a significant interaction ($F1,30 = 5.986$, $P = 0.020$) between PREPOST (pre vs. post retention-interval) x GROUP (sleep vs. wake). Post-hoc tests showed that performance remained stable after sleep ($P = 0.242$) but was reduced after wakefulness ($P = 0.002$). For the sleep-group we found that subjects showing higher sleep spindle activity during the experimental-night were able to enhance their performance over night ($r = 0.614$, $P = 0.015$). Furthermore there was a statistical trend for a negative relationship between REM sleep duration during experimental-night and overnight performance changes ($r = -0.480$, $P = 0.060$).
Conclusions: Sleep in comparison to wakefulness benefits the stabilization of performance in 3-ball cascade juggling. Slow sleep spindles and REM sleep seem to be involved in this process, though the direction of the effect differs.
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Learning, Memory and Cognition

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Slow oscillations during sleep orchestrate interregional communication in cortical networks

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Introduction: Large-amplitude sleep slow oscillations temporally coordinate faster neuronal oscillations. However, relatively little is known about the impact of slow oscillations on brain-wide spatio-temporal dynamics. Our aim was to investigate whether distributed cortical networks might become functionally and transiently coupled depending on the slow oscillation phase.

Methods: Human sleep was recorded through 128-channel EEG and current source density estimated, to minimize effects of volume conduction. Brain-wide functional connectivity dynamics were investigated across multiple frequency bands along the slow oscillation time course. Functional connectivity was assessed in terms of consistent phase locking and cross-frequency phase-amplitude relations between cortical sites.

Results: We demonstrate that interregional cortical communication depends on slow oscillations, as indexed by phase synchrony between cortical sites in the sleep spindle frequency range and cross-frequency coupling between slow oscillations, spindle and gamma activity. Furthermore, slow oscillations detected over different parts of the cortex show distinct modulation topographies.

Conclusions: According to our findings, the sleep state allows for highly complex spatiotemporal organization of neural activity. These dynamics appear to be shaped by the local occurrence of slow oscillations. These results suggest that sleep can support coordinated information processing at the level of distributed cortical networks. This is of considerable relevance for accounts of sleep-dependent memory reprocessing and consolidation, who's central premise holds that sleep-reactivation of distributed memory representations leads to synaptic modification of interregional cortico-cortical connections.

Disclosure: Nothing to disclose.

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Afternoon nap and exposure to bright light to prevent post-prandial decreases in task switching

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Objectives: Beneficial effects of a nap or bright light to overcome the post-lunch dip have been explored on various cognitive tests, but rarely on task switching. This study investigates the impact of these countermeasures on post-prandial alterations in task switching.

Methods: Twenty-five healthy adults participated in two randomized experimental conditions, either wake and nap, or bright light and placebo. In the 30-min nap/wake condition, participants either stayed awake watching a documentary or took a nap. In the 30-min bright light/placebo condition, participants watched a documentary under either bright blue light or dim orange light. For each trial, task switching presented a cue after which one of two presented stimuli had to be matched to a target.

Results: In the control condition (wake/placebo), a post-lunch dip in task switching emerged (increased switch-cost in errors, $P = 0.014$). Both interventions (nap/bright light) elicited a decrease of this post-lunch dip ($P = 0.019$), correlated with diminished fatigue and vigilance variability ($P = 0.017$, $P = 0.008$). Additional post-lunch benefits of bright light on cognitive flexibility were evidenced (decreased switch cost on RTs, $P = 0.051$). In the nap group, lower post-lunch dip in task switching correlated with more N1 ($P = 0.006$). Similar results were obtained for short and long cue-stimulus intervals indicating a modulation of reactive control processes more than proactive mechanisms.

Conclusions: Exposure to bright light during the post-lunch dip, easily applicable in daily life, results in similar beneficial effects than a short nap on task switching accuracy. In addition, bright light exposure could reduce switch cost in response speed during post-lunch dip.

Disclosure: Nothing to disclose.

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No effect of sleep on the generalization of fear learning

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Objectives: Sleep has been shown to be involved both in emotion regulation and in the active processing of information. We combined these two concepts and tested if sleep affected the generalization of fear learning.

Methods: In a fear conditioning paradigm, participants were shown images of a small and a big circle where one of them was paired with an aversive sound, making it the CS+. Fear was measured with skin conductance responses. Participants were then randomly divided into a sleep or a wake group. The sleep group took a 2 h nap while the wake group rested for 2 h. Participants were then exposed to the two circles seen before, combined with 8 novel circles that gradually varied in size from the small one to the big one. We looked at how many circle sizes away from the CS+ that participants still exhibited a fear response, and if this differed between the sleep and the wake group.

Results: We found no effect of sleep on the slope of the generalization across the different circles. There was a main effect of circle size, $F(1,25) = 10.42$, $P = 0.01$, but no main effect of sleep/wake, $F(1,25) = 0.40$, $P = 0.54$, and no interaction between sleep/wake X circle size, $F(1,25) = 0.62$, $P = 0.44$.

Conclusions: The fear conditioning manipulation worked, with a gradual increase of fear depending on the stimuli's similarity to the CS+. However, there was no effect of sleep or wake, which could possibly be explained by that just a 2 h nap not being a sufficient sleep manipulation to detect any differences.

Disclosure: Nothing to disclose.

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Factors influencing mechanisms supporting overnight declarative memory consolidation

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Objectives: Today there is little doubt concerning the significance of sleep for memory consolidation. Contemporary research has often attempted to reveal mechanisms supporting this process. Moreover,

it is widely accepted that sleep architecture, as well as sleep specific microstructures change with age. In the current study we sought to explore the effect of age on sleep-dependent declarative memory consolidations, sleep architecture, as well as sleep spindles and slow oscillations in insomnia.

Methods: 23 subjects with primary insomnia were divided in two age groups: younger (24.54 $\pm$ 5.28) and older (43.00 $\pm$ 3.84). Participants learnt a list of 80 word-pairs in the evening. Later they underwent two cued recall sessions, one before and one after 8 h of nocturnal sleep with full polysomnography.

Results: We found that only the older group displayed significant memory loss over the night. In this age group a shorter length of slow oscillation half waves was correlated with better memory performance. Other parameters that revealed associations with memory consolidation, such as slow oscillation density or amplitude, were merely due to age difference. No associations between memory and sleep spindles were revealed.

Conclusions: Our findings highlight the crucial influence of age for mechanisms of 'offline' memory consolidation, even over a rather narrow age range (19–48 years), in patients suffering from primary insomnia.

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Mathematical modeling and *ADORA2A* genotype elucidate individual differences in the effects of sleep loss on risky decision-making

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Objectives: Sleep loss (SleepDep) has been linked to faulty decision-making (DM; e.g., Chernobyl) but laboratory findings are inconsistent. This investigation combined mathematical modeling with adenosine A2A receptor (*ADORA2A*) genotyping to further understand individual differences in the effects of SleepDep on risky DM.

Methods: 22 males completed rested and SleepDep in-laboratory sessions 1 week apart with order counter-balanced (*ADORA2A* genotypes included 6 'C/C', 9 'C/T', and 7 'T/T'). The Iowa Gambling Task involves risky decisions between card decks and was administered at 13:40 at each session (after 5.7 h vs. 29.7 h of wakefulness). Hierarchical Bayesian implementation of the Prospect Valence Learning-Delta model yielded four parameters: *A*, sensitivity to reward and loss magnitude; *w*, weighting of losses relative to gains; *a*, valence updating and *c*, decision consistency.

Results: There was a main effect of SleepDep on *A* ($F_{1,19}$ = 22.88, P = 0.0001, 91% reduction in magnitiude sensitivity, Cohen's d effect size (ES) = 1.3). Further, there was a cross-over interaction between *ADORA2A*_gene and SleepDep on *w* ($F_{2,19}$ = 6.3, P = 0.008, ES = 0.23).

Conclusions: These results clarify previous inconsistent findings on SleepDep and risky DM. SleepDep has a large effect on mathematical parameter *A,* indicating that fatigue sharply blunts sensitvity to the magnitude of gains and losses. Further, SleepDep has differential influences on *w* for different *ADORA2A* genotypes. During sleep loss 'C/C'-genotypes paid relatively more attention to losses, while instead 'C/T' and 'T/T'-genotypes began to neglect losses and were reward-seeking. These findings elucidate how SleepDep degrades DM, and for whom.

Disclosure: Supported by travel grant of the ESRS Network of Sleep Research Laboratories.

Interactions between Sleep and Circadian Rhythm

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Chronotype-specific alterations in semantic priming performance during functional MRI (fMRI)

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Objective: Based on individual physiological cycles, humans can be classified as early (EC), late (LC) and intermediate (IC) chronotypes. Recent studies have verified that chronotype-specificity relates to performance on cognitive tasks: participants perform more efficiently when tested in the chronotype-specific optimal time of day than when tested in their non-optimal time. Nevertheless, imaging studies focussing on the underlying neural mechanisms of chronotype-specificities are sparse. Chronotype-specific semantic processing alterations have been neglected entirely.

Methods: 16 male, healthy ECs, 16 ICs and 16 LCs participated in a fast event-related functional Magnetic Resonance Imaging (fMRI) paradigm probing semantic priming 12 h after their individual wake up times. Subjects read two subsequently words (prime, target) and were requested to determine whether the target word was an existing word or a non-word. Reaction times, accuracy and fMRI semantic priming contrasts were analysed.

Results: Chronotype-specificity is associated with task-performance and brain activation. First, ECs exhibited slower reaction times than LCs. Second, ECs showed attenuated BOLD responses in several task-related brain areas, e.g. in the left postcentral, left and right precentral and in the right superior frontal gyrus. Additionally, increased BOLD responses were revealed for LCs as compared to ICs in task-related areas, e.g. in the right inferior parietal lobule.

Conclusions: The present study determined the underlying neural activation of chronotype-specificity during basic visual semantic processing. Importantly, our results lead to strong socio-economic implications (i.e. fixed vs. flexible working schedules) and clearly speak for the assessment of the subjects' chronotype for experimental study recruitments and/or clinical settings.

Disclosure: Nothing to disclose.

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Circadian regulation of EEG slow waves and phase coherence in human sleep

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Objectives: Both slow waves (0.5–4 Hz) and phase coherence are thought to reflect neural connectivity and to be modulated by brain maturation, learning and sleep history. We aimed to investigate the circadian modulation of slow wave parameters (SW) and phase coherence across multiple frequencies in NREM sleep.

Methods: 230 sleep periods of 34 young healthy participants scheduled across the circadian cycle in a 10-day forced-desynchrony protocol were analysed with qEEG and statistical methods.

Results: Circadian rhythmicity significantly modulated the incidence, amplitude, duration and the slope of the SWs in all brain areas. This circadian influence on some SW parameters such as amplitude, duration and slope was similar to or greater than the sleep-dependent modulation in several brain regions including central, temporal and occipital brain regions. Sleep-dependent modulation of characteristics of SWs was more prominent in frontal than in posterior brain areas. Interhemispheric coherence (Inter-HC) showed a strong significant sleep dependent increase in the delta, theta and sigma band. Intrahemispheric coherence (Intra-HC) showed a sleep dependent decrease only in the higher frequency range (>15 Hz). Intra-HC was under a considerable circadian variation across all frequency bands except the delta band whereas the circadian modulation of the Inter-HC was significant only for the alpha band.

Conclusion: These findings challenge concepts of exclusive sleep dependent regulation of SWs and imply a contribution of circadian rhythmicity to functional brain connectivity.

Disclosure: Nothing to disclose.

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Human cortical excitability depends on time awake and circadian phase

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Objectives: The dynamics of neuronal excitability is considered to be mainly driven by sleep homeostasis, which directly depends on time spent awake. However, no study has been properly designed to investigate a putative circadian timing system influence on human cortical excitability. Here we assessed this circadian modulation using transcranial magnetic stimulation coupled with electroencephalography (TMS/EEG).

Methods: Twenty-two healthy young men (18–30 years) underwent 8 TMS/EEG sessions during a 28 h sustained wakefulness under stringent constant routine conditions. Participants were stratified in two groups according to a polymorphism in *PERIOD3* (*PER3*), known to affect sleep-wake regulation (15 $PER3^{4/4}$; 7 $PER3^{5/5}$). Cortical excitability was inferred from the normalized amplitude of the first component of TMS-evoked EEG potentials over the prefrontal cortex, a brain region highly sensitive to sleep deprivation.

Results: Cortical excitability significantly increased with time spent awake. However, the dynamics of this change was not linear and presented a pronounced local decrease around the so-called evening wake-maintenance zone. Conversely, a marked local amplification was found at the end of biological night when the circadian system maximally promotes sleep. This time-course was best predicted by the interaction of linear (sleep homeostasis) and sine-wave (circadian) functions. Interestingly, analyses by genotypes showed that the overnight difference in cortical excitability between sleep and wake maintenance zones was more pronounced in $PER3^{5/5}$.

Conclusions: These results demonstrate that temporal changes in cortical excitability depend on the interplay between sleep homeostasis and circadian timing system.
Fundings: FNRS, AXA, WBI, ULg, FMRE, ARC, FEDER, RADIOMED.

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Impact of sleep pressure, circadian phase and the ADA polymorphism on cerebral correlates underlying working memory performance

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Objectives: A functional polymorphism in adenosine deaminase (ADA) modulates behavioural susceptibility to variations in sleep pressure as well as circadian sleep-wake regulation. Here we explored whether it also acts on sleep pressure- and circadian phase-dependent cerebral correlates underlying working memory performance.
Methods: Twelve G/A-and 12 G/G-allele carriers underwent a 40-hours sleep deprivation (SD) and multiple nap (NP) protocol. Blood-oxygen-level-dependent (BOLD) activity was assessed during an n-back task scheduled to the end of the biological day and night. Genotype-specific analyses focused on comparisons of (1) NP vs SD, and (2) day vs night during NP.
Results: Performance was worse during SD particularly at night ($P_{all} < 0.05$), but similar for both genotypes. The impact of sleep pressure condition on task-related BOLD activity was modulated by genotype: G/A-allele carriers decreased activity from NP to SD (1) in frontal, anterior cingulate and right temporal regions ($P_{corr} < 0.05$), a pattern not present in G/G-allele carriers. Concomitantly, frontal BOLD activity decreased in G/A-, but not in G/G-allele carriers from day- to nighttime [(2), $P_{corr} < 0.05$], encompassing an area modulated by sleep pressure (1) specifically in the G/A-genotype.
Conclusions: Our results indicate an increased susceptibility to sleep pressure variations in G/A-allele carriers at the cerebral level. They further point towards a stronger circadian modulation in task-related frontal BOLD activity in this genotype. Interestingly, a part of these frontal regions overlaps with an area varying according to sleep pressure levels, suggesting a genotype-specific common interface of circadian and homeostatic influences during working memory performance.
Disclosure: Nothing to disclose.

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Individual differences in the non-image forming effects of light on human sleep

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Objectives: Non-image-forming (NIF) responses to light modulate human physiology. However, how NIF light responses modulate human sleep and if these effects are different across individuals remain scarcely understood. Here we investigated NIF responses to light on sleep in individuals genotyped for the *PERIOD3 (PER3)* variable-number-tandem-repeat (VNTR) polymorphism.
Methods: Eighteen healthy young men (20–28 years; mean ± SEM: 25.9 ± 1.2) homozygous for the *PER3* polymorphism were matched by age, body-mass index and ethnicity. The study protocol comprised a balanced cross-over design during the winter, in which participants were exposed to light of 40 lux at 6500K (blue-enriched) and at 2500K (non-blue enriched), during 2 h in the evening.
Results: Blue-enriched light induced significant increases in all-night NREM sleep slow-wave activity (SWA: 1.0–4.5 Hz) in the occipital cortex only for the $PER3^{5/5}$ individuals, relative to the non-blue enriched ($P = 0.02$). Dynamics of SWA across sleep cycles indicated increased occipital NREM sleep SWA for virtually the entire sleep episode, but only in the $PER3^{5/5}$ individuals. Furthermore, they experienced blue-enriched light as being two times brighter, relative to the $PER3^{4/4}$ individuals ($P = 0.03$). Intriguingly, this subjective perception of brightness significantly predicted their increased occipital SWA throughout the sleep episode ($r = 0.34$, $P = 0.04$).
Conclusions: Our data indicate that humans homozygous for the $PER3^{5/5}$ allele are more sensitive to NIF light effects, as indexed by specific changes in their sleep EEG activity. Ultimately, individual differences in NIF light responses on sleep may depend on a clock gene polymorphism involved in sleep-wake regulation.
Fundings: Swiss Federal Office for Public Health

Insomnia – from Structure to Dysfunction

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Reduced anterior internal capsule white matter integrity in primary insomnia

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Objectives: Chronic insomnia is one of the most prevalent central nervous system diseases, however, its neurobiology is poorly understood. Up to now, nothing is known about the integrity of white matter tracts in insomnia patients.

Methods: In this study, diffusion tensor imaging (DTI) was used in a well characterised sample of primary insomnia (PI) patients and good sleeper controls to fill this void. Voxelwise between-group comparisons of fractional anisotropy (FA) were performed in 24 PI patients (10 males; 14 females; 42.7 6 14.5 years) and 35 healthy good sleepers (15 males; 20 females; 40.1 6 9.1 years) with age and sex as covariates.

Results: PI patients showed reduced FA values within the right anterior internal capsule and a trend for reduced FA values in the left anterior internal capsule.

Conclusions: The results suggest that insomnia is associated with a reduced integrity of white matter tracts in the anterior internal capsule indicating that disturbed fronto-subcortical connectivity may be a cause or consequence of the disorder.

Disclosure: Nothing to disclose.

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Differential brain structural correlates of insomnia severity in affective disorders

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Objective: Prevention targeting people at an increased risk to develop affective disorders may be the most viable approach to mitigate an increasing global burden. Insomnia is a major and modifiable risk factor for new-onset and relapse of affective disorders. Brain structural correlates of insomnia in affective disorders have remained virtually unexplored, while they would likely reveal targets to alleviate the risk and improve the trajectory of affective disorders.

Methods: In a cross-sectional design, brain morphometry and insomnia severity were assessed in 59 participants with major depressive disorder (MDD), 61 with anxiety disorder without and 78 with comorbid depression, and 62 controls. Whole-brain voxel-based morphometry of structural magnetic resonance imaging data was used to investigate the association of insomnia severity with gray matter (GM) density.

Results: Exclusively in patients with MDD, but not in controls or patients with anxiety disorder with or without comorbid depression, insomnia severity showed a strong negative association with GM density in a large cluster in the left thalamus that encompassed the complete pulvinar. The observed association in MDD was independent of severity of depression or use of antidepressant medication.

Conclusions: Given the pulvinar's unique direct bidirectional connectivity with the cerebral cortex, low pulvinar GM density may be responsible for the low coherence of sleep oscillations across distant cortical areas previously found in MDD. The selective involvement of the pulvinar in insomnia severity in MDD has implications for our understanding of insomnia. Depending on the affective disorder phenotype, different brain mechanisms might underlie seemingly similar sleep complaints.

Disclosure: Nothing to disclose.

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Cortical thinning in patients with persistent insomnia is associated with reduced structural connectivity in the default mode network

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Objective: Despite recent neuroimaging findings of various structural alterations in insomnia, the results have largely been inconsistent due to methodology differences.

The current study aims at assessing structural abnormalities in a large sample of patients with persistent insomnia (PI) compared to good sleepers (GS) using recently developed measures of cortical thickness and structural connectivity. This study particularly focused on regions of the default-mode network (DMN).

Methods: Fifty-seven patients presenting PI and 40 good sleepers (GS) underwent structural magnetic resonance imaging (MRI) acquisition. Based on literature review, we selected the cortical regions corresponding to the DMN. A seed-based structural covariance analysis measured cortical thickness correlation between each seed point and other cortical areas. Association of cortical thickness and the measured covariance with sleep quality (measured by Pittsburgh Sleep Quality Index, PSQI) and neuropsychological assessments were further assessed using linear regression models.

Results: Compared to GS, cortical thinning was found in PI in the anterior cingulate cortex, central cortex, and lateral prefrontal cortex after adjusting for age, sex, and depression levels. In PI, decreased structural covariance within regions of the DMN was observed, specifically decreased connectivity between anterior and posterior regions of the DMN. Decreased structural covariance within the DMN was also associated with lower PSQI scores and impaired working memory.

Conclusion: Our results suggest that insomnia patients may fail to disconnect anterior and posterior regions of the DMN during the wake to sleep transition due to structural disruption of frontoparietal

connectivity, which may lead to sustained sleep difficulties and cognitive impairment.
Disclosure: Nothing to disclose.

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Sleep restriction therapy for insomnia: an exploratory assessment of sleep and physiological markers of arousal in response to treatment

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Objectives: Higher arousal levels have been found in those with insomnia compared to controls. This study aimed to profile objective changes in sleep and physiological arousal pre-to-post sleep restriction therapy (SRT) for psychophysiological insomnia (PI).
Methods: Ten participants with PI underwent 6 weeks of SRT. To determine arousal, dependent variables were assessed pre and post-treatment including: objectively-defined total sleep time (TST), overnight plasma cortisol concentrations and core body temperature. It was hypothesised that objectively-defined sleep would improve, and measures of physiological arousal would reduce (cortisol and core body temperature).
Results: Confirming the benefits of therapy, Insomnia Severity Index scores decreased significantly (mean (SD): 18.2 (2.8) vs. 8.4 (4.8), $P < 0.01$). Improvements were found for TST (min): mean (SD): 313.7 (54.2) vs. 353.6 (40.9), $P < 0.05$. Plasma cortisol (μg/dL) did not reduce pre-to-post therapy but displayed significantly higher levels in the early morning (03:00–06:00) at post-treatment compared to baseline (mean (95% CI): 7.0 (5.9, 8.2) vs. 9.7 (8.5, 10.9), $P < 0.01$). Core body temperature (°C) was found to reduce significantly (mean (95% CI): 36.54 (36.3, 36.8) vs. 36.45 (36.2, 36.7), $P < 0.05$).
Conclusions: Effective SRT appears to increase objectively defined TST, early morning cortisol concentrations and decrease core body temperature in PI. This study suggests that SRT may improve sleep and physiological functioning through modifications in arousal. Further studies are required to evaluate potential changes in larger numbers of participants over the course of 24 h under constant routine conditions.
Disclosure: Nothing to disclose.

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Correlates of sleep misperception

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Introduction: Few studies have documented correlates of sleep misperception. Our objective is to link misperception to sleep severity, beliefs and attitudes and personality measures between insomnia individuals (INS) classified as paradoxical insomnia (PARA-I) or psychophysiological insomnia (PSY-I) and good sleepers (GS).
Methods: 122 individuals [(50 GS; M*Age*: 34.7, SD = 1.29); (72 INS; 42 PSY-I; M*Age*: 40.2, SD = 1.4 and 30 PARA-I; M*Age*: 40.0, SD = 1.7)] spent four nights in the laboratory. BDI, BAI, ISI, DBAS and NEO-FFI were completed. Difference scores were obtained by subtracting subjective (diary) from objective (PSG) measures of SOL, WASO and TST. Four misperception categories were created: A) $\leq$30 min; B) between 30 and 60 min; C) between 60 and 90 min and D) more than 90 min.
Results: Significant correlations were obtained for GS on Extraversion (WASO-B, r = 0.42) and Openness (SOL-B, r = 0.41). For INS, significant correlations were obtained for SOL-B and BAI (r = $-$0.30), BDI (r = $-$0.30), ISI ($-$0.32) and WASO-B and DBAS scores ($-$0.25).When INS were subdivided, associations were found for PSY-I for DBAS (WASO-C = 0.38), BDI (SOL-C = 0.38) and Conscientiousness (SOL-C = 0.32) while for PARA-I, they were DBAS and BDI (SOL-C = $-$0.57 and 0.55) and Conscientiousness (SOL-C = $-$0.44 and WASO-C = $-$0.53).
Conclusion: Results suggest that correlates of sleep misperception appear especially for WASO, only once it exceeds 60 min. In addition, they differ for GS and INS, albeit be PSY-I or PARA-I. All questionnaires, to a certain extent, could be helpful at targeting sleep misperception.
Disclosure: Nothing to disclose.

From Mice to Man and One Bird – Physiology of Sleep

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Prior light history impacts on cognitive brain function

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Objective: Recent data suggest that melanopsin has dual-state properties, such that its light sensitivity is modulated by prior light exposure. Accordingly, prior exposure to 590 nm, 515 nm and 480 nm monochromatic light would lead to higher, medium or lower subsequent melanopsin sensitivity, respectively. Here we tested if light history modulates the subsequent impact of light on cognitive brain function, and if this modulation is compatible with melanopsin dual-state properties.

Methods: Sixteen participants underwent 3 identical and consecutive functional magnetic resonance imaging (MRI) sessions during which they were exposed to a monochromatic green test-light (515 nm), while performing a simple auditory detection task (0-back task) and a more difficult auditory working memory task (3-back task). Seventy minutes before each session, participants were exposed to 10 min of orange (589 nm), green (515 nm) or blue (461 nm) monochromatic light.

Results: Prior exposure to orange, as compared to blue light, increased executive responses bilaterally in the dorsolateral prefrontal cortex, in the right ventrolateral prefrontal cortex, and in the pulvinar. Furthermore, prior exposure to green, as compared to blue light, increased executive responses in the left ventrolateral prefrontal cortex. Remaining comparisons (orange > green; green > orange; blue > orange; blue > green) had no significant prefrontal responses. This wavelength-dependent impact of prior light exposure is consistent with recent theories of light-driven melanopsin dual states.

Conclusion: Our results emphasize the key role of light for cognitive brain responses and are the strongest evidence in favor of a cognitive role for melanopsin. Ultimately, this photopigment may confer a form of 'photic memory' to human cognitive brain function.

Fundings: FNRS-FMRE-ULg-AXA.

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Dynamics of fractal indices extracted from human EEG suggest how NREM-related synchronous resets compete with self-organization and protect sleep unconsciousness via fragmentation of functional connectivity

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Objectives: Criticality reportedly describes brain dynamics. Some Critical Features (CFs), like

1. scale-free neural avalanches, are associated to Self-Organized Criticality (SOC); others, like
2. scale-free-network topology of functional connectivity, and
3. temporal long-range memory associated to renewal intermittency of the order parameters, are described by second-order phase transitions (SOPTs).

SOC's advocates question SOPT because it requires fine-tuning of control parameters. SOPT's advocates respond that inhomogeneity can spread critical points into broad critical regions. Here we investigate how CFs change in different sleep phases and whether resulting differences help understanding the connection between criticality and consciousness.

Methods: We recorded 29 128-channels nocturnal EEGs including pre-sleep wakefulness and all sleep phases, with different levels of mentation and consciousness. We used Hilbert transform to select spatially distributed phase/amplitude changes in EEG activity (Multi-Channel Rapid Transition Processes, MC-RTPs). CF #1 (avalanches) is studied by event-based cluster analysis of MC-RTPs; CF #2 (scale-free network) is studied via network analysis of supra-threshold pairwise long-time MC-RTPs correlations; CF #3 (infinite memory) is studied on MC-RTPs signal via Detrended Fluctuation Analysis.

Results: While SOC-related properties are unchanged, intermittency and complex functional connectivity are present during conscious phases (wakefulness, REM sleep), and break down during non-REM sleep (N2 and N3).

Conclusions: Results are not compatible with either SOC or SOPT with parameter changes associated to the passage from wakefulness to NREM sleep and/or from NREM to REM sleep. We provide a theory for fragmentation-induced intermittency breakdown mediated by NREM-sleep bistability (i.e. globally-resetting hyperpolarization induced by K+ channels opening).

Disclosure: Nothing to disclose.

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Cardiorespiratory control during sleep in histamine-deficient mice

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Objectives: The central histamine system is involved in wake-sleep control. It is debated whether this system is altered in narcolepsy-cataplexy, which entails cardiovascular derangements during sleep. We aimed to investigate whether histamine deficiency deranges cardiorespiratory control during sleep.

Methods: Eight histidine-decarboxylase knock-out (HDC-KO) male mice with congenital histamine deficiency and ten congenic (C57Bl/6J) wild-type (WT) controls were implanted with electrodes for sleep recordings and with a catheter for telemetric recording of mean blood pressure (MBP) and heart rate (HR). Recordings were performed on freely-behaving mice either in their own cages or in a whole-body plethysmograph for simultaneous monitoring of breathing.

Results: HDC-KO ate more food and weighted more compared with WT. Indexes of cardiac vagal and vascular sympathetic modulation were higher for HDC-KO than for WT. HDC-KO had enhanced increases in MBP and HR upon awakening from non-REM sleep and lower pre-awakening values of HR than WT. HR was also lower in HDC-KO than in WT during aroused wakefulness (sleep deprivation and cage-switch). Conversely, HR variability during non-REM sleep was higher in HDC-KO than in WT. HDC-KO and WT did not differ in terms of breathing during sleep, including the sleep apnoea index.
Conclusions: HDC-KO mice with congenital histamine deficiency show mild derangements in cardiovascular but not in respiratory control during sleep. This suggests that alterations of histamine transmission may modulate cardiovascular derangements during sleep in pathological conditions such as narcolepsy-cataplexy.
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Sleep and vigilance linked to melanism in wild barn owls (*Tyto alba*)

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Objectives: Understanding the function of variation in sleep requires studies in natural ecological conditions in which sleep evolved. Sleep has an impact on individual performance and hence may integrate the costs and benefits of investing in processes that are sensitive to sleep such as immunity or coping with stress. Because dark and pale melanic animals differentially regulate energy homeostasis, immunity and stress hormone levels, the amount or organization of sleep may covary with melanin-based colour.
Methods: We recorded the EEG of barn owl nestlings (66) in nature using a minimally-invasive method. A 24-hour period was scored for wakefulness, non-REM and REM sleep using 4s epochs by a scorer blind to all other variables. Additionally, we measured melanin-based colouration of nestlings and their parents as well as vigilance during family interactions.
Results: Wild, cross-fostered nestling barn owls born from mothers displaying more black spots had shorter non-REM sleep bouts, a shorter REM sleep latency and more wakefulness bouts. This sleep traits also correlated with male nestlings own level of spotting. Heavily spotted male nestlings and offspring of heavily spotted biological mothers switched sleep-wakefulness states more frequently. Also, nestlings from mothers displaying many black spots looked more often towards the nest entrance where their parents bring food and towards their sibling against whom they compete.
Conclusions: Owlets from heavily spotted mothers might invest more in vigilance thereby possibly increasing associated costs due to sleep fragmentation. Different strategies of the regulation of brain activity have evolved and are correlated with melanin-based colouration.
Disclosure: Nothing to disclose.

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Heartbeat evoked EEG responses from wake to sleep

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Objectives: EEG studies on interoceptive awareness have studied the so-called heartbeat evoked potential (HEP; e.g., Pollatos & Schandry, 2004), which is most prominent over somatosensory and frontal cortex. Our aim was to investigate whether this evoked response changes from wake to sleep. We calculated HEPs and heartbeat evoked phase responses. Furthermore, we were interested, whether the slow oscillation known to synchronize neuronal (cortical, but via efferent pathways also in other brain regions) activity might also synchronize (with) the heartbeat.
Methods: We studied 24 healthy sleepers (mean age = 24.42 years, SD = 2.59, 12 females). 8 h PSG was recorded using a 32-channel Synamps amplifier (NeuroScan Inc., Texas). Preprocessing and R-peak detection was done in Brain Vision Analyzer 2 (BrainProducts, Germany). Phase Locking analysis (PLI, PLV; Lachaux et al., 1999) and spindle/slow oscillation detection was done using in-house Matlab routines. HEPs were detected at around 250–400 ms post R-peak. ANOVAs and bootstrapping statistics were calculated.
Results: Frontocentral HEP amplitude decreased from wake to deep sleep, with a renewed increase during REM. Interestingly, heartbeats appearing simultaneously with a sleep spindle did not produce a clearly detectable response. Statistical ERP and PLI analysis confirmed these observations. Furthermore, heartbeats appeared more often at the beginning of the slow oscillation up-state as compared to the down-state.
Conclusions: If the heartbeat evoked EEG response is indeed a cortical response conditioning interoceptive awareness its decrease from wake to sleep is reasonable. It remains questionable, however, whether the slow oscillation influences the heart rate or whether some heartbeats might trigger slow oscillations.
Disclosure: Nothing to disclose.

Circadian or Sleep-wake Driven? Dissecting Central and Peripheral Transcriptome Dynamics

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Brain gene expression in the mouse; the complex interaction of time-spent-awake, time-of-day, and stress

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As with most studies aimed at identifying physiological variables that play a role in some aspect of sleep also the search for sleep's molecular correlates is complicated by the many processes that contribute to gene expression and by the protocols used to investigate them. For example, many researchers interested in that fraction of the transcriptome that is under circadian control, mostly sample a specific tissue across the day thereby discounting factors such as time-spent-awake prior to sampling. In the past we have shown that 80% of the transcripts that show a 'circadian' pattern of expression are only rhythmic because of the sleep-wake distribution and, as a consequence, their expression over the day is flat when time-spent-wake prior to sampling is controlled for (Maret *et al.* PNAS 2007). Similarly, studies aimed at identifying the transcriptome changes accompanying extended periods of wakefulness in animals have often overlooked the effects of increased corticosterone that invariably accompanies sleep deprivation. More recently, using adrenalectomy in mice, we demonstrated that two-thirds of the transcripts claimed to be sleep-wake driven are in fact corticosterone driven (Mongrain *et al.* SLEEP 2010). It is thus of interest to established how circadian, sleep-wake driven, and 'stress' related processes interact to affect gene expression. In an effort to disentangle these respective contributions, we developed a simple, semi-quantitative model for transcripts for which the expression integrates all three aspects using the clock gene *Period2* as an example (Curie *et al.* SLEEP 2013).

Disclosure: Nothing to disclose.

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Interaction of sleep timing and clock function in the regulation of circadian transcriptome rhythms

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Circadian clocks regulate 24-hr rhythms of physiology and behavior including the sleep-wake cycle. While the effect of clock function on sleep has been extensively studied, little is known about how sleep timing and sleep quality may feed back on clock regulation. In mammals, circadian rhythms are set by cellular clocks with a master pacemaker residing in the hypothalamus and subordinate clocks in central and peripheral tissues. These cellular oscillators translate time-of-day information into physiological signals by controlling tissue-specific transcriptional programs. We developed a mouse model of misaligned sleep to analyze the impact of sleep disruption on the regulation of circadian transcriptome rhythms. We found that in different tissues 24-hr rhythms of gene expression are dramatically altered after sleep misalignment, correlating with disrupted expression of core clock genes. By comparing adipose and liver gene rhythms with those in the basal hypothalamus tissue-specific effects of sleep mistiming became apparent. Our data suggest that diurnal transcriptional programs are highly plastic and the interaction of clock function and behavioral rhythms such as the sleep-wake cycle shapes the cellular transcriptional landscape to adapt physiological processes to external demands. When clock function was genetically disrupted, mice became largely resistent to the effects of sleep misalgnment, indicating that sleep may interfere with peripheral physiology via the regulation of the local clock machinery.

Disclosure: Nothing to disclose.

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Mistimed sleep disrupts the circadian regulation of the human transcriptome

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Sleep is important for good health, although a significant number of adults report having insufficient sleep, and ~20% of adults perform shift work, which is associated with both insufficient and mistimed sleep. Epidemiological data show that insufficient and mistimed sleep are associated with negative health outcomes such as obesity, type 2 diabetes, and cardiovascular problems. Some studies also highlight an increased risk for certain cancers among shift workers. However, we do not yet fully understand the molecular mechanisms that underlie these health risks.

In two studies, we have investigated the effects on the human whole blood transcriptome of (1) 40 h of total sleep loss after 1 week of insufficient sleep (5.7 h) compared to 1 week of sufficient sleep (8.5 h), and (2) when sleeping in or out of phase with the central circadian clock in a forced desynchrony protocol.

Compared with sufficient sleep, there was a seven-fold increase in the number of transcripts that showed increased or decreased expression levels in response to total sleep loss. By contrast, when sleep was displaced 12 h out of phase with the central circadian clock the number of transcripts with a circadian expression profile reduced from 6.4% when sleeping in phase to just 1% when sleeping out of phase. Furthermore, mistimed sleep disrupted the expression profiles of over one third of transcripts.

Gene ontology and interaction network analyses identified pathways and processes that are sensitive to insufficient and mistimed sleep, including those associated with immune and inflammatory responses, and those that regulate transcription and translation.

Disclosure: Nothing to disclose.

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Body temperature cycles: gatekeepers of circadian clocks

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Objectives: The circadian clock is a molecular timing mechanism that synchronizes cellular, physiological and behavioural processes

in light-sensitive organisms to geophysical time and ensures their proactive reaction to environmental cues. In mammals, the circadian clock consists of a master pacemaker situated in the suprachiasmatic nucleus of the ventral hypothalamus and subsidiary 'peripheral' clocks present in virtually all cells of the body. The master pacemaker senses the daily light-dark changes and conveys the environmental timing signals to the peripheral oscillators in the form of core body temperature changes, cyclic releases of hormones, and daily feeding-fasting cycles. The main goal of our study is to identify molecular pathways involved in the synchronization of peripheral clocks by daily oscillations in core body temperature.

Methods: We employ state-of-the-art mouse in vitro systems and a novel bioluminescence-based whole-body imaging technique in freely moving animals to elucidate temperature-dependent mechanisms that generate cyclic mRNA expression of a cold-inducible RNA-binding protein (CIRBP) and its role in the establishment of phase coherence and coordination of circadian physiology in mice.

Results: Our data suggest a major role of posttranscriptional gene regulation in temperature-dependent CIRBP expression in mouse cells. Reduction of CIRBP expression in cells and its ablation in mice leads to changes in stimulus-based phase adaptation of circadian clocks.

Conclusions: This study demonstrates the impact of core body temperature oscillations on post-transcriptional gene regulation. In turn, these posttranscriptional mechanisms are involved in the maintenance of phase coherence in the mammalian circadian timing system.

Disclosure: Nothing to disclose.

Sleep and Brain Maturation Development of Sleep-regulatory Mechanisms and Interactions between Sleep and Brain Maturation

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Post-weaning development of sleep and sleep-regulatory mechanisms in the rat

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Sleep-wake behavior undergoes substantial reorganization from infancy to adulthood, but the mechanisms driving normal sleep development are largely unknown. We recently examined different characteristics of the sleep-wake cycle and sleep homeostatic regulation in rats during early post-weaning, the time period between postnatal days 21 (P21) and P30. Our findings indicated that maturational changes in sleep-wake organization in rats parallel significant increases in sleep-related Fos-immunoreactivity in the preoptic hypothalamus. Further, we performed extracellular recordings of neuronal activity within the median preoptic nucleus (MnPN) during baseline (BSL) sleep-wake and in response to sleep deprivation (SD), across P20-P30; studied developmental changes in adenosine production in the basal forebrain (BF); and examined the effect of suppression of adenosine signaling during early post-weaning period on sleep normal development.

Sleep-active units discharged at higher rates at P30 vs. P20 during both spontaneous NREM and REM sleep (3.6 ± 0.5vs.1.7 ± 0.3, $P < 0.01$ and 3.7 ± 0.6vs.2.1 ± 0.3, $P < 0.05$, respectively). During SD, compared to BSL, discharge of sleep-active neurons in wake significantly increased by approximately 50–75% at P20 rats and by 100–175% at P30 rats and was higher at P30 vs. P20 (1.1 ± 0.2 vs. 0.7 ± 0.1 spikes/s, $P < 0.05$). SD-related increases (compared to baseline, 100%) in AD levels in the BF were seen in P30 (SD: $222\% \pm 9\%$; RS: $121\% \pm 30\%$), but not P22 rats (SD: $99\% \pm 6\%$; RS: $89\% \pm 10\%$).

These findings indicate that developmental increases in wake-related production of adenosine in the BF go in parallel with functional maturation of preoptic hypothalamus suggesting that these two critical sleep-regulatory mechanisms are involved in the maturation of sleep homeostasis.

Disclosure: Nothing to disclose.

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Life-long alterations of sleep patterns and emotional behavior after transient serotonin impairments during development

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Dysfunction of the serotonin system is involved in sleep and emotional disorders. Because serotonin (5-HT) has a facilitating role in development, the question arises about the long term impact of a serotonergic dysfunction in early life. Indeed, the selective serotonin reuptake inhibitors (SSRIs) are the most commonly used pharmacological treatment for depression, and there is mounting concern about their effects on the developing foetus in treated depressed pregnant women. In fact, such SSRI treatments often cause sleep and behavioural disorders in the infant but there are no data about their long-term effects, i.e., until adolescence/adulthood.

In animal models, transient neonatal exposure to SSRIs (fluoxetine or escitalopram) induces in the progeny a life-long depression-like phenotype in the form of sleep anomalies, anhedonia, increased helplessness and enhanced response to acute stress. We have shown that these alterations: 1- depend on the functional status of 5-HT_{1A} receptors that is disrupted by the SSRIs and: 2- can be prevented by augmenting the neonatal SSRI treatment with a 5-HT_{1A} receptor blocker, pindolol.

Interestingly in adult depressed patients, pindolol increases the therapeutic action of SSRIs, suggesting that it might be possible in pregnant mothers to augment the SSRI treatment with 5-HT_{1A} compounds that would both prevent the deleterious effects of SSRI on the progeny and increase the antidepressant therapeutic efficacy.

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Sleep maturation and developmental disorders

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Sleep is a mirror of cortical maturation during childhood. Recent data suggest a close interaction between sleep-dependent plasticity development, represented predominantly by slow-wave sleep, and neurocognition and behavior in children. Continuous spike and waves during slow-wave sleep (CSWSS) is connected with mental regression, language difficulties and behavioral problems. Similarly CSWSS in Landau-Kleffner syndrome leads to aphasia and behavioral changes; rolandic epilepsy with centrotemporal spikes represents a part of the clinical continuum. Children with specific language impairment and developmental coordination disorder reveal epileptic activity during sleep very frequently, too. Sleep dependent mechanisms are, therefore, involved in the development of motor skills, speech, cognitive learning, behavior as well as emotional processing. Children with attention deficit and hyperactivity disorder (ADHD) show a less mature topographic slow-wave activity, and changes were found also in the autistic spectrum disorders.

The relationship between sleep and cognition and behavioral/emotional regulation is bidirectional. NREM parasomnias and sleep related movement disorders in children are frequently connected with other developmental disorders (motor skills, speech, learning and behavior) suggesting a common mechanism of disordered matura-

tion. Connection of impaired sleep and its association with poor academic performance, influence of sleep deprivation on neurobehavioral functioning in children, long-term outcome of sleep breathing disorders, and association of eveningness with problem behavior in adolescents are all well-known symptoms. Impaired sleep is also believed to accompany some psychiatric diseases manifested during childhood and/or adolescence.

Disclosure: Nothing to disclose.

Sleep across the Ages

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Cortical thinning mediates age-related changes in NREM sleep oscillations during adulthood

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Objectives: Magnetic resonance imaging (MRI) studies showed that grey matter integrity is an important determinant of slow waves (SW) properties in young subjects. During aging, SWs become scarce and their amplitude decreases mostly in frontal regions, where cortical thinning is also predominant. We sought to assess the role of cortical thinning in age-related changes in SW properties.

Methods: Polysomnography was recorded in 30 young (20–30 y/o; 16 men) and 33 middle-aged (50–70 y/o; 15 men) subjects. Mean SW density and amplitude between pairs of frontal electrodes (F3-F4) was calculated for all-night non-rapid-eye-movement sleep. Subjects underwent a brain MRI, and cortical thickness (CT) was calculated. Mediation analyses were performed to investigate the role of cortical thinning in the age-related changes in SW.

Results: Compared to the young, middle-aged subjects showed lower SW density and amplitude ($P < 0.05$). Controlling for the effects of age, SW density was associated with CT in fronto-temporal gyri, while SW amplitude was associated with CT in fronto-parieto-occipital gyri ($P < 0.05$-corrected). Mediation analyses and effect size measures showed that thinning of the precentral and infero-temporal gyri explained a large proportion of the age-effect on SW density (K^2: 0.44), while thinning of the precuneus explained a small proportion of the age-effect on SW amplitude (K^2:0.22).

Conclusions: Our results shows that thinning of specific cortical regions are involved in SW changes during adulthood. Since these regions are involved in SW generation and propagation, future studies should assess how cortical and subcortical connectivity influences SW propagation during aging.

Disclosure: Nothing to disclose.

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Developmental changes in sleep oscillations during early childhood

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Objectives: Early childhood is a time of rapid maturation in functional skills (e.g., language, motor, cognition), brain morphology, and reported sleep duration, timing, and quality. Currently, early developmental changes in the sleep EEG are understudied. We investigated the trajectory of sleep oscillations as characteristic features of the human sleep EEG during early childhood.

Methods: All-night sleep EEG was recorded in 8 children (3 males) at three longitudinal time points (2.5–3y, 2Y; 3.5–4y, 3Y; 5.5–6y, 5Y). Sleep stages were scored according to standardized criteria. We detected oscillatory events [1] in the sleep EEG and studied how the event rates in specific frequency bands changed during development.

Results: Strongest changes were observed in light sleep. A striking finding was the almost complete absence of sleep spindles at 2Y in contrast to pronounced spindles observed at 5Y (significant increase, $P < 0.05$).

Similar to adults, large inter-individual differences were present. Thus, certain changes were observed in a subset of children only: some showed theta oscillations at 2Y, which almost disappeared at 5Y, while in most subjects delta events decreased across development.

Conclusions: Our findings, in particular the changes of delta and spindle oscillations, likely reflect maturational changes in the thalamo-cortical system during early childhood. Whether shifts in these oscillatory events are reflected in children's maturing cognitive capabilities remains an unanswered question.

[1] Olbrich, E. and Achermann, P. J. Sleep Res., 2005, 14: 337–346.

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Association between white matter integrity markers in the corpus callosum and NREM interhemispheric EEG coherence in aging

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Objectives: Studies in patients with corpus callosum (CC) section or agenesis support the role of white matter in interhemispheric EEG coherence during sleep. As aging is associated with NREM sleep and white matter integrity modifications, we aimed to investigate the link between the magnitude-squared coherence of the NREM EEG and white matter diffusion during aging.

Methods: One night polysomnographic recording was performed in 30 young and 30 older healthy participants. Stage 2 and SWS magnitude squared EEG coherence was computed between inter-hemispheric pairs of electrodes for delta (1–4 Hz) and sigma (12–14 Hz). Fractional anisotropy (FA) and mean diffusivity (MD) were estimated for three CC portions (anterior, middle and occipital) with diffusion magnetic resonance imaging.

Results: During stage 2, older subjects showed lower sigma and delta coherence for C3-C4, P3-P4 and T7-T8 and lower delta coherence for F7-F8 compared to young subjects. During SWS, older subjects showed lower sigma coherence for C3-C4, P3-P4, and T7-T8. Only older subjects showed significant correlations between coherence and CC integrity. During stage 2, higher FP1-FP2 sigma

coherence was associated with higher FA/lower MD in anterior CC whereas sigma coherence between C3-C4 and P3-P4 was positively linked to FA in middle CC. During SWS, higher Fp1-Fp2 sigma and delta coherence and higher F7-F8 sigma coherence were associated to higher FA in anterior CC whereas higher C3-C4 sigma coherence was associated with lower MD in middle CC.

Conclusions: Higher interhemispheric NREM sleep coherence is associated with higher white matter integrity markers in specific CC portions in older subjects.

Disclosure: Nothing to disclose.

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Effects of long-term caloric restriction on circadian rhythms of aged rats

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Aging involves changes in physiological functions. Long-term caloric restriction (LTCR) can prevent or delay age-related deteriorations and diseases. Here we assessed the effects of LTCR on circadian rhythms of aged rats.

26 male rats were submitted to a 40% caloric restriction from 8 to 21 months old (O-RC rats) while 13 control rats (O-AL) were fed ad libitum. Average weight was then 605 g and 1185 g, respectively. A group of 8 months old rats (M-AL rats) served as age controls. Telemetry probes for rest-activity, body temperature and heart rate were implanted and recordings took place for the next 6 days. Analyses were performed on the last 24 h, with ANOVAs on means of 4-hour bins, alpha = 0.05.

O-AL rats were significantly less active than O-RC rats and the latter were not different from M-AL rats. Only M-AL rats exhibited a circadian pattern of the rest-activity cycle. Heart rate was significantly faster in O-AL rats than O-RC and M-AL rats. Again, only M-AL rats showed a circadian pattern of heart rate. Body temperature was significantly higher in O-AL than O-RC rats, particularly during the dark (active) period. Values of M-AL rats were in between and the amplitude of the temperature circadian rhythms was higher in M-AL rats.

The present results show that LTCR may favorably impact the effects of aging on activity levels, heart rate and body temperature. However, it does not appear to prevent the loss of circadian rhythmicity. The neural mechanisms involved remains to be identified.

Disclosure: NSERC, FRQ-S, RQRV.

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Are age-related modifications in spindle characteristics linked to markers of white matter integrity?

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In normal aging, sleep spindles and white matter integrity undergo important changes. The goal of this study was to investigate the role of magnetic resonance imaging (MRI) white matter diffusion modifications in age-related reduction in spindle density and amplitude.

Thirty young (20–30 yo) and 33 middle-aged subjects (50–70 yo) underwent a night of polysomnographic recording and a 3T MRI acquisition including a diffusion sequence. Spindles were automatically detected on artefact-free non-rapid eye movement (NREM) sleep on F3 and P3 (linked-ears). Diffusion tensor imaging technic was used for voxelwise white matter diffusion analyses. Fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD) and radial diffusivity (RD) were measured. Mediation analyses were performed to estimate whether white matter diffusion markers could explain age-related effect on spindle characteristics.

Compared to the young, older participants showed lower spindle density and amplitude in F3 and P3. When controlling the effects of age, decreased F3 spindle amplitude was associated with increased RD bilaterally in the frontal lobe ($P < 0.05$). Crucially RD in these regions was increased in older subjects ($P < 0.05$). Mediation analysis revealed that increased RD in frontal areas partially explains age-related effect on sleep spindle amplitude ($P < 0.05$). No effect was found for other diffusion variables.

Our results indicate that alterations in white matter diffusion are associated with age-related modifications of specific spindle characteristics. Further analyses will estimate whether markers of white matter integrity may explain age-related changes in other spindles characteristics and NREM sleep oscillations.

Disclosure: Nothing to disclose.

Farewell to the Two-process Model?

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The two-process model: origin and perspective

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In the two-process model as developed in the early 1980's sleep is controlled by a process-S, representing the rise and fall of sleep demand resulting from prior sleep-wake history, interacting with a process-C representing circadian variation in sleep propensity. S and C together optimize sleep timing and intensity with respect to internal demand and external opportunity.

The theoretical distinction between S and C has been useful in understanding many aspects of sleep, most prominently 'internal desynchronization' and circadian vs. homeostatic aspects of physiology. Both S and C concepts met difficulties as they were further explored in mathematical detail. The simple S dynamics of the model became problematic when SWA dynamics appeared to vary between brain areas.

The C process was originally identified with the circadian pacemaker in the SCN. Some researchers even specifically attributed the direct control of activity and rest to the SCN. Yet, activity-rest rhythms under special circumstances (feeding schedules; methamphetamine) turned out to require neither the SCN nor circadian clock genes, and have an oscillatory basis themselves. Recent studies show that in animals the activity-rest cycle adaptively shifts from night to day under metabolic influence. The SCN itself remains rigidly tied to the day and night outside, acting as a clock entraining, not dictating other circadian processes. The original S-C model provides a basic framework for the much needed analysis of the role of metabolism in the temporal organisation of sleep and wake. It will require adjustment, not abandonment.

Disclosure: Nothing to disclose.

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Interaction of sleep homeostasis and circadian rhythms

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In mammals, homeostatic sleep pressure is reflected by electroencephalogram slow-wave activity (SWA, electroencephalogram power density <5 Hz) in non-rapid eye movement sleep. The timing of sleep is controlled by the circadian pacemaker, located in the suprachiasmatic nucleus (SCN). The circadian pacemaker generates electrical activity rhythms in the SCN which is high during the subjective day and low during the subjective night.

Whether homeostatic and circadian regulation of sleep function independently has been subject of discussion since the two were brought together in the two process model. It was shown that the timing of sleep is regulated independent from the homeostatic sleep need. However, other data indicated that there may be a continuous interaction between sleep homeostasis and the circadian clock.

To gain more insight, we recorded the electroencephalogram and SCN neuronal activity simultaneously in vivo in rats and showed that SCN neuronal activity is influenced by vigilance state changes. In addition, suppressing SWA by slow-wave deprivation, resulted in increased SCN activity, whereas total sleep deprivation resulted in increased SWA, and simultaneously a suppression of SCN neuronal activity. Recent fMRI studies show a similar negative relationship in humans.

The data suggest a continuous interaction between sleep homeostasis and the circadian clock. Our present work is concentrating on the consequences of increased homeostatic sleep pressure on circadian functioning. Behavioural studies show that sleep deprivation diminishes rest-activity phase shifting capacity. We want to resolve the neurophysiological mechanisms and investigate whether and how this can be influenced.

Disclosure: Nothing to disclose.

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The two-process model: Its impact on clinical research

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A fundamental test of the two-process model is deprivation of sleep and its rebound - and the predictions have functioned in many species. The first clinical application was immediate and obvious: could the remarkably rapid antidepressant effect of one night's sleep deprivation be related to abnormalities in process S? Thirty years later, contradictory findings range from low delta power to higher SWA in NREM sleep. New TMS/EEG data in bipolar depression reveal that cortical excitability, putatively a direct measure of Process S, increases as a function of time awake, more in clinical responders than in non-responders. Yet the model requires also addressing alterations in depression that could arise from Process C - the suprachiasmatic nuclei, their retinal input, strength of zeitgebers, etc. Importantly, light acts on the circadian pacemaker and has antidepressant properties. The usefulness of the model was rapidly recognised not only in affective and sleep disorders, but also in fields such as alertness management (fatigue and performance), development (adolescence) and ageing. As behoves a good hypothesis, it is elegant, and the accumulated data have helped us understand the regulation of sleep and wakefulness within its framework. However, outside the laboratory, other factors may be important in modulating vigilance and mood states: day-by-day variability in external inputs (e.g. light, noise), internal signals (stress, rumination, pain, drugs) and behaviour (posture, activity, meals, social setting). One new aspect is the role of skin temperature and thermoregulation in promoting sleep and maintaining alertness. Can the model accomodate the messy multifactorial real world?

Disclosure: Nothing to disclose.

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Sleep and the environmental 24-hour cycle

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Since its origin life had to adapt to the environmental cycle of light and darkness. Plants depend on light for their energy, and in animals feeding behavior and metabolism are closely associated with the environmental 24-h cycle. Forced desynchrony experiments in humans demonstrated the powerful influence of the circadian rhythm on sleep. In his studies of autonomic nervous functions in the 1930s Walter Rudolf Hess viewed sleep in the context of the 24-h cycle. He described sleep to be part of the trophotropic phase serving recovery

and waking to be part of the ergotropic phase characterized by interactions of the organism with the environment. Hess's view of sleep and waking has been recently revived in circadian rhythm research. Thus in analogy to his concept the clock is assumed to partition behavioral and metabolic processes into a sleep/fasting period and a wake/feeding period. The ubiquitous temporal organization of metabolism in association with the environmental cycle may be the guiding principle for the sleep-waking cycle. A major function of the sleep-wake dependent homeostatic process may be to reinforce the circadian rest-activity cycle and thereby to ensure the optimal temporal organization of energy metabolism.

Disclosure: Nothing to disclose.

Sleep and the Social Brain

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Sleep and emotion processing in children

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Early childhood is characterized by dramatic developmental changes in sleep and emotion processing (i.e., expression and regulation of emotion). Although sleep-dependent changes in emotion processing are increasingly recognized as central to psychopathology, experimental evidence in young children is lacking. We examined the effects of acute sleep restriction (nap deprivation) on toddlers' emotion expression and self-regulation. Toddlers (n = 10; 7 females; 30–36 months) followed a strict sleep schedule for 5 days before each of two afternoon assessments following Nap and No-Nap conditions. Children attempted 1 solvable (positive context) and 1 unsolvable puzzle (challenge context). Videotaped assessments were later coded for emotion expression displays and mutually exclusive self-regulation strategies. In the positive context, sleep restriction resulted in a 34% decrease in positive emotion facial displays. In the challenge context, nap deprivation led to a 31% increase in negative emotion facial displays and a 39% reduction in confused facial responses. Furthermore, nap-dependent effects on self-regulation strategies in the challenge context were observed: 5–7% decreases in healthy skepticism and negative self-appraisal and 9–10% increases in physical self-soothing, perseveration, and insistence on completing the unsolvable puzzle. Results suggest sleep serves an important role in the way toddlers respond emotionally to their dynamic daily world. Sleep-restricted toddlers are neither able to fully benefit from positive experiences nor are as they adaptive in challenging contexts. Over time, persistent burdening of children's emotional responses from chronically missed sleep may impair young children's emotion processing, posing potential risks for emotional and behavioral problems.

Disclosure: Nothing to disclose.

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Sleep, appearance and social interactions

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Social interactions are crucial for many aspects of life including a healthy relationship with your partner, successful collaboration with work colleagues, or when needing help from a stranger. The aim of the presentation is to go cover some of the emerging knowledge of how insufficient sleep affects functions relevant for social interactions, ranging from changes of cognitive functions, appearance, behaviour as well as interactions in real world settings.

There is support for a number of socially relevant cognitive functions including language ability, rational decision-making, and affective regulation to deteriorate with lack of sleep. Insufficient sleep can also affect mood, impulsivity, risk-taking, stress reactivity and cause worse reactions in frustrating situations. We have recently showed that sleep deprivation also affects appearance, including a number of facial cues relating to the eyes (e.g. dark circles under the eyes), the skin (e.g. paleness) and the mouth (e.g. droopy more corners of the mouth), which may explain the finding that sleep deprived people are perceived as less healthy, less attractive and more sad. In turn, these effects may also affect how other's wants to interact with sleep deprived people. Together, these findings suggest that social interactions may be impaired in individuals with insufficient sleep.

Disclosure: Nothing to disclose.

Technical Aspects of Scoring Sleep

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Sleep apnea diagnosis greatly varies with the hypopnea criteria applied

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Objectives: In 2007 hypopnea criteria A and B were proposed by the American Academy of Sleep Medicine (AASM) for scoring sleep-related breathing disorders (SRBDs). In 2012 they recommended new hypopnea criteria. We aimed to evaluate the impact of these criteria on the apnea hypopnea index (AHI) in patients with acute stroke or transient ischemic attack (TIA).

Methods: We performed polysomnographies (PSGs) in patients with TIA or stroke, and scored the studies according to the A-, B- and 2012-hypopnea criteria.

Results: 63 PSGs were eligible for hypopnea scoring. There was no difference in the number of patients diagnosed with the B- and 2012-criteria. Therefore they are mentioned as one. With the A-criteria, 47 patients (75%) were diagnosed with SRBD, but with the B/2012-criteria, 57 patients (90%) were diagnosed ($P < 0.0016$). In 30 cases, a change from the A- to the B/2012-criteria resulted in a change in diagnosis. 11 cases of 'no SRBD' changed to mild to severe SRBD. An AHI >15 is a typical indication for treatment. With the B- or 2012-criteria, we found an additional indication for treatment in 18 patients, compared to when the A-criteria were applied ($P < 0.0001$). 2 of these patients were labeled as 'no SRBD' with the A-criteria.

Conclusion: The difference is significant between the AHIs achieved by the A- and the B-/2012-hypopnea criteria, with much lower AHIs achieved with the A-criteria. As SRBD treatment lessens the risk of complications, correct identification of SRBD patients is of the utmost importance.

Disclosure: Nothing to disclose.

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Scoring criteria for polygraphy: a comparison with full polysomnography using four hypopnea definitions in a population based sleep cohort

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Objectives: Respiratory polygraphy (RP) is increasingly used as an alternative to polysomnography (PSG) for the diagnosis of sleep disordered breathing (SDB). However, recommendations for the scoring of RP recordings are still lacking. Pulse-wave amplitude (PWA) drops, considered as surrogates for EEG arousals, may provide a better definition of respiratory events for PM recordings. We aimed to investigate the performance of four different hypopnea scoring criteria for the diagnosis of SDB using 3% or 4% oxygen desaturation, including or not PWA drops in RP recordings compared to home full PSG.

Methods: Subjects drawn from a population-based cohort (HypnoLaus) underwent a complete home PSG. The PSG recordings were then rescored using only the parameters available on RP (EEG channels removed) with 'lights off' and 'lights on' times based on patients' report. The AHI of the four different RP scoring criteria were then compared to the PSG-based AHI.

Results: 312 subjects were included. Overall, RP-AHIs showed a good correlation with PSG-AHI although it tended to slightly underestimated it. The PG-AHI using 3% desaturation without PWA criteria showed the best diagnostic accuracy for AHI thresholds $\geq$5/h and $\geq$15/h (correctly classifying 94.6% and 93.3% of subjects respectively). For AHI $\geq$30/h however, the inclusion of PWA drops showed better accuracy (classifying correctly 94.2% subjects).

Conclusions: Interpretation of RP recordings using hypopnea criteria which include 3% desaturation without PWA drops showed the best correlation and diagnosis accuracy for mild and moderate SDB. Using PWA drops as surrogates for microarousals adds accuracy for the detection of severe SDB.

Disclosure: Nothing to disclose.

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Transcutaneous carbon dioxide during periodic breathing and upper airway flow-limitation during sleep

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Objectives: The increase of transcutaneous carbon dioxide levels from wakefulness to sleep is an indicator of decreasing sympathetic tone after sleep onset. We assessed the impact of various forms of SDB on the autonomic nervous system by measuring their average levels of $tcCO_2$ and comparing to $tcCO_2$ levels during wakefulness and steady breathing.

Methods: 555 consecutive cardio-respiratory sleep recordings were analyzed retrospectively for SDB sequences. SDB sequence was determined as ten consecutive events or 5 min of certain type of SDB. Absolute and relative $TcCO_2$ levels during different types of SDB were assessed with Kruskal-Wallis test.

Results: Forty-four patients (34 m/10f) with 88 SDB sequences were included to the study. Mean age was 53 (range 32–70) Mean apnea-hypopnea-index (AHI) was 21.8/h. Relative $TcCO_2$ levels increased in the following order: wakefulness (0%), CSA (48.9%), hypopnea (62.4%), OSA (88.6%), steady breathing (100%) and flow-limitation (132.9%). $TcCO_2$ was higher during flow-limitation than any other type of SDB ($P = 0.004$), $tcCO_2$ was lower during CSA than OSA ($P = 0.023$) and hypopnea lower than steady breathing $P = 0.003$).

Conclusions: SDB with periodic breathing are characterized by $tcCO_2$ levels higher than wakefulness but lower than during steady breathing. Flow-limitation is associated with the highest levels of $tcCO_2$. The findings are in line with the hypothesis that SDB with periodic breathing, but not flow-limitation, increase sympathetic activity during sleep.

Disclosure: Nothing to disclose.

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A validation study of the Watch PAT^{tm} in participants of the Akershus sleep apnoea project (ASAP)

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Current clinical guidelines open for the use of unattended portable screening devices for obstructive sleep apnoea (OSA). The WatchPAT^{tm} uses peripheral arterial tone (PAT), heart rate, actigraphy and oxygen saturation to estimate apnoea hypopnea index (pAHI). Previous validation studies have included few participants. The aim of the current study was to assess diagnostic properties of the WatchPAT^{tm} in a large, community-based sample.

The current study comprised 307 participants of the Akershus Sleep Apnoea Project (ASAP) that completed simultaneous registration with the WatchPAT^{tm} and manually scored polysomnography. A diagnosis of OSA was made by cut-off values of the AHI of ≥5, 15 and 30.

Unadjusted prevalences of OSA in this sample were 62%, 36% and 19% when OSA was defined by an AHI of ≥5, 15 and 30 respectively. When OSA was defined by an AHI ≥5, the sensitivity was 99% (97, 100) and the specificity was 33% (25, 42). By AHI ≥15, sensitivity was 96% (93, 100) and specificity was 64% (57, 71) and by AHI ≥30, sensitivity was 98% (95, 100) and the specificity was 80% (75, 85). Negative predictive values were 95%, 97% and 100% respectively. Positive predictive values were 70%, 60% and 53% respectively.

In this study conducted in a community-based setting, Watch Pat had a high negative predictive value, suggesting it can be used to rule out OSA. However, the positive predictive value was only moderate, suggesting that additional diagnostic tests may be needed to confirm a final diagnosis of OSA.

Disclosure: Nothing to disclose.

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Transition to home monitoring for OSA diagnosis: effects on test availability, waiting time, patients′ satisfaction and outcome in a large health provider system

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Introduction: During 2009, the Haifa district of Clalit health service (CHS) made a decision to switch from full night in lab polysomnography (PSG) to home studies for the diagnosis of obstructive sleep apnea (OSA). We sought to evaluate the effects of this change on accessibility, waiting time, satisfaction, costs and CPAP purchase by the patients.

Methods and materials: Data regarding sleep studies, CPAP purchase and waiting times were collected retrospectively from the computerized database of CHS. Patients′ satisfaction was assessed utilizing a questionnaire introduced by phone to a randomized small sample of 70 patients. All comparisons were made between the years 2007–2008 representing in laboratory studies and 2010–2011 when 76% of the studies were ambulatory.

Results: Of about 650000 insured individuals in the Haifa district of CHS, 1471 sleep studies were performed during 2007–2008 compared to 2794 tests during 2010–2011. The average waiting time was 9.9 weeks in 2007–2008 compared to 1.1 weeks in 2010–2011 ($P < 0.05$). 597 CPAPs were purchased in 2007–2008 compared to 831 in 2010–2011. The overall patients′ satisfaction was similar, but discomfort tended to be higher in the in-laboratory group (4.1 vs 2.7 in a scale of 0–10; $P = 0.11$).

Conclusions: Switching to ambulatory diagnosis improved the test accessibility (almost doubled the number of studies) and significantly reduced the waiting times. Patients′ satisfaction remained similarly high. The total number of CPAPs purchased by patients increased, in a smaller proportion relative to the increase in studies. The total direct cost of OSA management (diagnosis and treatment) was reduced.

Disclosure: Nothing to disclose.

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High cardiac vagal control during wakefulness predicts better subjective and objective sleep quality

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Objectives: The functioning of the parasympathetic nervous system - assessed using indirect measures of vagus nerve activation, or cardiac vagal tone (CVT) - has been linked to both physical and mental health. One particularly critical process for both physical and psychological health is sleep - yet, the links between CVT and sleep have remained relatively under-examined. We hypothesized that healthy adults with higher (vs. lower) CVT measured before sleep will experience better sleep quality assessed both subjectively (i.e., self-report) and objectively (i.e., polysomnography).

Methods: In the present study, 29 healthy young women watched a full-length neutral film and an aversive film (counterbalanced across subjects) during which CVT, measured by respiratory sinus arrhythmia (RSA), was assessed. Each following night, they underwent full polysomnography during which objective measures of sleep quality were assessed (e.g., sleep latency, number of arousals, and total sleep time). Subjective sleep quality was assessed with established questionnaires.

Results: As expected, higher RSA during the neutral film was associated with higher subjective and objective sleep quality (i.e., shorter sleep latency, fewer arousals within total sleep time) for both nights. Interestingly, for the night after the aversive film higher RSA was also related to more REM sleep. Higher RSA reactivity to the aversive film was associated with more REM sleep and less deep sleep.

Conclusions: These results indicate that high CVT measured before sleep is a predictor of healthy sleep. Sleep may be an important mechanism in studies linking CVT with physical or mental health outcomes.

Disclosure: Nothing to disclose.

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K-Complex characteristics in obstructive sleep apnea syndrome

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Objective: The K-Complex (KC) is an EEG-waveform, which is generated by networks located in the pre-frontal cortex (Riedner et

al., Prog Brain Res. 2011; 193: 201–218.). Sleep-apnea is known to affect in particular pre-frontal cortical functions.

According to the Sleep-Homeostasis-Hypothesis (SHY; e.g. Tononi & Cirelli, Neural Plast. 2012;2012:415250.), the main KC characteristics (amplitude, duration, and slope) depend on the degree of (pre-frontal) cortical connectivity.

Method: In order to confirm the predictions of SHY we investigated KC characteristics in a sample of 22 OSAS outpatients and in age- and sex-matched controls. In order to eliminate any confounding effects, we restricted analysis to KCs during N2 without any concomitant arousals or respiratory events. KC characteristics (number, amplitude, duration, and slope) were detected automatically by a wavelet-based method.

Results: Control subjects had a significantly higher number of KCs which are not associated with an arousal or/and a respiratory event compared to untreated patients at C4 (patients: 89.1 $\pm$ 51.0 vs controls: 203.5 $\pm$ 141.2; $P = 0.001$) and C3 (patients: 100.5 $\pm$ 60.0 vs controls: 204.2 $\pm$ 139.3; $P = 0.003$). Furthermore, KC-duration was significantly shorter in healthy controls (controls: 0.93 $\pm$ 0.11 vs patients: 1.00 $\pm$ 0.09 at C4, $P = 0.018$; controls: 0.92 $\pm$ 0.09 vs patients: 1.00 $\pm$ 0.09 at C3, $P = 0.011$).

In untreated patients, amplitudes of KC are slightly higher than in controls, but there was no significant difference observed between untreated patients and healthy controls.

Conclusion: The observed differences of KC-duration between OSAS patients and matched controls supports the Sleep-Homeostasis-Hypothesis.

Disclosure: Nothing to disclose.

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Physiologically-based brain state estimation and dynamics

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Objectives: In this study, a model-based approach is used to characterize brain states directly in terms of physiology. Unlike classical sleep stages such as Rechtschaffen and Kales, this approach is individualized and does not impose artificial discrete labels, instead providing a physiological representation of brain states.

Methods: An established mean-field model of the brain is used to predict the EEG power spectrum from activity and connectivity of key neural populations. Compatibility with classical sleep stages is quantitatively verified by comparing model predictions to experimental data from 28 healthy control subjects to identify the physiologies associated with classical stages. The model is fitted to experimental data to track brain states over time and determine the dynamics of the sleep-wake transition.

Results: The sleep stages are found to be associated with distinct physiological parameter regimes that allow the sleep-wake cycle to be represented as a trajectory in the model's parameter space. Wake states are broadly associated with positive corticothalamic feedback, and sleep stages are differentiated primarily by intrathalamic feedback strength. Tracking the brain state from EEG reveals complex dynamics that are consistent with the classical stages in the model but are considerably more localized in terms of physiology because they are individualized.

Conclusion: Individualized physiologically based brain states can be determined from EEG and offer a far more detailed representation of individual brain physiology and dynamics than is possible with classical stages, which can be reproduced in the model by discretizing the continuous parameter trajectories and averaging over individuals.

Disclosure: Nothing to disclose.

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The maintenance of wakefulness test: an electro-physiological measure to better evaluate adult patients with attention deficit/hyperactivity disorder

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Objectives: To quantify the objective level of sleepiness in Attention Deficit Hyperactivity Disorder (ADHD) adult patients, and to determine the relationship between excessive daytime sleepiness and their simulated driving performance.

Methods: 40 adult ADHD patients and 19 matched healthy control subjects were included. Participants answered the Epworth Sleepiness Scale (ESS). After a nocturnal polysomnography, they performed a 4 x 40 min Maintenance Wakefulness Test (MWT) and a 1 h driving session. The primary outcome measure was the mean sleep latency on the MWT. ADHD patients were divided into 3 groups defined by their MWT scores. Participants were allocated as follows: sleepy ADHD (0–19 min), intermediate ADHD (20–33 min), alert ADHD (34–40 min) and control group (34–40 min). The driving performance outcome was the mean of Standard Deviation of Lateral Position (SDLP) of the vehicle during the simulated session.

Results: The group mean ESS score was higher in ADHD patients (12.1 $\pm$ 4.4) than in controls (6.0 $\pm$ 2.7; $P < 0.001$). Based upon the MWT scores, 14 (35%) of our patients were in the sleepy group, 20 (50%) were in the intermediate group, and only 6 (15%) were in the alert group. Sleepy ADHD patients exhibited significantly deteriorated driving performance compared to the other 3 groups ($P < 0.01$).

Conclusion: Our study shows that a significant proportion of adult ADHD patients exhibit an objective excessive daytime sleepiness (EDS) which, in addition, impacts on simulated driving performance. EDS, therefore may be a key element to better evaluate these ADHD patients.

Disclosure: Nothing to disclose.

Investigating the Function(s) of Sleep from the Perspective of a Single Cell to the Systems Level

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Global sleep and single-cell rest

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Sleep is characterised by specific patterns of cortical and subcortical network activity. One of the main defining electrophysiological phenomena of non-rapid eye movement (NREM) sleep is the cortical slow oscillation, visible as slow waves at the level of electroencephalogram. Sleep slow waves are homeostatically regulated: they are enhanced after waking and progressively decrease in the course of sleep. Neither the mechanisms underlying sleep homeostasis nor its functional significance are understood. Important lessons can be learned from understanding the spatio-temporal dynamics of cortical activity during sleep. It was found in rodents that EEG slow waves are mostly local in the first minutes after falling asleep and progressively encompass wider cortical territories in the course of a sleep episode. It is proposed that slow waves originate from those cortical circuits, which were relatively more active during preceding waking and whose need for 'rest' is maximal. Higher-amplitude slow waves typical for sleep later in the episode may, in turn, reflect global synchronisation among distributed functionally interconnected networks. REM sleep also appears to have 'local' and 'global' features. Specifically, it was found that the instantaneous amplitude of EEG theta (6–9 Hz) activity during REM sleep shows slow fluctuations at around 1 Hz frequency, which at times show a high degree of spatial coupling across distant cortical areas, while mostly occur independently. It is concluded that complex spatio-temporal dynamics of EEG activity during sleep reflect sequential involvement of cortical circuits in specific types of network oscillations, which are relevant for restorative sleep functions and synaptic plasticity.

Disclosure: Nothing to disclose.

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Evolution of slow-wave sleep

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Mammals and birds are the only groups known to exhibit slow-wave sleep (SWS) characterized by high-amplitude, low-frequency EEG activity. The apparent absence of comparable activity in sleeping reptiles suggests that SWS evolved independently in mammals and birds. Determining the evolutionary steps leading to the convergent evolution of SWS may provide novel insight into the function(s) of this state's underlying neurophysiology, the slow-oscillation of neuronal membrane potentials between depolarized up-states and hyperpolarized down-states. Most EEG studies reported intermittent high-voltage spikes (HVS) in sleeping reptiles. Although it has been suggested that HVS are homologous to mammalian hippocampal sharp-waves, their relationship to components of the slow-oscillation has not been examined. We used high-density depth electrode arrays to compare the spatio-temporal distribution of sleep-related activity in anesthetized zebra finches and crocodiles, the closest living relatives to birds. In both, local field potentials were similar to EEG activity reported during spontaneous sleep. In finches, slow-waves were composed of frequent bursts of activity that propagated as complex waves. Interestingly, in crocodiles, HVS propagated with a general spatio-temporal pattern similar to the bursts in finches, suggesting homology. The most parsimonious interpretation of these findings is that components of SWS (up-states and down-states) were present in the common ancestor to mammals and birds, and that the ratio of time spent in up- relative to down-states increased independently in each group. If correct, the functional implications of the greater investment in up-states at the expense of down-states may be revealed through further comparisons of avian, mammalian, and reptilian brains.

Disclosure: Nothing to disclose.

What Keeps You Awake? Insomnia Subtypes

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The use of brain imaging to define subtypes of insomnia and corresponding different underlying mechanisms

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Insomnia is a prevalent severe disorder and a major risk factor for other disorders. Unfortunately, findings on its neuronal correlates have been scarce and equivocal, hampering the development of mechanistic models and rational intervention. A possible reason for the equivocal findings is that insomnia is not a single disorder, but comes in many subtypes with different underlying causes - just like 'dementia of old age' is now recognized to involve many different pathologies. We addressed the multiple subtype hypothesis through (1) large-scale multivariate internet assessment of stable characteristics, life events and health history followed by Latent Class Analysis (LCA), as well as through (2) structural magnetic resonance imaging of carefully selected subtypes followed by whole brain Voxel Based Morphometry (VBM).

LCA on 47 constructs measured by questionnaires in 1538 insomniac participants of the Sleep Registry (www.sleepregistry.org) revealed four distinct insomnia subtypes, differing with respect to depression, anxiety, perfectionism, rumination and pain, among others. Interestingly, subtypes differentiated hardly on sleep constructs.

VBM on 59 participants with major depressive disorder (MDD), 61 with anxiety disorder without and 78 with comorbid depression, and 62 controls revealed exclusively in MDD a strong negative association of insomnia severity with gray matter density in a large cluster in the left thalamus encompassing the entire pulvinar, independent of depression severity or use of antidepressants.

Concertedly, the findings support the hypothesis that multiple subtypes of insomnia exist. If not recognized accordingly, samples are likely to be too heterogeneous to find consistent psychometric characteristics and neural correlates of insomnias.

Disclosure: Nothing to disclose.

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Predicting transitions between acute and chronic insomnia using insomnia sub-types

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Despite our knowledge of the various sub-types of insomnia, in terms of symptom complaints, little systematic research exists into the temporal stability of these subtypes over the developmental course of the disorder. If temporal stability exists there is an increased likelihood that symptom complaints are a consequence of predispositional factors. As such opportunities would exist for tailoring treatments. The aim of the present study was to examine: a) the make-up of insomnia subtypes in an acute insomnia population, and b) whether insomnia subtypes changed over the course of the disorder. A longitudinal survey with a short temporal follow-up on individuals with acute insomnia (18–64 years) was conducted in the north of the UK. Of the 1245 individuals screened, 140 (11.24%) met DSM-5 criteria for Insomnia Disorder but reported having the disorder for less than 3 months (acute insomnia). From the cross-sectional data the predominant complaint was characterised as a problem with Sleep Onset (SO - 24.6%), Sleep Maintenance (SM - 10.1%), Early Morning Awakenings (EMA - 13.8), or a mixed complaint (51.4%). There were no differences between symptom groups on mood, perceived stress, or number of life events experienced. At follow-up, 35 participants had remitted and 55 met criteria for insomnia disorder. Stability of symptoms did not predict transition to chronic insomnia although those whose complaint consisted of a mixture of SO and EMA were most likely to remit (61.15%). The results are discussed in relation to treating insomnia during the acute phase.

Disclosure: Nothing to disclose.

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The use of internet to find insomnia subtypes: mining a large database

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Phenotypical variability in insomnia hampers progress in finding underlying mechanisms and genetic predispositions. Current revisions of diagnostic classification systems have given up subclassification of insomnia subtypes by sleep-related symptoms (difficulty initiating sleep, difficulty maintaining sleep, non-restorative sleep and daytime dysfunction) because of a lack of robustness. Furthermore, studies investigating physiological and psychological mechanisms of insomnia have given equivocal findings that may involve heterogeneity of the insomniacs investigated. Identification of endophenotypes is thus crucial. Phenotypical dissection of psychological or behavioral characteristics is an important step towards identifying such endophenotypes. This is done using the voluntary input of good and poor sleepers participating in the Netherlands Sleep Registry (http://www.sleepregistry.org), an online tool assessing multiple surveys and cognitive tests. In a large number of participants we assessed a wide range of variables, including both sleep-related variables and stable characteristics like personality traits, life events and disease history. Latent class analysis on the dataset identified distinct subtypes of insomniacs, distinguishable mostly on non-sleep related traits.

Presently the likely possibility that these subtypes (1) involve differential underlying brain mechanisms and (2) respond differentially to available non-pharmalogical treatments is investigated. Extensive brain imaging (HD-EEG, MRI, TMS) is used to investigate the first; multiple chronobiological treatments and cognitive behavioural therapy are used to evaluate the latter. Furthermore, the best discriminating set of questions are selected into a Sleep Phenotype Survey of acceptable length that can be used to find subtypes in existing cohorts, and to evaluate differential risks of these subtypes to develop other disorders, notably depression.

Disclosure: Nothing to disclose.

Metabolic, Cerebral and Behavioural Consequences of Sleep Loss and Circadian Misalignment

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Impact of circadian phase and prior wakefulness on cognition-related cerebral activity in humans

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Circadian and sleep-wake homeostatic processes modulate cognitive performance and its underlying cerebral correlates. We investigated brain activity during working memory performance in 24 healthy young participants by applying a 40-h multiple nap (NP) and sleep deprivation protocol (SD) in a within subjects design. Blood-oxygen-level-dependent (BOLD) activity was assessed using functional magnetic resonance imaging while performing a 3-back task at the end of the biological day (13 h after habitual wake-up) and night (21 h after habitual wake-up). Nap sleep efficiency (SE) assessed immediately after scanning under NP was considered to reflect the participants' strength of circadian wake (end of biological day) and sleep (end of biological night) promotion, respectively. At the end of the biological day, higher SE was negatively linked to anterior hypothalamic BOLD activity ($P_{corr} < 0.05$), particularly during SD. Furthermore, higher BOLD activity in this region was associated with better 3-back scores at the end of the biological day, independent of sleep pressure condition ($P < 0.05$). In the early morning hours, higher SE was linked to reduced BOLD activity in a task-active cortical network (e.g. bilateral middle frontal, cingulate, premotor cortex, $P_{corr} < 0.05$). Circadian wake promotion in the late evening hours seems thus associated with higher task-related hypothalamic BOLD activity, itself linked to better 3-back scores, while night-time circadian sleep promotion is mirrored by a reduced recruitment of cortical regions implicated in successful working memory performance.

*These authors equally contributed to the work.

Disclosure: Nothing to disclose.

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Sleep homeostasis and the circadian timing system set the dynamics and excitability of neuronal ensembles

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Cognitive brain function is regulated by the interplay between sleep homeostasis and the circadian timing system. The macroscopic brain correlates involved in this interaction are being uncovered, but microscopic cellular-level mechanisms remain largely unknown. We recorded neuronal responses to TMS pulses using hdEEG in 22 healthy young individuals over a stringent 29 h constant routine protocol during which participants performed cognitive test batteries. Dynamic causal modelling and neural mass modelling were applied to infer connectivity between pyramidal (PC) and stellate cells (SC) and inhibitory interneuron (II), as well as glutamate and GABA functions. Cortical excitability was computed from the slope and amplitude of the evoked responses recorded at scalp level and inferred at the brain surface. Mean firing rate, excitatory drive form SC to both II and PC as well as inhibitory feedback drives of II and SC showed a significant time modulation. The temporal changes in all these variables were best explained by an interaction between a linear and sinusoidal function. Similarly, cortical excitability changed with time awake and dynamics was matched by a linear-sinusoidal interplay. Finally, regression analyses indicated that changes in neural system organization and excitability were related to variations in performance and subjective feeling as well as with slow wave activity during previous baseline sleep. These results demonstrate that the temporal changes in the organization of the different cortical layers reflect the interplay between sleep homeostasis and the circadian clock. The data further suggest the theses neuronal changes set non-linear variations in cortical excitability and behavior.

Disclosure: Nothing to disclose.

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Diversity in sleep homeostatic and circadian regulation of plasma lipids in human

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In concert with the solar cycle, the circadian system ensures that lipid absorption, storage, and transport are temporally coordinated with rest-activity and feeding cycles. However, few studies have examined the role of circadian rhythms and the sleep homeostat in regulating plasma lipids. To address this, we used lipidomics approaches to profile the time course of 263 lipid species in 20 healthy males (aged 21–28 years) recruited from the general population. In a 4-day laboratory protocol, blood samples were drawn every 4 h over a span of 28 h, and plasma lipids were analyzed using mass spectrometry techniques. Across subjects, about 13% of lipid metabolites showed circadian variation, including triglyceride (TAG), phosphatidylcholine (PC), and sphingomyelin species. Using consensus clustering, subjects clustered into different groups based on strength of rhythmicity for a subset of TAGs and PCs, raising the possibility that there are different circadian metabolic phenotypes in the general population. Additionally, we found that about 18% of plasma lipids increased linearly during sleep deprivation, in particular TAG and PC species. By comparison, a small subset of plasmalogen PC species decreased reliably across subjects with increasing time spent awake, which could reflect increased oxidative stress associated with sleep deprivation. Our results suggest that plasma lipid levels are influenced by the circadian system and sleep deprivation. These findings have potential implications for lipid metabolism disorders linked to shift work.

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Sleep and Memory Consolidation: New Insights and Models

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New model detailing the role of the hippocampus in sleep-related procedural memory consolidation

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While several models of sleep-related memory consolidation have previously associated hippocampal activity with declarative memory, there is now increasing evidence that the hippocampus also plays a crucial role in procedural memory. In this presentation, I will review recent human functional neuroimaging studies demonstrating that the hippocampus is involved in the acquisition and sleep-related consolidation of procedural memories, and motor sequence-based skills in particular. More specifically, I will present evidence that hippocampal activity and its functional interactions with other brain structures, particularly competition with the striatum, contribute to the initial learning of sequential motor behavior. Interestingly, these early cerebral representations in the hippocampus and striatum, can predict subsequent sleep-related memory consolidation processes. I will also argue that sleep can reorganize the activity within, as well as the functional interactions between, these structures, ultimately favoring overnight performance enhancement. Finally, I will conclude by offering insights into the respective roles of these structures in procedural memory consolidation processes. I will present a new model, developed in collaboration with colleagues, in which we argue that in the context of motor sequence memory consolidation, the hippocampal system triggers subsequent sleep-dependent performance enhancement whereas the striatal system is involved in the maintenance of the motor behavior over time.

Disclosure: Nothing to disclose.

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Upgrading the sleeping brain with targeted memory reactivation

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A fundamental feature of human memory is the propensity for changes in information storage after initial encoding. Recent research findings favor the possibility that memory consolidation during sleep is instrumental for actively maintaining the storehouse of memories that we carry through our lives. In other words, the information that ultimately remains available for retrieval may be that which is reactivated during sleep.

Several studies have now shown that it is possible to externally reactivate specific memories during sleep via the method of Targeted Memory Reactivation (TMR). In our lab, TMR is accomplished by presenting low-intensity auditory cues during slow-wave sleep to prompt memory rehearsal without awakening. In this talk, I will summarize the current and future status of this research topic. I will notably present new findings about the boundary conditions for TMR benefits, and discuss the possibility of finding an electrophysiological signature of reactivation during human sleep using TMR.

Disclosure: Nothing to disclose.

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New insights on the consolidation of emotional memories during sleep

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Recent research has demonstrated that freshly encoded memory traces are replayed during sleep. This mechanism would allow some information to be integrated into an existing network of representations. During wakefulness, the brain is bombarded with large amounts of information. Thus, to better understand how replay during sleep contributes to memory processes, we need to determine what type of information is prioritized for subsequent replay during sleep. We hypothesized that information with an affective value, which might require long-term behavioral changes, would benefit from offline reprocessing during sleep. Thus, memories of emotionally or motivationally relevant experiences may have a higher probability of being reprocessed during sleep. Using simultaneous EEG-fMRI recordings, we measured brain activity while healthy participants played alternating blocks of two distinct games, one of which they would eventually win. Then, we also measured brain activity during different sleeps stages. Using a neural decoding approach we found that the pattern of brain activity associated with the rewarded game occurs spontaneously during deep sleep and more frequently than the non-rewarded game. In a second experiment, we artificially reactivated emotional memory traces during sleep using auditory cues in patients with intracranial EEG recordings. We observed that the cues associated with positive events would elicit distinct iEEG responses during sleep in brain regions involved in emotion and memory. Taken together, these findings suggest a general mechanism whereby the brain selectively consolidates memories with a high value for survival. The replay of relevant memories occurs during a physiological state, i.e. sleep, that is highly favorable for neural plasticity.

Disclosure: Nothing to disclose.

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Sleep-dependent motor memory consolidation from adolescence to adulthood

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Despite profound experience supporting the hypothesis that sleep plays a functional role in the consolidation of fine-motor sequence learning, the impact of sleep on the consolidation of motor adaptation tasks as well as complex gross-motor learning is still debated. Furthermore, in children (7–11 years) it has been shown that there is a lack of sleep-dependent motor memory consolidation. We here examined effects of sleep and wakefulness on 3-ball-cascade juggling in adolescents (12–15 years) in comparison to adults (19–29 years). Juggling requires accurate bimanual arm movements, grasping and visual tracking in the periphery; thus constituting a complex visuo-motor skill. Similar to earlier results in children we found that sleep in adolescents does not lead to an increase but to a decrease in motor performance, whereas across the wake retention interval performance remained stable. This was exactly contrary to the findings in our adult population: juggling performance after sleep

was stabilized but deteriorated after wakefulness. Whereas the sleep-dependent stabilization in the adults was positively associated with fast sleep spindle activity (13–15 Hz) but negatively with REM sleep during sleep after training, no such relationships were revealed for the adolescents. This absence of overnight consolidation in adolescents can be interpreted in terms of diminished capabilities to integrate complex sensory and sensorimotor inputs into already existing motor representations especially at an early stage of implicit motor learning (also see Wilhelm et al., 2012). Astonishingly, data contradicting the classical sleep-dependent memory consolidation hypothesis seem to be accumulating, particularly when focusing on motor learning and early development.

Disclosure: Nothing to disclose.

Hypersomnia: Diagnosis to Treatment

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Perception of sleepiness in a driving simulator is better than perception in the maintenance of wakefulness test

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Objectives: Healthy sleep deprived controls signalled their sleepiness after onset of the first sleep-fragment (SF) in one third of all trials of a maintenance of wakefulness test (MWT) but never in the driving simulator (DS). Here we aimed to validate these results in patients with sleep-wake disorders.

Methods: Overall 40 healthy sleep deprived controls were tested in the MWT (22.3 y ± 2.3). Thereof 16 completed four MWT's and 24 completed one single MWT and one DS trial. They were instructed to signal sleepiness as soon as they realized the first symptoms of sleepiness or tiredness by pressing a button. They were rewarded for optimal performance. So far only 12 patients with sleep-wake disorders were included, while testing them for their fitness-to-drive in 4 MWT's and a DS. A SF was defined by a miniperiod (≥3 s) of theta dominance in the EEG while the eyes were closed.

Results: In 11 of the 48 MWT's (23%) patients signalled sleepiness after the first SF in the MWT almost similar to controls (in 27 of the 88 MWT's, 31%). In the DS no SF and therefore no late signalling occurred in patients whereas at least one SF occurred in 13 of the 24 controls after sleep deprivation, but all controls signalled their sleepiness beforehand.

Conclusion: Similar to healthy controls, optimally treated sleep-patients can fall asleep without prior subjective perception of sleepiness in the MWT, but not in the driving simulator.

Disclosure: Nothing to disclose.

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Narcolepsy in Norway after 2009 ± H1N1-vaccination - the 4 year status

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Objectives: In 2009/2010, 2.2 of 5.1 million Norwegians were H1N1-vaccinated with Pandemrix followed by a >10-times increase in narcolepsy incidence.

We here present the 4-year update on Norwegian narcolepsy cases occurring after 2009.

Methods: Since autumn 2009, all new cases with symptoms of possible narcolepsy have been centrally reported to our center. Cases with sufficient information to confirm narcolepsy according to International Classification of Sleep Disorders 2nd edition were included.

Results: 124 new cases were reported; 38/124 were excluded due to insufficient information.

Narcolepsy was confirmed in 76 Pandemrix-vaccinated cases (♀:♂ 46:30; 71/76 < 18 years; median age 11); 58 diagnosed in 2010–11 and 18 in 2012–13. Abrupt cataplexy was present in 58/61; hypocretin deficiency in 51/51; HLA-DQB1*0602-positivity in 47/47. 12/18 cases diagnosed in 2012–13 actually had disease onset in 2010.

Further, narcolepsy was confirmed in 10 non-vaccinated cases (♀:♂ 5: 5, 5/10 < 18 years, 6 with cataplexy, 8 with hypocretin deficiency); 5 diagnosed in 2010–11; 5 in 2012–13 (one after possible H1N1-infection).

Significant increase in narcolepsy incidence was only found in the vaccinated group in 2010–11 ($P < 0.0001$). Prevalence of cataplexy or hypocretin deficiency did not differ between the vaccinated and non-vaccinated group.

Conclusions: We confirm that narcolepsy incidence in Norway seems only increased in the Pandemrix-vaccinated group in 2010–11. Like in other Nordic countries, some adult Norwegian cases now also appear. However, a considerable number of reported cases with possible narcolepsy still await a final diagnosis, which warrants further investigation of the situation in Norway.

Disclosure: Nothing to disclose.

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Oral JZP-110 (ADX-N05) for the treatment of excessive daytime sleepiness in adults with narcolepsy: results of a randomised, double-blind, placebo-controlled trial

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Objective: Evaluate JZP-110, a wake-promoting agent with dopaminergic and noradrenergic activity, for treatment of excessive daytime sleepiness (EDS) in adults with narcolepsy.

Methods: This double-blind, placebo-controlled study randomised adults with narcolepsy to once-daily placebo ($n = 49$) or JZP-110 ($n = 44$) doses of 150 mg/day (weeks 1–4) increased to 300 mg/day (weeks 5–12). Efficacy endpoints included change from baseline in average sleep onset latency (SOL) on the 40-min Maintenance of Wakefulness Test; Clinical Global Impression-Change (CGI-C); and change from baseline on the Epworth Sleepiness Scale (ESS).

Results: Week 4 changes from baseline were significantly greater with JZP-110 150 mg vs. placebo: increased SOL (9.5 vs 1.4 min; $P < 0.0001$), decreased ESS scores (5.6 points vs 2.4 points; $P = 0.0038$), and more patients with CGI-C improvement (80% vs 51%; $P = 0.0066$). At week 12, following 8 weeks of 300 mg/day, JZP-110 resulted in greater improvement from baseline than placebo on SOL (12.8 vs 2.1 min; $P < 0.0001$), ESS (8.5 points vs 2.5 points; $P < 0.0001$), and percentage of patients with CGI-C improvement (86% vs 38%; $P < 0.0001$). Three subjects (6.8%) on JZP-110 discontinued due to adverse events (AEs). The most common AEs with JZP-110 vs placebo were headache (16% vs 10%), nausea (14% vs 6%), diarrhoea (11% vs 6%), insomnia (14% vs 2%), decreased appetite (14% vs 0%), and anxiety (11% vs 0%). Two serious AEs (conversion disorder, acute cholecystitis) in the JZP-110 group were considered unrelated to treatment.

Conclusion: In adults with narcolepsy, JZP-110 doses of 150–300 mg/day were well-tolerated, and objective and subjective symptoms of EDS were significantly improved.
Disclosure: This study was funded by Aerial BioPharma.

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Modafinil improves real driving performance in patients with hypersomnia: a randomized double-blind placebo-controlled crossover clinical trial

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Objectives: Patients with excessive daytime sleepiness (EDS) are at high risk for driving accidents, and physicians are concerned by the effect of alerting drugs on driving skills of sleepy patients. No study has up to now investigated the effect of modafinil (a reference drug to treat EDS in patients with hypersomnia) on on-road driving performance of patients suffering from central hypersomnia. The objective is to evaluate in patients with central hypersomnia the effect of a wake-promoting drug on real driving performance and to assess the relationship between objective sleepiness and driving performance.
Methods: Randomized, crossover, double-blind placebo-controlled trial conducted among 13 patients with narcolepsy and 14 patients with idiopathic hypersomnia. Patients were randomly assigned to receive modafinil (400 mg) or placebo for 5 days prior to the driving test. Each condition was separated by at least 3 weeks of washout.Mean number of Inappropriate Line Crossings, Standard Deviation of Lateral Position of the vehicle and mean sleep latency in the Maintenance of Wakefulness Test were assessed.
Results: Modafinil reduced the mean number of Inappropriate Line Crossings and Standard Deviation of Lateral Position of the vehicle compared to placebo ($F(1,25) = 4.88$, $P < 0.05$ and $F(1,25) = 3.87$, $P = 0.06$ tendency). Mean sleep latency at the Maintenance of Wakefulness Test significantly correlated with the mean number of Inappropriate Line Crossings ($r = -0.41$, $P < 0.001$).
Conclusions: Modafinil improves driving performance in patients with narcolepsy and idiopathic hypersomnia. The Maintenance of Wakefulness Test is a suitable clinical tool to assess fitness to drive in this population.
Disclosure: Nothing to disclose.

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Sodium oxybate for the treatment of excessive daytime sleepiness and cataplexy in patients with narcolepsy: time to response

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Objective: To evaluate, through post-hoc analysis, the time to response with sodium oxybate (SXB) for the treatment of excessive daytime sleepiness (EDS) and cataplexy in patients with narcolepsy.
Methods: Data were from a randomised, placebo-controlled trial (GHB-2; $N = 136$) that evaluated 4-weeks of oral SXB 3 g, 6 g, and 9 g nightly, and its active drug open-label extension (GHB-3) for 12 additional months. Two responder definitions were developed based on analysis of the relationship of Clinical Global Impression of Change with Epworth Sleepiness Scale (ESS) and number of cataplexy attacks evaluated: EDS improvement determined by >20% decrease in ESS score, and ≥50% reduction in cataplexy attacks. Kaplan-Meier curves and median times to first response and maximum response were estimated.
Results: Among GHB-2 patients randomised to SXB, 77.6% (66 of 85) and 90.7% (78 of 86) of patients responded based on ESS and cataplexy definitions, respectively; median (95% CI) times to first response were 37 (31–50) days for ESS and 25 (17–29) days for cataplexy. Median times to maximum response were 106 (85–164) days for ESS and 213 (94–279) days for cataplexy. Results in GHB-3 among 29 patients initially randomised to placebo were generally consistent with those treated with SXB throughout, but with a longer time to achieve maximum response.
Conclusions: Clinically meaningful improvements in EDS and cataplexy were observed in ≥50% of patients within 2 months, with a longer period needed to achieve maximum response in most patients. Clinicians should recognise that the time course of response may take weeks to months.
Disclosure: This study was funded by Jazz Pharmaceuticals.

Circadian Rhythm Disorders from Clock to Clocking Off

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Core temperature and melatonin circadian rhythm period lengths are longer in delayed sleep phase disorder patients than controls

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Objectives: Delayed Sleep Phase Disorder (DSPD) is assumed to be caused by a persistent 2–6 h delay in the timing of patients' biological clocks. Another mechanism, the endogenous circadian rhythm period lengths (i.e., *taus*) of core temperature and melatonin may contribute to the maintenance of the phase delay and resistance to effective treatment. It was hypothesized that DSPD patients would display significantly longer *taus* compared to controls, thus contributing to its aetiology.

Methods: The ultradian routine method was employed consisting of ultra-short '1 h days', with alternating 20-min sleep opportunities and 40-min of enforced wakefulness. Sixteen controls and 19 DSPD patients, meeting ICSD-3 criteria, underwent an 80-h modified-constant routine weekend protocol to assess core body temperature and melatonin rhythm *taus*.

Results: An independent samples t-test showed DSPD patients had longer melatonin taus (M = 24h32 m $\pm$ 17 m) than controls (M = 24h19 m $\pm$ 15 m), P = 0.012 (one-tailed), d = 0.80. DSPD also had longer core temperature *taus* (M = 24h40 m $\pm$ 40 m) compared to controls (M = 24h16 m $\pm$ 38 m), P = 0.044 (one-tailed), d = 0.59. *Tau* measures were interrelated (r = 0.403, P = 0.016).

Conclusions: Longer *taus* may contribute to the aetiology of DSPD. A longer tau would produce a stronger tendency to phase delay. This would lead to greater delays when not opposed by Zeitgebers such as morning light on mornings of delayed awakenings. This stronger tendency to phase delay would also explain the difficulty in phase advancing DSPD patients and the high relapse rate following treatment. Results give further support for rigorous and persistent morning phototherapy and evening melatonin administration.

Disclosure: Nothing to disclose.

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Measuring melatonin in saliva before the start of light therapy in delayed sleep phase disorder

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Introduction: Dim light melatonin onset (DLMO) is a common way to measure the biological phase delay in delayed sleep phase disorder (DSPD). Sometimes DLMO is time consuming, expensive and difficult to obtain. In the present study a shortened way of estimating DLMO, before light therapy is commenced, was evaluated.

Method: Forty-five participants (23 women) with a mean age of 22 years, with diagnosed DSPD, were investigated. A sleep diary was kept for 1 week. Melatonin in saliva was then measured hourly during one late evening to obtain DLMO. DLMO was defined as the clock time when melatonin exceeded a threshold of 4 ng/L. All participants received 2 weeks of light therapy (LT) at 10 000 lux for 2 weeks. Based on the DLMO results at baseline the group was divided into participants with a DLMO before 23:00 and those with a DLMO after 23:00 to compare the results.

Result: Late DLMO at baseline was correlated with larger advance in sleep onset and sleep offset (rho = 0.58; P = 0.001 and r = 0.389; P = 0.037 respectively) from baseline to second week of LT. A significantly larger improvement in sleep onset (P = 0.037) and sleep offset (P = 0.014) from baseline to the second week of LT were seen for the group with melatonin values $\leq$4 ng/L at 23:00 compared to the group with melatonin values >4 ng/L at 23:00.

Conclusion: Improvements regarding diurnal rhythm after LT are significantly larger for those with a later DLMO. Testing melatonin in saliva at 23:00 could be a usable shortened test before LT is commenced.

Disclosure: Agneta Markström has had paid speaking engagemant on non-invasive ventilation and secretion mobilizing equipment for Respironics AB Sweden. There are no conflicts of interest to declare for any of the other authors.

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Difficult morning awakening from REM sleep and impaired cognitive function in delayed sleep phase disorder patients

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Objectives: Difficult awakening is a key symptom of delayed sleep phase disorder (DSPD), but none have quantified awakening thresholds in a sleep-laboratory. We assessed if cognitive function was impaired after awakening and if difficult awakening was associated with specific polysomographic features like slow-wave sleep stage N3.

Methods: Nine patients with DSPD and nine sex and age matched healthy controls were included. Polysomnography was performed at our University Hospital from midnight. An alarm clock was activated at 0700 am with sound intensity increasing from 72 to 104 dB. Participants performed a continuous performance test (CPT) the previous afternoon and immediately upon awakening.

Results: Three DSPD patients and zero controls did not wake up to the maximum 104 dB alarm sound. All these three patients were in

REM sleep when the alarm clock went off (difference in proportions $P = 0.047$). In patients, CPT reaction time was prolonged in the morning compared to the afternoon (ANOVA interaction $P = 0.01$). DSPD patients made more omission errors than controls regardless of time of the day (ANOVA main effect $P = 0.046$).

Conclusions: Difficult awakening from slow-wave sleep was not observed. A subgroup of DSPD patients may have a severe problem waking up from REM sleep. DSPD patients may also have a state-like impairment in cognitive function in the morning and a trait-like impairment not depending on time of day, compared to normal sleepers.

Disclosure: Nothing to disclose.

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How does alertness differ between healthy employees and those with shift work disorder?

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Objectives: Shift work disorder (SWD) is defined as insomnia or excessive sleepiness temporarily associated with a recurring work schedule that overlaps the usual time for sleep. In this field study we examined how alertness of employees with SWD varies in different shifts and days off compared to healthy counterparts.

Methods: Participants were 31 shift workers from a Finnish airline company who belonged either to the SWD ($n = 22$, men 77%, age range 27–59) or the control ($n = 9$, men 78%, age range 36–58) group, based on the occurrence of any work shift dependent frequent symptoms of insomnia or tiredness reported on a 6-item questionnaire. Participants estimated their lowest alertness of the past day with the Karolinska Sleepiness Scale (KSS) in a 3-week diary and the real time alertness with the KSS in connection with four shifts and two days off.

Results: Linear mixed model analysis adjusted for sex indicated lower alertness in the SWD group compared to the healthy group in connection with early morning shifts (shifts starting before 6 a.m.) ($P < 0.01$) and after the night shifts (the lowest alertness $P < 0.001$). The lowest alertness of the day did not differ between the groups on the days off, however the SWD group evaluated their real time alertness lower than the controls. Self-assessed chronotype did not differ between the groups.

Conclusions: The results indicate that the employees with SWD are distinguished from the healthy co-workers especially in early morning shifts by their lower level of alertness.

Disclosure: Nothing to disclose.

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Sleep schedules and social jetlag in students with delayed sleep phase disorder and controls

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Objectives: To compare habitual sleep schedules and social jetlag (discrepancy between midsleep on weekdays and weekends) in students with delayed sleep phase disorder (DSPD) and healthy controls.

Methods: A total of 40 students with DSPD and 21 controls participated. The DSPD group comprised 70% females and 30% males, mean age 20.7 ± 3.1 years. The control group comprised 71% females and 29% males ($P = 1.000$), mean age 21.2 ± 2.2 years ($P = 0.511$). Sleep diaries were kept for 7 days on a habitual sleep schedule. Data were analysed by t-tests and two-way ANOVAs (DSPD/control x weekday/weekend).

Results: Students with DSPD went to bed at 01:59 ± 113 min/03:10 ± 124 min (weekdays/weekends) and rose at 10:31 ± 151 min/12:36 ± 112 min, whereas controls went to bed at 23:54 ± 40 min/01:05 ± 87 min and rose at 08:15 ± 80 min/09:52 ± 69 min. Analyses showed a main effect of group (DSPD/control) for both bed ($F_{1,59} = 24.31$, $P < 0.0005$) and rise times ($F_{1,59} = 30.54$, $P < 0.0005$), as well as a main effect of time (weekday/weekend) for both bed ($F_{1,59} = 34.60$, $P < 0.0005$) and rise times ($F_{1,59} = 49.19$, $P < 0.0005$). There were, however, no group x time interaction effects neither for bed ($F_{1,59} = 34.60$, $P = 0.974$) nor rise times ($F_{1,59} = 49.19$, $P = 0.384$), and the degree of social jetlag did not differ between the groups (DSPD 79 ± 84 min, controls 90 ± 85 min; $t_{59} = 0.49$, $P = 0.625$).

Conclusions: Sleep schedules were delayed by more than 2 h in students with DSPD compared to controls. However, both groups reported delayed weekend sleep schedules and the degree of social jetlag did not differ between the groups.

Disclosure: Nothing to disclose.

Metabolomics in Sleep Research: Integration from Animals to Humans

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Lipid profiles after experimental restriction of sleep and in an epidemiological cohort reporting insufficient sleep

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Sleep restriction increases the risk for many common diseases. Many of these pathologies are associated with inflammation, e.g. type 2 diabetes and atherosclerosis. The development of insulin resistance during sleep restriction has been well documented in healthy volunteers, describing the development of pathologies in glucose metabolism. However, lipid metabolism - the central pathology of atherosclerosis - has not been frequently assessed in sleep restriction studies, and when measured, the changes have reported to be either small or non-existent.

In the present study, we applied transcriptomics and modern lipidomics approaches to study changes in lipid metabolism during sleep restriction in healthy volunteers (sleep was restricted to 4 h per day during five consecutive days; SR) and in an epidemiological cohort with questionnaire data on subjective sleep insufficiency (SSI).

The genome wide gene expression studies revealed that genes related to immunological activation were up-regulated while those related to lipid metabolism were down-regulated in both the SR and SSI groups. Lipidomics profiles, assessed with 1NMR, showed that during the five day sleep restriction, the number of LDL particles decreased while there was no change in the number of HDL particles. However, in the SSI group, there was no difference in LDL particle number as compared to good sleepers, but the number of HDL particles was decreased.

We conclude that the down-regulation of lipid metabolism takes place already after 1 week of sleep restriction at transcriptional level, and persists also in the long run, while changes in the actual lipid profile develop more slowly.

Disclosure: Nothing to disclose.

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Chronic sleep restriction alters metabolomic profiles in healthy humans

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Objectives: Sleep restriction degrades neurobehavioral functions including behavioral attention, cognitive throughput and memory, and increases sleepiness. However, there are substantial, stable and trait-like individual differences in such responses to sleep restriction with some individuals showing no neurobehavioral decrements (resilient), other showing intermediate responses, and others showing marked decrements (vulnerable). The current study examined whether metabolomic markers could differentiate such vulnerable and resilient individuals.

Methods: N = 10 healthy subjects (27.5 $\pm$ 5.6y; 5 females; 9 African Americans) participated in one of two 14–20 day laboratory protocols. Metabolomic blood samples were taken following 10–12 h fasting after: 1. one night of baseline sleep [10 h time in bed (TIB), 2200 h-0800 h]; 2. chronic sleep restriction (5 consecutive nights of 4 h TIB, 0400 h-0800 h); and 3. one night of recovery sleep (12 h TIB, 2200 h-1000 h). The 10-min Psychomotor Vigilance Test (PVT), Digit Symbol Substitution Task (DSST), Digit Span (DS), Karolinska Sleepiness Scale (KSS) and Profile of Mood States (POMS) were administered every 2 h while awake. OPLS regression was used for statistical analysis.

Results: One metabolite associated with six neurobehavioral variables during sleep restriction, but not at baseline or recovery: DS, KSS, DSST, POMS-vigor, PVT lapses (response times >500 ms) + false starts (premature responses or response times <100 ms) and PVT response speed. Higher levels of this metabolite predicted poorer DS, DSST and PVT performance, and higher KSS scores.

Conclusions: This study provides the first experimental evidence that one metabolite may be a significant predictor of differential vulnerability to sleep restriction using reliable neurobehavioral outcomes in healthy adults.

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Effect of sleep deprivation on human plasma metabolome rhythms

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Objectives: The metabolic pathways involved in human sleep and during sleep deprivation have not yet been systematically studied using a metabolomics approach. We thus aimed to characterise plasma metabolite rhythms during a 24 h wake/sleep cycle followed by 24 h of wakefulness using untargeted and targeted liquid chromatography-mass spectrometry (LC-MS) metabolomics.

Methods: Following an adaptation night, 12 healthy young males remained in controlled laboratory conditions with respect to environmental light, sleep, meals and posture during a 16 h wake/8 h sleep opportunity followed by 24 h of wakefulness. Blood samples were collected for 48 h at 1- and 2-hourly intervals for melatonin and LC-MS analysis, respectively.

Results: Principal component analysis revealed a clear time of day variation during the wake/sleep cycle as well as during 24 h of wakefulness in both untargeted and targeted analysis. Of 171 metabolites quantified, daily rhythms were observed in the majority (n = 109), with 78 of these maintaining their rhythmicity during 24 h of wakefulness, most with reduced amplitude (n = 66). By contrast fewer ions/metabolites were significantly changed during sleep deprivation. In the targeted analysis only 27 of the 171 metabolites were significantly increased during sleep deprivation (including

tryptophan, serotonin, taurine, some acylcarnitines, glycerophospholipds and sphingolipids).

Conclusions: The increased levels of serotonin, tryptophan and taurine may explain the antidepressive effect of acute sleep deprivation and deserve further study. Metabolic profiling during sleep and sleep deprivation and characterization of 24 h rhythms under these conditions offers a unique view of human sleep-wake regulation.

Disclosure: BBSRC (UK) supported.

Sleep-related Neurostimulation: Mechanisms and Clinical Implications

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Investigating sleep homeostasis by means of transcranial magnetic stimulation

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Investigations into mechanisms underlying the homeostatic regulation of sleep have provided fruitful insights into functions of sleep. Transcranial magnetic stimulation (TMS) in combination with EEG allows investigating such mechanisms in humans. For example, rTMS induced potentiation of cortical circuits, lead during subsequent sleep to a localized increase in EEG slow wave activity (SWA), the well established electrophysiological correlate of sleep homeostasis. Similarly, paired associate stimulation paradigms were used to depress or potentiate sensorimotor cortex and resulted, during subsequent sleep, in corresponding local changes in SWA. Such results support the synaptic homeostasis hypothesis by Tononi and Cirelli, which considers that waking is generally accompanied by the strengthening or potentiation of synapses. According to the hypothesis, sleep slow waves are not only reflecting such synaptic potentiation but are also responsible for synaptic re-normalization, a generalized decrease in synaptic strength that recalibrates neural circuits. The simultaneous application of TMS and EEG may provide insights into this re-normalization process during sleep. TMS induced EEG responses represent a unique measure of the excitability of a particular cortical area, which supposedly changes as a function of synaptic strength. Thus, we were able to show that excitability of the human frontal cortex progressively increases with time awake, from morning to evening and after one night of sleep deprivation, and decreases after recovery sleep. Such results suggest that sleep may control cortical excitability, which might be related to the well-known effects of sleep deprivation on seizures, hallucinations, and depressive symptoms.

Disclosure: Nothing to disclose.

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Closed-loop stimulation of sleep oscillations

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Sleep promotes memory consolidation, but the neurophysiological mechanisms mediating this effect have been unraveled only partially. The slow oscillation hallmarking the electroencephalogram during slow wave sleep is assumed to represent an essential element in this regard. Cortical slow-oscillatory activity in a top-down fashion orchestrates other subcortical rhythms: within a slow oscillation, thalamo-cortical spindle activity is nested which in turn entrains hippocampal sharp-wave ripples. Together, these phenomena might mediate the transfer of memory traces temporarily stored in the hippocampus to cortical structures for long-term storage.

This functional importance has stimulated attempts to manipulate slow oscillatory activity through external stimulation. While previous studies enforced rhythms on the brain irrespective of the endogenous activity, closed-loop control represents an innovative alternative: Utilizing the ongoing EEG activity, the stimulation is fine-tuned to the brain's own rhythm, latching onto slow oscillations which typically display a temporal jitter. This enables a synchronization of the desired manipulation to the slow oscillatory rhythm and thereby increases the efficacy.

In a series of experiments we have explored the merits and limitations of this approach by employing auditory or transcranial direct-current stimulation as a means to manipulate both slow oscillations and sleep spindles and to probe their functional role in memory consolidation. Altogether, our results indicate that closed-loop stimulation is a promising approach to increase the efficacy of sleep rhythms and to investigate their functional relevance. Moreover, this approach may be useful to treat pathological conditions, like attention deficit hyperactivity disorder, that are associated with sleep disturbances and cognitive impairments.

Disclosure: Nothing to disclose.

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The impact of high-frequency stimulation on sleep

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The general public is exposed to RF fields from various sources, e.g. radio and TV transmitters, mobile communication devices and their respective base stations. Especially the increasing use of mobile mobile phones has lead to concerns about possible health effects due to RF-EMF exposure in parts of the population. The Eurobarometer 73.3 on electromagnetic fields (EU, 2010), which investigated public perception of potential health risks of EMFs in 26.600 subjects from 27 EU member states, points out that 33% of the poll believed that their health is affected to a large extent by mobile phone base stations. The corresponding figure for mobile phones is 26%. Among the most often reported non-specific symptoms attributed to EMF exposure are headache and sleep problems. Most of the early experimental human studies investigating effects of short-term RF-EMF exposure on sleep have shown an effect on the power spectra of the non-REM sleep EEG especially in the spindle frequency range. It has been shown that pulse modulation of the RF signal plays an important role. More recent studies underline that

1. power spectra differences are observed not only in the spindle frequency range, but in varying frequency ranges,
2. are not restricted to NREM sleep or NREM stage 2 sleep and
3. occur not only at the beginning of the night (SCENIHR 2014).

Overall studies vary with regard to

1. exposure conditions and set-ups,
2. the number of investigated outcome parameters, and
3. statistical properties.

Nevertheless effects of RF-EMF exposure on the sleep-EEG are observed with some consistency in experimental human studies.

Disclosure: Nothing to disclose.

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The modulation of sleep continuity through transcranial direct current stimulation (TDCS)

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Introduction: The aim of this study was to provide proof-of-concept that sleep continuity in humans can be modulated by local activity changes of the cerebral cortex through the non-invasive brain stimulation technique transcranial direct current stimulation (tDCS). This proposition is based on preclinical work suggesting that sleep emerges from synchronized deactivation in a cortico-thalamo-cortical feedback-loop and human studies indicating an association between cortical deactivation and sleep.

Methods: Eighteen healthy individuals (40–65 years) underwent a within-subject, repeated measures protocol across five nights in the sleep laboratory. One adaptation night was followed by a baseline night and three experimental nights with polysomnographic monitoring. A repetitive tDCS protocol (anodal activation, cathodal deactivation and sham stimulation) was applied directly prior to sleep in the experimental nights (bifrontal stimulation, 1 mA on each side). The stimulation conditions were implemented in a counterbalanced order and were separated by 1 week.

Results: A within-subject repeated-measures ANOVA revealed a significantly decreased total sleep time in the activation compared to the deactivation and sham condition, primarily driven by a reduction of stage 2 sleep in the activation condition. The intervention was well tolerated and the participants were unaware of the stimulation conditions.

Conclusion: This study provides first evidence that sleep continuity in healthy individuals can be modulated by local cortical activity changes through tDCS. Future studies are needed to test whether disturbed sleep in patients with insomnia can be improved.

Disclosure: Nothing to disclose.

Impact of Sleep Disordered Breathing in Neurological Sleep Disorders

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Sleep disordered breathing and paradoxical insomnia

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The essence of insomnia is a predominant complaint of dissatisfaction with either duration or quality of sleep. A diagnosis of insomnia is based on three fundamental criteria: recurring difficulties with sleep, adequate opportunities for sleep, and impairment of daytime functioning. These symptoms may also be present in other primary sleep disorders. Moreover, insomnia may coexist with these disorders, and sleep apnea is found in at least 30% of insomnia patients. The resulting clinical picture may be complex and difficult to tackle diagnostically and therapeutically. Paradoxical insomnia refers to a complaint of severe insomnia that is not on a par with objective evidence of sleep disturbance. Typically patients claim to have been awake for most of the night, whilst polysomnography shows little or no abnormalities in the hypnogram. Sleep apnea and paradoxical insomnia incidentally coexist. The particularities of this association will be discussed in the presentation.

Disclosure: Nothing to disclose.

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Role of sleep disorder breathing in REM sleep behavior disorder

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REM sleep behavior disorder (RBD) is characterized by motor and vocal dream-enacting behaviors and nightmares associated with increased electromyography activity during REM sleep.

Patients with severe obstructive sleep apnea (OSA) without RBD may report nightmares and abnormal sleep behaviors due to apneic-related arousals. In other words, severe OSA may mimic true RBD symptomatology. In these pseudo-RBD cases, CPAP therapy eliminates the nightmares and abnormal sleep behaviors. This indicates that polysomnography is mandatory to diagnose RBD (showing excessive electromyographic activity in REM sleep) and to exclude its clinical mimics such as OSA.

In patients with true-RBD, the excessive EMG activity occurring in the pharyngeal muscles in REM sleep may protect to severe OSA. However, OSA and RBD may coexist by chance. In these cases, apneic events in REM sleep hampers the correct diagnosis of RBD by polysomnography because sleep disruption does not allow evaluate properly the quantity of electromyographic activity in REM sleep. Elimination of OSA with CPAP is then useful to quantify properly the electromyographic activity in these cases when OSA interfered. In true RBD patients with coexistent severe OSA, therapy with CPAP reduces (but does not eliminates) the frequency and intensity of both nightmares and dream-enacting behaviors.

In RBD subjects with Parkinson disease and dementia with Lewy bodies, sleep disordered breathing is not more common than in matched healthy controls. In contrast, in RBD patients with multiple system atrophy, central sleep apnea, Cheyne-Stokes respiration and laryngeal palsy resulting in stridor and OSA are common.

Disclosure: Nothing to disclose.

Behavior Problems and Treatment Possibilities in Child and Adolescent Sleep Problems

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Internalizing behavior problems in primary school children with insomnia

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Introduction: Several studies indicate that children with insomnia also have internalizing behavior problems. In the present study, we investigated whether these problems improve after the successful treatment of sleep disorders. Results were compared to a waiting list control group and 12-month follow-up data are available.

Methods: 48 families with children aged 5–10 years with insomnia were treated with the sleep training 'KiSS'. This sleep training is a short-term multimodal therapy with six sessions (three for children and three for parents) which integrates hypnotherapeutic and cognitive-behavioral interventions and psychoeducation. Internalizing behavior problems were measured with the German version of the Child Behavior Checklist (CBCL) before the training, immediately after the training, and three, six and twelve month later.

Results: At the beginning of the investigation the children had slightly higher internalizing behavior problems compared to the clinical norm values of the CBCL; with no differences between the therapy and the control group. Internalizing behavior problems were reduced in both groups, after the waiting time and the treatment, but the reduction was significantly stronger in the treatment group. The effects decreased until 1 year after the sleep training.

Conclusion: A treatment with the multimodal sleep training 'KiSS' leads to positive changes in children with internalizing behavior problems. With only three sessions for parents and three sessions for children the training is economical. Thus, the sleep training 'KiSS' can be seen as a positive contribution to treatment of childhood insomnia.

Disclosure: Nothing to disclose.

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Melatonin treatment and classical conditioning in children with delayed sleep phase

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The positive effects of melatonin treatment in children with sleep onset problems usually disappear when treatment is discontinued. We investigated whether classical conditioning might help to preserve treatment effects of melatonin.

After a baseline week, 16 children (mean age 9.78 years) received melatonin treatment for 3 weeks, followed by a week in which they received half the dose, and a stop week. Classical conditioning was applied by having children drink biological lemonade while taking melatonin, and by using a lamp that was turned on when children went to bed. Variables measured were sleep (sleep diaries, actigraphy), Dim Light Melatonin Onset, and health, behavior problems, and parenting stress. The results were compared with a control group consisting of 41 children (mean age 9.43 years) who received melatonin without classical conditioning.

Melatonin treatment was effective in advancing DLMO and reducing sleep onset problems, and in addition positive effects were found on sleep quality, health, behavior problems, and parenting stress. After stopping melatonin, sleep returned to baseline levels. Interestingly, for both groups behavior problems and parenting stress remained significantly lower. Results did not differ between the experimental and control group, so we concluded that there was no effect of classical conditioning. However, when we excluded children with comorbid conditions, classical conditioning did seem to subdue the negative effects of withholding melatonin.

This study suggests that classical conditioning does not help to preserve the efficacy of melatonin treatment after its discontinuation. However, classical conditioning may be effective in children without comorbid problems.

Disclosure: Nothing to disclose.

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Aggression and violent behavior and sleep problems in young students

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A cumulatively impaired sleep quality is a frequently seen phenomenon, especially in samples of adolescents and young adults due to specific vulnerability factors such as the pubertal shift in circadian preference. One of the recently emerging consequences of a diminished sleep quality is an increase in hostile and aggressive conduct within laboratory settings as well as in the field. However, little is known regarding the intervening variables that effectuate this association. In accordance with the contemporary literature, the hypothesis of a deficit in executive functioning was translated into a structural equation model and tested in a sample of 1879 young students (26.1% male) with a mean age of 21.5 years $\pm$ 2.01; range: 17 - 25 years). Evaluation of the revised model structure resulted in a sufficient model fit. The model yielded significant and clinically relevant path loadings from the latent sleep variable to different aspects of executive functioning (β = 0.82) and from executive functioning to the degree of self-reported aggressivity (β = 0.66). A significant interrelation between aggression and the severity of insomnia symptoms as assessed by the PSQI was also demonstrated. Despite the high level of convergence between these results and the hypothesis of a sleep-related deficit in executive functioning this association remains to be validated within a laboratory setting and by implementing objective measures. Nonetheless, these preliminary findings highlight the importance of sleep-inherent regeneration for emotional functioning. The magnitude of the reported effect sizes emphasizes the relevance of this interrelation in daily life.

Disclosure: Nothing to disclose.

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Efficacy of cognitive behavior therapy in adolescents with insomnia: an RCT with group-CBTi, internet-CBTi and a waiting list condition

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Objectives: Research indicates that adolescents are at risk for insomnia and insomnia can have severe negative impacts on behavioural, cognitive and emotional functioning. Treatment of insomnia has been examined extensively in adults, but studies with adolescents are sparse.

Methods: We randomly assigned 115 adolescents with DSM-5 primary insomnia to Cognitive Behavioural Therapy for Insomnia (CBTI) in groups (N = 38), individual CBTI through an internet website (N = 39), or a waiting list condition (N = 38). CBTI consisted of six weekly sessions and a booster session after 2 months. We measured sleep with daily sleep logs and actigraphy, and questionnaires for symptoms of insomnia and chronic sleep reduction at baseline, post treatment and two moths follow-up.

Results: After treatment there was more improvement in the primary outcome measure sleep efficiency (proportion of actual sleep during time in bed), for both treatment groups compared to the waiting list group, which was confirmed by improvements in several other sleep variables. Symptoms of insomnia and chronic sleep reduction, except irritability, also improved more for the treatment groups compared to the waiting list group. There were no significant differences between outcomes of the two treatment groups, and there was a trend of continuing improvements at 2 months follow up.

Conclusions: To our knowledge this is the first RCT with CBTI for adolescents. Preliminary results demonstrated the efficacy of CBTI for the treatment of insomnia in adolescents. Further investigations into the efficacy of the separate CBTI-components and mediating factors are suggested.

Disclosure: Nothing to disclose.

Complex breathing disorders during sleep

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Natural evolution of complex sleep apnea: polysomnographic results

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Introduction: Obstructive sleep apnea patients who exhibit ≥5 central apneas per hour of sleep (AI) under otherwise sufficient treatment of obstructive sleep apnea by CPAP (obstructive and mixed AI <5) fulfill criteria for complex sleep apnea. It is uncertain which patients develop complex sleep apnea and how stable over time complex sleep apnea is.

Methods: After receiving full night diagnostic polysomnography (PSG), patients with obstructive sleep apnea received a second full night PSG in their first night with stable CPAP treatment (after one night nCPAP titration). Patients used CPAP for 3 months and were re-studied with full night PSG.

Results: 12.2% (82) of the initial 675 patients exhibited complex sleep apnea in the first night with stable CPAP. They were older (59.8 vs. 55.5 years, $P = 0.001$) and had a higher diagnostic Apnea-Hypopnea Index (AHI; 37.5 vs. 31.4. $P = 0.003$) compared to those who did not develop complex sleep apnea. Their higher AHI was exclusively due to more central and mixed apneas (both $P < 0.05$) in the diagnostic PSG. Sleep variables in the diagnostic PSG did not differ for patients with and without complex sleep apnea, but in the first night with stable CPAP, complex sleep apnea patients had lower sleep efficiency, more wake after sleep onset and more sleep stage N1 ($P < 0.05$).

76% of patients with and 74% of patients without complex sleep apnea were available for the 3 months follow-up. 13% of each group did not continue with CPAP. 40 (74%) of the 54 patients with initial complex sleep apnea available for follow-up did no longer have complex sleep apnea. 16 of 382 patients (4.2%) without initial complex sleep apnea had novel complex sleep apnea in the follow-up PSG. Even though most (16) of the 30 patients with complex sleep apnea at follow were not a part of the group with initial complex sleep apnea, similar characteristics of age and sleep structure were present for both complex sleep apnea groups.

Conclusion: Most patients with initial complex sleep apnea do no longer have complex sleep apnea after 3 months - it seems that complex sleep apnea is not a stable disorder. Complex sleep apnea probably impairs sleep quality, but it could also work the other way: complex sleep apnea could be a phenomenon appearing in older patients with a large proportion of central apneas before treatment in nights with (spontaneous?) low sleep quality with many sleep wake transitions which promote central breathing disorders. If complex sleep apnea was constantly impairing sleep, the disorder should be more stable than our results indicate and these patients could be expected to be sleepier. But that is not the case, as rather similar ESS scores indicate (ESS 7.3 vs. 6.5 at follow up, $P = 0.3$).

Disclosure: Nothing to disclose.

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The role of the 'central' component in the pathophysiology of complex breathing disorders during sleep

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Sleep specialists are being confronted with an increasing number of patients with complex breathing disorders during sleep related to obesity hypoventilation (OHS), opioid induced sleep apnoea, overlap syndrome and OSA related to neuromuscular disorders. These disorders constitute the end points of a spectrum with distinct yet interrelated pathogenic mechanisms for OSA, CSA, sleep hypoventilation and CSR. Airflow is recurrently interrupted or reduced, while breathing effort is reduced simultaneously. Instability of the breathing pattern can go along with an increase in upper airway resistance, increased collapsibility of the upper airway and discoordination of local reflex mechanisms, and can cause obstructive apnoeas. Unstable and irregular breathing in itself can lead to periodicity and central apnoeas. In neuromuscular disease, OHS and narcotic use, decreased chemical drive and/or failing respiratory function are associated with CSA and usually also with ongoing hypoventilation during wakefulness, characterised by chronic daytime hypercapnia. The OHS combines abnormalities of ventilatory control, thoracic mechanisms, sleep-disordered breathing and neurohormonal disturbances, such as leptin resitance, each of which contributes to varying degrees in individual patients to the development of OHS. The coexistence of OSA and COPD seems to occur by chance. However, accentuated physiologic alveolar hypoventilation, ventilation-perfusion mismatch, reduced contractility of respiratory muscles, increased physiological dead space, lower oxygen levels, lung inflation, (respiratory) muscle atrophy and intermittent hypercapnic events resulting from apnoeas and hypopnoeas contribute to the final clinical picture. Some patients present with preserved or enhanced chemical drive on the one hand, and blunted chemical drives on the other hand. Altogether, the wide range in chemical drives illustrates the existence of different phenotypes in overlap patients, but also reflects a gradual adaptation of chemoreceptors (CO2 desensitisation) secondary to mild elevation of serum HCO3- that can occur even during acute hypercapnia.

Conclusions: Complex breathing disorders during sleep do not represent a single disease, but is likely the result of any one of a number of processes that yield instability of respiratory control. Knowledge of shared mechanisms may help to identify these patients and guide therapy.

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Disclosure: Nothing to disclose.

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Therapeutical approach of complex breathing disorders during sleep

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The complexity of sleep related breathing disorders (SRBD) has been increasingly realized in recent years. Patients present with the coexistence of obstructive (OSA) and central sleep apnoea (CSA). In addition, comorbidities such as morbid obesity, chronic obstructive pulmonary disease or neuromuscular disorders impose clinical problems including air trapping, different aberrations of the pulmonary compliance or instability of the upper airways. SRBD may be differentiated in those with reduced (hypercapnic) and increased (non-hypercapnic) breathing disturbances. These complex findings have to be addressed by different applications of positive airway pressure during the breathing cycle, various adaptations to upper airway obstruction or periodic breathing and lung inflation. The varying upper airway obstruction may be addressed by automatic adaptation of the expiratory pressure. The difference between expiratory pressure and inspiratory pressure defines a tidal volume applied by the device. It may be varied according to the required minute ventilation in hypoventilatory disorders or anticyclically in patients with periodic breathing. To allow more comfortable ventilation for the patient, the pressure may be relieved during early expiration (pressure relief). Most recent algorithms combine automatic adaptation of the expiratory pressure, pressure relief during early expiration and automatic adaptation of the pressure support. However, critical evaluation of the technical approaches is needed to find the optimal therapy for the individual patient.

Disclosure: Nothing to disclose.

Sensorimotor Processes in REM Sleep: from RBD to Rat Pups to Robots

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Neuro-circuits controlling muscle atonia during paradoxical (REM) sleep

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Paradoxical sleep (PS) is characterized by muscle atonia induced by ponto-medullary-spinal pathways. It was first demonstrated that a pontine area recently named sublaterodorsal tegmental nucleus (SLD) contain the neurons inducing the muscle atonia of PS. Besides, it was shown that glycine induces the hyperpolarization of motoneurons during PS. We recently define in detail the network responsible of muscle atonia during PS combining Fos staining, retrograde tracing and immunohistochemistry or 'in situ' hybridization of markers of cholinergic, glutamatergic, GABAergic and glycinergic neurons. We showed that glutamatergic neurons localized in the SLD triggered muscle atonia during PS by means of their descending projections to GABA/glycinergic neurons localized in the ventral medullary formation namely the ventral gigantocellular reticular nucleus (GiV). We further showed that these neurons project to the spinal cord and are activated during PS. To directly demonstrate the role of these glutamate and GABA/glycinergic neurons in PS atonia, we inactivated SLD glutamatergic or GiV GABA/glycinergic transmission using transfection with AAVs of short hairpin RNA specific of the mRNAs of the vesicular glutamate 2 (vGLUT2) or GABA/glycine vesicular (vGAT) transporters. These animals display absence of atonia and large movements during PS confirming the role of the SLD glutamatergic neurons and the GABA/glycinergic neurons in the induction of muscle atonia during PS. In line with these results, we propose that REM sleep behavior disorder (RBD) is due to a specific degeneration of PS-on glutamatergic neurons localized in the SLD or the glycinergic/GABAergic premotoneurons localized in the GiV.**Disclosure:** Nothing to disclose.

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Developing the sensorimotor system in our sleep

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How are the 'rudimentary' movements of fetuses and infants transformed into the coordinated, flexible, and adaptive movements of adults? Some believe that adult behaviors are built from 'motor primitives,' endowed units of behavior, hardwired in the central nervous system, that arise fully formed without the need for experience. In contrast, an increasing number of developmental scientists and roboticists are emphasizing how infants *discover* how their bodies are built. Not surprisingly, this process of discovery has been presumed to occur only when infants are awake, reflecting the common wisdom that sleep is a period of sensory isolation and behavioral stillness. But this is far from the truth. Instead, during active (or REM) sleep, every skeletal muscle in the body twitches, causing jerky movements of arms and legs, fingers and toes, eyes, and (in rodents) whiskers. These movements are particularly prominent during the perinatal period when active sleep predominates. Although considered for millenia to be by-products of dreams (think dogs 'chasing rabbits'), research in infant rodents over the past decade has fundamentally altered our conception of the neural causes and functional consequences of this behavior, with important implications for our understanding of typical and atypical development and recovery of function after injury or disease. Also, recent work from my laboratory shows that twitches are uniquely different from wake movements with regard to how they are processed by the sensorimotor system. This surprising feature of twitching may hold the key to understanding its role in driving activity-dependent development of the sensorimotor system.
Disclosure: Nothing to disclose.

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Sleeping robots: How sleep behaviour drives the development of spinal circuits

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Sleeping is not a typical subject of investigation in artificial intelligence and robotics. Arguably, a sleeping robot could be regarded as a non-behaving creature which would defeat its purpose as a functional machine. However, when looking at the sleep of biological creatures, it is clear that such a state is not completely devoid of behaviour. On the contrary, during REM sleep a significant amount of body motion is produced by spontaneous motor activity. This type of activity takes the form of myoclonic twitches which generate spontaneous contractions in every muscle of the body. These contractions occur in the absence of sensory activity, and have been hypothesized to contribute to the development and refinement of neural circuits. In our experiments, we actuated a robotic platform with analogues of myoclonic twitches. The platform is equipped with artificial muscles and three sensory modalities which are reminiscent of the following spinal proprioceptors: the muscle spindles, the Golgi-tendon organs, and the cutaneous receptors. Our results show that by correlating the sensory and motor signals during the twitching activity we can obtain equivalents of the most basic reflex circuits in the spinal cord. Overall, they suggest that myoclonic twitches might be important for the development of motor control, by maintaining peripheral reflex circuits aligned with the morphology of the body throughout the entire lifetime of the animal.
Disclosure: Nothing to disclose.

Memory, Cognition and Dreaming

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Memory deficits associated with sleep loss can be prevented by targeting a single phosphodiesterase isoform selectively in excitatory neurons of the hippocampus

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Objectives: Millions of people regularly obtain insufficient sleep which results in cognitive impairments. We previously showed that 5 h of sleep deprivation leads to attenuation of the cAMP pathway in the hippocampus which is reversed by systemic delivery of the non-specific phosphodiesterase 4 (PDE4) inhibitor rolipram. We also found that sleep deprivation for 5 h leads to increased protein levels of the cAMP-degrading PDE4 isoform PDE4A5. However, no studies assessed whether the upregulation of PDE4A5 is solely responsible for the cognitive deficits associated with sleep loss.

Methods: We used a viral approach to express the following transgenes in excitatory neurons of the hippocampus:

1. a catalytically inactive dominant negative form of PDE4A5 (PDE4A5DN),
2. wild-type PDE4A5 (PDE4A5WT), or
3. enhanced green fluorescent protein (eGFP) virus.

Results: Overexpression of PDE4A5DN in hippocampal neurons prevented memory deficits associated with sleep loss without affecting memory formation in the absence of sleep deprivation. Overexpression of PDE4A5WT increased hippocampal PDE4 activity and reduced cAMP levels selectively in the hippocampus. Furthermore, overexpression of PDE4A5WT impaired long-term potentiation and impaired the formation of long-term memories in hippocampus-dependent learning tasks.

Conclusions: Together, these findings suggest that PDE4A5 in the hippocampus is *the* critical mediator of the memory and plasticity deficits associated with sleep loss. Studies are currently underway to determine the downstream mechanisms by which PDE4A5 ultimately leads to cognitive and memory deficits. This work may contribute to new therapeutic strategies to ameliorate the cognitive deficits caused by sleep deprivation.

Disclosure: Nothing to disclose.

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Selective intervention in hippocampal vs. cortical consolidation

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Rationale and aim: For memory traces to be successfully recalled, they need to be consolidated. Different factors are thought to influence this process with

1. sleep during the consolidation period allowing for 'systems consolidation' and thus a cortically based memory; whereas
2. novelty exposure strengthens a hippocampal trace via neuromodulation.

Do such cortical and hippocampal consolidated traces differ qualitatively or in their behavioural expression? To investigate this, rats were trained on two competing memories with training to one followed by sleep and the other by sleep deprivation plus novelty.

Methods: Rats were trained to learn two opposite escape locations in a watermaze over 2 sessions, with sleep or novelty + sleep deprivation following session 1 and the alternative intervention after session 2 (counterbalanced). Probe trials without any platform present were conducted at varying times afterwards (Expt 1: 24 h, 7d and 21d (within-subjects); Expt 2: 7d and 21d only).

Results: In probe tests at 24 h, the rats remembered both locations but showed a preference for the location whose encoding was followed by novelty. This hippocampal memory trace did not survive to 7d. However, in Expt 2 and the absence of the 24 h probe, the novelty-enhanced memory trace did survive. Performance was at chance by 21d.

Conclusion: These data indicate that cortical memory is more resistant to interference, but at the cost of being less exact and vivid, while hippocampal memory enables a stronger behavioural response.

Disclosure: Nothing to disclose.

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Working memory ability and topographical distribution of sleep slow wave activity in children and adolescents

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Objectives: Working memory (WM) is the ability to simultaneously keep in mind and manipulate information. Sleep slow wave activity (SWA), the key characteristic of deep non-REM sleep, has been shown to be an indicator for cortical maturation as well as for use-dependent changes in brain functioning. This study assesses maturational and/or use-dependent differences in SWA topography between children and adolescents with high and low WM abilities, thus investigating a developmental period in which major WM improvements occur.

Methods: WM was assessed in 40 subjects (13.2 ± 0.28 years). Low vs. high performers were distinguished according to the group

median. All-night high-density EEG (128 channels) was recorded. Power maps were calculated based on the average SWA of the first hour of NREM sleep.

Results: WM scores were significantly different between the groups with 113.3 ± 1.63 and 97.8 ± 1.58 points in high and low performers respectively ($P < 0.01$). Sleep architecture was not different between the two groups. High performers exhibited significantly more SWA than low performers over a prefrontal/frontal cluster of six electrodes (increase: 14.28 ± 0.86%, $P < 0.05$).

Conclusion: Children and adolescents with better working memory abilities show more SWA in an area known to be involved in WM performance. This may either reflect a more mature neural network underlying this key cognitive process or it may illustrate the increased use of WM functions in these children and adolescents.

Disclosure: Nothing to disclose.

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Motor memory consolidation depends upon reactivation driven by the action of sleep spindles

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Objectives: The consolidation of motor sequence learning (MSL) is enhanced during sleep. Yet the physiological mechanisms and neural substrates responsible for this process remain controversial. Spindles and correlated changes in striatal and hippocampal activity contribute to motor sequence memory consolidation. Up until now, however, evidence supporting this view has been entirely indirect, as it is not known if reactivation of brain regions involved in MSL during sleep is time-locked to spindles. We hypothesized that regions activated during MSL practice would be reactivated during subsequent sleep, and this spindle-triggered reactivation would be correlated with offline gains in motor sequence memory performance.

Methods: Thirteen participants were trained in the evening on two separate visits, either on an explicit MSL or control task in the MRI scanner. Following training, subjects were asked to sleep in the scanner for up to ~2.25 h where simultaneous EEG-fMRI was used to record post-training sleep EEG and BOLD signals. Subjects were re-tested the following morning to measure gains in performance.

Results: Brain regions within the striato-cerebello-cortical and hippocampal networks recruited during training on the MSL task were also activated during sleep, time-locked to spindles, and the degree of this reactivation was correlated with enhanced performance the next day. Furthermore, reactivation of the hippocampus and putamen was associated with slow and fast spindles, respectively, and thus, may be involved in consolidating unique aspects of the motor memory trace.

Conclusions: Post-learning striato-cerebello-hippocampo-neocortical reactivation associated with sleep spindles is critical for motor memory consolidation.

Disclosure: Nothing to disclose.

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The schema effect and sleep-dependent memory consolidation

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Objectives: The acquisition of knowledge is more effective if the new information can be incorporated into an associative schema. This advantage for schema-linked learning is thought to be driven by accelerated consolidation mechanisms. Whether or not sleep-dependent consolidation is involved in this process remains unclear. Here, we explore the interaction between sleep-dependent consolidation and schema-linked learning.

Methods: After establishing a schema over several days, participants encoded new facts that were either related to the schema (schema memories) or unrelated (non-schema memories). The encoding was done in two sessions, 24 h apart (consolidated and unconsolidated memories). Overnight sleep was polysomnographically monitored, and memory was tested in an MRI scanner directly after the second encoding.

Results: Participants showed a greater advantage for schema-linked learning after consolidation ($P = 0.003$). Interestingly, this interaction between schema and consolidation correlated positively with the spindle density ($r = 0.6$, $P = 0.006$), and negatively with the percentage of stage 4 (S4) sleep ($r = -0.62$, $P = 0.003$). A median split analysis further suggested that the spindle density was associated with the retention of schema memories ($P = 0.003$), while S4 sleep was associated with the retention of non-schema memories ($P = 0.002$). Functionally, we observed two separate clusters in the left medial temporal lobe, including hippocampus and parahippocampus, where the interaction between schema and consolidation was predicted by spindle density and time in slow wave sleep.

Conclusion: Our results provide initial evidence for an association between schema-linked learning and sleep-dependent memory consolidation, and suggest that deep sleep and sleep spindles may play differential roles.

Disclosure: Nothing to disclose.

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Sleep- and hippocampus-dependent memory consolidation in patients with obstructive sleep apnea

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Objective: Obstructive sleep apnea (OSA) is a common disorder with multiple consequences including negative effects on cognitive function. Several domains of cognitive function have been reported to be impaired in OSA patients, but few studies systematically investigated the effects of OSA on sleep dependent memory so far. Aim of the study was to compare healthy controls with OSA patients with regard to declarative, procedural and hippocampus-dependent spatial memory.

Methods: Eighteen OSA patients (apnoe-hypopnoe-index [AHI] 20.5 ± 3.7/h, age 51 ± 2 years, 9 females) were compared to 18 healthy controls (AHI 2.4 ± 0.8/h, age 48 ± 2 years, 9 females). A training session in the evening including a wordlist task (WL), a mirror tracing task (MT) and a spatial learning task in a virtual maze (VMT) was followed by a standard polysomnography and a recall session in the morning.

Results: Although there was no difference in total sleep time and sleep efficiency, the OSA group performed worse in the procedural and declarative tasks (controls vs. OSA: MT 135.2 ± 10.2% vs. 106.5 ± 9.1, t-test $P < 0.05$; WL −19.2 ± 2.9% vs. −30.7 ± 5.3%,

t-test $P < 0.05$) and showed a tendency towards impaired spatial memory consolidation (VMT delayed recall index 49.7 ± 6.9% vs. 35.7 ± 6.7%, t-test $P = 0.08$).

Conclusions: In our sample of patients with OSA, sleep dependent memory consolidation in well established tests for procedural and declarative memory was impaired. Also hippocampus dependent spatial memory consolidation seems to be affected, however, the statistical power of these preliminary results is low. Additional experiments are necessary to understand the underlying mechanisms.

Disclosure: Nothing to disclose.

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A nap to recap: daytime sleep strengthens rewarded relational memory

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Objectives: Sleep contributes to memory consolidation. Yet, the factors influencing the selection of freshly encoded information for consolidation during sleep remain largely unknown. Here, we hypothesized that motivational relevance prioritizes rewarded information for subsequent reprocessing during sleep, and may thus yield better long-term memory. Moreover, we asked whether recollective experience, as assessed by confidence ratings, would also be stronger for rewarded memories.

Methods: Participants first learned sequences of pictures, half of which were associated with high and half with low reward. Then, they either took a 90-min nap or spent an equivalent period awake monitored by polysomnography (Sleep and Wake group, respectively). We then assessed memory for the picture sequences as well as confidence ratings, both immediately and 3 months later. fMRI data were acquired during the learning, test, and retest sessions.

Results: Our results show that reward enhanced memory consolidation at test for Sleep and Wake groups, and at long-term retest for the Sleep group only. The processing of rewarded memories was associated with increased hippocampal activation for the Sleep group as compared to the Wake group and sleep spindles boosted increase in memory performance from learning to test. Furthermore, sleep enhanced confidence ratings for highly rewarded hits at test and retest and this effect was associated with increased hippocampal activation.

Conclusions: Our results suggest that sleep favors the selectivity of long-term consolidation by retaining the most important memories, and enhancing subjective confidence for these memories. Such effects are mediated by hippocampal circuits and enhanced by sleep spindles.

Disclosure: Nothing to disclose.

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Circadian regulation in cognition and subjective assessment of waking function in humans

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Objectives: Our waking function is regulated by endogenous circadian rhythmicity in interaction with a sleep-wake homeostat. To what extent the magnitude of the circadian and homeostatic influences varies across cognitive domains and subjective dimensions, is unclear. We addressed this question by assessing performance in several subjective scales and cognitive tasks, in a 28-h forced-desynchrony (FD) protocol.

Methods: We measured subjective sleepiness, perceived effort, mood, attention and working memory in 36 healthy young men and women. All data were assigned a circadian and time-awake coordinate, by aligning them relative to (1) Dim Light Melatonin Onset computed from hourly plasma melatonin samples and (2) Wake-Time on each FD day, respectively. They were then analysed using a mixed-model ANOVA with circadian melatonin phase and time-awake as fixed factors.

Results: As predicted, there was a significant circadian ($P < 0.05$) and homeostatic ($P < 0.05$) modulation, such that, mood, sleepiness, perceived effort, attention and accuracy of working memory were worst during the biological night and deteriorated with time awake. But, the magnitude of this modulation, as indexed by effect size (f2), was greater in the subjective dimensions than in any cognitive domain. Furthermore, the homeostatic effect was greater than the circadian effect in the subjective dimensions, whereas this difference was minimal in cognition.

Conclusions: That circadian and homeostatic factors influence both subjective measures and cognition is well established. That the homeostatic effect is greater than the circadian effect, and more so in subjective dimensions is more novel with theoretical and practical implications.

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The nature of delayed dream incorporation: personally significant events persist, but not major daily activities or concerns

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The greatest incorporation of daytime stimuli into dreams occurs on the night after, and 5–7 nights after stimuli, termed the day-residue and dream-lag effects respectively. This study compares the time-course of incorporation into dreams of three categories of daytime stimuli.

38 participants (33 females, mean age 23.9 years) kept a daily log for 14 days, on which they recorded their major daily activities, personally significant events and major concerns. They also kept a dream diary. Two weeks after the logs and diaries were completed, participants compared all daily logs to all dream reports and identified any correspondences between items on the logs and each dream report. The mean number of incorporations of log items was computed for each period of log completion to dream occurrence, for the three log categories. Participants with above and below median total number of incorporations were analysed separately. Comparing mean number of incorporations per dream, a significant (U-shaped) difference in incorporation across the 7 nights after the day of occurrence of the log items was found only for personally significant events, and only for the below-median total correspondences participants (Friedman test, $P = 0.029$; day-residue and dream-lag effects, both ps< 0.05).

Personally significant events may better evidence the dream-lag because they are emotionally more salient than daily activities, and more specific to a particular day than are concerns. These data fit with the selective pattern of brain activity during REM that encompasses the anatomy of autobiographical self and emotional salience.
Acknowledgement: Study funded by UK ESRC.

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Risk factors for frequent nightmares among the general Finnish adult population

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Objectives: Nightmares are intensive disturbing dreams that awake the dreamer from sleep. Occasional nightmares are common and harmless, but frequent nightmares can be a serious problem and are often related to mental disorders.

The current study investigates risk factors for frequent nightmares among the general Finnish adult population. The aim was to investigate several previously unexplored potential contributing factors for nightmares as well as to test whether many already known correlates of nightmares can be replicated in these data.

Methods: The current study utilized data from The National FINRISK study from Finland. The surveys consist of random cross sectional population samples from adults aged 25–74 who fill in a comprehensive health questionnaire including items on sleep and mental well-being. Nightmares were assessed with self-estimated frequency during the last month. In the current study surveys from years 2007 and 2012 were used (N = 13 922).

Results: Preliminary analyses show that insomnia and depression symptoms as well as the use of hypnotics and antidepressants are major risk factors for frequent nightmares ($P < 0.001$). Strong associations also exist between nightmares and life dissatisfaction, self-estimated poor physical health, heavy use of alcohol and several measures of self-estimated anxiety and stress symptoms ($P < 0.001$).

Conclusions: A wide variety of factors related to psychological and physical well-being are associated with nightmare frequency with a modest effect size. As such frequent nightmares seem to related to general decrease in well-being that may be caused by many different circumstances.

Disclosure: Nothing to disclose.

Paediatrics: What`s Normal, What`s Not

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Influence of body growth on sleep during the first days of life in preterm neonates

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Neonates lose around 10% of their birthweight after birth and weight gain is thus very important in the first weeks of life. Sleep processes are implicated in energy-balance regulation and can be altered by nutrition. Here, we assessed the influence of body growth on sleep structure during the first days of life in preterm neonates.

Overnight polysomnography was performed in 49 healthy preterm neonates at their 9th (N9) day of life. Two groups were constituted according to postnatal growth: a weight gain-group (WG, WG at N9: $+94 \pm 67$ g/kg) and a weight loss-group (WL, WL at N9: -59 ± 42 g/kg). Sleep structure was analysed (EEG and eye movements) by using frequency, duration and percentage of active (AS), quiet (QS), indeterminate (IS) sleep stages and wakefulness after sleep onset episodes.

Gestational age and cumulated energetic intake were identical in the two groups. A negative correlation was found between postnatal growth and birthweight. The latter was lower in the WG group (WG: 1009 ± 202 vs. WL: 1433 ± 251 g). The proportion of AS was higher in the WG than in the WL group (62 ± 8 vs. 56 ± 9%, respectively) whereas the proportion and frequency of IS were lower (24 ± 6 vs. 28 ± 6% and 1.4 ± 0.3 vs. 1.6 ± 0.4 h^{-1}, respectively). Positive WG is associated with a higher proportion of AS at the cost of IS. Since the amount of AS should be increasing at this age, the present results suggest that maturational development is improved by a better body growth in the first days of life of preterm neonates.

Disclosure: Nothing to disclose.

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Very preterm children, compared to full-term children, show alterations in objective sleep, behavior and emotion, and cortisol secretion during middle childhood

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Background: Very preterm children are at higher risk to develop behavioral and emotional difficulties and poor sleep. Additionally, prenatal and early postnatal exposure to adversities may alter very preterm children's hypothalamic-pituitary-adrenocortical activity (HPAA). Little is known about associations between objective sleep, HPAA, and behavioral/emotional difficulties in very preterm children compared to full-term children.

Methods: Fifty-eight very preterm children (<32nd gestational week) and 55 full-term children aged 6;0 to 10;10 years underwent one night of in-home polysomnographic sleep assessment. HPAA was assessed via saliva sampling in the morning (cortisol awakening response, CAR) and in the evening (diurnal variation). Parents completed the Strengths and Difficulties Questionnaire to assess children's behavioral/emotional difficulties and a subscale of the Children's Sleep Habits Questionnaire to assess sleep disordered breathing.

Results: Compared to full-term children, very preterm children showed more total behavioral/emotional difficulties, more emotional symptoms, poorer sleep (more stage 2, less slow wave sleep (SWS), more nocturnal awakenings), and faster decreasing evening cortisol levels. The associations of sleep and HPAA with behavioral/emotional difficulties did not differ between very preterm and full-term children. In both groups, Stage 2 sleep was associated with more total behavioral/emotional difficulties. Blunted CAR and lower evening cortisol levels were associated with more conduct problems.

Conclusions: At the age of 6–10 years, very preterm children, compared to full-term children, show more behavioral/emotional difficulties, poorer sleep and an altered HPAA. Poor sleep and HPAA show similar associations with behavioral/emotional difficulties in very preterm and full-term children.

Disclosure: Nothing to disclose.

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Evaluation of school-based sleep interventions: does adjunct bright light therapy and parental involvement improve treatment outcomes?

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Objectives: Whilst the evidence for clinical interventions for adolescents' sleep is good, application to a broader context (i.e., school settings) suggests limited efficacy. This may be due to adolescents perceiving barriers and lack of support to change sleep behaviours. We present here a randomised controlled trial of a sleep education program (SEP) with adjunct bright light therapy (BLT) and/or parental involvement (PI).

Methods: 193 adolescents (age = 16.3 ± 0.4 years, 79%f) were randomly assigned to SEP+BLT, SEP+PI, SEP+BLT+PI, or classes-as-usual (CAU; control). SEP involved 4 x 50-min classes (over 4 weeks) based on a Motivational Interviewing (MI) framework (Cain, Gradisar and Moseley, 2011, Sleep Med). Groups with BLT attempted a weekend phase advance using portable green light LED glasses (500 nm; Re-Timers). Parents of adolescents in the PI groups received weblinks to weekly YouTube videos (~2–3 min long) outlining what their teen was learning and how they could assist. CAU adolescents continued their regular school classes (with no sleep information).

Results: Consistent effects were found for all intervention groups, including advanced sleep onset on school nights (d = 0.49-0.53) and weekends (d = 0.26–0.37), increases in TST (School: d = 0.35–0.58; Weekends: d = 0.24–0.27), and decreased depression (d = 0.32–0.34). No changes occurred for the CAU group (d = 0.03–0.14). Surprisingly, weekend out of bedtime did not advance in all four groups (d = 0.02–0.09).

Conclusions: This sleep education program based on an MI framework produced some meaningful sleep benefits to adolescents.

However, brief adjunct light therapy and parental involvement do not confer additional benefits. Increased ′dosages′ of bright light and parental involvement need to be tested.

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Incident sleep-disordered breathing associated with cardiovascular risk factors: the Penn State Child Cohort

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Objective: The independent association between sleep-disordered breathing (SDB) and cardiovascular risk in adults is well established. The purpose of this study was to identify incident SDB and its association with cardiovascular risk in a population based sample of adolescents.

Methods: The Penn State Child Cohort is a representative random sample of 700 children aged 5–12 years (8.6 $\pm$ 1.7 years) at baseline. Of these subjects 421 have been reevaluated 8 years later as adolescents (17.0 $\pm$ 2.3 years). Three blood pressure (BP) assessments (adjusted for age, gender, and height) in the seated, supine and standing positions were completed using an automated device. Vascular reactivity was assessed in terms of the difference between supine and standing BP. A metabolic syndrome risk score was based on the sum of age and gender standardized residuals of HDL, tryglyceride, HOMA, waist circumference and seated MAP (Eisenmann 2010).

Results: We observed 10.6% incident SDB at follow up with 100% remission of SDB at baseline. Incident SDB was not significantly associated with elevated diastolic BP. However, systolic BP assessed across all positions, except supine, as well as vascular reactivity was significantly elevated in those with incident SDB. In addition, we observed a significantly increased metabolic syndrome risk score in those with incident SDB ($P < 0.001$).

Conclusions: Incident SDB was significantly associated with elevated systolic BP. Incident SDB was also significantly associated with increased systolic vascular reactivity and metabolic syndrome risk. These factors have been associated with increased risk of CVD and the development of hypertension in adults.

Disclosure: NIH R01 HL603772, R01 HL97165, UL1 RR033184, C06 RR16499.

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Increased cortisol levels are associated with polysomnographic sleep disturbance in adolescence

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Objectives: Increased hyperactivity of the hypothalamic-pituitary-adrenal axis is associated with significant nighttime sleep disturbances in adults. However, studies examining this association in adolescents are very limited. This study assessed the association of salivary evening and morning cortisol levels with polysomnographic (PSG) parameters in a general population sample of adolescents.

Methods: A sample of 421 adolescents ages 12–23y underwent a 9-h PSG recording. PSG parameters of sleep onset latency (SOL), wake after sleep onset (WASO), total wake time (TWT), total sleep time (TST), sleep efficiency (SE), and percentages of stages 1, 2, slow-wave sleep (SWS), and rapid-eye movement (REM) were ascertained. Saliva samples were collected in the evening and morning during the in-lab study and assayed for cortisol. We examined the association of salivary cortisol levels with PSG variables, controlling for age, gender, race, and body mass index percentile.

Results: Higher evening cortisol levels were significantly associated with higher SOL ($P = 0.035$), WASO ($P = 0.013$), and TWT ($P = 0.006$) as well as lower TST ($P = 0.010$), SE ($P = 0.007$), and marginally with percent REM sleep ($P = 0.105$). Morning cortisol levels were not significantly associated with PSG parameters (all $P > 0.207$).

Conclusions: Similar to adults, increased evening cortisol levels are associated with significant nighttime sleep disturbance in adolescence. The association of sleep disturbance with HPA axis activation in adolescence suggests that chronic insomnia, particularly in those with objective sleep disturbance, may have an adverse impact on physical and mental health in young individuals.

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Gender differences in the relative effect of sleep disordered breathing and obesity on neurocognitive functioning in adolescents

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Objectives: Sleep disordered breathing (SDB) has been associated with impaired neurocognitive functioning. No study to date has examined the relative association of SDB and obesity with neurocognitive performance in a general population sample of adolescents.

Methods: The Penn State Child Cohort is a random sample of 700 children aged 5–12 years (8.6 $\pm$ 1.7y) at baseline of whom 421 were followed-up 8 years later during adolescence (17.0 $\pm$ 2.3y). All subjects underwent a 9-h polysomnography, neurocognitive testing, anthropometric measures, and Dual-energy X-ray Absorptiometry (DXA) scans.

Results: SDB was associated with impaired general ability ($P < 0.07$) and achievement ($P < 0.05$) however, we found a significant interaction between female gender and SDB on general ability ($P < 0.05$) and that obesity mediated the association of SDB with achievement ($P < 0.01$). Obesity was associated with impaired vigilance ($P < 0.05$), processing speed ($P < 0.01$), working memory ($P < 0.05$), and response interference ($P < 0.05$). Finally, we found significant interactions between male gender and obesity on vigilance ($P < 0.05$) and processing speed ($P < 0.05$).

Conclusion: Obesity is more strongly associated with impaired executive functions and achievement than SDB per se in adolescents. Interestingly, SDB is associated with impaired general ability in female adolescents, while obesity is associated with impaired vigilance and processing speed in male adolescents. These data suggest gender differences in the neurocognitive vulnerability to the effects of SDB and obesity that may further our understanding of different clinical presentations of SDB in men and women.

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Habitual sleep variability, not sleep duration, is associated with abdominal obesity in adolescents - Penn State Child Cohort Study (PSCC)

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Objectives:

Investigate: (1) habitual sleep duration (HSD) and variability (HSV) in relationship to abdominal obesity in a population-based sample of adolescents; and

(2) nutrient intakes as mediating factors.

Methods: Actigraph and sleep diary were used in the PSCC follow-up examination (N = 421) for 7 consecutive nights to estimate nightly total sleep time (TST) and then calculate the 7-night mean and standard deviation of TST, as measures of HSD and HSV, respectively. Abdominal obesity was assessed by dual-energy x-ray absorptiometry, including android/gynoid fat ratio (AGR), and visceral fat area (VFAT, cm^2). The Youth/Adolescent Food Frequency Questionnaire was used to obtain 1-year average total energy intake, energy intakes from protein, fat, and carbohydrates, respectively. Linear regression models were used to associate HSD and HSV with abdominal obesity and identify mediating factors.

Results: The mean age was 17 years, with 52% male and 78% white. The mean (SD) of HSD and HSV were 7.00 (0.83) and 1.19 (0.61) hours, respectively. After adjusting for age, sex, race, BMI-percentile, and HSD, higher HSV was associated with AGR (β = 0.02, SE = 0.01, $P < 0.05$), and VFAT (β = 6.86, SE = 2.82, $P < 0.05$). HSD was not associated with abdominal obesity in HSV-adjusted models. Higher HSV was associated with higher caloric intake, especially calories from fat and carbohydrate. After adjusting for caloric intakes, the regression coefficients from HSV were attenuated by at least 20%.

Conclusion: Higher HSV, not HSD, is associated with abdominal obesity, which can be partially explained by HSV-associated energy intakes from fat and carbohydrate in adolescents.

Disclosure: NIH R01 HL603772, R01 HL97165, UL1 RR033184, C06 RR16499.

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REM sleep and emotional face memory in typically developing children and children with autism

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REM sleep is involved in emotional memory processing. We tested the relationship between REM sleep markers and memory consolidation in autistic (AUT) and typically developing (TD) children.

Twenty-six boys (13 AUT:10.23 $\pm$ 2.09 years, 13 TD:10.23 $\pm$ 2.01 years) were recorded for two consecutive nights. Recall of previously unknown faces showing positive, negative or neutral emotions was assessed before/after night 2 (immediate/delayed recall). Improvement scores (delayed minus immediate recall performance) on accuracy (AIS) and reaction time (RTIS) were calculated for total hits and each emotion type. REM sleep duration, REM density and EEG activity (Beta and Theta bands; P7,P8,O1,O2 electrodes) were computed for night 2. Groups were compared with t-tests and correlations between REM sleep measures and improvement scores were tested with Pearson's r.

No group differences for REM sleep duration, REM density, Beta EEG activity. AUT showed more Theta activity than TD at P7 (45.79 $\pm$ 72.11 vs. 21.50 $\pm$ 12.43) and longer reaction times for delayed recall of neutral faces (1353.35 $\pm$ 484.38 vs. 1006.99 $\pm$ 308.61). TD showed positive correlations between AIS for neutral emotions and EEG at every electrodes (Beta: 0.58 to 0.73; Theta: 0.58 to 0.66) and a positive correlation between RTIS over total trials and REM density (r = 0.58). AUT children showed different patterns: positive correlations between RTIS for negative emotions and Beta activity at P7,P8,O2 (0.62 to 0.63) and a positive correlation between RTIS for positive emotions and theta O1 activity (r = 0.56). TD and AUT children showed a relationship between REM sleep and emotional memory. Results suggest an atypical sleep processing of emotional memory in autism.

Disclosure: Nothing to disclose.

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The effect of nighttime sleep patterns on sensitivity to reward in healthy adolescents

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Objective: To examine the effect of nighttime sleep patterns (NSP) on sensitivity to reward in otherwise healthy adolescents.

Methods: The 78 participants were part of a longitudinal study starting in infancy, 43% were female and mean age was 15.4 $\pm$ 0.3 y. Motor activity was recorded for a week with actigraphs (Actiwatch-16/64) worn in the nondominant wrist, yielding the identification of NSP -total sleep time (TST) and number of awakenings (NA)-through an automated method (Actiware®). We categorized NSP for weekdays and weekend days according to their median values. Participants performed the Reward task which is an oculomotor test of inhibitory control: subjects were instructed to avoid looking at visual stimuli of incentivized trials (reward, avoid loss, and neutral) appearing on the screen and look in the opposite location (correct response).

Results: The median values for TST were 7.9 $\pm$ 1.6 h and 8.4 $\pm$ 2.7 h, and for NA 1.0 $\pm$ 1.6 and 2.0 $\pm$ 1.9 during weekdays and weekend days, respectively. Compared to adolescents with lower NA, those with higher NA presented shorter latency to incorrect responses on avoid loss trials during weekdays (286.1 vs. 305.6 ms, $P < 0.05$). Relative to subjects with higher TST, subjects with lower TST showed reduced latency to correct responses on reward trials during weekend days (392.1 vs. 441.4 ms, $P < 0.01$).

Conclusions: Our results show that NSP modulate the sensitivity to reward in adolescents. Further, such a modulation appears to occur differently on weekdays and weekend days.

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Parkinson's Disease and Sleep: A Multifaceted Interaction

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Sleep changes as a prodromal marker of Parkinson's disease

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Longitudinal studies in Parkinson disease (PD) have shown that the prevalence of sleep disorders increases with advanced disease. However, two sleep disorders, excessive daytime sleepiness (EDS) and REM sleep behaviour disorder (RBD), have been described to antedate the development of the classical motor signs and symptoms of PD. One epidemiological work from the Honolulu-Asia Aging Study showed that aging men who reported 'being sleepy most of the daily' had a threefold excess risk for developing PD after a 7-year follow-up. The origin and nature of EDS was not investigated. This study needs to be replicated. In fact, recent studies have shown that EDS is not more frequent in untreated de novo PD subjects than in matched healthy controls. More robust data exist regarding RBD as the first manifestation of PD. The majority of idiopathic RBD (IRBD) subjects followed in sleep centers will be diagnosed with PD and other synucleinopathies such as dementia with Lewy bodies and multiple system atrophy. In a recent study involving 174 IRBD patients, the risk of a defined neurodegenerative syndrome was 33.1% at 5 years, 75.7% at 10 years, and 90.9% at 14 years. IRBD patients with decreased striatal dopamine transporters imaging, substantia nigra hyperechogenicity, color visual deficits and hyposmia have an increased short-term risk for developing a synucleinopathy. IRBD is an optimal population to be tested with disease-modifying agents in order to stop or slow down neurodegeneration in the brain.

Disclosure: Nothing to disclose.

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Sleep benefit in Parkinson's disease

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Sleep disorders are common among patients with Parkinson's disease (PD). However, there are also reports of PD patients experiencing a beneficial effect of sleep. Upon awaking in the morning some patients describe a good mobility, as if they are in an 'on' state induced by medication, contrary to what would be expected after a night without medication. This intriguing phenomenon is known as sleep benefit. So far, most studies used questionnaires to assess the presence and characteristics of sleep benefit. These studies found a rather consistent prevalence of 30–50% of patients reporting to be familiar with the phenomenon. In a recent prospective study by our group using both a 7-day symptom diary and a more traditional sleep benefit questionnaire, we found a prevalence of sleep benefit of 32% and 31% respectively. However, the results of both instruments did only partially overlap, so they probably assessed different aspects of sleep benefit. These results suggest that sleep benefit is a more heterogeneous and possibly more subjective phenomenon than previously thought.

Preliminary analyses of a controlled follow-up study using objective quantitative motor tests after nocturnal sleep and daytime naps, show that the subjective experience of sleep benefit does not match to an actual improvement in motor functioning. These new data suggest that sleep benefit is probably an altered experience of motor symptoms, possibly caused by refreshing properties of sleep, instead of a Parkinson-specific actual reduction in symptoms.

Disclosure: Nothing to disclose.

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Mechanisms of sleep disturbances in Parkinson's disease

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Sleep disturbances are frequent and disabling in Parkinson's disease. They may result from lesions within the sleep/wake or clock systems, from motor and psychological problems and from the deleterious effects of antiparkinsonian drugs. The three mechanisms are often associated in a single patient. Several evidences show that the networks controlling arousal (mostly noradrenaline, serotonin, dopamine and hypocretin) are affected in Parkinson's disease, contributing to increase daytime sleepiness. Similarly, the executive systems of REM sleep-associated muscle atonia in the pontine tegmentum are early damaged (sometimes years before the onset of parkinsonism) in PD patients with REM sleep disorders, in proportion with the rate of REM sleep without atonia. Plus, cholinergic systems seem primarily disturbed in these patients. Whether the circadian rhythm is advanced in PD is unclear. During the episodes of wake during the night, many patients experience restless legs, pain, dystonia, severe bradykinesia, dysuria and anxiety, which prolonged the wake after sleep onset. Sleep apnea in PD are not associated with higher daytime sleepiness or any subjective feelings, but sleep latency tests (and not perceived sleepiness) are improved with continuous positive airway pressure. Eventually, dopamine agonists (and sometimes levodopa alone) can induce sleepiness and sometimes sleep attacks. In contrast, patients with impulse control disorders or dopamine abuse have compulsions at night (gaming, playing, sex) which maintain them awake several hours, leading to a pseudo-insomnia.

Disclosure: Nothing to disclose.

OSA in Europe; Phenotypes, Metabolism, Accident Risk, and Treatment

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Metabolic effects of OSA

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Obstructive sleep apnoea (OSA) is associated with increased risk of metabolic dysfunction, but the intimate link with obesity makes an independent relationship difficult to identify. Several studies have analyzed the potential independent contribution of OSA to the pathogenesis of metabolic abnormalities, including type 2 diabetes, the metabolic syndrome and non-alcoholic fatty liver disease. OSA and adipose tissue likely interact in the development of metabolic dysfunction. Adipocytes are sensitive to hypoxia, which results in the activation of both inflammatory and hypoxia-inducible factor (HIF)-1 dependent pathways, which are important mechanisms in the development of metabolic dysfunction and cardiovascular disease.

Population studies have identified a significant cross-sectional relationship between OSA severity and both prevalence of T2DM and insulin resistance, but some studies have been limited by comparative small size, reliance on patient self-reporting, or the use of administrative databases or fasting plasma glucose measurement for diagnosis. The measurement of glycosylated hemoglobin (HbA1c) levels identifies a significantly greater burden of occult disease than does fasting glucose. Recent reports from the European Sleep Apnoea Database (ESADA) confirm a high prevalence of T2DM and associated poor disease control in OSA, independent of all recognised confounding variables. Furthermore, OSA severity independently predicts impaired glycaemic health in non-diabetic subjects, as evidenced by elevated HbA1c levels, which has implications for cardiovascular co-morbiditities.

The metabolic syndrome is highly prevalent in OSA, and is particularly associated with the presence of visceral fat accumulation and non-alcoholic steatohepatitis (NASH). Lifestyle interventions in OSA focussing on diet and exercise may particularly benefit metabolic dysfunction.

Disclosure: Nothing to disclose.

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Traffic accident risk in European patients with obstructive sleep apnea

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Objectives: Obstructive sleep apnea (OSA) is associated with an increased risk of motor vehicle accidents (MVA). Excessive daytime sleepiness (EDS) is a common symptom of OSA thought to cause MVAs. OSA may successfully be treated with Continuous positive airway pressure (CPAP) and has been found to reduce MVA risk. No causality has been observed between OSA severity and the MVA risk. The prevalence of previously identified risk factors (RF), associated with MVA history were assessed in the European sleep apnea patient database (ESADA).

Methods: RFs such as long driving distance, short habitual sleep time, driving license, and use of hypnotics were assessed.

Results: Clinical patients with suspected OSA (n = 8476, age 51.5 (12.5) years, body-mass-index 31.0 (6.6) kg/m^2, 82% driver's license holders) were included. RF for MVAs; Epworth Sleepiness Scale $\geq$16; habitual sleep time $\leq$5 h; use of hypnotics; driving $\geq$15000 km/year, were analyzed across European regions, with only a lower rate in the Eastern region (P = 0.001). The mean number of RF increased across classes of OSA severity. Frequent driving was prevalent (14.0 [IQR 8.0–20.0] 103 km/year) and 33% of drivers had severe OSA (Apnea-Hypopnea-Index 50.3 [38.8–66.0] n/h). At least one RF was identified in male and female drivers, 69% and 51%. Obesity, shorter sleep time, and younger age were associated with traffic exposure ($P \leq 0.03$).

Conclusion: The RF associated with MVA were common among European patients with suspected OSA but varied between geographical regions. Frequent driving, a RF for MVA, was overrepresented. Evaluation of MVA RF is important to detect OSA patients at risk for MVAs.

Disclosure: Nothing to disclose.

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OSA treatment outcome in Europe

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Objectives: The European Sleep Apnea Cohort (ESADA) study is a pan-European, multi-centre, prospective study involving 24 sleep clinics across 15 European countries and Israel with the aim to identify cross-sectional and longitudinal associations with cardiovascular and metabolic morbidity and mortality. During this presentation the impact of CPAP and oral device therapy on a number of metabolic parameters will be reviewed in a subset of patients from the ESADA cohort that got long-term follow up. 351 OSA patients (between 18 and 80 years old) treated with CPAP therapy and 172 patients who got oral device therapy were included (397 males and 126 females). A significant symptomatic improvement (ESS) was observed in both the CPAP (-3.07 ± 4.66; $P < 0.05$) and oral device therapy group (-2.16 ± 3.54; $P < 0.05$) therapy. In the CPAP group, a significant decrease was observed in serum creatinine (-0.05 ± 0.14 mg/dl; $P < 0.05$), cholesterol level (-7 ± 39 mg/dl; $P < 0.05$), triglycerides (-29 ± 112 mg/dl; $P < 0.05$), without any change in urine malbumine or Hs-CRP. Unexpectedly, HbA1c increased statistically significantly ($+0.7 \pm 2.7$%). With oral device therapy, significant changes were only found in cholesterol level (-29 ± 78 mg/dl; $P < 0.05$) and Hs-CRP (-0.18 ± 0.42 mg/dl), while all other parameters remained unchanged, including HbA1C.

In conclusion, OSA therapy can have some beneficial effects on metabolic derangements. However, the observed changes are inconsistent in CPAP vs. oral device therapy users. Findings will be discussed and data from literature will be reviewed.

Disclosure: Nothing to disclose.

Cell and Molecular Biology and Genetics

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Effects of circadian typology and partial and total sleep deprivation on the human transcriptome

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Objectives: Circadian typology (CT) correlates with sleep-wake timing, circadian period, and aspects of sleep homeostasis. However, how CT affects human genome-wide gene expression is not known. Here, we measured sleepiness and the blood transcriptome in individuals who differed with respect to CT during total sleep loss after 1 week of sufficient or insufficient sleep.

Methods: Twenty-six participants were subdivided according to CT into morning (MT, n = 9, age = 28.3 $\pm$ 4.4SEM), intermediate (IT, n = 9, age = 28.0 $\pm$ 4.3) and evening (ET, n = 8, age = 25.9 $\pm$ 4.2) groups. They underwent 1 week of sleep extension (SE, 10 h) or restriction (SR, 6 h), followed by a 40-h sleep deprivation constant routine (CR), during which blood was collected for measurement of melatonin (hourly) and gene expression (3-hourly).

Results: Melatonin peak expression during the CR was delayed in ET (05.47 $\pm$ 0.46SEM) compared to IT (03.52 $\pm$ 0.35) and MT (03.99 $\pm$ 0.57; P = 0.002). After SR, sleepiness scores during the CR were higher in MT (5.99 $\pm$ 0.16SEM) compared to ET (4.81 $\pm$ 0.17; P = 0.032). Transcriptome analyses showed an interaction between CT and sleep condition in 225 transcripts; MT mainly had lower expression after SR compared to IT and ET. Top ranking genes were associated with photoreception, pupil constriction, and the circadian ubiquitin ligase complex. A main effect of CT was more pronounced after SR in 38 transcripts, where expression levels in MT were generally different to both IT and ET. These transcripts included growth hormone releasing hormone and insulin-like growth factor.

Conclusions: These data show that MT are more vulnerable to the effects of partial sleep loss in both measures of sleepiness and the transcriptome.

Disclosure: Nothing to disclose.

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A role for mGluR5-mediated signaling in regulating neurophysiological markers of sleep homeostasis in humans

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Objectives: Fragile X mental retardation protein (FMRP), encoded by the *FMR1* gene, was proposed as a molecular marker of sleep need in animals. FMRP modulates neuronal plasticity by interacting with metabotropic glutamate receptors of subtype 5 (mGluR5), which induce the formation of inositol-triphosphate (IP3). mGluR5 availability is enhanced following sleep deprivation in human volunteers. Here we investigated effects of sleep loss on endogenous glutamate, glutamine, and myo-inositol (IP3 precursor), and their relationships with mGluR5 availability and EEG activity in NREM sleep.

Methods: J-resolved single-voxel proton magnetic resonance spectroscopy at 3 Tesla (n = 17) and whole-brain PET measurements with ^{11}C-ABP688 (n = 26) after 9 and 33 h of wakefulness were consecutively conducted in randomized, cross-over fashion. Sleep was polysomnographically recorded in baseline and recovery nights. Data were compared between two *FMR1* genotypes, thought to differ in FMRP expression. Statistical analyses included mixed-model ANOVAs and Spearman correlations.

Results: In baseline and sleep-deprived conditions, mGluR5 availability was associated (p_{all}< 0.04) with myo-inositol levels (r > 0.56), EEG slow wave activity (SWA: r > 0.44), and < 1 Hz slow oscillation activity (SOA: r > 0.71). Glutamate/glutamine levels were not altered by sleep deprivation (p_{all}>0.5). Finally, *FMR1* genotype distinctly modulated the effects of sleep loss on mGluR5 availability, SWA and SOA (p_{all}< 0.02).

Conclusions: Data suggest that sleep deprivation alters mGluR5-dependent downstream signalling without affecting endogenous glutamate/glutamine levels. Functional changes in mGluR5 signalling may provide a neurochemical mechanism contributing to the sleep-loss-induced rebound in established EEG makers of sleep need.

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Length polymorphism in the human clock gene *Period3* and diurnal preference, subjective sleepiness and the response to morning light

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Objectives: The length polymorphism of the human clock gene *Period3 (hPer3)* has been associated with diurnal preference, with the longer allele *Per*^{5} linked with morningness. In addition, *Per*$^{5/5}$ subjects seem particularly sensitive to light at night. The aim of this study was to confirm the association *Per3*-diurnal preference, and to test the effect of morning light administration in relation to genotype.

Methods: 551 healthy subjects donated buccal DNA samples and completed the Horne-Östberg diurnal preference questionnaire. A subgroup of 359 also completed 12-day sleep logs and hourly assessments of subjective sleepiness over one waking day. Finally, eleven *Per*$^{5/5}$ and thirteen *Per*$^{4/4}$ homozygotes performed timed urine collections for 6-sulphatoymelatonyn (aMT6s) measurement before/after 2 weeks of morning light treatment.

Results: 497 subjects out of 551 were genotyped: 41% were *Per*$^{4/4}$, 14% *Per*$^{5/5}$ and 45% *Per*$^{4/5}$; 21% were evening, 21% morning, and 58% intermediate types. A significant association was confirmed between chronotype and genotype (χ^2=13.5, P = 0.009), with the frequency of the *Per*^{5} allele higher in the morning compared to the evening types (0.39 vs. 0.29, P = 0.05); *Per*$^{5/5}$ subjects were significantly less sleepy in the morning hours compared to *Per*$^{4/4}$. After light administration, 14 subjects (eleven *Per*$^{4/4}$, three *Per*$^{5/5}$)

showed an advance in their aMT6s peak time, 4 a delay (all *Per*$^{5/5}$) and 6 no significant change. Regardless of direction, the change was more pronounced in the *Per*$^{5/5}$ (43 vs. 35 min).

Conclusion: The *Per*^{5} allele is associated with morningness and might affect the outcome of light therapy.

Disclosure: Nothing to disclose.

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Melatonin receptor locus associates with shift work intolerance - genome-wide study and replications

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Objectives: Shift work is a common environmental factor causing misalignment of sleep-wake cycle from the physiological circadian rhythms which can lead to symptoms of fatigue. However, inter-individual variability in response to shift work is large. In this study we examined genetic factors predisposing to intolerance to shift work.

Methods: Intolerance to shift work was assessed by measuring job-related exhaustion (exhaustion scale of Maslach Burnout Inventory) in shift workers. Genome-wide association study (n = 179) and the first replication study (n = 241) were performed in population-based samples from the Health 2000 study. Further replication for one variant was performed in shift workers of two occupational cohorts: a Finnish airline company sample consisting of in-flight (n = 263) and non-flight (n = 343) workers and a sample of shift-working nurses (n = 73).

Results: The strongest signal in the population-based samples, coming from the variant close to the melatonin receptor locus, was replicated in the in-flight workers of the airline cohort and showed the same effect size in the nurse cohort but not in the non-flight workers. The meta-analysis reached genome-wide significance (P < 5x10E-08), when restricting the airline sample to in-flight workers who typically encounter frequent and large circadian misalignment in their irregular schedule including long shifts and time-zone transitions.

Conclusions: To our knowledge, this is the first non-candidate based study exploring liability to negative health effects in shift work. The results suggest that genetic factors affecting inter-individual differences among shift workers can be identified, and at least some of them are linked to melatonin signaling.

Disclosure: Nothing to disclose.

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EEG-vigilance regulation in carriers of bipolar disorder risk alleles

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Objectives: Although Bipolar Disorder (BD) has been shown to be highly heritable, genome-wide association studies identified only a modest number of robust chromosomal risk loci thus far. One strategy of disentangling the impact of genetic markers on heterogeneous diseases is investigating disease-related endophenotypes. According to the vigilance regulation model of affective disorders (Hegerl & Hensch, 2012), manic and depressive episodes are characterized by profound alterations in vigilance (i.e., central nervous arousal). The present study aimed to assess whether carriers of BD risk alleles differ in vigilance regulation compared to non-risk carriers when faced with a twenty-min eyes-closed resting EEG paradigm.

Methods: We selected participants of the large scale Leipzig Health Care Study, who completed a comprehensive medical and psychological examination and were free of any current psychiatric or neurological disorder. During the EEG paradigm, participants were allowed to follow their natural decline of vigilance. EEGs were analysed applying the Vigilance Algorithm Leipzig (VIGALL), a LORETA-based tool assessing the dynamics of vigilance. Subsequently, participants were genotyped for ten of the most replicable BD risk variants utilising TaqMan OpenArray Plates.

Results: Our final sample comprised 587 participants (mean age: 70.9; 332 male). Vigilance regulation was most strongly linked to a polymorphism within CACNA1C (rs1006737; P = 0.002) with risk-allele carriers showing faster declines of vigilance.

Conclusion: The association of rs1006737 is in line with the vigilance regulation theory of affective disorders. Further studies are needed to replicate this finding and should elucidate possible causal pathways in vigilance regulation.

Disclosure: Nothing to disclose.

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Orexin physiologically regulates beta-amyloid and tau metabolism: a cerebrospinal-fluid in vivo study

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Objectives: It has been demonstrated that beta-amyloid$_{1–42}$ ($A\beta_{1–42}$) metabolism is physiologically regulated by orexin signaling in animal models. We assessed cerebrospinal-fluid (CSF) orexin, $A\beta_{1–42}$ and tau proteins levels in a population of healthy subjects (HS) in order to investigate if orexin physiologically has effect on $A\beta_{1–42}$ and tau metabolisms.

Methods: We measured CSF orexin, $A\beta_{1–42}$ and tau proteins levels obtained from lumbar puncture (LP) in a group of HS, admitted to our department in the suspect of polyneuropathy, which was ruled out after diagnostic investigations. HS provided their informed consent to the study.

LP was performed in the morning and CSF orexin, $A\beta_{1–42}$ and tau proteins levels were determined using commercially available sandwich enzyme-linked immunosorbent assays.

Results: Thirty-four HS (15M19F, aged 20–83) were included in the study. No HS subject showed pathological CSF orexin (<110 pg/mL), $A\beta_{1–42}$ (<500 pg/mL) or tau (>350 pg/mL) levels. We found that orexin levels were positively correlated with $A\beta_{1–42}$ (R = 0.42, P = 0.013) as well as tau proteins (R = 0.57, P = 0.0003) concentrations.

Conclusions: In our population of HS, we documented that CSF orexin levels significantly correlated with $A\beta_{1–42}$ and tau proteins, known as Alzheimer Disease biomarkers. This observation, coupled with previous animal model studies, suggests that orexin seems to play a critical role in regulating $A\beta_{1–42}$ and tau levels possibly affecting their metabolism.

Therefore, our data may provide further evidence that orexin could be implicated in the metabolic cascade alteration of beta-amyloid and tau proteins supporting their pathological precipitation into senile plaques and neurofibrillary tangles, respectively.
Disclosure: Nothing to disclose.

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The protector effect of transgene GDNF on sleep in MPTP mouse model of Parkinson's disease

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Mice C57BL/6 at age of 2.5–3 months with preliminary implanted (under general avertin anesthesia) electrodes for cortical and hippocampal EEG were injected through bilateral intracerebral cannulas with NEK293 cells transgene for glial-derived neurotrophic factor (*Gdnf*) in amount of 100–200 thousand cells in 1 microliter of Henks solution to striatum (caudatum/putamen). Cells were transfected using plasmid construction containing modified gene of *Gdnf*, gene of resistance to gentamicin and gene of green fluorescent protein (*gfp*) for control of administration. Control animals received *gfp*-transgenic HEK293 cells. Three days later mice were subcutaneously injected with 40 mg/kg of neurotoxin MPTP selectively destroying dopaminergic system. EEG and video continuous 24-hr recordings were performed just before, 7 and 14 days after toxin administration. Then animals were tested behaviorally in RotaRod apparatus, killed and brains were studied immunohistochemically for tyrosine hydroxylase immunopositive neurons (THIN). Control animals demonstrated,

1. significant increase in activity and wakefulness and decrease in slow wave and paradoxical sleep by 14th day since toxin administration during dark period of nyctemeron;
2. sharp decrease in RotaRod time exposure;
3. decrease in amount of THIN in substantia nigra/pars compacta by 70%.

Administration of GDNF resulted in smoothing of changes of activity and waking-sleep cycle, increasing in exposition on RotaRod and lesser decreasing in amount of THIN (by 35%). The conclusion is, transplantation of NEK293 cells containing transgene protein GDNF into striatum of experimentally neurodegenerative mice induces protector-like effect.
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Microphage migration inhibitory factor −173 G/C promoter polymorphism and serum levels correlate with obstructive sleep apnea

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Objectives: Obstructive sleep apnea (OSA) has been shown to activate pro inflammatory cascade which promotes endothelial and cardio metabolic dysfunction. We hypothesized that MIF levels could be associate with the severity of OSA and −173 G/C gene polymorphism may alter their cardio metabolic risk. We looked for correlation if any with serum MIF levels and −173 G/C gene polymorphism in OSA.
Method: 99 subjects (mean age 44 years) with suspected sleep disorders were evaluated. All subjects underwent overnight full-montage digital polysomnography (Alice-Le, USA). Serum MIF was evaluated by enzyme linked immune sorbent assay (ELISA). The PCR products were sequenced to check the MIF −173 G/C polymorphism with the BigDye® Terminator v3.1 Cycle Sequencing Kit (ABI, USA) on an ABI Genetic Analyzer 3730 (ABI, Japan).
Results: 47 subjects had OSA and 52 did not have OSA. Mean BMI was 32 Kg/m^2. The mean serum MIF levels was higher in subject with OSA (16.8 ng/mL) as compare to subjects without OSA (9.34 ng/mL) respectively. The mean MIF levels in mild, moderate, and severe OSA was 10.53, 14.84 and 20.93 ng/mL. Overall MIF −173 G/C single nucleotide polymorphisms (SNPs) G, G/C and C, was 60.6%, 34.3% and 5.1% respectively.
Conclusion: Serum MIF levels is significantly associated with severity of OSA (P = 0.02, OR- 1.039) and BMI (P = 0.004, OR-1.1). MIF −173 G/C SNPs in MIF gene should be investigated in a large population of subjects with OSA.
Disclosure: Nothing to disclose.

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Viral insertion screen implicates the conserved vertebrate gene *dreammist* in larval zebrafish sleep regulation

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Objectives: To identify novel regulators of sleep in larval zebrafish.
Methods: Using an automated high throughput tracking system, we observed the sleep-wake behavior of larval zebrafish larvae harboring viral-induced disruptions in gene function. Up to 1000 larvae are placed into 96-well plates and simultaneously observed on a 14:10 light:dark cycle for three days. Our analysis software automatically scores features of larval zebrafish sleep, including sleep bout timing and duration, sleep latency, and waking locomotor activity.
Results: Through the viral insertion screen, we identified a novel gene, *dreammist* (dmist), that when disrupted in homozygotes results in significantly decreased sleep compared to wild type (WT) siblings (ANOVA, P < 0.05). *Dmist* is predicted to encode a small (70aa) peptide that is conserved among vertebrates, including fish, birds, mouse, and human. *Dmist* encodes an N-terminal signal sequence, predicting it enters the secretory pathway, and the mature domain shares a 60% similarity between zebrafish and humans. In situ hybridization and RT-PCR shows *dmist* expression in the zebrafish larval brain, particularly around the ventricle from

24 h post-fertilization, but gene expression is not rhythmically expressed.

In contrast to gene disruption, using a heat shock promoter to dive transient over-expression of dmist throughout the larval brain increases sleep compared to WT siblings (ANOVA, $P < 0.05$).

Conclusions: Taken together, this data indicates that *Dmist* is a novel, conserved neuropeptide involved in promoting larval zebrafish sleep. On-going experiments seek to put Dmist in context with other known zebrafish sleep/wake regulators, especially the hypocretin/orexin system.

Disclosure: Nothing to disclose.

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Connexin30 knock-out mice display less spontaneous locomotor activity, more sleep pressure and a reduced expression of metabolism-related genes

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Recent reports point out the involvement of astrocytes in sleep regulation. Astrocytes form local networks through gap junctions (GJ) by which metabolites can be transported. Recently, we showed that sleep deprivation (SD) induced an increase in connexin 30 (Cx30) mRNA, a major component of the astroglial GJs, and that Modafinil increases astrocytes coupling measured by dye diffusion in patched-cells. Here, we hypothesize that, in turn, the absence of Cx30 could impact the ability to maintain normal wakefulness in Cx30-KO mice. To verify this issue, spontaneous locomotor activity of KO and WT mice were recorded during 6 days. Mice were also implanted for polysomnographic recording and underwent an instrumental (ISD) or a 'gentle' (GSD) sleep deprivation of 6 h. In addition, the mRNA levels of genes linked to energy metabolism were also measured by qPCR in different brain structures.

In Cx30-KO mice, locomotor activity is significantly lowered for dark (−27%) and light (−38%) periods. Preliminary data show that during ISD the Slow Wave Sleep (SWS) duration was greater in KO mice (+50%) as well as the number of stimulations required to maintain KO mice awake for GSD (+49%). qPCR analysis revealed significant decreases in mRNA levels coding for the neuronal monocarboxylate transporter (8 to 12%), the lactate dehydrogenase A (14 to 20%), the glycogen phosphorylase (9 to16%) and the protein targeting to glycogen (13 to 21%).

These results suggest that impairment of astroglial GJ impacts the ability of mice to maintain active waking periods, possibly by alterations of neurometabolic coupling mechanisms.

Disclosure: Nothing to disclose.

Sleep Deprivation

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Sleep-loss related decrements in night-time vigilance performance: cerebral correlates and the impact of genetic vulnerability

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Objectives: Sleep-loss-dependent modulation of cognition-related cortical and subcortical brain activity was suggested to be affected by a polymorphism in the clock gene *PERIOD3 (PER3).* Here we investigated the impact of differential sleep pressure levels and *PER3* on cerebral correlates underlying vigilance performance during late night, when circadian sleep promotion is maximal.

Methods: Fifteen homozygous carriers of the long repeat allele ($PER3^{5/5}$) and 14 homozygous carriers of the short repeat allele ($PER3^{4/4}$) underwent a 40-h sleep deprivation (SD) and a 40-h multiple nap protocol (NP). Blood-oxygen-level-dependent (BOLD) activity was assessed with fMRI during a 10-min Psychomotor Vigilance Task (PVT) at the end of the biological night (3 h prior habitual wake-time).

Results: PVT reaction times were slower in SD than NP ($P < 0.05$); but similar for both genotypes ($P > 0.05$). *PER3* modulated BOLD activity such that activation in attention-related brain regions (e.g., inferior frontal gyrus (IFG), anterior cingulate, inferior parietal and thalamic regions, $P_{corr} < 0.05$) increased in $PER3^{4/4}$carriers from SD to NP, but mostly decreased in $PER3^{5/5}$ carriers. Seed-based connectivity analysis pointed to a stronger connectivity between a brainstem region (part of reticular formation) with the thalamus and left IFG in $PER3^{4/4}$ carriers. Further, a time-on-task-dependent activity increase in the thalamus under SD was present only in $PER3^{4/4}$ carriers ($P_{corr} < 0.05$).

Conclusions: Cerebral coping mechanisms with sleep-loss related vigilance decrements in the late night are affected by a *PER3* polymorphism. Higher activations of arousal-promoting brain areas suggest a stronger wake-promotion in the more resilient genotype ($PER3^{4/4}$) in general and also with increasing time-on-task.

Disclosure: Nothing to disclose.

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Sleep restriction alters immune functions and metabolism - transcriptomic and metabolomic studies in humans

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Objectives: Short or insufficient sleep has been associated with increased risk for metabolic diseases, such as atherosclerosis and type II diabetes. The development of these diseases have a strong immunological component. To elucidate the molecular mechanisms linking sleep homeostasis to immune functions and metabolism, we studied transcriptomic and metabolomic profiles of partially sleep-deprived subjects.

Methods: The sleep of healthy young males ($N = 14$) was restricted to 4 h/night for 5 nights. Fasting blood samples were collected in the mornings after 2 nights of baseline, 5 nights of partial sleep restriction (SR), and 2 nights of recovery.

Serum lipid profiles including lipoprotein particle species, cholesterol, and triglycerides were measured with NMR metabolomics. Total RNA was extracted from blood mononuclear leukocytes, and RNA expression was analysed using Affymetrix whole genome micro-arrays complemented with pathway analyses of differentially expressed genes.

Results: The most enriched pathways among genes that were up-regulated after SR were interleukin-8 production and B-cell activation ($P < 0.001$). Down-regulated pathways were involved in metabolic processes, such as cholesterol transport and homeostasis ($P < 0.001$). However, the lipoprotein profile after SR seemed beneficial with less low density lipoprotein (LDL) particles ($P < 0.01$), apolipoprotein B ($P < 0.005$), and LDL cholesterol ($P < 0.0005$).

Conclusions: Cumulative sleep restriction activates immune responses and decreases reverse cholesterol transport at the level of transcription in leukocytes. We propose that the low-grade inflammation state evoked by sleep loss may contribute to the development of cardiovascular diseases. Our data from a Finnish population sample ($N = 472$) support these findings on epidemiological level.

Disclosure: Nothing to disclose.

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Sleep homeostasis in genetically modified loss-of-function and gain-of-function brain-derived neurotrophic factor (BDNF) mice

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Objectives: Previous studies show that cortical brain-derived neurotrophic factor (BDNF) is causally linked to homeostatic sleep regulation. In addition to cortex, also the cholinergic basal forebrain (BF) is crucially involved in the regulation of arousal and sleep homeostasis. In the present study we investigated if BDNF plays a role in the BF mediated regulation of arousal and sleep homeostasis.

Methods: Loss-of-function C57BL/6 mice ($n = 6$) heterozygous for BDNF-null gene and gain-of-function C57BL/6 mice ($n = 6$) overexpressing the neurotrophic tyrosine kinase receptor (TrkB) gene and their wildtype (wt) littermates ($n = 6 + 6$) were under anesthesia implanted with EEG electrodes and unilateral microdialysis quide cannulae aimed at the BF. After recovery microdialysis probes were inserted into the BF and continuous sampling of microdialysates and EEG was initiated. A 24 h baseline followed by a 6 h sleep deprivation (SD; by gentle handling) with 18 h recovery was performed. Adenosine (ADE) and lactate (LAC) concentrations were measured from microdialysates whereas EEG was processed for vigilance stages and power spectral analysis.

Results: During SD the heterozygous BDNF-null mice accumulated less homeostatic sleep pressure as calculated by increased low frequency waking theta (4–7 Hz) EEG power as compared to their wt littermates but interestingly had more pronounced increase in the

extracellular ADE concentration. In contrast, TrkB overexpressing mice had more NREM sleep recovery after SD than their wt littermates.

Conclusions: These results show that sleep homeostasis is blunted in mice with lower BDNF levels whereas mice with elevated BDNF receptor expression show increased response to SD.

Disclosure: Nothing to disclose.

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Sleep homeostasis *in vitro*

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Introduction: Sleep is the behavioral state that plays important roles to construct our circadian daily life and hemeostatic need for rest. Although slow wave activity during NREM sleep is the best marker of sleep need in vivo, how this activity relates to cellular up and down states of single cortical neurons is still unclear. The most dominant feature of the spontaneous neural activity of dissociated cortical cultures is their synchronized bursting similar to deep NREM sleep.

Method: We have analyzed spontaneous neural activities in primary mouse cortical cultures by Multi Electrode Array (MEA) system at baseline and during recovery, 24 h after a single stimulation by a cocktail of excitatory neurotransmitters. We have developed algorithms to detect and characterize the burst-pause activity and its changes during recovery.

Results: Our detailed analysis indicated significant differences between baseline and recovery, including a higher synchronization (initial slope), and faster desynchronization (final slope) of bursting activity during recovery. Up state was prolonged in duration during recovery, while inter-burst interval was shortened. Also, the cross-correlation between electrodes increased during recovery. Spectral analysis if bursting activity indicated a higher power during recovery with a significant shift in power from 0.20 Hz to 0.40 Hz.

Discussion: Detailed analysis of spontaneous activity of simple neural networks in vitro shows surprising similarities in terms of homeostatic adaptation to stimulation, very similar to the homeostatic adaptation of the brain to enforced wakefulness.

Hinard et al., J Neuroscience, 2012, 32:12506–17.

Disclosure: Nothing to disclose.

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Light irradiance influences sleep homeostasis through melanopsin-based phototransduction

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Objectives: Light influences sleep and waking through circadian and direct effects, yet its putative influence on sleep homeostasis remains unclear. We previously reported that melanopsin (*Opn4*), a retinal photopigment, affects sleep homeostasis. Here we sought to determine whether light irradiance influences the sleep homeostatic process in melanopsin KO mice.

Methods: Backcross male *Opn4*$^{-/-}$ mice and their littermate controls were exposed to three different light intensities (<10, 150, or 600lux, n = 6–8/group) for 7 days (exposure duration based on a previous preliminary study). Sleep was recorded under baseline conditions and during a 6-h sleep deprivation by gentle handling. EEG power spectrum was performed, specifically to quantify EEG delta power, a reliable marker of sleep need.

Results: Wild-type mice showed significant (P < 0.05) increases in delta power as a function of light intensity, with the highest under 600 lux (240% of baseline, Delta determined during the dark period) during the day preceding the sleep deprivation, vs. 150 lux (170%) and <10 lux (141%). Following sleep deprivation both groups of mice, <10 and 150 lux, increased whereas 600 lux remained stable (244%). Furthermore, theta activity during waking (a marker of alertness) was also increased with intensity in these mice. *Opn4*$^{-/-}$ reacted less strongly to the sleep deprivations and showed overall lower delta power amounts. Interestingly, the genotype difference was more evident as light intensity increased.

Conclusion: These preliminary results indicate a positive relationship between light intensity and the increase in sleep-need with time-spent-awake, an effect mediated primarily through melanopsin-based phototransduction.

Disclosure: Nothing to disclose.

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Effects of COMT inhibitor tolcapone on mood and working memory during sleep deprivation

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Objectives: Common variation in genes regulating dopaminergic neurotransmission, including catechol-O-methyl-transferase (COMT) and dopamine transporter (DAT), impact on rest-activity patterns (Valomon et al., 2014) and neurophysiological markers of sleep-wake regulation (Holst et al., 2014). COMT degrades dopamine in prefrontal cortex; it can be inhibited by tolcapone, used in Parkinson therapy. To examine a causal relationship between dopaminergic neurotransmission and the consequences of sleep loss, we investigated the effects of tolcapone on mood and working memory in sleep-deprived volunteers.

Methods: 2 x 100 mg tolcapone were administered to 12 adult young men after 11 and 23 h of 40 h prolonged wakefulness (randomized, double-blind, placebo-controlled, cross-over design). The Karolinska Sleepiness Scale, the Profile of Mood States and a visual 2-back task were regularly conducted. Repeated measure mixed-model analyses of variance were applied.

Results: Symptoms of sleepiness, fatigue, irritability, and depression increased with time awake, while speed and accuracy on the 2-back task decreased. Compared to placebo, tolcapone tended to lower fatigue and irritability (P = 0.05 and P = 0.08). Moreover, it improved response speed (P < 0.03), yet not accuracy, on the 2-back task.

Conclusions: These preliminary results of an ongoing study indicate that pharmacological inhibition of COMT improves impaired mood states and working memory after sleep deprivation, suggesting that altered dopaminergic signaling contributes to these consequences of sleep loss in healthy volunteers. The observed large inter-individual differences in the effects of tolcapone may reflect different genotypes of the functional Val158Met polymorphism of *COMT*.

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Sleep loss changes executive brain responses in the wake maintenance zone

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Objectives: Brain mechanisms underlying executive processes are regulated by circadian and sleep homeostatic processes. Furthermore, during sleep deprivation (SD), cognitive performance and neural responses are differentially modulated by a clock gene *PERIOD3* polymorphism. Here, we investigated interindividual differences on executive brain responses under SD. Critically, we focused on the circadian evening wake maintenance zone (WMZ), a key time-point for sleep-wake regulation.

Methods: Thirty healthy young volunteers, genotyped for the *PER3* polymorphism (10 $PER3^{5/5}$; 20 $PER3^{4/4}$ homozygotes), underwent 42-h SD under constant routine conditions. They performed a 3-back working memory task in 13 successive fMRI sessions. To compare neural activity in the WMZ before and during SD, sessions were realigned according to individual dim light melatonin onset.

Results: We tested for a group ($PER3^{5/5}$>$PER3^{4/4}$) by session effect (WMZ before vs. during SD). From the first evening WMZ (i.e. during a normal waking day) to the second (i.e. following 40 h of continuous waking), $PER3^{5/5}$ individuals relative to $PER3^{4/4}$ showed significantly larger increase in responses in the left mid-cingulate, bilateral precuneus and thalamus. Interestingly, these regions are involved in executive processes and arousal regulation (thalamus).

Conclusions: These results show that the strong circadian wake-maintenance signal depends on sleep pressure, in a *PER3*-genotype dependent manner. Interestingly, pronounced genotype differences were observed in the thalamus, an area that compensates potential lower cortical activity under SD.

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Regional differences in the impact of sleep deprivation on sleep EEG power in early to mid adolescence

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Objectives: A developmental decline in slow-wave activity (SWA) along with a progression of maximal SWA from posterior to anterior regions has been shown across adolescent development under baseline sleep conditions [1]. SWA also shows a robust increase following sleep deprivation. We examined whether the increase in SWA to sleep deprivation varied across regions from early to mid adolescence.

Methods: Polysomnography was recorded from 11 EEG derivations during baseline (14 h prior wakefulness) and recovery (32 h prior wakefulness) sleep in 13 early (mean = 10.3 (0.48) years) and 30 mid adolescents (mean = 15.4 (0.49) years). A mixed model ANOVA with between subjects factor age (early vs. mid adolescent) and within subjects factor region (11 derivations) was used to compare regional difference in SWA from mid to late adolescence for baseline and recovery nights separately.

Results: We found the expected decline in SWA from mid to late adolescence for baseline ($P < 0.0001$) and recovery ($P < 0.0001$) nights. Furthermore, we found an interaction of derivation with age for baseline ($P = 0.001$) and recovery ($P < 0.0001$). Both nights showed more SWA at anterior vs. posterior derivations in the older group.

Conclusions: We confirmed a shift of non-REM sleep SWA from posterior to anterior areas with age in adolescents on baseline and recovery nights. These results provide evidence that brain regions with most SWA at baseline express greatest recovery after extended wakefulness, as indexed by SWA increase.[1] Kurth et al. (2010) JNeurosci 30:13211–13219

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Neural correlates of sustained attention under sleep deprivation during a constant routine: circadian and homeostatic interaction

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Objective: Sustained attention refers to the ability to maintain attention over extended periods of time. The interaction between circadian and homeostatic processes regulates time-of-day modulation in alertness and sustained attention. We investigated the neural correlates of sustained attention during a 42-h constant routine, while participants performed the psychomotor vigilance task (PVT) during successive 13 functional magnetic resonance imaging (fMRI) sessions.

Methods: Thirty-three healthy young volunteers (age 19–26; 17 women) participated to the study. Analyses aimed at characterizing the modulation of cerebral responses induced by PVT across fMRI sessions. Objective (theta wake EEG activity) or subjective (Karolinska Sleepiness Scale, KSS) measures of sleepiness were used as regressors in these fMRI analyses.

Results: Data revealed significant activation/deactivation patterns in a well know attentional brain network. This network included the middle frontal gyrus, intraparietal sulcus, middle occipital gyrus and cerebellum (all $P_{corr} < 0.05$). Interestingly, these areas were observed irrespective of the type of regressor used (theta activity and KSS). Furthermore, analyses of these fMRI brain areas estimates across sessions showed both sinusoidal (circadian) and quasi-linear (homeostatic) patterns.

Conclusion: Our results indicate that cerebral response to a sustained attention task is similarly modulated by both subjective and objective sleepiness across time. Moreover, both circadian and homeostatic factors modulate the hemodynamic responses within this fronto-parieto-occipital network.

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Effect of partial sleep deprivation on empathy for pain in an fMRI experiment

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Objectives: Sleep loss is known to affect emotional and social functions. Several studies have investigated the neural network underlying empathy for pain, and this network includes bilateral insulae and caudal anterior cingulate cortex, partly overlapping with areas activated when experiencing pain. Our aim was to study how partial sleep deprivation affects subjective unpleasantness and changes in activity in brain networks underlying empathy for pain.

Method: Healthy volunteers (n = 21, mean age = 24 years, SD = 3 years, 10 females) participated in a functional magnetic resonance imaging (fMRI) experiment, once after normal sleep and once after only sleeping 3 h. During fMRI, participants viewed pictures of hands being stung by needles or poked with a Q-tip. Mean values from predefined regions of interest were extracted and analysed.

Results: Partial sleep deprivation caused participants to report increased levels of unpleasantness ($P < 0.01$) when viewing pain stimuli. Across sleep conditions, pain stimuli caused increased activity in anterior insulae ($P < 0.005$) and caudal cingulate cortex ($P < 0.001$). Sleep deprivation caused a decrease in activity in cingulate cortex ($P = 0.057$). Higher sleepiness, as measured using the Karolinska Sleepiness Scale, was likewise associated with decreased activity in medial cingulate cortex ($P = 0.033$). In bilateral insulae, decreased activity was non-significantly associated with sleep deprivation, left ($P = 0.17$) right ($P = 0.19$), and self-rated sleepiness, left ($P = 0.07$) right ($P = 0.08$).

Conclusion: Partial sleep deprivation affects both subjective and caudal anterior cingulate cortex responses to other's pain.

Disclosure: Nothing to disclose.

Consciousness and its Boundaries: Lessons from Sleep

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Cortical mechanism of loss of consciousness: the role of bistability

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During NREM sleep early in the night consciousness fades while neuronal firing rates and synchronization levels can be similar to those observed in quiet wakefulness. In a recent series of experiments we recorded brain responses to direct cortical stimulations in humans during wakefulness, NREM sleep, REM sleep both non-invasively (using a combination of transcranial magnetic stimulation and electroencephalography) and invasively (by employing intracranial electrical stimulation/recordings in neurosurgical patients). These measurements show that, while during wakefulness and REM sleep the brain is able to sustain long-range, differentiated patterns of activation, during NREM sleep this ability is lost: cortical neurons, despite being active and reactive, become unable to engage in long-range, complex patterns of causal interactions. I will argue that this loss of complexity is due to bistability between up- and down-states in cortical circuits, a basic mechanism that may also account for loss of consciousness in anesthesia and in brain-injured patients.

Disclosure: Nothing to disclose.

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The boundaries of consciousness: lucid dreaming

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During rapid eye movement (REM) sleep, most of our vivid dream mentations occur. During REM sleep, activity levels in many brain regions are close to or even exceeding levels during wakefulness, whereas other regions are rather low in activity. The interplay between wakelike activity and regional deactivation may explain delusions, missing insight and lack of logic in dreams. Furthermore, mostly during phasic REM sleep, the brain is secluded from external influences, but is functioning in a closed-loop mode. In contrast to non-REM sleep, however, thalamocortical coupling is restored in phasic REM sleep, which may be a prerequisite for consciousness to reoccur. While during ordinary dreams, a basal form of consciousness is present, insight into the dream state during lucid dreaming may reflect a level of higher-order consciousness, without any changes in the brain's background activity level. Using combined EEG/fMRI experiments we investigated which brain regions may support this categorical change in consciousness. We identified areas in the dorsolateral prefrontal cortex, temporal and parietal cortex to be associated with presence of lucidity. Our findings complement EEG data which showed that dorsolateral prefrontal gamma power is a signature of lucid dreaming.

Disclosure: Nothing to disclose.

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The boundaries of consciousness: NREM and REM parasomnias

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NREM sleep parasomnias include arousal disorders (sleepwalking, sleep terrors and confusional arousals, often mixed in a single patient), sleep-related eating disorder and sexsomnia. Rare but concordant findings suggest that these patients are in a mixed state between sleep and wakefulness. During the abnormal motor behaviors, patients have the eyes open and apparently move and speak as they would during wakefulness, but some of their brain areas are still asleep (and sometimes dreaming). Consequently, their consciousness is altered: mental confusion, disorientation in time and space, inappropriate behavior, behavior in sharp contrast with their normal personality, anesthesia and partial or complete amnesia are indicative of this alteration. Similarly, during REM sleep behavior disorders, patients enact out some violent nightmares by loss of normal muscle atonia, leading them to potentially injure themselves or their bed-sharer, in partial or complete awareness that they are in reality lying in their bed. These two categories of parasomnia may have legal and ethical implications, as patients can develop a supranormal strength with aggressive or defense behaviors, leading to rare cases of severe injuries, sexual assault and homicide. In this case, they are categorized as insane automatisms.

Disclosure: Nothing to disclose.

Impact of Sleep Loss on Mood: From Animal Models to Humans

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Impaired sleep patterns and homeostasis in animal models for anxio-depressive disorders

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Impaired sleep is often accompanied by many psychiatric as well as neurological diseases. Among them, changes in sleep patterns or sleep habits are also recognized as a premorbid symptom, particularly well described in depression. To investigate the molecular link between sleep and mental illness, several mouse models for mood disorders were generated in our institute and underwent sleep assessment.

Two different lines of anxio-depressive models will be focused in the symposium; 1) a robust mouse model of trait anxiety showing high (HAB) and low (LAB) anxiety-related behavior, and 2) a humanized mouse mutant in which the murine P2RX7 gene was substituted by the depression-associated variants of human P2RX7. Homeostatic control over sleep loss was evaluated by responses to acute (6 h only) or sub-chronic (6 h/day for a week) sleep deprivation (SD).

Under baseline conditions, HAB mice, compared with LAB, displayed faster sleep-wake cycles with constantly higher slow-wave activity (SWA) during non-REM sleep but responded normally to SD. In contrast, heterozygous P2RX7 mutant mice were characterized with low SWA and barely spent in deep non-REM sleep. They showed normal homeostatic responses to acute sleep loss; however after sub-chronic SD, elevated occurrences of REM sleep decreased.

Totally different sleep phenotypes were observed in these separate anxio-depressive models. They both preserved sleep homeostasis, whereas sleep quality was severely affected. Although their sleep phenotypes are ascribable to different molecular mechanisms, a genetic disposition vulnerable to mood regulation impairs sleep in animals. Poor consolidation of sleep detected here might have underscored their anxiogenic behavior.

Disclosure: Nothing to disclose.

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Insomnia as a risk factor for depression

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Psychiatric sleep research in the last decades has focused on the issue of the specificity of REM sleep abnormalities for depressive disorders vs. other mental disorders. In contrast, not much attention was paid to sleep continuity disturbances, i.e. prolonged sleep latency, increased frequency of nocturnal awakenings or early morning awakening. In the meantime, a change of research paradigm has taken place: instead of searching for specific markers for depression, the transdiagnostic character of sleep continuity alterations has been proposed leading to a renewed interest in these sleep variables in psychiatric research. Furthermore, besides being symptoms of depression, sleep continuity alterations have been identified to be early premorbid signs or even independent predictors for developing depression. In a meta-analysis (Baglioni et al., 2011), we were able to demonstrate that insomnia at a given time (without significant co-morbid psychopathology) was predictive of developing depression - subjects with insomnia alone had a two-fold risk to become depressed in the next years. These results raise the question whether the treatment of insomnia may be preventive for the development of more severe mental disorders. Interestingly, recently it was shown that insomniac symptoms may also serve as risk factors for the development of suicidal ideation and suicide.Thus symptoms of insomnia are of high clinical relevance and future research should clarify whether the early and adequate treatment of these symptoms may prevent mental disorders.

Baglioni, C, Battagliese, G, Feige, B, Spiegelhalder, K, Nissen, C, Voderholzer, U, Lombardo, C, Riemann, D: Insomnia is a predictor of depression: a meta-analytic evaluation of longitudinal epidemiological studies. Journal of Affective Disorders, 2011, 135, 10–19.

Disclosure: Nothing to disclose.

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Genes involved in circadian rhythmicity and sleep homeostasis

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Genetic studies on model organisms have been successful in underpinning mechanisms involved in circadian rhythmicity and sleep homeostasis. They have been supported by experimental studies in humans and by the initial studies striving for finding direct associations between genetic variations and sleep phenotypes. The latter have been valuable in providing evidence for a role of functionally relevant genes in sleep regulation, such as f.ex. clock genes in circadian phenotypes and sleep disturbances, genes of the adenosine pathway in sleep architecture and sensitivity to sleep disturbance, and genes involved in ATP-gated ion channels or NO metabolism for total sleep length. Despite these successes, genetic determinants behind the large inter-individual variability in normal sleep characteristics in population are yet unveiled for the most part. Considering the adaptive nature of sleep and contribution of both genetic and environmental factors on sleep phenotypes according to twin studies, a significant proportion of the genetic influences on sleep is likely to be affected by environmental factors. In order to reveal such interplay, large and preferably longitudinal samples with appropriate measures are needed, not forgetting the plausible presence of population-specific genetic and environmental factors. At molecular level, the environment's effect on function of genome is likely to occur via epigenetic mechanisms, such as DNA methylation, histone protein modifications or expression of non-coding RNA molecules. Data on involvement of such mechanisms also in regulation of sleep is emerging. As epigenetic changes are dynamic by nature and typically tissue- and cell-specific, combining information from experimental models and human studies will be a necessity also in future.

Disclosure: Nothing to disclose.

What`s Hot in Sleep-disordered Breathing

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The accumulation of hypoxemia, a newly developed index, well predicts vascular endothelial dysfunction in patients with sleep disordered breathing

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Objectives: Sleep-disordered breathing (SDB) affects cardiovascular system through intermittent hypoxemia during sleep. The intermittent hypoxia reportedly injures the vascular endothelial cells, and might play a key role in developing vascular diseases. However, the relationship is not clear enough in the clinical practices. Thus, we assessed what index of oxygen desaturation related with vascular endothelial dysfunction.

Methods: We obtained several indices representing oxygen desaturation (apnea-hypopnea index [AHI], 3% oxygen desaturation index [3%ODI], lowest SpO_2 [Low_SpO_2], and averaged SpO_2 [Avg_SpO_2]) by polysomnography and flow-mediated vasodilation (%FMD) by ultrasound method in 32-SDB patients (Age: 59 $\pm$ 13 years, Male: 29). We developed a new simple index, an accumulated desaturation index (Acc_SpO_2), which was simply generated as a product of averaged desaturation (%) and whole sleep duration (hour): Acc_SpO_2=(100%-averaged oxygen saturation during sleep) X total sleep time. We assessed the relationships between these indices related to oxygen desaturation and %FMD using Pearson's or Spearman's correlation coefficient.

Results: The mean values of AHI, 3%ODI, Low_SpO_2, Avg_SpO_2 and Acc_SpO_2 were 41.5 $\pm$ 20.7/h, 34.0 $\pm$ 20.1/h, 76.3 $\pm$ 10.1%, 94.4 $\pm$ 1.4% and 37.8 $\pm$ 11.9%*h, respectively. The mean value of %FMD was 4.2 $\pm$ 2.3% which suggested impaired endothelial function. The %FMD had a significant correlation with Acc_SpO_2, but not with AHI, 3%ODI, Low_SpO_2 or Avg_SpO_2 (Acc_SpO_2: r = 0.51, $P < 0.01$, AHI: r = 0.05; 3%ODI: r = 0.15; Low_SpO_2: r = 0.11; Avg_SpO_2: r = 0.25).

Conclusions: The accumulated desaturation (i.e. Acc_SpO_2), not the frequency or the lowest desaturation, related to vascular endothelial dysfunction. Current results indicated that the total duration of oxygen desaturation might be the most important trigger for vascular diseases in patients with SDB.

Disclosure: Nothing to disclose.

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Sleep-disordered breathing in patients with acute ischemic stroke and transient ischemic attack: short-term evolution and effects on vascular/clinical outcome - the SAS CARE 1-study

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Background/objectives: Sleep disordered breathing (SDB) represents an independent risk factor for cardiovascular morbidity and mortality. The aim of this observational multicenter prospective study (SAS-CARE 1/supported-by-Swiss-National-Foundation-grant-320030_125069) was to assess the effects of SDB on clinical evolution and cardiovascular parameters within the first 3 months after stroke/TIA.

Patients/methods: Patients from five centers were studied within 7 days from stroke onset and 3 months later. Assessment included conventional polysomnography, analyses of stroke characteristics and severity (NIH stroke scale/NIHSS), 24-h-blood pressure, heart rate variability, endothelial function (by ENDOPAT), humoral markers of oxidate stress, vascular and clinical outcome (modified Rankin scale, mRS).

Results: The enrollment in this study was completed in December 2013 with a total of 209 patients (68% males, mean age 61 years, 88% strokes, 42% partial anterior infarcts) Mean NIHSS on admission/after 3 months was 4/1. SDB (AHI $\geq$ 10) was found in 57% in the acute phase and in 47% of patients 3 months later.

Age and history of hypertension were independent predictors of moderate to severe SDB (AHI $\geq$ 20) in the acute and subacute, BMI only in the acute phase. Systolic blood pressure values (mean, maximum, variability) correlated with AHI at 3 months (mean: r = 0.344/P = 0.001; max: r = 0.313/P = 0.001, var = 0.240/P = 0.01). No correlation was found between SDB and both NIHSS and mRS. Currently, ENDOPAT, heart rate variability and humoral data are analyzed.

Conclusions: Our data suggest that SDB

1. is common in stroke/TIA patients, also after 3 months,
2. is associated with high systolic blood pressure values, but
3. not with stroke severity and short-term outcome.

Disclosure: The main investigator of this study (Prof. C.L. Bassetti) received financial support for this study also from ResMed Inc. and Respironics Inc.

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Recurrence of sleep apnea after withdrawal of upper airway stimulation - a randomized controlled study

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Introduction: Upper airway stimulation (UAS) has been demonstrated to reduce sleep apnea severity in a large cohort study (STAR trial). This study was designed to examine the effect of 1 week therapy withdrawal on sleep apnea and quality of life measures.

Methods: A total of 46 consecutive responders to UAS from a prospective phase III trial which implanted and followed 126 subjects were randomized 1:1 to either the therapy ON group or the therapy OFF group for a minimal of 1 week of therapy withdrawal. Outcome measures included AHI, ODI, and sleep-related quality of life (Epworth Sleepiness Scale, Functional Outcomes of Sleep Questionnaire). The same outcomes were collected again at 18 months with therapy ON for both groups.

Results: In the randomized assessment, AHI did not change in the ON group (7.2 $\pm$ 5.0 vs. 8.9 $\pm$ 9.1, $P = 0.21$), but in the OFF group, AHI increased significantly (7.6 $\pm$ 4.0 vs. 25.8 $\pm$ 16.2 event/hr, $P < 0.001$). Therapy withdrawal also resulted in significant changes in the therapy OFF group in ODI, FOSQ, and ESS, compared to the therapy ON group. At 18 months with therapy ON in both groups, all objective and subject outcome measures showed sustained improvement similar to those observed at 12 months.

Conclusion: Withdrawal of therapeutic upper airway stimulation results in worsening of both objective and subjective measures of obstructive sleep apnea.

Disclosure: Nothing to disclose.

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Short term outcomes for obstructive sleep apnoea patients treated with hypoglossal nerve stimulation

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Objectives: The development of new methods for treating obstructive sleep apnoea (OSA) is important. We report the findings of a randomised controlled trial of one novel treatment, hypoglossal nerve stimulation. This trial was commenced in 22 centres worldwide, but was prematurely closed by the company (Apnex Medical) due to an unfavourable interim analysis. We report here the 6 month results of the 21 participants from our centre.

Methods: The device consisted of an implanted neurostimulator, a pacing lead and a respiratory sensing lead. Participants with an apnoea hypopnoea index (AHI) of 20–80 who had failed usual treatment options were enrolled. All underwent surgical implantation, then were randomly allocated (2:1) to have the device activated 1 month or 7 months post implantation. Outcome assessment at 6 months post randomisation included sleep measures and behavioural outcomes. Responders were a priori defined as achieving AHI <20 with at least 50% reduction from baseline.

Results: All data are mean (SEM). The device was implanted in 4 females, 17 males, mean age 54.3 (1.7) years. There was a significant improvement from baseline AHI in both active (34.1 [3.5] to 22.1 [5.2]) and control groups (40.9 [6.5] to 29.7 [6.2]). However, the only inter-group difference was in the Beck Depression Index. Using logistic regression, responder status was predicted by oxygen desaturation but not by treatment group and there was an association with obesity (BMI).

Conclusion: Although early studies suggested that this may be a promising therapy, the current data fail to confirm this.

Disclosure: The study was funded by the manufacturer, Apnex Medical. The company did not contribute to this analysis or the abstract.

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Effect of upper airway stimulation on improving sleep quality and quality of life in moderate to severe obstructive sleep apnoea

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Objectives: The objective of this study was to evaluate the effects of Upper Airway Stimulation (UAS) on sleep quality and quality of life (QOL) in CPAP-intolerant OSA patients.

Methods: A prospective, multi-centre clinical trial evaluated the safety and efficacy of an implantable neurostimulation system (Inspire II, Inspire Medical Systems, Minneapolis, USA) for CPAP-intolerant OSA by nocturnal stimulation of the hypoglossal nerve. Patients had a baseline polysomnography (PSG) prior to device activation, titration PSGs at 2 and 6 months after UAS implantation, and primary endpoint PSG at 12-months. All PSGs were scored by a single reviewer in a core lab. Patients also completed the Epworth Sleepiness Scale (ESS) and the Functional Outcomes of Sleep Questionnaire (FOSQ) at each visit.

Results: PSGs were performed in 126 patients (83% males) at baseline, and 124 patients completed the 12-month visit. Mean age was 54.5 years. At the primary endpoint visit, UAS improved OSA severity, quality of life, and sleep quality. AHI was reduced from 29.3 events/h to 9.0 events/h, arousals were reduced from 28.9/h to 14.8/h. QOL measures were also improved (ESS: 11.6 $\pm$ 5.0 to 7.0 $\pm$ 4.2; FOSQ: 14.3 $\pm$ 3.2 to 17.3 $\pm$ 2.9, $P < 0.001$ for both). Stage N1 and N2 sleep decreased (11.5% to 9.3%, and 64.3% to 64.2%, respectively, $P < 0.001$), while N3 sleep increased from 8.5% to 10.8% ($P < 0.05$). REM sleep was unchanged (15.7% to 15.6%, $P = 0.08$).

Conclusions: Upper airway stimulation for CPAP-intolerant OSA improved sleep quality and QOL measures. Improvements were likely due to the therapeutic effect of UAS on reducing the AHI.

Disclosure: This study was sponsored by Inspire Medical Systems, Minneapolis, USA

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Poor brain bioenergetics during resting wakefulness are related to neurobehavioural deficits in severe obstructive sleep apnea

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Objectives: Obstructive sleep apnea (OSA) is a well-established cause of impaired daytime functioning. However, there is a complex inter-individual variability in the neuroanatomical and neurobehavioural deficits in OSA. We previously reported defects in brain bioenergetics during apneic sleep in severe OSA patients. In this study, we investigate whether poor brain bioenergetics during resting wakefulness are related to neurobehavioural decrements.

Methods: Patients attended the sleep laboratory in the evening and were kept awake over-night. Performance testing on the psychomotor vigilance task (PVT, 10-min sustained attention task) occurred at 21:00, 23:00, 01:00, 03:00 and 05:00. We assessed brain bioenergetics (inorganic phosphate/adenosine tri-phosphate ratio, Pi/ATP) in the temporal lobe during resting wakefulness at 07:00 in a 1.5T MRI scanner using phosphorous magnetic resonance spectroscopy (^{31}P MRS) techniques.

Results: We studied 13 males with severe OSA (age 49 $\pm$ 11 years, BMI 33 $\pm$ 7 kg/m^2, respiratory disturbance index [RDI] 77 $\pm$ 22 h^{-1}). A higher Pi/ATP ratio in the brain (poorer brain bioenergetics) was significantly correlated with worse PVT performance across the testing period (average number of lapses greater than 500 ms, r = 0.59, P = 0.03). In contrast, the conventional RDI measure of disease severity was not significantly correlated with performance.

Conclusions: Poorer brain bioenergetic activity was related to worse performance in these patients. Neuroimaging appears to provide more accurate objective correlates of negative functional effects in OSA and to predict inter-individual variability. We speculate that better or adaptive brain bioenergetics may protect a patient from the insult of repetitive hypoxia / sleep fragmentation. This may explain why some OSA patients are relatively asymptomatic compared with others.

Disclosure: Nothing to disclose.

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Long term effects of compliance with positive airway pressure (PAP) therapy in patients with obesity hypoventilation syndrome (OHS)

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Objectives: To assess the role of different levels of compliance and long-term effects of positive airway pressure (PAP) therapy on gas exchange, sleepiness, quality of life, depression and death rate in patients with obesity hypoventilation syndrome (OHS).

Methods: One hundred fifty two patients with newly diagnosed OHS, who have been recommended PAP therapy, were followed up for a minimum of 2 years. The hours/day and percentage of days PAP was used were monitored. Subjective daytime sleepiness, reflected by Epworth sleepiness scale (ESS), quality of life (Short Form 36-SF-36) and patient's level of depression (Beck Depression Inventory-BDI) were recorded together with the death rate before and at the end of the follow up period.

Results: At the end of the follow-up period (mean duration, 50 months), PaO_2 had increased from baseline (P = 0.007) and $PaCO_2$ had decreased (P < 0.0001). PAP therapy also significantly improved ESS (P < 0.0001), BDI (P < 0.0001) and SF-36 (P < 0.0001) scores. During follow-up, ten patients died (two of them due to the progression of respiratory failure). Patients who used PAP therapy for >6 h/day had a considerably greater improvement in blood gases and questionnaires scores than less adherent patients.

Conclusions: Increased hours of use and long-term therapy with PAP are effective in the treatment of patients with OHS. Clinicians should encourage adherence to PAP therapy in order to provide a significant improvement in clinical status and gas exchange in these patients.

Disclosure: Nothing to disclose.

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A sleep apnea related risk of vehicle accident is reduced by CPAP - Swedish traffic accident data acquisition (STRADA) registry

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Objectives: Obstructive sleep apnea (OSA) is associated with excessive daytime sleepiness (EDS) and two to seven times increased risk of motor vehicle accidents (MVAs) compared with the general population. The MVA rate in patients with suspected OSA, clinical features and the effect of treatment on risk prediction was investigated.

Methods: Clinical sleep laboratory patients were cross-analyzed with a matched control group from the general population. The 10-year incidence of MVA among patients (n = 1478, 70.4% males, mean age 54 (13) years) and accidents (n = 21118) in the general population was analyzed. Risk factors associated with MVA risk were determined in patients with OSA.

Results: Observed accidents among patients (n = 74) were compared with the expected number (n = 29.91, risk ratio 2.47, P < 0.001) predicted from the control population. Observed MVAs were more prevalent among younger (18–44 years) patiens but estimated OSA related excess accident risk was most prominent in elderly (65–80 years, risk ratio 3.5) drivers. Risk factors within the OSA patient cohort (high traffic exposure $\geq$15 000 km/year, Epworth Sleepiness Score $\geq$16, habitual sleep time $\leq$5 h/night and use of hypnotics) were associated with increased accident risk (odds ratio 1.2, 2.1, 2.7 and 2.1, respectively, all $P \leq$ 0.03. Compliance with CPAP ($\geq$4 h/night), was associated with a reduction of MVA frequency (7.6 to 2.5 accidents/1000 drivers/year).

Conclusions: The motor vehicle accident risk in this large cohort of unselected sleep apnea patients suggests a need for accurate tools to identify individuals at risk. Conventional metrics of sleep apnea severity (e.g. apnea-hypopnea-index) failed to identify patients at risk.

Disclosure: Nothing to disclose.

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Effectiveness of two maintenance diets following a very low energy diet to reduce cardiometabolic risk in obese sleep apnea patients: a randomised controlled trial

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Objectives: We investigated whether patients with obstructive sleep apnea (OSA) could maintain significant weight loss and cardiometabolic improvement achieved through a very low energy diet (VLED) using a low glycemic index high protein diet (LGHPD) regime compared to a standard hypocaloric diet based on the Australian Guide to Healthy Eating (AGHED).

Methods: We recruited obese adult OSA patients (apnea hypopnea index $\geq$5 events/h, body mass index $\geq$30 kg/m^2) Patients received 2 months VLED (<900calories/day) before randomisation to LGHPD or AGHED. These two iso-caloric diets were prescribed according to calculated energy requirements using dietary modelling. Participants received 4 months lifestyle counselling and outcomes were measured at 0, 2 and 6 months. Outcomes reported mean$\pm$SD and mean change (95%CI).

Results: We recruited 44 obese patients of which 2 withdrew from the VLED. 20 patients were randomised to AGHED [weight = 111.7 $\pm$ 20.3 kg, age = 50 $\pm$ 9 years, 12 mechanically treated (MT)] and 22 to LGHPD (113.4 $\pm$ 18.7 kg, age = 49 $\pm$ 10 years,12MT). Following 2-months VLED, body composition parameters and most cardiometabolic markers improved significantly. At 6 months, weight loss ($P < 0.0001$): AGHED = $-$13.5 kg ($-$16.2 to $-$10.9), LGHPD = $-$13.4 kg ($-$16.0 to $-$10.7) and body fat via bioelectrical impedance analysis ($P \leq 0.002$): AGHED = $-$4.2 kg ($-$6.9 to $-$1.6), LGHPD = $-$5.9 kg ($-$8.5 to $-$3.2) were sustained to a significant degree. Significant improvements in cardiometabolic markers included triglycerides, fasting blood glucose and insulin in all patients ($P < 0.01$), systolic blood pressure and high density lipoprotein cholesterol in the AGHED only ($P < 0.05$) and resting pulse in the LGHPD only ($P < 0.0001$).

Conclusions: Patients with OSA can maintain significant weight loss and cardiometabolic improvement through a calorie controlled maintenance diet for 6 months.

Disclosure: Nothing to disclose.

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CPAP use improves sexual function in men with OSA and erectile dysfunction (ED): a randomised controlled study

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Objectives: ED is common in OSA. Uncontrolled studies suggest CPAP improves erectile function. PDE-5 inhibitors for ED may worsen OSA. This study was to evaluate CPAP vs. sham CPAP, and Vardenafil vs. placebo, on sexual function in men with OSA and erectile dysfunction.

Methods: 61 men with OSA (AHI > 20) and ED were randomised to 12 weeks CPAP or Sham CPAP, and 10 mg daily Vardenafil or placebo in a factorial design study. Sleep related erections (SRE, subset of $n = 35$) were recorded, as well as subjective sexual function, quality of life and treatment satisfaction. A sub-analysis in participants who used CPAP or Sham >4 h/night was also performed ($n = 20$).

Results: CPAP improved overall sexual satisfaction compared to sham CPAP ($P = 0.04$), increased the number of SRE's ($P < 0.01$) and improved vigilance ($P = 0.01$) and vitality ($P = 0.03$). In those who used CPAP more than 4 h/night, erectile function and sexual desire increased with CPAP vs. sham ($P = 0.04$ & $P = 0.03$ respectively). For adherent participants, self-esteem, social function, and mental health all increased while depression and stress reduced (all $P < 0.05$). Vardenafil improved SRE quality ($P = 0.01$), and had higher treatment satisfaction ($P = 0.001$) but did not improve subjective erectile function compared to placebo ($P = 0.069$) and did not worsen OSA.

Conclusion: Adherent CPAP use improves sexual function, and several parameters of mental health, however, adherence to CPAP was low in this study. Participants who received vardenafil or were adherent to CPAP were more satisfied with this treatment for erectile function compared to placebo.

Disclosure: Nothing to disclose.

From RBD to Restless Legs

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Data-driven modeling of sleep EEG and EOG reveals stages indicative of pre-Parkinson and Parkinson's disease

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Question: Will unsupervised modelling of sleep EOG and sleep EEG reveal sleep characteristica indicative of pre-Parkinson and Parkinson's disease (PD)?

Methods: Polysomnographic (PSG) data from 10 age-matched control subjects were used to develop an EOG sleep model and an EEG sleep model. The sleep models were applied on full-night PSG data from 24 additional control subjects, 26 patients with periodic leg movements (PLM), 31 patients with idiopathic REM sleep behavior disorder (iRBD) and 36 PD patients. Based on the data-driven sleep models, features reflecting sleep characteristics in the EEG and EOG activity were computed. The total amount of data was devided in a training dataset containing 16 subjects from each of the four groups, and a validation dataset containing the remaining subjects. The features derived were evaluated and the most discriminative ones between iRBD/PD (neurodegenerative diseases (NDD) cases) and PLM/controls (motor, but non-NDD cases) were found by training a Lasso regularized Regression model using eight-fold cross-validation on the training dataset.

Results: The best classification model included four features derived from the EEG data, and the NDD patients in the validation dataset could be classified with a sensitivity of 91.4% and a specificity of 61.1%. The most discriminative features were found to be thresholded amounts and stability of EEG topics reflected to REM, N3 and N1/N2, respectively.

Conclusions: This study suggests that the amount of N3 and R and the ability to maintain NREM and REM sleep determined by a data-driven sleep model can be used as potentially early PD biomarkers.

Disclosure: Nothing to disclose.

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A distinct sleep pattern in the novel parasomnia associated with Iglon5 antibodies

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Objective: IgLON5 parasomnia is a novel neurological syndrome with antibodies against IgLON5 and prominent sleep dysfunction and pathological features suggesting a tauopathy. We report the sleep pattern of this novel parasomnia.

Methods: Video-polysomnographic studies of four patients (3 males, median onset age: 56 years) with IgLON5 parasomnia were scored according to standard criteria with modifications to include additional stages, such as undifferentiated NREM sleep (UN-NREM) and poorly structured stage-N2 (PS-N2). Vocalisations were classified as simple or complex, and motor events as jerks, simple, or finalistic. Rapid periodic leg movements (RPLM) were repetitive leg movements separated by less than five seconds.

Results: Sleep efficiency ranged from 44 to 89%. RPLM were present in four patients during wakefulness and continued briefly after sleep onset. In all patients, sleep initiation and re-entering of sleep after awakening was abnormal with UN-NREM [0–67% of the total sleep time (TST)] or PS-N2 (14–36% TST) with frequent vocalisations, simple movements and finalistic behaviours. Normal N1 and N2 sleep were infrequent. Normal N3 stage was present (8–42%). UN-NREM and PS-N2 predominated in the first half of the night, normal N3 in the second half. In all patients, REM sleep (0–18%) occurred as REM sleep behaviour disorder (RBD) with frequent jerks. Stridor and obstructive sleep apnoea (OSA) predominated during normal N3 stage (AHI: 20–44).

Conclusions: IgLON5 parasomnia is characterized by distinctive abnormal sleep architecture with UN-NREM or PS-N2 with simple and finalistic movements, normalisation of NREM sleep by the end of the night, RBD, and stridor with OSA.

Disclosure: Nothing to disclose.

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Sensitivity and specificity of two screening questionnaires for REM sleep behaviour disorder and relationship with REM sleep without atonia in patients with Parkinson's disease

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Objectives: to assess the sensitivity and specificity of the REM Sleep Behaviour Disorder (RBD) single-question screen (RBD1Q)[1] and the RBD-Screening Questionnaire (RBDSQ)[2] in patients with Parkinson's Disease (PD) and their relationship with REM sleep without atonia (RSWA).

Methods: Thirty-two non-demented PD patients (M = 18;mean age:63 ± 8 years) consecutively evaluated at a movement disorder center, filled out both RBD1Q and RBD-SQ, before undergo a full-night video-polysomnographic recording. RSWA was evaluated using the Montreal method[3] (%tonic 30-s epochs and %2-s mini-epochs containing phasic chin EMG activity), the SINBAR[4] (%30-s epochs containing any chin or FSD EMG activity) and the automatic Atonia Index.[3] RBD was diagnosed in 19 patients following the ICSD-3 criteria.

Results: Sensitivity of the RBD-1Q and of the RBD-SQ was 52.6% and 47.4%, and ROC was 0.79 and 0.78 respectively, while specificity was 100% for both questionnaires. Two visual methods, the Montreal %tonic chin 30-s epochs and the SINBAR %30-s epochs containing any chin/FSD activity showed 100% sensitivity, 76.9% specificity and ROC=0.93. Atonia Index performed slightly

lower with sensitivity 94.7%, specificity 69.2% and ROC = 0.84. The phasic parameter performed significantly worse.
Conclusions: Screening questionnaires showed good specificity but low sensitivity; conversely, visual and automatic evaluation of RSWA showed high sensitivity and good specificity for RBD in PD patients. PD patients might underestimate their RBD during sleep and/or they might show relatively frequent RSWA without fulfilling the required diagnostic criteria for RBD.
[1]Postuma et al., Mov Dis 2012
[2]Stiasny-Kolster et al., Mov Dis 2007
[3] Ferri et al., Sleep Med in press
[4]Frauscher et al., Sleep 2012
Disclosure: Nothing to disclose.

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Electroencephalographic and autonomic alterations in nightmare disorder during pre-and post-REM periods

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Objectives: Abnormal arousal processes and wake-like alpha activity during sleep were reported as pathophysiological features of Nightmare Disorder. We hypothesized that in Nightmare Disorder, wake-like cortical activity and peripheral measures linked to arousals would be triggered by the initiation of REM periods.
Methods: We examined electroencephalographic (EEG), motor and cardiac activity in nightmare (NM) and control (CTL) subjects during sleep-state-transitions. Based on the second-nights' polysomnographic recordings of 19 NM and 21 CTLs, we examined the absolute power spectra focusing on the alpha range, measures of heart rate variability (HRV) and motor (muscle tone) activity during pre-REM and post-REM periods, separately.
Results: The NM group exhibited increased alpha power during pre-REM, but not in post-REM periods. CTLs showed increased HRV during pre-REM periods in contrast to post-REM ones, but NM subjects did not exhibit such sleep state-specific differences in HRV, showing more stable values across the examined sleep states and less overall variability reflecting generally attenuated parasympathetic activity. These differences were independent of trait anxiety. Moreover, in both groups, significant differences emerged regarding cortical and motor activity between pre-REM and post-REM conditions, reflecting the heterogeneity of NREM sleep.
Conclusions: Our findings indicate that NM subjects's sleep is particularly compromised during NREM-REM transitions. The coexistence of sleep-like and wake-like cortical activity in NM subjects seems to be triggered by REM/WAKE promoting neural activity.
Disclosure: This research was supported by the European Union and the State of Hungary, co-financed by the European Social Fund in the framework of TÁMOP 4.2.4. A/-11-1-2012-0001 'National Excellence Program'.

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24-Hr treatment of restless legs syndrome patients with an insufficient response to short-acting dopamine agonists: a comparative study using multiple immobilization tests

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Objectives: Current treatment options for restless legs syndrome (RLS) / Willis-Ekbom disease (WED) include dopaminergic agents (DA) with elimination half-lives that cover the main symptomatic period at night. However, RLS/WED symptoms emerging during the daytime are common even during treatment. The purpose of this study was to investigate whether insufficient response to a short-acting DA is associated with the emergence of daytime symptoms and whether treatment with long-acting dopamine agents can improve response.
Methods: Thirty patients diagnosed with idiopathic RLS/WED with an insufficient response to pramipexole (IRLS>15) underwent a 9-week, open crossover study, switching from a 4-week treatment with pramipexole (0.25 mg bid) to rotigotine (2–3 mg/d). Multiple suggested immobilization test (mSIT; 8AM to 12PM) and polysomnography were performed on two consecutive days at the end of each treatment, and were scored by blind raters. Secondary endpoints included mean change across conditions in rating scales.
Results: A positive correlation was found between IRLS scores at baseline and mSIT scores before 7PM, suggesting that higher IRLS scores were associated with daytime symptoms ($r = 0.49$; $P < 0.01$). Compared to pramipexole, rotigotine improved the Leg Movement Index on mSITs ($P < 0.05$), PLMI and sleep architecture during PSG, as well as symptom severity as assessed by rating scales.
Conclusions: Our findings suggest that daytime symptoms are common during RLS/WED treatment with short-acting DAs, and contribute to treatment failure. In patients with an insufficient response to pramipexole, rotigotine leads to an improvement of RLS symptoms both during the day and at night.
Disclosure: Nothing to disclose.

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High values of nocturnal blood pressure coexist with high number of PLMS in patients with insomnia

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Objectives: The aim of this study was to check if insomnia patients with increased nocturnal blood pressure (BP) have higher number of periodic limb movements in sleep (PLMS).
Methods: Polysomnographic recordings of 60 consecutive insomnia patients were analyzed. The subjects were at first divided into two groups: Patients with normal nocturnal BP values were included into Group I and patients with nocturnal systolic BP >120 mmHg or nocturnal diastolic BP>75 mmHg were included into Group II. Indices of periodic limb movements in sleep (PLMS-I) and of periodic limb movements in sleep with arousal (PLMSA-I) were compared between the groups. Total Sleep Time (TST), Sleep latency (SL), Sleep Efficiency (SE), Sleep stages latencies, Awakenings index (AW-I), Arousals index (AR-I), wake after sleep onset (WASO) were also compared.
Results: Patients from Group II were older than patients from Group I (49.1 years vs. 40.1 years, $P < 0.05$), with no difference in sex distribution between the groups. PLMS-I was significantly higher in Group II (19.9 vs 6.5, $P = 0.0066$) as well as PLMSA-I (3.0 vs 1.4,

$P = 0.0414$). Patients from Group II had significantly shorter TST (6.11 vs 6.76; $P < 0.05$) and SL (0.35 vs. 0.59 h; $P < 0.05$). They had significantly longer REM latency (2.42 vs. 1.73 h; $P < 0.05$) and WASO (1.65 vs. 1.12 h; $P < 0.05$).

Conclusion: PLMS-I is higher in insomniac patients with increased nocturnal blood pressure. Normalization of PLMS-I should be considered as a possible method of normalizing nocturnal blood pressure in patients with insomnia.

Disclosure: Nothing to disclose.

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Genetic risk loci for restless legs syndrome are not related to multimorbidity

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Objectives: Restless legs syndrome (RLS) is associated with multimorbidity. In this relationship, the potential role of the known risk loci for RLS has not yet been studied. Our aim was to evaluate whether the presence of RLS risk alleles predicts increased comorbidity in the general population.

Methods: Two independent, observational cohort studies were used: the Dortmund Health Study (DHS, $n = 1{,}312$) and the Study of Health in Pomerania (SHIP, $n = 4{,}308$). Age-stratified, random sample drawn from the respective city registers. RLS status was assessed according to the RLS standard minimal criteria. Comorbidity index was calculated by adding up the following conditions: diabetes, hypertension, myocardial infarction, obesity, stroke, cancer, renal disease, anemia, depression, thyroid disease, and migraine. Thirteen SNPs associated with elevated risk of RLS were genotyped.

Results: The mean age was 52.6 ± 13.7 years (DHS) and 49.7 ± 16.4 years (SHIP), and the proportion of women was 53.1% (DHS) and 51.1% (SHIP). The mean number of comorbid conditions was 1.4 ± 1.2 and 1.6 ± 1.3 in DHS and SHIP, respectively. In multivariate regression models, the presence of any RLS risk allele was not associated significantly with the comorbidity index in any of the studies or in the pooled sample.

Conclusions: These results suggest that the increased multimorbidity in RLS is not explained by known genetic risk factors for RLS.

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Prevalence of sleep bruxism in a general population sample: comparison of symptoms, masseter muscle activity and sound monitoring

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Objectives: Sleep bruxism (SB) is a sleep-related movement disorder that can cause pain and dysfunction in the orofacial region. Limited data is available on how prevalent SB is in the general population.

Methods: In an epidemiological study on asthma and allergy (www.ecrhs.org) a random population sample 40–65 years was additionally invited for a type 3 home sleep study (T3, NoxMedical, Reykjavik, Iceland) including electromyography of masseter muscles and sound recording. Identification of SB was based on manual scoring by AASM 2014 diagnostic criteria. Bruxism episode index (BEI) was calculated per hour of sleep (phasic, tonic and mixed). Low frequency SB was characterized by BEI ≥ 2 - 3.99 and high frequency SB by BEI ≥ 4.

Results: Altogether 380 (83.5%) answered the questions on SB; of those 39 (10.3%) reported grinding/clenching teeth at least weekly. Whole night measurements for $n = 367$ showed a 19.6% prevalence of SB in the general population ($n = 19$ with high frequency SB and $n = 53$ with low frequency SB). The subjects with high frequency SB had average BEI ($\pm$ SD) 6.1 ($\pm$ 1.9). A total of 305 subjects had both questionnaire and a measurement of bruxism. The majority of subjects reporting teeth grinding did not have measurable SB (84.4%) and the majority of those with measured SB did not report grinding teeth (91.8%). A significant relationship was found between reporting SB and reporting morning headaches (x^2 test, $P = 0.04$).

Conclusion: SB is common in the general population. The discrepancy between measurable SB and SB symptoms suggests that diagnostic criteria need improvement.

Disclosure: ES Arnardottir is a consultant with Nox Medical.

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Mortality and social consequences of REM sleep behaviour disorder for patients and their partners. A controlled national study

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Objectives: We aimed to evaluate the total costs of REM sleep Behaviour Disorder (RBD) for patients and their partners as this is poorly described.

Methods: Using records from the Danish National Patient Registry and other public databases (1997–2012) we identified 356 RBD patients and their partners ($N = 201$). They were compared to respectively 1422 and 804 controls subjects (ratio 1:4) randomly selected with respect to age, gender and geographic location Mortality, direct and indirect costs were evaluated for patients and their partners. Direct costs including frequencies of primary and sector contacts and procedures, and medication from primary and secondary sectors were obtained from the Danish Ministry of Health, the Danish Medicines Agency, and the National Health Security. Indirect costs, which included labor supply and social

transfer payments, were based on income data derived from the Coherent Social Statisticswere evaluated for patients and their partners.

Results: RBD presented lower survival than control subjects (0.910; 0.872–0.937 vs. 0.933; 0.899–0.956, HR = 2.32, $P = 0.0002$). RBD patients had higher rates of health-related contact, medication use, unemployment, and lower income level. Excess yearly direct net health costs and indirect costs including social transfer payment were: €7287 after diagnosis. There were no significant differences among partners as compared to their controls.

Conclusions: RBD is associated with increased mortality and health related burden, and has socioeconomic consequences.

Disclosure: Nothing to disclose.

When Sleep Attacks Vigilance

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Measurements of vigilance impairment in patients with sleep disorders

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Excessive daytime sleepiness (EDS), an increased tendency or need to fall asleep, is the key symptom of many sleep disorders. EDS was shown to be accompanied by vigilance impairment in a variety of sleep disorders such as narcolepsy and obstructive sleep apnoea syndrome (OSAS). Recent studies indicate that measurements of sleepiness and vigilance are complementary. Firstly, we provide protocols for the use of the Sustained Attention to Response Task (SART), a vigilance test. Secondly, we provide evidence for the valuable combination of ESS or MWT with the SART to assess treatment effects in narcolepsy. In addition, we discuss the treatment effects of (1) continuous positive airway pressure on vigilance and sleepiness in OSAS, and (2) sodium oxybate on vigilance and sleepiness in narcolepsy. The latter study also provides a comparison of vigilance tests.

Disclosure: Nothing to disclose.

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Inter-individual differences in sustained attention resulting from sleep deprivation

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There are considerable inter-individual differences in sustained attention deficits due to sleep loss, and these differences in vulnerability to sleep loss constitute a trait. Broad searches for predictors of vulnerability to sleep loss have revealed that genetic polymorphism explain some of the inter-individual variability, but much of the between-subjects variance remains to be explained. Recently it was proposed that allostatic changes in homeostatic sleep/wake regulation as a consequence of prior chronic sleep restriction may also play a role. Inter-individual differences in performance impairment due to sleep loss extend beyond sustained attention, and they appear to be task-dependent. Neuroimaging data of the brain indicate that regional differences in neuronal processing capacity may be involved. Theoretical considerations and cognitive modeling results suggest that such regional differences may entail differential resilience to degradation of cognitive processing as a consequence of local sleep. Much has been learned about inter-individual differences in vulnerability to sleep loss; yet, 10 years after they were first demonstrated to be a trait, they still provide a rich platform for scientific discovery.

Disclosure: Nothing to disclose.

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A harmacogenetic perspective on vigilance regulation during sleep deprivation

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The psychomotor vigilance task (PVT) is currently the dominant assay of sustained attention in sleep deprivation paradigms. It is thought that due to 'wake-state-instability', PVT performance after prolonged wakefulness is characterized by increased variability, slowing and elevated propensity to lapse. Nevertheless, not only sleep-loss-induced impairments but also baseline performance on the PVT is highly variable among healthy individuals. These inter-individual differences may reflect different endogenous sleep propensity. Pharmaco-genetics provides a powerful approach to identify molecular mechanisms contributing to state- and trait-like inter-individual differences on the PVT. Our studies revealed that functional polymorphisms of genes affecting adenosinergic (*ADA*, *ADORA2A*), glutamatergic (*FMR1*) and dopaminergic (*DAT1*, *COMT*) neurotransmission impact on PVT speed in rested and sleep-deprived state. Furthermore, *ADORA2A* and *COMT* genotype modulate the effects of caffeine and modafinil on response speed after sleep deprivation, whereas functional variation of *COMT* predicts the increase in lapse-frequency after sleep loss. These data show that adenosinergic, glutamatergic and dopaminergic mechanisms regulate PVT response speed, which relies on a fronto-parietal sustained-attention-network and the motor system, including the striatum. In contrast to *ADA*, *ADORA2A*, *FMR1* and *DAT1*, the *COMT* gene is hardly expressed in basal ganglia. The distinct effect of *COMT* genotype on PVT lapses after sleep loss suggests that local expression of genes within the sustained-attention-network differently contributes to trait- and state-like individual differences in PVT performance. These findings may offer a unique opportunity for the development of personalized improvement of distinct aspects of impaired vigilance as a consequence of sleep loss and sleep disorders.

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Non-visual effects of light on alertness and cognitive performance: measures and inter-individual differences

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Non-visual or non-imaging forming light in humans reduces sleepiness, increases alertness and cognitive performance and also interferes with our sleep acutely or via its circadian phase shifting properties. There is a clear dose- time of day- and wavelength dependency with a strong 'blue-shift' most probably also involving melanopsin as a mediator of non-image forming light responses in humans.

Blue-enriched light at low levels (40 lux) and light from LED-backlit computer screens elicited significant alerting responses as indexed by subjective and objective correlates of sleepiness, along with better well-being and cognitive performance in attention, working memory and declarative learning tasks during the late evening. Blue-enriched light induced robust effects on sleep consolidation and sleep EEG power density, with fewer nocturnal awakenings and reduced frontal NREM EEG slow-wave activity (2.5–4 Hz) during the first sleep cycle, as compared to non-blue enriched light. Interestingly, the response to light showed clear inter-individual differences, such that women preferred 'warm' (2500 K) than blue-enriched light at 6500 K, which was not the case for men. Furthermore, we have first evidence that a polymorphism in the clock gene PERIOD3 may modulate some

of the non-visual responses to blue-enriched light in the evening including its effects on sleep.

These results seem to indicate that the regulation of human neuroendocrine, alerting and neurocognitive responses to light are far more complex and nuanced than initially thought. In a broader perspective, this should increase our awareness of the impact of both natural and artificial light for human health and societal well-being.

Disclosure: Nothing to disclose.

Brain Histamine in Narcolepsy: Neurobiological and Therapeutic Implications

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Increase of histaminergic tuberomammillary neurons in narcolepsy

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Objectives: Narcolepsy is caused by loss of the hypothalamic neurons producing the orexin/hypocretin neuropeptides. One key target of the orexin system is the histaminergic neurons of the tuberomammillary nucleus, an essential wake-promoting system. As cerebrospinal fluid histamine levels may be low in patients with narcolepsy, we examined histaminergic neurons in patients with narcolepsy and in 2 mouse models of narcolepsy.

Methods: We stereotaxically counted the number of hypothalamic neurons producing orexin, melanin-concentrating hormone, and histamine in 7 narcolepsy patients and 12 control subjects. We also examined these systems in 6 wild-type mice, 6 orexin/ataxin-3 transgenic mice, and 5 orexin ligand knockout mice.

Results: Compared to controls, narcolepsy patients had 94% more histaminergic TMN neurons. This increase was higher in 5 narcolepsy patients with >90% orexin neuron loss than in 2 patients with <75% orexin neuron loss. Similarly, the number of histaminergic TMN neurons was increased 53% in orexin ligand knockout mice, whereas orexin/ataxin-3 transgenic mice showed an intermediate 28% increase. Another research group (John, et al, 2013) has found similar changes in patients with narcolepsy.

Conclusions: This surprising increase in histaminergic neurons in narcolepsy may be a compensatory response to loss of excitatory drive from the orexin neurons and may contribute to some of the symptoms of narcolepsy such as preserved consciousness during cataplexy and fragmented nighttime sleep. In addition, this finding may have therapeutic implications, as medications that enhance histamine signaling are now under development.

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Novel therapeutic approach in narcolepsy: clinical trials of an antagonist/inverse agonist of the histamine H3 receptor

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We assessed the efficacy and safety of Pitolisant, a selective histamine H3 receptor inverse agonist activating histamine neurons, in narcolepsy.

We randomly assigned 95 adult patients with narcolepsy, free of psychostimulants for at least 14 days and with EDS (Epworth Sleepiness Scale-ESS ³ 14/24) to Pitolisant (20 or 40 mg), Modafinil (200 or 400 mg) or Placebo given *per os* daily during an 8-week double-blind phase. A 3-week individual titration was followed by a 5-week stable dose and then, 1-week withdrawal phase. Primary outcome was ESS improvement with Pitolisant compared to Placebo (superiority) or Modafinil (non-inferiority). Secondary outcomes were EDS assessed by Maintenance of Wakefulness Test-MWT and Sustained Attention to Response Task -SART, cataplexy frequency, and adverse events including withdrawal syndrome occurrence.

At week 8, a significantly better mean change in ESS adjusted for baseline was observed in the Pitolisant group compared to Placebo (5.8 vs. 3.4, $P = 0.024$); with no significant change compared to Modafinil but non inferiority was not reached. Responders to treatment (ESS $\leq$ 10) were 13.3%, 45.2% and 45.5% for Placebo, Pitolisant and Modafinil. Significant EDS improvement was confirmed on MWT and SART for Pitolisant vs. Placebo, without significant difference with Modafinil. Cataplexy frequency was reduced in the Pitolisant group only. No serious adverse events and no withdrawal syndrome occurred with Pitolisant but 10% of patients taking Modafinil.

Pitolisant once-a-day was efficacious on core symptoms of narcolepsy and well tolerated. It offers a new therapeutic opportunity for this disease.

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Sleep Analysis: from Animals to Humans

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Central and peripheral metabolic changes induced by gamma-hydroxybutyrate

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Gamma-hydroxybutyrate (GHB) was originally introduced as an anesthetic but became a substance of abuse by bodybuilders first, then a recreational or club drug. Sodium salt of GHB is currently used for the treatment of cataplexy in narcolepsy patients. The mode of action and metabolism of GHB is not well understood. Although GHB is an agonist of GABAB receptors, high doses of GHB are supposed to be metabolized to GABA with divers behavioral effects. GHB stimulates growth hormone release in humans and induces weight loss in treated patients, suggesting an unexplored metabolic effect.

In different experiments the impact of GHB administration on central (cortex) and peripheral (liver) biochemical processes involved in the metabolism of the drug, as well as the effects of the drug on metabolism were evaluated in mice.

Respiratory ratio decreased under GHB treatment, independent of food intake, suggesting a shift in energy substrate. GHB treated C57BL/6J and GABAB null mice but not ob/ob mice gained less weight than matched controls. GHB dramatically increased corticosterone level but did not affect growth hormone or prolactin. Metabolome profiling showed that an acute high dose of GHB did not increase the brain GABA level. Both in the brain and liver, GHB was metabolized into succinic semialdehyde by hydroxyacid-oxoacidtranshydrogenase. Interestingly, in spite of glucose availability, brain preferentially used other sources of energy. Chronic administration decreased s-adenosylhomocysteine, oxidized gluthathione, and increased omega-3 fatty acids.

Our findings indicate unexpected metabolic changes with important protective effects for GHB.

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Baclofen enhances sleep, improves functional recovery and promotes neuroplasticity after stroke in rats

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Objectives: Sleep disruption in the acute phase after stroke has detrimental effects in both humans and animals. Conversely, the effect of sleep promotion is unknown. Baclofen (Bac) is a known NREM sleep promoting drug in both humans and animals. The aim of this study was to investigate the effect of Bac in a rat model of focal cerebral ischemia (isch).

Methods: 24 h after induction of stroke (MCAo) rats were treated with Bac (10 mg/kg) or saline and then twice daily during 10 consecutive days. Three groups of rats were designed: Bac/isch, saline/isch and Bac/sham. Sleep was assessed by EEG recordings and sensorimotor function by single pellet reaching test (SPR). To identify potential underlying mechanisms, axonal sprouting and neurogenesis were evaluated. Brain damage was assessed by Nissl staining.

Results: Repeated Bac treatment after MCAo affected sleep, motor function and neuroplasticity but not the size of brain damage. NREM sleep amount was increased significantly during the dark phase in Bac/isch compared to saline/isch group (days 2, 6 and 11). SPR performance dropped to 0 immediately after MCAo in both ischemic groups and recovered slowly thereafter. However, Bac-treated ischemic rats performed significantly better than saline-treated animals. Axonal sprouting in the ipsilesional motor cortex and striatum, and neurogenesis in the peri-infarct region were significantly increased in Bac/isch group.

Conclusion: Delayed repeated Bac treatment after stroke increased NREM sleep and promoted both, neuroplasticity and functional outcome. These data support the hypothesis of the role of sleep as a modulator of post-stroke recovery.

Disclosure: Nothing to disclose.

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A role for group-I metabotropic glutamate receptors (mGluR1/5) in sleep-wake regulation

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Objectives: Glutamate signalling is tightly controlled across the sleep-wake cycle. Studies in humans revealed enhanced availability of subtype 5 metabotropic glutamate receptors (mGluR5) after sleep deprivation (SD). This increase positively correlated with SD-induced subjective sleepiness and the rebound in EEG delta power in recovery sleep, indicating that mGluR5 contributes to sleep homeostasis. To further study the roles of mGluR5 in sleep-wake regulation, we examined the effects of genetic ablation of mGluR5 on sleep and locomotor activity and the possible compensatory effects on mGluR1 expression in mice.

Methods: EEG/EMG recordings in baseline and recovery from a 6-h SD, and behavioral adaptation to environmental changes by measuring 11-day-locomotor activity after separation and cage changing with infrared sensors were quantified in wild-type (WT), heterozygous (Het), and mGluR5 knock-out (KO) animals (n = 2–11/genotype). Whole brain mGluR1 expression was quantified by qPCR.

Results: Compared to WT littermates, mGluR5 KO showed a significantly attenuated build-up of EEG delta power during wakefulness, both during undisturbed baseline and SD. KO mice also exhibited reduced locomotor activity in the dark phase across 1 week, while the other two genotypes did not ($F_{18,174}$ = 2.6, P = 0.0006) evidence of reduced capacity to adapt to a novel environment. Up-regulated mGluR1 mRNA was found in KO compared to WT.

Conclusions: Deletion of mGluR5 in mice importantly affects sleep homeostasis. Whether compromised adaptation to environmental changes could be related to impaired sleep-wake regulation or other possible underlying causes will be determined in ongoing studies.

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Sexual arousal, a role of histamine and orexin neurons

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Objectives: Sexual arousal ensures the necessary waking state, allowing anticipation/performance of sexual activities and so is a prerequisite for reproduction. We hypothesize that a full expression of such a behavioral state requires optimal activities of the brain arousal systems notably histamine (HA) and orexins (Ox) neurons.

Methods: Wild-type, histidine-decarboxylase (hdc) or/and Ox-knock-out (KO) mice were chronically implanted for sleep-wake monitoring under baseline conditions (12 h light/dark cycle) and during the sexual arousal test, which consisted of placing during 4 h a female mouse into the home cage of a male, the two mice being separated by a transparent plexiglass. Sexual arousal is defined as increased wakefulness (W) in the male mice.

Results: The presence of a female mouse elicited in the male a significant increase in W. This increase is not significant if another male was introduced. Ovariectomized or Tamoxifen (estrogen receptor antagonist)-pretreated female mice did not elicit sexual arousal in male animals. Male mice pretreated with androgen receptor antagonist Flutamide did not show any increased W facing a female. Acute application of HA synthesis inhibitor or Ox1-receptor antagonist abolished sexual arousal. Finally, whereas sexual arousal was intact in hdc or Ox KO mice, it was totally absent on double KO mice lacking both HA and Ox.

Conclusions: Both the HA and Ox systems, most likely driven by sex hormones, promote sexual arousal. Chronic HA or Ox loss could be compensated by up-regulated adaptive mechanisms, which become ineffective when both HA and Ox were deficient.

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Scoprism: a new algorithm for automatic sleep scoring in mice

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Objectives: Scoring of wake-sleep states by trained investigators is a time-consuming task in many sleep experiments. We aimed to validate SCOPRISM, a new open-source algorithm for sleep scoring based on automatic graphical clustering of epoch distribution.

Methods: We recorded sleep and blood pressure signals of 36 narcoleptic mice, 7 leptin knock-out mice, and 43 wild-type control mice in the PRISM laboratory. Additional groups of mice (n = 13) and rats (n = 6) recorded in independent labs were used to validate the algorithm across laboratories.

Results: The overall accuracy, specificity and sensitivity values of SCOPRISM (97%, 95%, and 94%, respectively) on PRISM lab data were similar to those calculated between human scorers (98%, 98%, and 94%, respectively). Using SCOPRISM, we replicated the main sleep and sleep-dependent cardiovascular findings of our previous studies. Finally, the cross-validation analyses showed that the SCOPRISM algorithm performed well on mice, and better on mouse than on rat data.

Conclusions: We (cross) validated SCOPRISM, a new, automated and open-source algorithm for sleep scoring on a large population of mice, including different mutant strains and 2 subgroups of mice recorded by independent labs. SCOPRISM is a very simple algorithm with the possibility to evaluate its efficacy following a quick and easy visual flow chart. This algorithm may help accelerate basic research on sleep and integrative physiology on genetically-engineered mice.

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EEG slow-wave characteristics in sleep after daily torpor in Djungarian hamsters

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Objectives: In Djungarian hamsters the initial slow-wave activity (EEG power in the 0.5–4.0 Hz band; SWA) immediately following an episode of daily torpor is consistently enhanced above values obtained during a day without torpor, reminiscent to the SWA increase after sleep deprivation (SD). It is unknown whether the mechanisms are similar.

Methods: Individual EEG slow-waves recorded from the parietal cortex in adult male Djungarian hamsters (n = 8, 8:16 LD) during the initial NREM sleep after torpor were analyzed. For comparison, a baseline day period with a similar amount of NREM sleep (50.0 ± 3.4 vs 44.9 ± 4.9 min, n.s.) and brain temperature (34.9 ± 0.2 vs 34.9 ± 0.2 °C, n.s.) was chosen. We identified slow-waves as negative deflections of the filtered (0.5–4 Hz) EEG below a zero-line.

Results: SWA during NREM sleep was higher after torpor (150.1 ± 11.2 vs 108.0 ± 7.1, % of a mean 8-h light period value, $P = 0.017$). Slow-wave incidence, amplitude and duration were higher after torpor compared to baseline (by 21.9 ± 8.1, 7.2 ± 2.0 and 3.9 ± 1.5% respectively, $P < 0.05$), suggesting that the SWA increase is mainly due to more frequent incidence of EEG slow-waves. We then matched baseline and torpor slow-waves according to amplitude and compared their up- and down-ward slopes. Interestingly, the slopes during baseline and after torpor were virtually identical ($P = 0.83$ and $P = 0.24$ for up- and down-slopes respectively).

Conclusions: This finding is in contrast with the steeper slope of slow-waves after SD reported earlier in rats. Therefore, our data suggest that mechanisms underlying increased NREM sleep SWA after torpor may differ from those after SD.

Disclosure: Nothing to disclose.

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Characterisation of the development of sleep disturbances in the unpredictable chronic mild stress murine model of major depression

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Objectives: There is growing evidence of a bidirectional relationship between sleep disturbances and major depression (MD). Our aim was to characterise the time-course of the emergence of sleep disturbances and the depressive-like symptoms in a murine model of MD.

Methods: Male, adult, BALB/c mice were subjected to a 9-week unpredictable chronic mild stress (UCMS) paradigm, consisting of daily exposure to social and environmental mild intensity stressors in a randomised way. The UCMS-induced physical and behavioural effects were compared with an undisturbed control group (n = 9/group). EEG/EMG recordings (48-h) were performed weekly. Preliminary analyses of sleep data (n = 7/group) were carried out on 24-h recordings performed at baseline (i.e., before UCMS), as well as after 2 and 5 weeks of UCMS.

Results: The UCMS paradigm induced a decrease of self-care and motivational behaviour respectively after 1 and 2 weeks of UCMS, which is characteristic of a depressive-like disorder. Preliminary analyses showed a substantial increase in REM sleep appearing after 2 weeks (only in the 12-h light period) and 5 weeks (24-h) of UCMS, compared to the control group. Furthermore, while the UCMS group displayed an increase in NREM sleep during the dark period after 5 weeks, a reduction was observed during the light period, with concomitant changes in wakefulness.

Conclusions: The current study suggests that this paradigm represents a promising translational model of the emergence of sleep disturbances in MD. Analyses are ongoing to further characterise the time-course of sleep alterations and other behavioural and neurochemical changes induced by the UCMS paradigm.

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Slow wave activity and cerebral blood flow are anti-correlated during sleep

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Objectives: Simultaneous EEG-fMRI recently has been used to localize sleep-associated brain activity. However, no study employed arterial spin labelling (ASL)-MRI during sleep (measure of absolute cerebral blood flow; CBF).

Previous EEG-PET studies described negative regional CBF correlations with slow-wave activity (SWA; spectral power 1–4.5 Hz; indicator of non-REM sleep intensity) in (pre)frontal areas [1].

Thus, we investigated CBF and its relation to slow-wave activity (SWA) using EEG-ASL.

Methods: Healthy males (4 h sleep restriction the night before) were instructed to sleep while 64 channel-EEG and ASL-MRI were simultaneously recorded at 3T.

EEG data were pre-processed (standard procedures) and remaining artefacts removed (independent component analysis). C3A2 power spectra of cleaned data were computed at scan midpoints. ASL images were realigned, CBF images calculated with in-house MATLAB scripts [2], co-registered with individuals anatomical images and normalized to standard space.

Time courses of SWA and each voxels' CBF were smoothed, detrended and correlated.

Results: Preliminary analysis revealed negative CBF correlations with SWA, mainly in the (pre)frontal cortex ($r = -0.2$ to -0.6, Bonferroni correction $P < 0.01$). Positive CBF-SWA correlations appeared in a small occipital cluster ($r = 0.2$ to 0.6, Bonferroni correction $P < 0.01$).

Conclusions: Consistent with above-mentioned study, CBF and sleep SWA were largely anti-correlated, pointing to reduced CBF during NREM sleep. Reduced energy consumption by the neuronal burst firing underlying slow wave generation might explain these negative correlations.[1] Dang-Vu TT et al., Neuroimage 2005:28:14 [2] Wang J et al., Magn Reson Med 2003:49:796

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Dynamics of human cortical ensembles are set by circadian system and sleep homeostasis

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Objectives: Animal and human studies indicate linear alterations in inhibitory/excitatory neurotransmission during sleep and wakefulness, suggesting an exclusive sleep homeostatic influence. However, recent data posit a circadian, non-linear influence on neuronal function. We investigated whether this circadian drive impacts on human brain function in vivo.

Methods: We applied neural mass models using dynamic causal modeling (DCM), a Bayesian technique for neuronal identification, to transcranial magnetic stimulation (TMS)-evoked EEG signals from the prefrontal cortex (PFC, highly sensitive to sleep pressure). Twenty-two healthy young participants (18–30y) underwent 8 TMS-EEG recordings, during 28-h of sustained wakefulness, under stringent constant routine conditions. All significant effects are $P_{corr} < 0.05$.

Results: Using DCM, we estimated GABAergic/glutamatergic functions, inhibitory/excitatory drives, and inhibitory/excitatory action potentials across PFC neuronal subpopulations. Overall control (self-inhibitory gain) within superficial pyramidal cells and inhibitory interneurons decreased with time awake, with nadir and peak in the circadian evening wake-maintenance zone and early morning sleep-maintenance zone, respectively. Conversely, GABAergic function and inhibitory action potentials across neuronal subpopulations increased with time awake, with local decrease and increase during wake- and sleep-maintenance zones, respectively. Excitatory action potentials slightly increased with time, with local decrease in the wake-maintenance zone. All time-courses were best predicted by the interaction of sine-wave (circadian) and linear (sleep homeostasis) functions.

Conclusions: Our results provide a proof-of-principle that inhibitory/excitatory changes in neuronal subpopulations reflect the interaction of circadian system and sleep homeostasis. Ultimately, the data provide a unique window on the hidden neuronal milieu setting the temporal organization of human brain function.

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Sleep and psychiatric disorders: a meta-analysis of the last 20 years of research

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Objectives: Sleep disturbance is common in psychopathology. Nevertheless the sleep changes associated to the most prevalent mental disorders are not fully understood. The aim of this study was to conduct a meta-analysis of polysomnographic (PSG) studies in patients with different mental disorders.

Methods: This meta-analysis was conducted in accordance to the MOOSE guidelines. PSG studies evaluating patients with different mental disorders compared to healthy controls were identified through a search in Pubmed and PsycInfo databases from 1992 to 2012. Keywords included PSG, sleep architecture, sleep recordings or sleep stages and key search terms for mental disorders. Effects were summarized using standardized mean differences and pooled with the random-effect model. Subgroups analyses were conducted to observe the effect of sex, age and comorbidity with other mental disorders.

Results: Our final sample included 98 PSG studies conducted with patients with affective (43); anxiety (19); ADHD (9); schizophrenia (8); autistic (6); eating (5); borderline personality (5); and Asperger syndrome (3) disorders. All conditions, excluding ADHD, were associated with PSG alterations. No sleep parameter was found to be specifically impaired in only one condition, except REM density which was altered only in affective disorders. Single disorders, in the absence of any comorbidity, were associated with less sleep disturbances compared to studies that included comorbidities.

Conclusions: The results support the notion that sleep is an important dimension for brain and mental health. Psychiatric clinical practice may benefit from the inclusion of sleep quality interventions in the treatments of the most prevalent mental disorders.

Disclosure: Nothing to disclose.

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Implementation of dynamic lighting in a nursing home: impact on agitation

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Objectives: Disturbances of circadian rest-activity rhythms in demented patients often culminate in the clinical problem of evening and nighttime agitation. The aim of the current study was to test the impact of a dynamic lighting system on agitation and rest-activity cycles.

Methods: From midwinter 2012 on, a ceiling mounted dynamic lighting system was installed in the dayroom and programmed to produce high illuminance with higher blue light proportions during the day and lower illuminance without blue light in the evening. Thirteen residents with dementia were regularly assessed with the Cohen Mansfield Agitation Index (CMAI), completed by trained nursing stuff. Additionally, rest-activity cycles were continuously monitored for 6 months by a wrist worn activity watch. Preliminary analysis of the activity data 2 weeks before and 2 weeks after the dynamic lighting installation was performed by using the Wilcoxon-Test for matched pairs (before vs. after the lighting installation).

Results: The dynamic lighting significantly reduced the CMAI sum-scores from 30.2 ± 5.1 to 27.9 ± 2.6 (mean $\pm$ SD; $N = 12$; $P < 0.05$). Analysis of the CMAI sub-scores revealed that under the dynamic lighting mainly non-physically aggressive behaviors were reduced. Preliminary results from the rest-activity analysis did not show differences of circadian amplitude, and other circadian variables before and after the lighting installation.

Conclusions: The dynamic lighting in the living room significantly reduced agitated behaviour in demented patients, indicating short-term benefits from higher daily light exposures. Whether such lighting impacts also on long-term (circadian) rest-activity cycles needs to be further analyzed .

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Sleep-disordered breathing in the acute phase of transient ischemic attack and minor stroke

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Objectives: Obstructive sleep apnea represents an independent risk factor for cerebrovascular events. Here we describe the clinical and sleep related respiratory features of a consecutive series of patients with acute minor ischemic stroke (MS) or transient ischemic attack (TIA) enrolled in a previous cross-sectional study (Ciccone et al., Thorax 2013).

Methods: We prospectively considered patients admitted to 13 stroke units for acute MS or TIA submitted to a cardio-respiratory sleep study within 10 days of the onset of symptoms.

Results: We enrolled 356 patients. A Sleep Disordered Breathing (i.e. apnea hypopnea index >5, SDB) was found in 67.7% of patients.

The SDB was prevalently obstructive in 153, mixed in 55 and central in 33 patients. Non parametric statistical analyses (Kruskall-Wallis, Mann-Whitney, Chi-Square tests) revealed different variables significantly associated with SDB: age, male gender, oral anatomy according to Mallampati, body mass index, neck circumference, neurological deficits, previous cardiovascular events, hypertension, diabetes, hypercholesterolemia, carotid artery stenosis, and high risk of SDB at the Berlin questionnaire.

Patients with a pure central SDB (33 subjects) did not show a statistical significant association with hypertension, diabetes and a high risk of SDB at the Berlin questionnaire.

Conclusions: Our data show a high prevalence of SDB during the acute phase of a mild cerebrovascular event. The presence of a SDB should be investigated in patients admitted in a stroke unit, especially in subjects with a history of hypertension, diabetes, previous cardiovascular events and a high risk of SDB at the Berlin questionnaire.

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Sleep and gastrointestinal cancer risk in the MCC-Spain case-control study

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Objectives: Sleep duration is a modifiable risk factor associated with mortality and possibly cancer risk in humans. A few studies suggest that both long and short sleep may increase risk of colorectal cancer. In this large population based case control study we evaluated sleep duration but also sleep quality and timing with relation to gastrointestinal (colorectal and gastric) cancer risk in both sexes.

Methods: 1731 colorectal, 483 gastric cancer cases and 3940 randomly selected population controls, enrolled in 11 Spanish regions, were included. Information on habitual sleep duration, quality and timing, as well as shift work history, socio-demographic and lifestyle factors was collected by face-to-face interviews. We used unconditional logistic regression analysis adjusting for potential confounders.

Results: We found a U-shaped association between sleep duration and gastrointestinal cancer ($P < 0.001$). Both long ($\geq$9 h; OR 1.64; 95% CI 1.37–1.97) and short ($\leq$5 h) sleep duration (OR 1.12; 95% CI 0.94–1.35) increased gastrointestinal cancer risk, compared to 7 h sleep per night. ORs for long sleep were 1.61 (95% CI 1.33–1.95) for colorectal and 1.77 (95% CI 1.27–2.47) for gastric cancer, respectively. Sleep onset after 2:00 h was associated with a higher risk for gastrointestinal cancer (OR 1.36; 95% CI 1.09–1.70).

Conclusions: In this large population based study we found an increased gastrointestinal cancer risk associated with both long and short sleep and late sleep onset.

Disclosure: Nothing to disclose.

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Chronotype in adult epilepsy patients: a questionnaire and DLMO determination based study

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Objectives: This study aimed to assess chronotype in adult epilepsy patients and to evaluate the associations between the chronotype and disease and demographic features.

Pateints and methods: Sixty adults (46.5 $\pm$ 13.85 years of age; 27 males), 80.8% diagnosed with focal (63.5% temporal lobe; 17.3% extratemporal lobe) and 19.2% with undetermined epilepsy; 33.3% pure sleep, 26.6% wake and 30.0% random seizures; 83.3% seizures free, all on AEDs treatment, were investigated with Morningness-Eveningness Questionnaire (MEQ) and an at-home 5-point salivary melatonin semicurve. Healthy subjects matched for age and sex served as controls.

Subject groups were compared using univariate analyses.

Results: Epilepsy patients significantly differed from controls for: Morningness chronotype (50.0% vs. 31.7%; $P = .03$); Mid sleep on working days (MSwd; 2:57 $\pm$ 0:51 vs. 3:21 $\pm$ 0:38; $P = .006$) while they didn't differ for: Mid sleep on free days corrected for sleep lenght (MSfdC; 3:34 $\pm$ 0:54 vs. 3:52 $\pm$ 0:48); Social jet lag (1:17 $\pm$ 1:01 vs. 1:12 $\pm$ 0:52) Pitsburgh score (5.0 $\pm$ 3.3 vs. 4.9 $\pm$ 3.1)

Mean DLMO in epilepsy patients was determined at 21:38 $\pm$ 1:21 (range 19:01–1:08) and significantly correlated with MEQ score ($r = -0.42$ $P = .001$) and MSfdC ($r = 0.49$; $P = .001$).

Epilepsy subjects with morningness chronotype were older (51.1 $\pm$ 13.5 vs. 41.9 $\pm$ 12.8, $P = .009$) and showed less Social Jetlag (0:53 $\pm$ 0:59 vs. 1:38 $\pm$ 0:55, $P = .006$).

Discussion: Our findings are in line with literature showing that epilepsy patients are morning oriented people. DLMO consistently correlates with the subjective measures of chronotype. Morningness epilepsy patients are older and their sleep schedule does not vary significantly between working and free days.

Disclosure: Nothing to disclose.

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Insomnia and nightmares and associations with PTSD and depressive symptoms among the survivors from the Norwegian terror 22/7 2011 attack on Utøya

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The 2011 attack at Utøya was a national tragedy where 69 people were killed, most of them adolescents. The objective of this study was to describe the long-term effects of the incident on the prevalence of insomnia and nightmares, and associations of psychiatric disorders among the survivors.

Methods: 33 survivors of the Utøya attack and 39 controls, age-/gender and socio-demographic matched, partcipated 18–30 months after the attack. Insomnia was assessed by BergenInsomniaScale and questions taken from sleep and dream diaries were employed. Psychiatric symptoms were evaluated in 20 survivors by using MINI.

Results: Prevalence of insomnia was 57.1% among survivors and 20.5% in controls ($P < 0.001$). Survivors reported shorter sleep duration ($P < 0.01$), difficulty to fall asleep ($P < 0.001$), distress/impairment in social/occupational/educational life due to excessive sleepiness ($P < 0.001$) and were more unsatisfied with their sleep ($P < 0.001$) than controls. In the subgroup of survivors, insomnia was present in 83.33% with recurrent depression, 80% with panic disorder and 75% with PTSD. Nightmare was reported by 82.2% of the victims, consisting of more negative content (42.8%) and strong feelings (57.1%) vs 59.0%, 28.2% and 2.5% in controls ($P < 0.05$, $P < 0.001$ and $P < 0.05$, respectively). In the subgroup, all those who reported nightmares were diagnosed with recurrent depression, panic disorder and/or PTSD. One survivor, no controls used hypnotics.

Conclusions: Survivors report more insomnia and nightmares 18–30 months after the Utøya attack compared to controls. Insomnia and nightmares were highly present in the survivors diagnosed with depression, panic disorder and PTSD.

Disclosure: Nothing to disclose.

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Blocking blue light during mania; markedly increased regularity of sleep and rapid improvement of symptoms: case reports from an ongoing randomized controlled trial

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Objectives: Mania is difficult to treat and pharmacological treatment is still insufficient. Irregular sleep is a core symptom of mania. Recently, blocking blue light by means of wearing orange-tinted glasses has proved a promising new treatment option. Here, we present two case reports illustrating the effectiveness of blue-blocking treatment in improving sleep and reducing manic symptoms.

Methods: Case 1: A woman (38) wore blue-blocking glasses (14 h/7 days) in addition to pharmacological treatment, during two separate manic episodes.

Case 2: A man (58) in a manic state wore clear-lensed glasses as control-condition (14 h/7 days), followed by 6 days of the blue-blocking regime.

Outcome measures were Young Mania Rating Scale (YMRS) ratings and actigraphy.

Results: In case 1 YMRS scores declined by 32% and 71% during the two repeated interventions respectively. In case 2 YMRS scores declined by 90% during the blue-blocking condition.

Comparing the week of control condition with the last 3 days of blue-blocking for case 2, night-sleep declined from 527 ± 160 to 419 ± 21 min, day-sleep declined from 24 ± 36 to 6 ± 10 min. Average motor activity/min during night-sleep declined from 14 to 7. The standard deviation of 'sleep start' and 'sleep end' declined from 116 to 12 and from 62 to 16, respectively. Similar results regarding changes in sleep and symptoms of mania were reproduced with an interval of 18 months for case 1.

Conclusions: These cases highlight the close interconnection between light, sleep and manic symptoms, and support the effectiveness of blue-light blocking in treatment of mania.

Disclosure: Nothing to disclose.

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Sleep and circadian rhythms in the bipolar phenotype: a comparison of high-risk individuals defined by hypomania or a family history of affective disorders

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Objectives: To compare sleep and circadian characteristics of medication-naïve individuals identified by different risk factors for mood disorder; either elevated risk by family history or symptoms of hypomania.

Methods: Two groups considered to be at high-risk of developing mood disorder were separately defined and recruited: Hypomania-group scored high (7–12) on the Mood Disorder Questionnaire ($N = 19$) and the Genetics-group had a first-degree relative diagnosed with an affective disorder but were not being themselves affected ($N = 21$). Controls of Hypomania-group consisted of MDQ low scorers (0–2, $N = 21$) and controls of Genetics-group consisted of healthy, age-matched individuals ($N = 19$). Individuals with current or prior psychiatric disorder were excluded. All participants wore an Actiwatch-Light (1-min epoch) for 9–28 days and recorded daily activities in a diary. They were assessed for chronotype using the Morningness-Eveningness questionnaire. Genetics-group and their controls provided 48-h urine samples for melatonin analysis.

Results: Both groups had significantly more physical movements during sleep (i.e. as fragmentation index) than controls (mean: 35.7 ± 8.6 vs 30.0 ± 8.7 respectively, $P < 0.005$). Genetics-group had a later sleep onset compared to all other groups (0141 vs 0105, $P < 0.03$). All groups were similar in sleep latency, wake-up time, chronotype distribution and melatonin rhythm (Genetics-group and respective controls).

Conclusions: Significantly more physical movement during sleep is associated with a family history of mood disorder or a hypomania phenotype. If this sleep phenotype can be replicated in other vulnerable groups across the affective spectrum, it could become an important target for interventions to prevent onset of mood disorder.

Disclosure: Nothing to disclose.

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Association of sleep disorders with psychosocial factors in female population aged 25–64 years in Russia: MONICA-psychosocial epidemiological study

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Objective: To study the prevalence of sleep disturbances (SD) and its relation with other psychosocial factors in female population aged of 25–64 years in Russia (Novosibirsk).

Methods: Under the third screening of the WHO 'MONICA-psychosocial' (MOPSY) program random representative sample of women aged 25–64 years (n = 870) were surveyed in Novosibirsk. The response rate was 72.5%. Estimation of sleep was assessed by the questionnaire Jenkins. Chi-square test (χ^2) was used to asses the statistical significance.

Results: The prevalence of SD in the female population aged 25–64 years was 65.3%. Poor sleep associates with high personal anxiety more frequently (93.8%) than good sleep ($P < 0.01$). The rate of major depression was 4-fold higher in women with poor sleep ($P < 0.001$). Prevalence of high vital exhaustion as well as low close contacts index grows linearly with deteriorating quality of sleep ($P < 0.001$). Changes in marital status are 2-fold higher and conflicts in family are also increased in women with SD ($P < 0.05$). Those women rarely have the opportunity to relax at home ($P < 0.05$). With regard to job stress poor sleep is associated with stopping or reducing the additional work in 2-times higher. Women with SD in 3-times more likely to report decline in their working capacity and responsibility at work ($P < 0.001$).

Conclusions: The prevalence of SD in female population 25–64 years in Russia is high. SD often related to high personal anxiety and vital exhaustion, major depression, high job and family stress.

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301

Sleep quality in hospitalized medical patients: influence of light, noise, and switch to daylight saving time

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Objective: To assess sleep quality in a group of well-characterised medical inpatients, in relation to light/noise levels, and the switch to daylight saving time.

Methods: Between 1st March and 30th April 2013 (switch 31st March), 132 consecutive inpatients (76 ± 12 years; hospitalization: 9 ± 7 days) underwent daily sleep assessments by standard questionnaires/diaries; use of psychoactive drugs/hypnotics was recorded. They slept in double or quadruple rooms, all facing South, and were qualified as sleeping near/far from the window. Those whose stay included pre/post-switch days were excluded. Luminance was measured by a luxmeter placed at each patient's eye-level, four times per day (08.00, 14.00, 19.00, 24.00). Noise was measured at the same times, in the middle of each room, by a phonometer.

Results: Sixty-one patients provided reliable questionnaires/diaries, and they reported sufficient sleep quality and moderate daytime sleepiness. Those who slept near the window were exposed to more light in the morning (before switch: 214 ± 74 vs. 148 ± 69; after switch: 192 ± 71 vs. 135 ± 34 lux, $P < 0.001$) and slept better (before switch: 7.3 ± 1.8 vs. 5.9 ± 2.3; after switch: 7.8 ± 2.1 vs. 6.9 ± 1.9 on 1–10 scales, $P < 0.05$/ $P < 0.1$). Noise levels were higher than recommended for care units (>30 dB) but comparable across times, room type and before/after the switch. No significant differences were observed in sleep parameters before/after the switch. However, the percentage of days in which patients were administered hypnotics decreased (32 vs. 12%, $P < 0.02$).

Conclusions: Natural light may play a role in inpatient sleep quality and more attention to light/noise in hospital planning seems worthy.

Disclosure: Nothing to disclose.

Poster Sessions

Pharmacology and Biochemistry

P305

Side-effects of benzodiazepines in psychiatric outpatients

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Objective: Despite knowledge of possibility of developing dependence in long term use, and limited evidence to their efficacy, benzodiazepines continue to be among the most commonly prescribed drugs. The most common adverse effects are: drowsiness, sedation, dizziness and ataxia.

The purpose of this study was to determine the frequency of adverse effects of benzodiazepines in psychiatric outpatients.

Methods: The study included consecutive patients that attended outpatient unit at the 'Saint Nicolae' Hospital. Patients were asked to fill in the questionnaire on adverse effects of benzodiazepines.

Results: Of 78 patients that have participated in the study, 54% men. 80% of patients used benzodiazepines at least once in their lifetime, 64% of women and 93% of men. Benzodiazepines were used in the last seven days by 39% of women and 86% of men. The benzodiazepines most used were alprazolam 40%, and diazepam 20%. 10% of men used more than one benzodiazepine daily. The mean number of adverse effects in both men and women were 4.6. The most evident difference in side-effects was the high prevalence of dizziness in women (31%) and low in men (7%). One third of women and one quarter of men stopped using benzodiazepines.

The number of side effects was equal in those who stopped to use the drugs, and in those who continued the usage.

Conclusion: Outpatients use benzodiazepines too often. Although more than 90% of patients experience side effects, they continue the use of benzodiazepines.

Disclosure: Nothing to disclose.

P306

Off-label use of low-dose quetiapine and mirtazapine for insomnia is growing

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Objectives: Registered hypnotics, particularly benzodiazepines, have various disadvantages, like the rapid development of tolerance. In clinical practice low doses of sedative antipsychotics and antidepressants seem to be broadly prescribed to treat sleep disturbances. Since these drugs are not registered for such an indication, this is off-label use. The aim of this study was to investigate the prescription rate of low doses of quetiapine and mirtazapine and the characteristics of both patients and prescribers.

Methods: A large pharmacy prescription database was used (IADB.nl) containing data from 1994 to 2012, covering an estimated population of 600 000 patients. Off-label use was defined as once daily $\leq$100 mg quetiapine or $\leq$15 mg mirtazapine.

Results: Off-label doses were prescribed to 44.3% (3599/8127) and 37.1% (6587/17 745) of quetiapine, mirtazapine users respectively. The number of off-label prescriptions significantly increased over the years. Since a couple of years more patients start with quetiapine and mirtazapine in an off-label dose than a registered dose. Approximately 30% of the off-label quetiapine users and 60% of the off-label mirtazapine users had no psychiatric co-medication, suggesting that they are free of severe mental health problems. Prescriptions for these patients came predominantly from general practitioners.

Conclusions: The rising off-label use of low doses of quetiapine and mirtazapine, not only in psychiatric patients but also in healthy individuals, is worrying. Scientific evidence supporting these drugs as alternatives for registered hypnotics is limited. There is urgent need of studies investigating their (long-term) influence on sleep and next day functioning as well their side effects.

Disclosure: Nothing to disclose.

P307

The longer term effects of caffeine withdrawal

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Objectives: Caffeine ingestion before bed has been shown to lower the quality and quantity of sleep. Caffeine withdrawal may be suggested to help treat insomnia. Most studies have shown negative effects during the first few days of caffeine withdrawal including headaches, lethargy, and irritability. The present study investigated the effects of caffeine withdrawal over an extended period of several weeks.

Methods: Participants were 23 healthy young adult caffeine consumers. In addition to a caffeine consumption diary they recorded subjective evaluations of their day at 6 pm each day on a web based survey. The evaluations included headache symptoms, alertness, moods, sleep, and overall quality of daily functioning. Measures were collected daily for a baseline week of normal caffeine consumption, a week of gradual withdrawal, and four additional weeks of caffeine abstention.

Results: During the week of withdrawal reported headaches and sleep length increased while alertness and overall day quality decreased compared to baseline caffeine consumption. However, by the last week of abstention all of these measures had returned to be comparable to the baseline week.

Conclusions: From this initial pilot study of the longer term subjective effects of caffeine withdrawal it appears that if the initial negative effects of caffeine withdrawal can be tolerated, continued abstention brings daytime functioning back to baseline levels. Further studies including randomized placebo control trials using objective measures of sleep and performance are required to confirm these initial pilot findings.

Acknowledgement: Kristen Johansson carried out this study as part of her Psychology Honours degree.

P308

Assessment of tasimelteon efficacy in totally blind individuals with non-24-h sleep-wake disorder in the set study

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Objective: To assess the Safety and Efficacy of Tasimelteon (SET) in Non-24-Hour Sleep-Wake Disorder (Non-24). Tasimelteon, a circadian regulator, has specific and potent affinity for the MT_1 and MT_2 melatonin receptors. Tasimelteon is being developed to treat Non-24 in the totally blind, a serious circadian rhythm disorder with no EMA-approved treatment.

Methods: In the SET study (n = 84) patients were treated with either tasimelteon (20 mg) or placebo. Circadian period was assessed from urinary 6-sulfatoxymelatonin (aMT6s) and cortisol rhythms. Clinical endpoints included nighttime and daytime sleep measures and Clinical Global Impression of Change (CGI-C).

Results: Tasimelteon entrained the circadian clock more than placebo at month 1 (aMT6s: 20.0 vs. 2.6%; cortisol: 17.5 vs. 2.6%). Entrainment rate in a subset of patients who received ~7 months of tasimelteon treatment was 59% (10/17). Tasimelteon induced a greater clinical response (entrainment plus improvement on a Non-24 Clinical Response Scale; 23.7 vs. 0%), improved CGI-C (2.6 vs. 3.4), increased sleep in the worst quartile of nights (LQ-nTST; 57 vs. 17 mins), decreased daytime sleep in the worst quartile of days (UQ-dTSD; 46 vs. 18 mins), and corrected the midpoint of sleep timing (MoST) by 21 mins/day compared to placebo. Tasimelteon was safe and well-tolerated.

Conclusion: Tasimelteon entrained the circadian pacemaker in totally blind patients with Non-24 and improved multiple measures of sleep, wake, and global functioning. While SET was not designed to address the time to response, adequate treatment duration is likely to be important in clinical practice.

Disclosure: Sponsored by Vanda Pharmaceuticals.

P309

Assessment of maintenance of effect of tasimelteon in totally blind individuals with non-24-h sleep-wake disorder - RESET Study

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Objective: To assess the safety, efficacy, and maintenance of effect of tasimelteon (20 mg) in Non-24-Hour Sleep-Wake Disorder (Non-24) in the totally blind. Tasimelteon, a novel circadian regulator with selective agonist activity for MT_1 and MT_2 melatonin receptors, was previously shown to entrain the central pacemaker and improve sleep-wake measures in the SET study. Non-24 is a serious circadian rhythm disorder highly prevalent in the totally blind with no EMA-approved treatment.

Methods: In the **R**andomized-withdrawal study of the **S**afety and **E**fficacy of **T**asimelteon (RESET) twenty patients were treated with tasimelteon (20 mg) for 8 weeks in an open-label run-in phase and then randomized to placebo or continue tasimelteon treatment for 8 weeks. Circadian period was assessed from urinary 6-sulfatoxymelatonin (aMT6s) and cortisol rhythms. Clinical endpoints included nighttime and daytime sleep measures.

Results: Tasimelteon maintained entrainment compared to placebo (aMT6s: 90 vs. 20%; cortisol: 80 vs. 20%). Total nighttime sleep in the worst quartile of nights was 67.2 min longer and total daytime sleep duration was 59.4 min shorter in tasimelteon-treated compared to placebo ($P < 0.05$). The midpoint of sleep timing (derived from both nighttime and daytime sleep) increased 36 min in tasimelteon-treated patients ($P < 0.05$). Tasimelteon was safe and well-tolerated.

Conclusion: Tasimelteon entrained the circadian pacemaker in totally blind patients with Non-24. Discontinuation of tasimelteon treatment resulted in loss of entrainment and a simultaneous ~60 min decrease in nighttime sleep and an equivalent increase in daytime sleep. The RESET study demonstrates the necessity for continued tasimelteon treatment to maintain circadian entrainment in Non-24.

Disclosure: Sponsored by Vanda Pharmaceuticals.

Physiology

P310

First-night effect on heart rate variability and salivary cortisol secretion

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Objective: To investigate the impacts of 'the first-night effect' on autonomic nervous and endocrine systems during sleep and after awakening.

Method: Polysomnography recordings of 16 male students (aged 21–23 years) were performed on two distinct nights (from 0:00 to 6:00 a.m.) with a >3-day interval between the first night (FN) and the subsequent night (SN). Each subject's saliva was collected during sleep and after awakening by a saliva aspiration system we developed, with which saliva can be continuously collected throughout the night without disturbing the wearer's sleep.

Results: The subjects' polysomnographic profiles illustrated the first-night effect: their FN sleep efficiency was significantly lower than that on the SN ($P < 0.05$). The heart rate (HR) and the high-frequency component (HF) of HR variability in the former half of the night were significantly higher ($P < 0.05$) and lower ($P < 0.05$) on the FN compared to those of the SN. After awakening, HR and HF were significantly lower ($P < 0.05$) and higher ($P < 0.05$) on the FN compared to those of the SN. Salivary cortisol concentration during sleep was significantly higher in the former half of the FN compared to that of the SN ($P < 0.05$).

Conclusion: Enhancement of the hypothalamic-pituitary-adrenal and sympathetic nervous system (SNS) activation in the former half of the FN, and following predominant parasympathetic nervous system activation after awakening were observed in this study. Prominent psychological stress during the FN may cause these negative impacts on autonomic nervous and endocrine system during sleep, resulting suppressed spontaneous SNS arousal on awakening.

Disclosure: Nothing to disclose.

P311

Electroacupuncture of Feng-Chi acupoints on epilepsy-induced sleep alterations

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Objectives: This study investigated effects of low frequency (10 Hz) electroacupuncture (EA) of Feng-Chi acupoints on epilepsy-induced sleep disruptions and elucidated the role of amygdala opioid receptors.

Methods: Male Sprague-Dawley rats were used for electroencephalography (EEG) and sleep recordings. The 10 Hz EA was performed 30 min prior to the dark period in three consecutive days. Focal epilepsy was induced by microinjection of pilocarpine into the left central nucleus of amygdala (CeA) in the third experimental day. Co-administration of opioid receptor antagonists into amygdala was used to elucidate the role of opioid receptors.

Results: Administration of pilocarpine into CeA induced focal epilepsy and decreased both rapid eye movement (REM) sleep and non-REM (NREM) sleep. NREM and REM sleep respectively decreased from 50.5 $\pm$ 1.9% and 15.3 $\pm$ 1.3%, obtained from sham control rats, to 33.8 $\pm$ 3.2% ($P < 0.05$) and 8.9 $\pm$ 1.0% ($P < 0.05$) after administering pilocarpine. The 10 Hz EA of Feng-Chi acupoints significantly reversed epilepsy-induced decrease of NREM sleep to 45.8 $\pm$ 2.3% ($P < 0.05$ vs. the pilocarpine effect), but had no effect on the REM sleep disruption. The effect of 10 Hz EA on epilepsy-induced decrease of NREM sleep was blocked by microinjection of μ-receptor antagonist (naloxonazine) into the CeA, but was not affected by naloxone, κ- (*nor*-binaltorphimine) or δ-receptor antagonist (natrindole).

Conclusions: Our study suggests that 10 Hz EA of Feng-Chi acupoints exhibited benefit of improving epilepsy-induced sleep disruptions. Our results further demonstrate that μ-opioid receptors in the CeA mediated EA's effect on blocking epilepsy-induced sleep disruption.

Disclosure: Nothing to disclose.

P312

Auditory stimulation evokes slow oscillations and spindle activity

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Objectives: Recently, online phase locked paired sound stimulation has been used to enhance slow oscillations during sleep and to improve overnight memory recall. We wanted to confirm and extend these findings.

Methods: Total of 25 subjects were analyzed. Baseline night was followed by sound stimulation and sham stimulation nights in random order. In subset of 15 subjects EEG responses were correlated with overnight word pair memory recall performance.

Results: Only Cz referenced to the average of mastoids is reported here. Slow wave locked auditory stimulation caused significant difference in both negative and positive half wave of the following slow wave, when compared to the sham stimulus condition. Similarly, also the fast spindle activity was increased by sound stimulation during the positive phase of the slow oscillation following sounds. Both median and mean response analyses led to similar conclusions. There was no significant correlation between overnight change in amount of recalled word pairs and evoked delta or spindle activity.

Conclusions: Low level auditory stimulation evokes both delta and spindle activity. As mean and median provided similar results, it's unlikely that observed changes would be due to infrequent high amplitude events. Evoked changes in slow oscillations or fast spindles in initial analyses were not correlating with memory recall. Neural mechanism responsible for observed group level improvement (abstract: Huotilainen Minna et al.) remains to be resolved.

Disclosure: Nothing to disclose.

P313

The ABCB-1 genotype influences human sleep

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Objectives: The ABCB (MDR) 1-gene product P-glycoprotein is an integral membrane protein that actively translocates substrates out of the intracellular compartment. One of the major sites of its action is the blood-brain-barrier. It is highly expressed in brain capillary endothelial cells and involved in limiting the access of substrate drugs to the brain. A single nucleotide polymorphism (SNP) of the ABCB1-gene was identified by Uhr et al and showed a different treatment response to antidepressants depending on the genotype. We tested the hypothesis that healthy human subjects with different genotypes of that SNP will have different brain levels of sleep regulating endogenous substances resulting in differences of sleep electroencephalogram (EEG).

Methods: 40 young healthy volunteers participated in the study and were selected for their ABCB1-genotype (10 males TT, 10 males CC/CT, 10 females TT, 10 females CT/TT). After a night of adaptation sleep EEG was recorded from 23:00 to 07:00. It was analyzed by conventional and by quantitative analysis.

Results: In male subjects the time spent in rapid eye movement (REM) sleep (TT mean $\pm$ standard error of the mean [SEM] 90.3 $\pm$ 9.6 min vs. CC/CT 63.3 $\pm$ 7.8 min), wakefulness (TT 47.2 $\pm$ 9.7 min vs. CC/CT 85.0 $\pm$ 10.7 min) and total sleep time (TT 442.6 $\pm$ 10.2 min vs. CT 402.0 $\pm$ 14.9 min) differed between genotypes. In females no effect of genotype on sleep EEG was found.

Conclusions: Our findings suggest an influence of the ABCB-1 genotype on sleep regulation in male subjects.

Disclosure: Nothing to disclose.

P314

Spatio-temporal dynamics of micro-arousals in human: an intra-cerebral study

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The three main stages of vigilance classically described in human are wakefulness, NREM and REM sleep, each of them characterized by a specific brain activity. However, many clinical situations such as parasomnia or sleep inertia, and recent experimental works suggest that transitional stages can be observed. Micro-arousals appear as a relevant phenomenon to study brain ability to commute from a state of vigilance to another.

Using intra-cerebral recordings in 8 drug-resistant epileptic patients we studied EEG activity during « spontaneous » or nociceptive induced micro-arousals in NREM and REM sleep. Wavelet spectral analyses were performed to compare EEG signal before and during micro-arousals in the thalamus, and primary, associative or high order cortices.

First results show that spectral composition of EEG signal during micro-arousal significantly differs from that of sleep (NREM or REM) but also from that of wakefulness. Activity modifications related to micro-arousals exhibit high inter- and intra-subject reproducibility at the thalamic level whatever the condition considered (sleep stage or micro-arousal trigger). In contrast, cortical patterns of activation are much more variable, even in a same cortical area. The highest variability is observed for « spontaneous » micro-arousals during NREM light sleep in associative areas.

These results point to a high heterogeneity of cortical intermediate states between wakefuness and sleep and argue for local mechanisms of regulation of these transitional states.

Disclosure: Nothing to disclose.

P315

The consequences of gestational intermittent hypoxia on new born mice

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Introduction: Obstructive sleep apnea (OSA) is a public health issue. Pregnancy is associated with a high prevalence of OSA. However, the consequences of gestational OSA are unknown. We hypothesized that intermittent hypoxia (IH), characteristic of OSA, induces prenatal and neurodevelopmental abnormalities of cardiorespiratory and cognitive functions, which could be related to a systemic and tissue inflammation.

Methods: A classic model of IH was applied to pregnant mice using 5% FiO2, 30 cycles /h,10 h/day, during the last 10 days of gestation. The IH model was characterized by monitoring transcutaneous oxygen saturation and the mothers' weight. The pups' evaluation consisted of daily weighing, measuring cardio respiratory parameters at basal state and during hypoxic and hypercapnic challenges at 5 and 12 days of age. Cognitive functions were evaluated by the object recognition test (ORT) at 60 days of age. Cytokine assays was performed in serum and tissue samples (Merck Millipore ®, Magp-mag-24k -Billerica, Massachusetts).

Results: The IH induced oxygen desaturations and delayed weight gain in pregnant mice without showing inflammation. The study of IH exposed pups revealed 1 / transient respiratory anomalies such as an increase in basal normoxic ventilation (Ve, Ttot), 2 / a persistent growth retardation at all ages till 30 days and 3 / no differences in cognitive function.

Discussion: These results are consistent with the current literature and suggest an impact of IH. The prospects inspired by our work are the study of the consequences of a less severe IH model, closer to human pathology.

Disclosure: Nothing to disclose.

P316

Enhancement of nightlong salivary melatonin secretion by a feeble light exposure during sleep

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Objective: To investigate the effect of feeble light exposure on salivary melatonin secretion during sleep.

Method: Ten male university students (aged 20–25) who voluntary participated in this study were instructed to sleep in a laboratory room from 0:00 to 6:00 a.m. with each condition [feeble light (FL) or control] on two distinct nights in a counterbalanced order. In the FL, feeble

LED lighting (50 lx) was exposed to subjects in the midst of their sleep for 90 min (from 1:30 to 3:00). Each subject's saliva was collected during sleep and after awakening by a saliva aspiration system we developed, with which saliva can be continuously collected throughout the night without disturbing the wearer's sleep.
Results: Melatonin concentration significantly increased during the light exposure period in the FL comparing with the control ($P < 0.05$), and underwent relatively higher value in the FL than that of the control ($P < 0.1$) thereafter. The heart rate and the high frequency component of its variability was significantly higher ($P < 0.05$) and lower ($P < 0.05$) in the middle section of the lighting period (from 2:00 to 2:30) in the FL. There found no significant difference between the FL and control night in the scores of subjective questionnaires, which are POMS, PSS, and STAI taken before and after the sleep.
Conclusion: Our results suggest that exposure to feeble LED lighting can increase melatonin secretion, even though it was not so luminous to disturb subject's sleep, and it might involve enhanced cardio-sympathetic nervous activity.
Disclosure: Nothing to disclose.

P318

Cortical downstates and breakdown of causality within sleeping brain: an intracerebral study in humans

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Objectives: Recent studies suggest that during non-rapid eye movement sleep (NREM), when consciousness fades, the occurrence of hyperpolarized, silent down-states in cortical neurons may impair the ability of thalamocortical circuits to generate complex patterns of causal interactions, a theoretical requirement for consciousness.
Methods: To confirm this hypothesis and to deepen the mechanism underlying this phenomenon we perform single pulse electrical stimulation (SPES) and simultaneous intracerebral recording, during wakefulness and sleep, in 8 patients undergoing neurosurgical evaluation for intractable epilepsy. The resulting evoked potentials were then analyzed using time-frequency spectral analysis (Wavelet), and phase locking measures both at the single contact level (phase locking factor - PLF) and at all contacts level (phase locking value - PLV).
Results: Our results show that during wakefulness, SPES evoked a sustained response made of recurrent waves of activity characterized by different components (>4 Hz) persisting until 300–500 ms. Conversely, during NREM sleep SPES evoked one high amplitude and long lasting (300–600 ms) slow wave (< 4 Hz). This slow wave was associated with a suppression of EEG-gamma activity (>20 Hz) power, thus reflecting a cortical downstate, and was followed by a corresponding breakdown of synchronization both within a given contact (PLF) and between different contacts (PLV), reflecting a breakdown of causality.
Conclusions: These findings suggest that cortical downstate is a key mechanism responsible for the disruption of the causal structure of cortical networks during NREM sleep.
Disclosure: Nothing to disclose.

P319

Theta wave bursts during rapid-eye-movement sleep in histamine-deficient mice

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Objectives: We recently described the occurrence of short (1–2 s) high-amplitude and pointed theta wave bursts (7 Hz, TWB) during rapid eye movement sleep (REMS) in orexin (ORX) deficient narcoleptic mice (Bastianini et al., J. Sleep Res. 2012). Histamine produced by tuberomammilary neurons is a biogenic amine involved in wakefulness control. An alteration of the histamine system in narcolepsy-cataplexy is debated. We aimed to verify if impairment of histamine signaling leads to TWB during REMS.
Methods: Twelve histidine-decarboxylase knock-out mice (HDC-KO) with congenital deficiency of the histamine-synthetizing enzyme and eleven congenic wild-type (WT) control mice were instrumented with electrodes for sleep recordings. Three additional WT mice were also instrumented with a cannula for intracerebroventricular (icv) infusion of alpha-fluoromethyl-histidine (α-FMH, 15 μmol/Kg), an inhibitor of the histamine-synthetizing enzyme, or vehicle.
Results: TWB previously described in ORX-deficient narcoleptic mice occurred during REMS in 100% of HDC-KO mice. Similar EEG events occurred in a significantly lower fraction (9.1%) of WT mice and with a significantly lower occurrence rate (0.4 vs. 2.7 per hour of REMS). In HDC-KO mice, the occurrence rate of TWB significantly increased after 6 h of total sleep deprivation (5.1 per hour of REMS). TWB during REMS were also recorded in WT mice after icv infusion of α-FMH, but not of vehicle alone.
Conclusions: TWB during REMS are produced by an impairment of either ORX or histamine signaling.
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P320

Time structure of physiological hind-limb movements during sleep in rats and mice: toward rodent models of periodic limb movements (PLM) and restless legs syndrome (RLS)

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Objectives: Understanding the physiology of tibialis anterior muscle (TA) activity during sleep in rodents is necessary to develop rodent models of periodic limb movements (PLM) and the restless legs syndrome (RLS). We aimed to develop a common methodological approach for recording rodent TA activity and describe its time structure.
Methods: Eight wild-type rats and eight wild-type mice were implanted with electrodes for recording the electroencephalogram and electromyogram (EMG) of postural (neck) and bilateral TA muscles. Recordings were performed for >24 h on undisturbed and freely-behaving animals. An algorithm for computer detection of TA-EMG bursts was developed and validated against visual scoring by consensus between two investigators (A. Silvani and M. Manconi) of a total of 1883 TA-EMG bursts during non-REM sleep in the light period.
Results: The incidence of visually-scored TA-EMG bursts was similar for the left and right hind limbs and was higher for mice than for rats. The burst duration and inter-movement intervals were similar for mice and rats and had modes <1 s and 4–5 s, respectively. The algorithm for TA-EMG burst detection had a sensitivity of 91% and 87% and a false positive rate of 34% and 34% for mice and rats, respectively.
Conclusions: The methodological approach we developed resulted feasible and reliable for monitoring and computer-assisted detection of limb movements during sleep in rats and mice.
Acknowledgements: The project was supported by an International Short Visit grant of the Swiss National Science Foundation (to A. Silvani) and a grant from UCB-Pharma (to M. Manconi).

P321

Cholinergic basal forebrain structures are not essential for the mediation of the arousing action of glutamate

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Objectives: Cholinergic basal forebrain (BF) structures contribute to cortical activation and receive rich innervations from the ascending activating system. They are involved in the mediation of the arousing action of noradrenaline and histamine. Glutamatergic stimulation in the BF results in cortical acetylcholine release and suppression of sleep. However, it is not known to what extent the cholinergic vs. noncholinergic BF projection neurons contribute to the arousing action of glutamate (GLUT). To elucidate the roles of cholinergic BF structures, we administered *N*-methyl-D-aspartate (NMDA), a GLUT agonist into the BF in intact rats and after destruction of BF cholinergic cells by 192-IgG-saporin (SAP).
Methods: In 7 Han-Wistar rats with implanted EEG/EMG electrodes and guide cannulae for microdialysis probes 0.23 μg SAP was administered into the BF, the 7 control animals received artificial cerebrospinal fluid (CSF). Two weeks later a microdialysis probe targeted into the BF was perfused for 3 h with CSF on the baseline day and with 0.3 mM NMDA on the subsequent day. Sleep-wake activity was recorded for 24 h on both days.
Results: NMDA exhibited a robust arousing effect both in the intact and the lesioned rats. Non-REM sleep (intact rats baseline day: 59.6 $\pm$ 2.1%, NMDA day: 26 $\pm$ 4%; lesioned animals baseline day: 61.6 $\pm$ 3.6%, NMDA day: 25.2 $\pm$ 4.5%) and REM sleep (intact rats baseline day: 10.7 $\pm$ 1.3%, NMDA day: 2.4 $\pm$ 0.8%; lesioned animals baseline day: 11.5 $\pm$ 1.8%, NMDA day: 2.1 $\pm$ 0.7%) were decreased significantly during the 3-h NMDA perfusion.
Conclusion: Cholinergic BF structures are not essential for the mediation of the arousing action of GLUT.
Disclosure: Nothing to disclose.

P322

The circadian effect of light stimulation on rats' body temperature and heart rate

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Light has a powerful influence on behaviour and physiology. The study aimed to investigate any potent circadian effects on body temperature (BT) and heart rate (HR) following bright light exposure.
Method: Rats were exposed to a single 2 h blue or white light stimulation (1500 lux, both) 2 h pre dark(D)/active phase or 2 h pre light(L)/inactive phase. Peripheral BT and HR were telemetrically monitored 4 post days.
Result: Blue light reduced mean 24hBT values across days recorded (-0.09°C, $P > 0.01$; -0.42, -0.55, -0.51°C, $P < 0.001$ all). After a transient decrease, the mean 24hHR increased (-1.2 bpm n.s.; +20.5, 20.6 and 17.2 bpm, $P < 0.01$ all), changes particularly evident in inactive phase. White light induced a modest decrease in BT (-0.07, -0.08, -0.07, -0.12°C, $P < 0.01$ all) and in HR (-7.5, -8.6, -7.8 bpm, $P < 0.05$; -4.6 bpm, n.s).
Light exposure pre L altered BT post day 1 only. In inactive phase, blue light increased (+0.16°C, $P < 0.001$), while white light decreased BT (-0.20°C, $P < 0.001$). Blue light decreased HR all post days in active phase (-7.5, -7.4 bpm, $P < 0.001$, both; -5.6 and -5.2 bpm, $P < 0.01$ both). White light pre L did not change HR.
Conclusion: A single 2 h light exposure resulted in prolonged effect on physiological parameters, but only if light was given before the active phase. Blue light was more powerful than white light. BT decreased and HR increased. Blue light before inactive phase decreased HR and induced transient changes in BT. Circadian timing of light exposure has a significant effect on physiological measures in rats.
Disclosure: Nothing to disclose.

P323

Cardiac autonomic modulation is preserved during sleep in patients with spinal cord injury

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Objectives: Spinal cord injuries (SCI) are associated with an altered cardiovascular autonomic control. It has been established that sympatho-vagal balance varies across sleep stages. So far, no data are available on the effects of SCI on autonomic regulation during sleep. Therefore, we investigated changes of sympatho-vagal

balance during sleep in SCI patients, taking into account the level of the lesion.

Methods: Overnight polysomnographic (PSG) recordings were obtained in 27 patients with cervical (Cerv, $n = 12$) and thoracic (Thor, $n = 15$) SCI and in a group of healthy subjects (Controls, $n = 8$). ECG and respiration were extracted from PSG and divided into wake (W), non-REM 2 and 3 (N2 and N3) and REM sleep stages. Autonomic control was assessed by means of symbolic analysis (SA), a non linear tool that identifies three main indices, 0V%, index of sympathetic modulation, 2LV% and 2UV%, markers of vagal modulation.

Results: Total variability was reduced in SCI**.** SA showed a decrease of 0V%, marker of sympathetic modulation, in N2 and N3 compared to W and REM; an increase of 2LV% and 2UV%, marker of parasympathetic modulation, in N2 and N3 compared to W and REM was observed in SCI patients. These modifications were independent by the level of the lesion and similarly to Controls.

Conclusions: In SCI patients, cardiac autonomic control changed across sleep stages, with a reduction of sympathetic and an increase of parasympathetic modulation during NREM compared to W and REM, similar to Controls. Thus, cardiac autonomic dynamics throughout sleep stages are maintained in SCI.

Disclosure: Nothing to disclose.

P324

Dawn simulation light: a potential cardiac events protector

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We consciously control our sleep-wake timing, by the use of alarm clocks to wake-up in the morning. Increases of major cardiovascular events in the morning hours represent a common feature and are thought to be partially due to abrupt changes in the sympatho-vagal balance, namely sympathetic surges during the transition from sleep to wakefulness. Here, we explored whether a more gradient transition from sleep to wakefulness via a dawn simulation light around awakening has the potential to reduce morning cardio-vascular vulnerability.

After a night of 6-h sleep restriction, participants were awakened 2 h before their habitual wake-time. In a counterbalanced within-subject design, we applied a habitual auditory alarm clock or a dawn simulation light alarm clock (DSL) starting 30-min before and ending 30-min after scheduled wake-up time. Importantly, for both conditions participants remained in bed in a supine position until 30-min following their awakening. Seventeen healthy young men met the inclusion criteria. We observed a significant gradient reduction in heart rate during the transition from sleep to wakefulness when applying DSL as compared to the classical alarm clock. Likewise, Heart-rate-variability smoothly increased throughout the 30-min sleep episode preceding scheduled wake-up in the DSL condition.

Dawn simulation might protect the heart by an evolving preparation of cardiac physiology for the wake-up process. Application of a dawn simulation, which more closely approximates natural lighting conditions in the morning, might therefore be considered as an effective tool to help waking up reducing the cardiovascular vulnerability of the waking up process.

Disclosure: Nothing to disclose.

P325

Sleep spindles do not inhibit behavioural and cortical responses to nociceptive stimuli: a surface and intracerebral electrophysiological study

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Generated by thalamic reticular nuclei, sleep spindles are transmitted into the thalamo-cortical network during nonREM sleep. They are supposed to have a sleep-protecting role by inhibiting sensory inputs. The aim of the present study was to test their inhibitory effect on behavioural and cortical responses evoked by nociceptive stimulations. Two electrophysiological experiments were conducted, using surface recordings in 9 healthy subjects, and intracerebral recordings in 9 epileptic patients. Thermo-nociceptive stimulations, calibrated slightly above the individual pain thresholds, were delivered during the whole night. The presence of arousal reactions and the cortical responses were analysed in sleep stage 2, according to whether the stimulations were delivered during or apart from sleep spindles. Spindles were detected on fronto-parietal electrodes for surface recordings and within the thalamus for intracerebral ones.

In both studies, behavioural results showed no significant difference in arousal reactions proportions between the two stimulation conditions (during spindles 26%; apart from spindles 31%). Electrophysiological results showed that cortical evoked responses had comparable latencies and amplitudes whether the stimulations were delivered during or apart from sleep spindles. This was the case on surface recordings as well as on intracerebral ones in the posterior insula, known to systematically respond to nociceptive stimuli.

Thus, the hypothesis of a spindles inhibitory effect on sensory inputs, suggested by studies performed with auditory stimuli, does not apply to nociceptive ones. The specificity of spino-thalamic pathway, with few inhibitory modulations at thalamic level, and the crucial role of nociceptive information for homeostasis may explain these unexpected results.

Disclosure: Nothing to disclose.

P326

Exercise is associated with changes in sleep architecture during stress

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Objectives: Exercise is associated with good sleep but there is a lack of consensus. This study aims to investigate the stress-sleep-exercise connection further.

Methods: 28 teachers were recorded with PSG in their homes during a (predicted) high stress and a low stress condition (and a habituation night).

Results: On the day of the high stress PSG recording the participants exercised for 17.7 $\pm$ 3.7 min (median 15 min, range 0–60 min), 43% did not exercise at all that day and in the low stress condition for 23.4 $\pm$ 3.8 min (median 30 min, range 0–60 min), 21% reported 0 min of exercise. 60%, exercised for 30 min or longer during low stress and 32% during high stress condition. None of the PSG variables, including bedtime and time of rising, during the low stress condition was related to exercise. During high stress exercise duration was negatively related to TST ($r = -0.600$, $P < 0.01$), REM ($r = -0.511$, $P < 0.01$) and stage 2 ($r = -0.516$, $P < 0.01$). The

latter variables plus age, sex, BMI, bedtime and wakeup time were entered in a multiple stepwise regression. Only TST remained significant (adj R^2 = 0.37; F(1/25) = 16, 44; β = -, 221; $P < 0.001$).
Conclusion: Since bedtime and time of rising was adjusted for, it appears that high exercise activity is related to shorter sleep without shorter time in bed. TST between the two conditions did not differ. It is suggested that exercise is associated with shorter sleep during stress.
Disclosure: Prof. Åkerstedt reports consultancy fees from Astra Zeneca, Philips and Sanofis-Aventis, but unrelated to this project.

P327

EEG biomarker for pain sensitivity

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Objectives: Subjective or objective sleep quality is correlated with pain sensitivity and tolerance. Sleep restriction increases pain sensitivity and decreases pain tolerance. This study investigates potential biomarkers for the pain perception.
Methods: Healthy controls (n = 25; all male; age 28.4 $\pm$ 4.3, BMI 22.6 $\pm$ 2.2) attended a sleep center for polysomnography at baseline and after a week of sleep restriction (2 h bedding opportunities). In the following morning, resting EEGs without and with pain stimuli (capsaicin) was recorded. Subjective pain sensitivity and tolerance were reported. Power spectra were calculated for quantitative analysis. Paired t-test and Pearson's correlation were performed.
Results: Stimuli enhanced the alpha (8–12 Hz) spectral power (in %) significantly at the baseline (39.8 $\pm$ 3.2 vs. 35.0 $\pm$ 3.2, $P < 0.01$). This enhancement was associated with EEG D/A (delta (0.5–4.5 Hz) to alpha ratio) during NREM sleep (Pearson's r = 0.423, $P < 0.05$). However, these were not observed under sleep restriction. Sleep restriction reduced the alpha significantly (22.8 $\pm$ 3.0 vs.35.0 $\pm$ 3.2 without stimuli; 25.2 $\pm$ 3.1 vs.39.8 $\pm$ 3.2 with capsaicin). Subjective pain sensitivity increased (6.4 $\pm$ 2.1 vs. 5.5 $\pm$ 1.4, $P < 0.01$) and pain tolerance decreased (40.5 $\pm$ 16.1 vs. 52.3 $\pm$ 12.0, $P < 0.01$). The reduced subjective pain tolerance was correlated to the changes in the alpha under sleep restriction (r = -0.441, $P = 0.04$).
Conclusion: Greater EEG D/A could be a potential biomarker for enhanced pain sensitivity measured by increased alpha spectral power.
Disclosure: Nothing to disclose.

P328

The structure of the sleep-wakefulness cycle and memory processing in 'depressive' and 'non-depressive' rats

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Objectives: Alteration of the structure in the sleep-wakefulness cycle (SWC) and some kinds of cognitive impairment observe at depression. The main object of the study was analysis of the differences in the structure of SWC, learning and memory trace consolidation in 'depressive' (D) and 'non-depressive' (ND) rats in correlation of μ-opioid receptors density in the brain.
Methods: Experiments were conducted on the albino adult rats (n = 30) using the following methods:

1. the Porsolt's and sucrose (32% liquid) preference tests for identify of depressiveness signs;
2. SWC registration (Cadwell system);
3. Passive and active avoidance tests used for study of learning and memory consolidation;
4. Biochemical investigation of opioid μ receptors density in the brain (MOR-1);
5. Statistical method (the Student's t-test).

Results: In the D animals compared to ND fragmentation of the SWC, average of the duration and frequency of PS phases was higher ($P < 0.05$).
In the ND and D group's performance of passive avoidance reaction was not full in the - 85% and 82%, accordingly; however the learning criterion of the active avoidance reaction was the same (50 $\pm$ 4). The animals of the both group successfully performed the avoidance reaction after 24 h ($P < 0.003$, $P < 0.000006$).
The density of μ-receptors was higher in the amygdala in D rats compared to ND rats.
Conclusion: The disorder of the SWC is more noted in the D animals; which correlate with high density of μ-receptors in the brain structures especially in amygdala. Though, the memory processing is not disturbed.
Disclosure: Nothing to disclose.

P329

Modulation of spontaneous cortical synchronization by transcranial alternating current stimulation: effects on resting wake and sleep

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Objectives: Recent studies showed that transcranial Direct Current Stimulation (tDCS) applied during wake and sleep can interact with the ongoing brain physiology resulting in frequency-specific enhancement of cortical activity.
This study evaluates the ability of transcranial Alternating Current Stimulation (tACS) on temporal lobes to induce cortical synchronization in resting wake EEG and its possible effects on ensuing sleep.
Methods: Effects on wake EEG were evaluated on a sample consisting of 21 subjects participating each one to two stimulation protocols (active and sham) separated by 1 week at least (wake-session). The protocol was: 5-min of pre-stimulation wake EEG (28 cortical derivations), 10-min of 5 Hz tACS in the active condition (sham = 10-s), 5-min of post-stimulation wake EEG.
In sleep-session, 14 experimental subjects were involved in the same stimulation protocol followed by 2-hrs nap.
Results: Results on wake EEG show significant increase of EEG power in Delta and Theta bands on bilateral temporo-parietal derivations (t > 2.086, $P < 0.05$) in active condition compared to sham condition.
At this stage of the study, statistical comparisons between EEG topographic values during first NREM cycle only show a weak enhancement in Delta and Sigma power after tACS.

Conclusions: These results indicate that temporal-tACS induces an increase of cortical activity in the range of slower EEG frequency bands consistent with an effective manipulation of physiological sleepiness. However, stimulation does not seem to affect similarly the ensuing sleep.
Disclosure: Nothing to disclose.

P330

Waking-promoting effects of orexin injection in the Raphe Pallidus in the rat

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Objectives: Orexin neurons within the lateral hypothalamus have been shown to project to the Raphe Pallidus (RPa), a key relay brainstem area in the cold-defence pathway (Tupone et al., J Neurosci., 2012). The present study was aimed to assess thermoregulatory and wake-sleep effects of orexin injection within the RPa in the free behaving rat.
Methods: Seven male Sprague-Dawley rats (300–350 g) adapted to normal laboratory conditions (12 h–12 h light-dark cycle, ambient temperature 24°C) were implanted, under general anaesthesia (Diazepam, 5 mg/kg, i.m., Ketamine, 100 mg/kg, i.p.), with electrodes for the EEG, and nuchal and diaphragm EMG recording, a thermistor for brain temperature (Tbrain) recording, a catheter for arterial pressure recording and a microcannula for drug delivery in the RPa. After a 1-week recovery, animals were injected with either orexin-A (30 pM, 150 nL) or vehicle (saline, 0.9%) on two consecutive days during the light period.
Results: In the first hour after orexin injection, Tbrain peaked from 36.89 $\pm$ 0.20 to 37.50 $\pm$ 0.30°C, while it remained stable (from 37.14 $\pm$ 0.25 to 37.08 $\pm$ 0.13) after saline (orexin vs. saline, $P < 0.05$). In the same time window, the relative amount of waking was largely increased and that of sleep was reduced, although to different extents:

1. wake: saline 39.3 $\pm$ 6.7%; orexin, 82.8 $\pm$ 5.8%; $P < 0.01$;
2. NREM sleep: saline, 55.4 $\pm$ 5.7%; orexin, 15.2 $\pm$ 4.9%; $P < 0.01$;
3. REM sleep; saline 5.3 $\pm$ 2.3%; orexin: 2.0 $\pm$ 1.5%; statistically not significant.

Conclusions: The direct activation of orexin-A receptors on neurons within the RPa led to an increase in Tbrain which was accompanied by a clear enhancement of waking.
Disclosure: Nothing to disclose.

P331

Diet-induced obesity rats are hypertensive across the different wake-sleep states

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Objectives: In obese humans, arterial pressure (AP) is higher during the day and decreases less during the night than in lean subjects (Kotsis et al., Hypertension, 2005). At present, no data are available concerning changes in AP related to wake-sleep states in the diet-induced obesity (DIO) rat, the most reliable animal model of human obesity. The present study was aimed to fill this gap.
Methods: Fifteen male Sprague-Dawley rats, adapted to normal laboratory conditions (ambient temperature: 25°C; light-dark (L-D) cycle 12 h–12 h) were randomly assigned to two experimental groups:

1. NC ($n = 7$), fed for 8 weeks a standard diet;
2. HC ($n = 8$), fed for 8 weeks a hypercaloric (35% of fat) diet. Animals were implanted under general anesthesia with: i) two epidural electrodes for EEG recording; ii) an intra-arterial catheter for AP telemetric recording;
3. a hypothalamic thermistor to measure deep brain temperature. Following 1 week of recovery from surgery, animals were studied for two consecutive days.

Results: The results showed that mean AP was higher in HC than in NC rats across the different wake-sleep states during both L-D periods: L) Wake, NC = 88.7 $\pm$ 5.0, HC = 95.1 $\pm$ 1.3; NREM sleep, NC = 85.1 $\pm$ 5.2, HC = 91.4 $\pm$ 1.1; REM sleep, NC = 88.5 $\pm$ 4.4, HC = 96.6 $\pm$ 1.2; $P < 0.05$ for all comparisons; D) Wake, NC = 91.4 $\pm$ 5.7, HC = 99.5 $\pm$ 1.4; NREM sleep, NC = 85.0 $\pm$ 5.9, HC = 93.0 $\pm$ 1.3; REM sleep, NC = 85.9 $\pm$ 4.7, HC = 96.5 $\pm$ 1.2; $P < 0.05$ for all comparisons.
Conclusions: Our results show that DIO rats develop a stable hypertensive state irrespectively of the wake-sleep states. These animals may represent a good model for studying the mechanisms underlying obesity-related hypertension in humans.
Disclosure: Nothing to disclose.

P332

The interaction of thermoregulatory and sleep systems during sleep onset: a simultaneous cerebral and muscular hemodynamic measurement with near-infrared spectroscopy

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Objective: Thermoregulatory system (TRS) and sleep regulatory system (SRS) play essential roles to control brain temperature across circadian cycle. To examine whether metabolism or blood perfusion contributes to brain temperature we measured hemodynamics at sleep onset using near-infrared spectroscopy.
Methods: We assessed HbO_2, deoxy-Hb, and blood volume (BV) over the left forehead and biceps at sleep onset in 14-healthy adults. Sleep related changes in hemodynamics were quantified by comparing muscular and cerebral mean values during wakefulness, stages N1, N2, and slow-wave-sleep (SWS; t-test, $P < 0.05$). The correlations between inflection points (IPs) of cerebral hemodynamics and SWS latencies, and slopes of cerebral hemodyamics were tested (Pearson's correlation, $P < 0.05$).
Results: Cerebral HbO_2 and BV gradually decrease while deoxy-Hb increases after entering N1 to their IPs before SWS onset, and return to change reversely during SWS. The occurrence time of IPs correlates with SWS latencies. By contrast muscular BV continuously increases from N1 to SWS. Slopes of cerebral BV and HbO_2 are correlated with each other before and after IPs, indicating brain perfusion mainly depends on increasing arterial supply. The slopes of cerebral HbO_2 and deoxy-Hb only correlated after IPs, suggesting metabolism before IPs may be regulated by TRS and SRS while it is mainly controlled by SRS during SWS.

Conclusion: Declining brain perfusion at sleep onset is driven to suppress metabolism as indicated by declining BV and HbO_2. Instead, increasing brain perfusion during SWS mainly due to increased vasodilation may enhance heat loss as a possible mechanism to reduce brain temperature.
Disclosure: Nothing to disclose.

P333

Genetic inactivation of glutamatergic neurons within the pontine sublaterodorsal tegmental nucleus induces REM sleep behaviour disorder (RBD) in rats

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Objectives: Functional neuroanatomical data suggest that glutamatergic neurons of the pontine sublaterodorsal tegmental nucleus (SLD) generate muscle atonia during paradoxical (REM) sleep (PS). To test this hypothesis in rats, we inactivated the glutamatergic transmission in these neurons using in situ injection of adeno-associated virus (AAVs) carrying short hairpin RNA (shRNA) targeting vesicular glutamate transporter 2 (vGluT2) mRNA.
Methods: Under stereotaxic control, rats were infused bilaterally in the SLD with vGluT2-shRNA-mcherry-AAVs or control-shRNA-mcherry-AAVs (300 nL) and prepared for polysomnography. After 10 days required for complete removal of vGluT2 mRNAs from the glutamatergic neurons, EEG/EMG recordings synchronized with video were performed to quantify muscle tone, movements and oneiric behaviours during PS. Rats were sacrificed thirty-three days post-injection and vGluT2 mRNA were labelled using in situ hybridization to delineate AAVs injection sites and assess the targeting specificity of the shRNA.
Results: The complete removal of vGluT2 mRNAs from glutamatergic SLD neurons induces a significant reduction of PS amounts (40% of reduction *vs* control rats quantified 30 days post-injection). Preliminary EMG and actimetry analyses further indicate that PS bouts are characterized by a preserved, although irregular, muscle tone and the presence of abnormal motor behaviours.
Conclusions: The present data demonstrate for the first time that glutamatergic SLD neurons are responsible for inducing muscle atonia during PS. Further, inactivation of the glutamatergic transmission in these neurons induces dream-enacting behaviours, similar to REM sleep Behavior Disorder (RBD) described in humans and thus constitutes an original rodent model of this pathology.Supported by France Parkinson
Disclosure: Nothing to disclose.

P334

Modifications of sleep structure induced by cold acclimation in rats

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Objectives: Sleep is sensitive even to slight changes in core and surface body temperature. Usually both of them are variously affected during different stages of cold acclimation. How these changes influence sleep during cold acclimation is still poorly investigated. The aim of our work was to study the modifications in sleep structure induced by cold acclimation.
Methods: Long-term (LTA) and short-term acclimation (STA) were used in the experiments. STA was carried-out by exposing animals over two days to −12 or +10°C in the light period for 15 min hourly, for a total of nine exposures per day; LTA was achieved by keeping rats at +4°C for 30 days. Sleep stages were scored off-line by visual inspection of 4 s epochs. The hourly time series data were analyzed by the cosinor method.
Results: Besides increasing in NREM and REM sleep amount after LTA, REM sleep amount and NREM sleep episodes duration after STA −12°C and NREM sleep amount and its episodes duration after STA +10°C the cold acclimation procedures dampened the circadian rhythmicity of sleep after STA −12°C and LTA. Moreover REM sleep rebound after both STA −12°C and LTA had a wave-like character with the period lengths differing from that of the control. STA +10°C increased mesor and amplitude of NREM sleep circadian pattern, but had no effect on REM sleep.
Conclusions: Cold acclimation changes sleep amount and its circadian rhythmicity in different ways probably depending on the character of cold influence (rhythmic or constant) and degree of temperature load.
Disclosure: Nothing to disclose.

P335

Targeting inactivation of Hcrt receptors in dopaminergic and noradrenergic neurons alters the EEG spectral profile during wakefulness

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Objectives: Hypocretin-1 and hypocretin-2 (also named Orexin A and Orexin B) are peptide neuromodulators produced by a small population of neurons in lateral hypothalamus and project throughout the brain, particularly to the wake-promoting monoaminergic and cholinergic cell groups, which express one or both of the hypocretin receptors. The effect of chronic disruption in any specific Hcrt-to-target connection remains unexplored. The aim of present research is to dissect this neuronal circuitry, exploring the impact on the EEG activity of deficiency in one or both receptors in different cell groups.
Methods: Using the Cre/loxP system, we created inducible knockout alleles of both Hcrt receptor genes (HcrtR1 and HcrtR2), allowing inactivation of one or both receptors in selected target populations. Mice lacking HcrtR1, HcrtR2, or both in dopaminergic neurons, and mice lacking HcrtR1 in noradrenergic cells were generated, and their EEG thoroughly analyzed.
Results: Mice with specific Hcrt signaling inactivation in noradrenergic and dopaminergic neurons each show characteristic alterations in specific frequency bands of the wakefulness spectra and different response to sleep deprivation.
Conclusions: Different branches of the Hcrt circuitry are differentially involved in generating different EEG spectral components of wakefulness brain activity.
Disclosure: Nothing to disclose.

P336

Successful physical exercise-induced weight loss is modulated by habitual sleep duration in the elderly: results of a pilot study

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Objectives: Although it is widely accepted that physical exercise promotes weight loss, physical exercise alone had been found to result in only marginally weight loss compared to no treatment. Interestingly, both subjective and objective sleep duration have been shown to be negatively correlated to the body mass index (BMI). Despite of this growing evidence for a relation between sleep duration and body weight the role of habitual sleep duration in physical exercise-induced weight loss has not been studied so far.

Methods: Twenty-two healthy elderly aged 61–76 years (mean 68.36 years, 55% female, Pittsburgh Sleep Quality Index ≤ 5, BMI mean 25.15 kg/m^2) either took part in a 12-weeks aerobic endurance training (3 x 45 min/week) or in a relaxation control (2 x 45 min/week). The BMI was assessed prior to and after intervention. Subjects maintained sleep logs every morning/evening during the training period.

Results: Besides a significant main effect of the type of training, a significant interaction effect of type of training and habitual sleep duration was observed: While after treadmill training subjects who slept less than 7.5 h/night during intervention reduced their BMI by nearly 4%, a comparable decrease in the BMI was found neither in subjects who slept more than 7.5 h nor after relaxation training independent of sleep duration.

Conclusions: Although results should be interpreted with caution due to the small sample size, this is the first study to indicate that physical exercise might compensate for disturbed body weight regulation associated with short sleep duration.

Disclosure: Nothing to disclose.

P337

Inter-individual differences in the effects of night-time noise exposure on sleep and cognitive performance during daytime

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Objectives: Sleep characteristics and night-time noise annoyance show considerable inter-individual variations. Here we tested whether a clock gene polymorphism in *PERIOD3* (*PER3*), implicated in human sleep-wake regulation, is linked to inter-individual response differences to night-time noise exposure during sleep and its repercussions on daytime functioning.

Methods: Eighteen male homozygous carriers of the long (*PER3*$^{5/5}$, $n = 9$) and short (*PER3*$^{4/4}$, $n = 9$) repeat allele underwent four continuous nights and days in the laboratory. The first night served as baseline sleep episode, followed by 2 nights during which freight train noise was played back into the sleeping room (60 trains per night, equivalent continuous sound pressure level during night: 40 or 50 dB (A) respectively) and by a noise-free recovery night. Daytime psychomotor vigilance (PVT) performance was assessed every 4 h. Polysomnography was carried out continuously, and sleep stages were manually scored.

Results: Subjective noise annoyance and sleep fragmentation were significantly more pronounced in PER3$^{5/5}$ than PER3$^{4/4}$ carriers ($P = 0.02$; $P = 0.003$). *PER3*$^{5/5}$ carriers responded to noise exposure with increased wakefulness and Stage 1 during the noise nights, while slow wave sleep was significantly reduced only in *PER3*$^{4/4}$ but not in *PER3*$^{5/5}$carriers (gene x night P at least 0.012). PVT performance deteriorated in the course of the experiment in the *PER3*$^{5/5}$ carriers only while remaining stable for the *PER3*$^{4/4}$ carriers (gene x time $P = 0.03$).

Conclusions: Our pilot data indicate that *PER3*$^{5/5}$ carriers are more susceptible to the effects of night-time noise exposure during sleep, as indexed by subjective and objective correlates of sleep quality and vigilant attention performance.

Disclosure: Nothing to disclose.

P338

Slow wave sleep in the chronically fatigued: spectral power distribution patterns in chronic fatigue syndrome and primary insomnia

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Objectives: Chronic Fatigue Syndrome (CFS) and Primary Insomnia (PI) are distinct conditions sharing non-restorative sleep and fatigue complaints without excessive daytime sleepiness (EDS). Impaired sleep homeostasis functioning has been suspected in both CFS and PI.

Methods: We compared perceived sleep quality, fatigue and sleepiness symptom-intensities, polysomnography (PSG) and slow wave sleep (SWS) spectral power distributions of drug-free CFS ($n = 30$) and PI ($n = 15$) patients without comorbid sleep or mental disorders, with a good sleeper control group (GSC; $n = 22$) of similar gender distribution ($P = .253$), age ($P = .318$) and BMI ($P = .606$).

Results: Compared to GSC, higher fatigue without EDS ($P < .001$) and impaired perceived sleep quality ($P < .001$) were confirmed in both patient groups. PSG mainly differed in sleep fragmentation ($P = .001$) and SWS durations (GSC vs CFS: $P < .05$). Spectral analysis revealed a similar deficit in central ultra-slow power (0.3–0.79 Hz) proportion during SWS for both CFS ($P < .05$) and PI ($P < .05$) and an increase in frontal rapid frequency power proportions during SWS in PI only (theta, alpha and sigma; all P's $< .005$). The latter was correlated to affective symptoms (all P's $< .05$) whereas central ultra-slow deficit was related to fatigue severity ($P < .001$) and sleep quality impairment ($P < .001$).

Conclusions: In combination with normal (PI) or even increased SWS durations (CFS), we found consistent evidence for lower proportions of slow oscillations during SWS in PI and CFS. Our findings suggest a compensation of an intrinsically altered process within SWS, expressing homeostatic dysregulation.

Disclosure: Nothing to disclose.

P339

Olfaction and sleep - a rodent EEG experiment

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Objectives: Olfaction is rodents' most important sense, and removal of animal's ability to smell has been used e.g. as a model for depression. We wanted to see how temporary loss of olfaction would affect sleep.

Methods: Adult rats were treated with 3-MI to temporarily destroy their olfactory sensory cells and thus to prevent any olfactory sensation for a period of time. Being able to renew, the olfactory sensory cells would grow back letting the animals regain their olfactory sense. Animals' ability to smell was tested weekly before and after the 3-MI treatment.

EEG and EMG were gathered from each animal to gain information on 3-MI treatment effects on sleep. Data were gathered before (control week) and after 3-MI treatment and 10-day recovery time (3-MI weeks). Two baseline days before a sleep deprivation day and the sleep deprivation day (with 3 h sleep deprivation) from each week (one control week and altogether five 3-MI weeks) were selected for further analysis. The data from the selected days were scored for different vigilance states (Wake, NREM, REM) in 4s epochs using an automatic scoring script and checked manually to exclude artefacts. EEG power was analysed in different time periods and in different vigilance states.

Results: Each animal served as its own control (control week vs. 3-MI weeks). Differences between control week and 3-MI weeks were found in vigilance state distributions and in EEG power.

Conclusions: Further analyses are required to shed light on these yet inconclusive findings.

Disclosure: Nothing to disclose.

P340

Thalamic and neocortical differences in the relationship between delta and sigma time courses of human sleep EEG

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Objectives: Capitalizing on basic neurophysiological observations regarding the spindle (sigma; 12–16 Hz) and delta (1–4 Hz) electroencephalographic (EEG) oscillations, particular attention has been paid to these rhythms and their relationship during sleep. Several studies reported an overall reciprocal relationship between sigma and delta power time courses as measured by a single correlation coefficient over NREM episodes. Here, by exploiting sleep intracerebral EEG (Stereo-EEG, SEEG) recordings we aimed at investigating this relationship across distant cortical and subcortical regions including thalamic nuclei.

Methods: Nine patients (5 M, 4 F) diagnosed with drug-resistant focal epilepsy underwent SEEG for the presurgical assessment of the epileptogenic zone. Inclusion criteria encompassed the presence of at least one bipolar SEEG lead investigating the thalamus. SEEG leads containing epileptiform activity were discarded. All the remaining contacts were analyzed (spectral analysis; 6-seconds epochs) and the time-course of sigma and delta activity was calculated for all the recording contacts. Cross-correlation analysis (lag-zero) was performed across all contacts between sigma and delta time-course activity across all sleep stages.

Results: In agreement with previous studies, for all patients, cross-correlation analysis between the time-course of sigma and delta activity performed both within and across neocortical contacts showed an overall reciprocal relationship (range -0.5 /-0.8). Intriguingly, when calculated for the thalamus, the correlation coefficient was found positive, both within thalamic contacts as well as between thalamic and neocortical contacts (range 0.7 / 0.9).

Conclusions: Our findings, although preliminary, suggest the coexistence of overnight patterns of distinct oscillatory activity between thalamic and neocortical regions.

Disclosure: Nothing to disclose.

P341

Study of the dynamic information between heart and brain networks during nocturnal sleep

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Objectives: Dynamic interactions between heart and brain during sleep were studied by Entropy based-measures to determine cerebral process in regulatory controls of both systems.

Methods: Normalized high frequency spectral component of heart rate variability (HF_{nu}) and all normalized sleep EEG power bands (δ, θ, α, σ and β) were computed from nocturnal sleep ECG and EEG of 10 healthy men aged between 18–23 years. During whole night and different sleep stages (light, deep, and REM sleep), dynamical interactions in brain-to-heart and brain-to-brain physiological networks were analyzed by Entropy measures.

Results: All sleep characteristics were concordant with classical literature. The predictive information confirms the existence of structured dynamics during sleep both for HF_{nu} and for each EEG power. Information transfer evidences the brain system associated to β-rhythm as the one transferring the largest amount of information to heart system. The predictive information about brain subsystems was higher for δ-rhythm. Nodes corresponding to slower EEG frequencies (δ, θ, and α) received more information than that sent out towards other nodes. Nodes describing σ and β activities were characterized by small number of incoming links and large number of outgoing links. The brain-to-heart and brain-to-brain information transfers lost progressively significance from light to deep and REM sleep.

Conclusions: Network node described by β-EEG power acted as a neurophysiological hub which conveys the largest amount of information flowing between heart and brain nodes. This network was sustained mostly by transitions across different sleep stages and vanished progressively from light to deep and REM sleep.

Disclosure: Nothing to disclose.

P342

Impaired slow wave sleep downscaling in patients with hypsarrhythmia

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The restorative function of deep non rapid-eye-movement (NREM) sleep has been linked to neuronal recovery, i.e. by a re-normalization of synaptic weights (synaptic downscaling). Synaptic downscaling is thought to be induced by the cortical slow oscillation during NREM sleep and is reflected in an overnight decrease of the slope of slow waves. It has been proposed that a stable slow oscillation requires high spatial synchronization across cortical networks. The EEG of West syndrome patients, a severe epileptic encephalopathy of infancy, is characterized by hypsarrhythmia, a chaotic pattern of random high voltage spikes and waves during sleep. Such asynchronous neuronal activity may interrupt the cortical slow oscillation and thereby impair synaptic downscaling.

The overnight decrease in the slope of slow waves and the amount of global slow waves, a marker of global synchronization, was analyzed in 14 West syndrome patients (6.0 $\pm$ 0.6 months), and compared to healthy age and gender matched controls (5.6 $\pm$ 0.6 months).

Infants with West syndrome revealed a reduced overnight decrease in the slope of slow waves compared to controls ($P < 0.05$). Moreover, the proportion of globally occurring slow waves was also significantly lower in patients (patients: 12.8 $\pm$ 1.6%, controls: 23.2 $\pm$ 1.9%, $P < 0.001$).

The physiological decrease of the slope of slow waves across the night was reduced in infants with West syndrome, indicating impaired synaptic downscaling. Moreover, the lower amount of global slow waves in West syndrome patients may reflect reduced global synchronization of slow waves during NREM sleep, which in turn may contribute to the impaired synaptic downscaling.

Disclosure: Nothing to disclose.

P343

The effect of hypnotics on auditory arousal thresholds in older adults

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The ability to respond quickly from sleep to emergency signals is assumed, however previous research has found that being under the influence of alcohol affects a person's ability to respond to their smoke alarm, even at very low levels. Relatively little is known about the impact hypnotics have on the response to emergency signals, such as smoke alarms, in older adults.

Methods: The repeated measures experiment involved monitoring the sleep patterns and arousal thresholds of 12 participants (10 males and two females aged between 65 to 80 years with an average age of 71) in their homes over 11 nights, modulating hypnotic intake (using their usual hypnotic) and alarm presentation (the current 3100 Hz sine wave compared with the 520 Hz square wave). The alarms were presented when the drug was at peak concentration.

Results: Hypnotic ingestion increased arousal thresholds by approximately 9 dBA. More than double the proportion of participants slept through the 3100 Hz sine wave at 75 dBA when under the influence of their hypnotic compared to the no hypnotic condition (17% cf. 8% respectively). The 520 Hz square wave significantly outperformed the standard smoke alarm (3100 Hz sine wave).

Conclusions: The findings suggest that hypnotics significantly compromise arousal thresholds amongst older adults. Together with the previous literature, the findings present a challenge to the effectiveness of existing fire detection and alerting technology amongst vulnerable groups and support the continued adoption of the 520 Hz square wave.

Disclosure: Nothing to disclose.

P344

Comparison of the levels of drowsiness obtained via a new photooculography-based drowsiness scale and via a simple variation of the Karolinska Drowsiness Scale (KDS)

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Objectives: Drowsiness is a major cause of accidents and oculography is one of the most sensible approaches for quantifying the level of drowsiness (LoD). We have thus developed a new drowsiness scale that uses images of the eye, called photooculography (POG), to produce a LoD. Since polysomnography (PSG) is the 'gold standard' for sleep, we have also defined a new LoD based on EEG and EOG signals that is obtained by aggregating scores produced by our interpretation of the 'Karolinska Drowsiness Scale (KDS)'.

Methods: We conducted an experiment in which 27 healthy volunteers were asked to perform three visual reaction-time tests in different sleep-deprivation conditions (with up to 28 h of sleep deprivation). During each test, we continuously recorded POG images and PSG signals. For each minute of test,

1. we automatically extracted ocular parameters from the POG images and produced a POG-based LoD, and
2. we manually determined a PSG-based LoD by aggregating KDS scores, assigned every 20s, according to the presence of alpha rhythm and/or theta activity and/or slow eye movements.

Results: Preliminary results (13 subjects) indicate that our POG-based LoD varies in accordance with our PSG-based LoD. The Pearson's correlation coefficient between our POG-based LoD and our PSG-based LoD is significant (0.62). Both types of LoDs also increase with sleep deprivation and with the reaction time.

Conclusions: This study showed that our POG-based LoD is well correlated with our PSG-based LoD, and has thus significant potential for quantifying the level of drowsiness of subjects accomplishing a task.

Disclosure: Nothing to disclose.

P345

Extreme violation of sleep hygiene: the effect of sleeping against the biological clock during a multiday relay event

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Objectives: Sleep hygiene is important for sleep quality and optimal performance during the day. However, it is not always possible to follow sleep hygiene requirements. In multiday relay events, athletes have to sleep immediately after physical exertion and sometimes against their biological clock. In this study we investigated the effect

of having to sleep at an abnormal circadian time on sleep duration during a multiday relay athletic event.

Methods: Eight runners and two cyclists performing a 500 km relay race were followed. They were divided into two groups that took turns in running and resting. As a result, sleep times varied between normal and abnormal times. All athletes wore actigraphs to record the duration and onset of sleep.

Results: Linear mixed model analyses showed that athletes slept on average 43 min longer when they slept during usual (night) times than during abnormal (day) times. In general, sleep duration decreased during the race.

Conclusions: This study shows that, even under extreme violation of sleep hygiene rules, there still is an apparent effect of circadian rhythm on sleep duration in relay race athletes. This means that whenever possible, athletes should either attune their activities as much as possible to their circadian rhythm, or try to adjust their circadian rhythm to the requirements of the event in which they participate. Exogenous melatonin may help to shift the 24-h rhythm, but further research is necessary to investigate whether melatonin could also be used to shorten the sleep-wake rhythm.

Disclosure: Nothing to disclose.

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P346

Daytime sleepiness levels are associated with academic performance and psychological health in UK adolescents

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Objectives: Sleep problems and depression are common in adolescence and may interfere with academic performance, but well-defined large epidemiological studies are limited in this age group. We aimed to examine the potential associations between daytime sleepiness and psychological health and academic performance across core subjects.

Methods: A total of 664 UK adolescents (11–13 years) participated in the Midlands Adolescent Schools Sleep Education Study (MASSES), a cross-sectional study to assess potential relationships between levels of daytime sleepiness and psychological wellbeing. A sub-sample of 110 participants were assessed for potential associations between daytime sleepiness and academic performance. Participants completed two validated questionnaires (Schools Sleep Habits Survey and Cleveland Adolescent Sleepiness Questionnaire), and wore wrist actigraphy for 7 days to estimate sleep duration. Academic performance level for Mathematics, English and Science were obtained from school records.

Results: After adjustment for a range of potential confounders including actigraphy estimated sleep duration, there was a significant negative association between daytime sleepiness level and Science $\beta = -0.40$, $P = 0.005$; Mathematics $\beta = -0.49$, $P = 0.041$ (girls only) but not English $\beta = -0.22$, $P = 0.186$. Higher levels of daytime sleepiness were significantly associated with increased subjective unhappiness $F = 27.58$, $P < 0.001$; worry $F = 20.18$, $P < 0.001$; feeling hopeless about the future $F = 32.05$, $P < 0.001$ and feeling nervous/tense $F = 15.48$, $P < 0.001$.

Conclusions: Higher levels of daytime sleepiness have detrimental effects on academic achievement and psychological health. A better understanding of adolescent sleep behaviors, other lifestyle factors and daytime functionality is required and could help to improve performance and mental health status in this vulnerable group.

Disclosure: Nothing to disclose.

P347

A new face of sleep: the impact of post-learning sleep on recognition memory for face-name associations

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Sleep improves consolidation of many types of new memories. However, prior studies have not examined the memory for face-name associations. The recognition of a new face along with the associated name is an important human cognitive skill, and is impaired in patients with MCI or dementia. Here we investigated whether post-presentation sleep impacts recognition memory of new face-name associations.

Fourteen participants (23.33 ± 2.05) were tested twice. They were presented photos of 20 faces with a corresponding name. Twelve hours later, they were shown each face, once with the correct and once with an incorrect name, and asked if each face-name combination was correct and to rate their confidence. In one condition the 12-h interval between presentation and recall included an 8-h sleep opportunity ('sleep'), while in the other condition they remained awake ('no sleep').

There were more correct and highly confident correct responses when the interval between presentation and recall included a sleep opportunity ($P < 0.03$). The number of correct responses in the 'sleep' condition was not correlated with duration of TST, REM, NREM, N1 or N2, but was negatively correlated with N3 ($r = -0.72$, $P < 0.01$). Improvement between the 'no sleep' and 'sleep' conditions was not correlated with duration of TST or any sleep stage.

These data suggest that a sleep opportunity improves the ability to correctly recognize face-name associations. The mechanism of this improvement does not appear to be linked to the duration of sleep, consistent with the protective effect of sleep on memory consolidation.

Disclosure: Nothing to disclose.

P348

Sleep's effect on motor skills: strong offline gains or a methodological bias?

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The Finger Tapping Task (FTT) is commonly used in sleep research to probe procedural memory. The Offline Improvement (OI%) is calculated as the difference between the testing and training sessions using the mean number of correctly typed sequences (mnCTS) on the last 3 trials (3L) of the training session (TS). However, performance often deteriorates at the end of the TS, due to fatigue or boredom. Therefore, the aim of the study was to compare the OI% calculated by the 3L and by the 3 best trials (3B).

Thirty young adults performed the training session of the FTT and half of them took a 90 min post lunch nap, while the rest remained in quiet wakefulness. Next, all participants performed the testing session of the FTT.

Before the retention interval the mnCTS was similar between groups: 3L: wake = 14.1 ± 2.3; sleep = 14.4 ± 1.7; $P > 0.05$; 3B: wake = 15.3 ± 2.4; sleep = 15.5 ± 2.0; $P > 0.05$. When using the 3L, the sleep group showed a 14.9 ± 12.3% gain, whereas if the 3B were used, only a 6.9 ± 10.8% improvement was observed ($P = 0.0016$, paired t-test). As for the wake group, the 6.9 ± 13.3% gain calculated with the 3L turned into a −2.3 ± 8.6% decrement, when using the 3B ($P = 0.0084$, paired t-test).

Our data suggests that sleep's effect on motor skills may have been overestimated in most studies, from an apparent gain of ~15% to an actual improvement of ~5%.

Support: CAPES and CNPq.

Disclosure: Nothing to disclose.

P349

Facial emotion recognition, neurobehavioral performance, and sleep associated with care at the time of death among shift-working caregivers

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Objectives: This study examined how care at the time of death was associated with facial emotion recognition, neurobehavioral performance and sleep in shift-working caregivers.

Methods: Fourteen shift-working caregivers in a dementia ward participated in this 2-week observational study (30.2 $\pm$ 0.5 years, 7 females). The participants were required to record their fatigue, sleepiness, stress and facial emotion recognition by visual analogue scales and to complete a psychomotor vigilance task by using an actigraph (AMI) after each shift. Then, they were asked (yes/no) whether there were elderly persons at the time of death under nursing care in their ward during their working time. They also rated emotional levels of facial expressions of other persons by using pictures of neutral faces and faces with fatigue, stress, vigor and aversion. Sleep was measured by the actigraph. Data were analyzed with a two-way (care [yes, no]) x shift [night, day]) mixed-model ANOVA.

Results: Significantly more sleepiness, lower performance and worse sleep quality were observed when there were elderly persons at the time of death under nursing care. Additionally, estimated aversive levels for both the aversive and neutral faces were significantly more increased in the care condition than in the non-care condition. Besides, working the night shift made them estimate significantly higher aversive levels for neutral face.

Conclusions: Our findings suggest that the experienced (or anticipated) workloads of providing care at the time of death affect not only alertness and sleep quality but also ability to recognize others' negative emotional states.

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The effect of dim light at night on brain activity during working memory task

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Objectives: We aimed to investigate the effect of dim LAN exposure during sleep in healthy young male subjects.

Methods: Twenty-three healthy young male volunteers were recruited for the study, and were divided into two groups depending on the exposed light randomly. (11 subjects for 5 lux group and 12 subjects for 10 lux group). During the first night, all subjects slept in darkness. On the second night, subjects exposed to two different dim lights depending on groups during whole sleep. All subjects underwent BOLD fMRI testing after the second and the third night. During BOLD-fMRI subjects performed a visual N-Back task.

Results: After 10 lux LAN exposure, there was reduced BOLD signal response in the inferior and middle frontal area. However, after 5 lux LAN exposure, there was no difference. As compared to 5 lux exposure group, 10 lux LAN exposure group had significantly more deactivation in the inferior frontal region. Compared to simple letter (0-back) identification and 1-back task, performing the 2-Back task decreased the BOLD signal in the inferior frontal and middle temporal region.

Conclusion: We found that dim LAN during sleep affects brain activity during working memory task. Moreover, there was significant frontal deactivation in 10-lux LAN exposed group, not in 5-lux group. Inferior frontal cortex activity was reduced at the most difficult working memory load. This finding suggests the adverse effects of dim LAN during sleep on daytime cognitive function, and the need to avoid light exposure above 5 lux during sleep even dim light.

Disclosure: Nothing to disclose.

P351

Spindles affection by use of negative emotional stimulations

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Objectives: In this study, the effects of negative emotional stimulations on spindle in sleep stage 2 are considered. With respect to spindle alternations, the causality relation between type of answers and spindle alterations after negative emotional stimulations are considered.

Methods: Eight subjects (5 men, 3 women, age range: 22–24 and the average age: 24.3) were selected. Negative emotional stimulations had applied before afternoon nap by use of International Affective Picture System (IAPS) dataset. After performing post-nap tests, correlation between number of spindles and type of responses were considered.

Results: Demonstrated that the negative emotional stimulations are caused more spindles decreasing that are derived to higher correct response in the subjects. Also the numbers of false responses areincreased with increasing number of spindles.

Conclusion: Spindle decreasing directs to better memory consolidation in negative emotional events.

Disclosure: Nothing to disclose.

P352

Sleep does not cause false memories on a story-based test of suggestibility

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Sleep contributes to the consolidation of recent memories, but there is evidence that the processes involved can also result in the formation of plausible, but false memories. Previous studies have examined this using the Deese, Roediger, McDermott false memory paradigm, in which participants learn lists of semantically related words, from which a critical lure, representing the theme of the list, is omitted. Participants are tested on recognition memory for both the studied words and the (false memory) critical lure. Mixed results have been found. Some studies show an increase in both veridical and false memory after a night of sleep compared to wake, other studies demonstrate a decrease in false memories after sleep. This study examined the effect of sleep on false memory using the Gudjonsson Suggestibility Scale. Participants listened to a short story about a bicycle accident, either in the morning (wake group, $n = 58$) or in the evening (sleep group, $n = 54$). Twelve hours later, after either a

period of wake or sleep, they answered 15 leading/suggestive questions and 5 factual/non-suggestive questions about the story. No significant difference was found between the sleep and wake groups on number of suggestible responses to the 15 leading questions: sleep group, M = 6.30 (SD = 3.69); wake group, M = 5.78 (3.53); F (1,111) = .581, $P > .05$. No effect of sleep on false memory was thus found using a method that involves narrative memory, and which also involves recognition and recall processes when a response is produced.

Disclosure: Nothing to disclose.

P353

Emotion regulation and maladaptive beliefs in relation to morningness/eveningness

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Objectives: To evaluate whether different chronotypes display different emotion regulation style and beliefs.

Methods: Until now, we recruited 87 participants (86.7% women), aged 25.6 ± 7.8 years, who completed a battery of tests that evaluate emotion regulation style (Difficulties in Emotion Regulation Scale -DERS), irrational beliefs (Shortened General Attitude and Belief Scale -GABS), automatic thoughts (Automatic Thoughts Questionnaire -ATQ- and Automatic Thoughts Questionnaire-positive), as well as circadian rhythmicity (Composite Scale of Morningness). The completion was online (SurveyGyzmo platform) and data was analysed in IBM SPSS Statistics 20.

Results: Compared to morning types, evening ones reported significantly more difficulties in regulating their emotions (DERS score: 89.3 ± 22.3 vs. 69.8 ± 15.6; t(48) = 3.56, $P = .001$), as well as more negative automatic thoughts (ATQ score: 40.8 ± 16.4 vs. 24.5 ± 12.7; t(48) = 3.92, $P < .001$) and more irrational beliefs (GABS score: 73.7 ± 18.4 vs. 60.4 ± 15.0; t(48) = 2.79, $P = .007$). Morningness was found to be significantly and negatively linked with DERS (r = -.393, $P < .001$) and ATQ scores (r = -.353, $P = .001$). Positive automatic thoughts were not linked with these variables and were not significantly different amongst chronotypes.

Conclusions: Emotion regulation style, as well as automatic negative thoughts and irrational beliefs are significantly worse amongst evening chronotypes, while morningness is inversely linked with ATQ and DERS scores.

Disclosure: Nothing to disclose.

P354

Temperament moderates the association between sleep duration and cognitive performance in children

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Objectives: Sleep restriction affects cognitive performance. Individual differences in sensitivity to sleep restriction have been shown in adults. We here investigated whether individual differences in temperament traits moderate the association of sleep duration with sustained attention, inhibition, and working memory in children.

Methods: 123 children (42% boys) aged 9–11 years participated. Sleep diaries and Early Adolescent Temperament Questionnaire-Revised were completed at home to assess sleep duration and four temperament traits: negative affectivity, extraversion, effortful control, and affiliativeness. Computerized assessment of sustained attention (short-form Psychomotor Vigilance Task, PVT); inhibition (PVT Go/No-Go adaptation); working memory (visual Digit Span) at school.

Results: Although regression analyses showed no overall association of sleep duration with sustained attention, there was a significant effect modification by extraversion and negative affectivity. Surprisingly, among children with low extraversion or high negative affectivity, a longer sleep duration was associated with worse sustained attention. Sleep duration was not associated with inhibition, but was negatively associated with working memory. This association was most pronounced in children with high negative affectivity. Effortful control and affiliativeness did not moderate associations of sleep duration with cognitive performance.

Conclusions: Individual differences in temperament determine associations between sleep duration and cognitive performance. Short-sleeping introvert and negatively affective children show better sustained attention and working memory performance than long-sleeping children with these temperaments. Mild sleep restriction in these children might lower their elevated baseline physiological arousal levels, which is more optimal for cognitive performance.

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P355

Integration of explicit and implicit memory systems evolves over sleep

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Objectives: It has been suggested that beyond stabilization and enhancement, sleep also changes the quality of memory traces. Here, we test whether sleep influences performance and brain activity indicating a transformation of memory in multi-item rule extraction.

Methods: In three experiments, 185 subjects learned a feedback-driven classification task and acquired explicit (item knowledge) and implicit memory (rule proficiency). Subjects were randomly assigned to learn the task either in the morning or in the evening. The test session followed immediately ($n = 45$) or 12 h later, with subjects spending the time in between either asleep ($n = 50$) or awake ($n = 50$). 40 subjects performed the test session following sleep ($n = 21$) or wakefulness ($n = 19$) in a 3T fMRI scanner.

Results: By nested structural equation modeling we show that over sleep, but not over wakefulness, the structure of memory changes, making explicit and implicit representations independent from each other. This change is reflected in better memory performance. Functional imaging data shows that improved performance in sleepers is related to stronger recruitment of implicit memory-associated structures, like the caudate nucleus, during an explicit item recognition memory task. Stronger recruitment of the hippocampus, which is usually associated with explicit memory, is found in implicit rule memory transfer. In a cooperative task, using explicit item

knowledge and implicit rule proficiency, the sleep group showed higher activation in both the hippocampus and the caudate nucleus.
Conclusions: Overall, we find a sleep-induced cooperation of explicit and implicit memory systems and a change in memory structure, together with improved memory performance.
Disclosure: Nothing to disclose.

P356

Sleep accelerates learning-related changes in brain activity

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Objectives: Sleep is assumed to modify the traces of memories in the brain. Our study aimed to examine the effects of repeated learning and sleep on the declarative memory trace as seen in fMRI activity.
Methods: 32 subjects acquired a list of 28 concrete nouns in seven repetitions in a 3T fMRI scanner. A second session employing the same task followed 12 h later. Here, half of the words were old, while the others were new. Subjects were randomly assigned to having the first session in the morning or in the evening, thus spending the time in-between awake or sleeping for 8 h.
Results: We found that hippocampal and medial prefrontal cortex (mPFC) activity decrease over encoding repetitions, while activity in the precuneus increases. For mPFC and precuneus we found the same effect over repetitions during recall. 12 h later, in the second session, we find discrepant activity patterns over repetitions for the sleep and wake groups. The sleep group shows further decrease of hippocampal and increase in precuneus activity only for new words, but not for old words, whereas this was seen for both old and new words in the wake group.
Conclusions: Our findings demonstrate the distinctive paths memories take during consolidation in sleep and wakefulness. Retention during wakefulness leaves the memory trace unchanged and we witness still ongoing consolidation during additional learning. Offline reprocessing during sleep however might have a similar effect to additional learning repetitions, thus enabling memory formation to complete ahead of time.
Disclosure: Nothing to disclose.

P357

Gender difference in sleep structure and cognitive function in the elderly

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Objectives: A decrease in slow wave sleep (SWS) is known to be related to aging especially in male, and changes of cognitive function with aging have been reported to show gender difference. This study was to investigate cognitive function and sleep structure in the elderly according to gender to find whether gender difference in sleep structure may be associated with cognitive functions.
Methods: From November 2010 to January 2012, cross-sectional and community-based study was performed on 696 subjects aged 60 years or older in an urban area of South Korea. A total of 348 subjects completed semi-structured interviews, self-report scales and laboratory polysomnography. Cognitive function tests were done in 339 subjects.
Results: Of the 339 subjects (female, 206), apnea-hyponea index (AHI) and stage 1 sleep (S1)% were higher in male than in female ($P < 0.001$; $P < 0.001$), but SWS% were higher in female than in male ($P < 0.001$). In cognitive function test, female subjects demonstrated higher scores in verbal registration (VR), Trail Making Test B (TMTB), Benton Visual Retention Test A (BVRTA), and Stroop color test (SCT) after adjusting potential confounding factors ($P = 0.003$; $P = 001$; $P = 004$; $P < 001$). VR was related with S1% and S3%, and association was also found between VR and AHI, and between BVRTA and SCT, and S1%.
Conclusions: Gender differences were observed in four of cognitive function tests, which could be explained by increase of S1% and AHI, and decrease of SWS% in male. Decrease of deep sleep in male might adversely impact on cognitive function in the elderly.
Disclosure: Nothing to disclose.

P358

Sleep deprivation affects working memory in low but not in high complexity for the N-Back test

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Sleep clearly influences learning and memory since sleep deprivation and stress impairs both cognitive processes. Working memory is an essential cognitive process and refers to a short-term holding of incoming information required to update the long-term mnemonic storage. Nevertheless, the influence of sleep deprivation on working memory has scarcely been studied. In this study we evaluated working memory using the N-back test after increasing periods of wakefulness. Healthy young males were kept awake for 36 h and the two N-back tasks with low (1 and 3) levels of complexity were applied every 6 h. Additionally, salivary cortisol was determined along the study. Unlike the control non-deprived participants, the sleep deprived volunteers showed a significant decrease in their efficiency to solve the 1-Back task after 24 h of sleep deprivation. However, no differences were observed after 30 and 36 h of sleep deprivation. Concerning the 3-Back task no differences were observed after sleep deprivation. Regarding reaction time, the deprived group manifested slower responses for the 1-Back task and for the 3-Back task after 30 h and 36 h of sleep deprivation, respectively. Cortisol levels presented the normal daily oscillation and no differences were observed be- tween groups. This data suggests that sleep deprivation affects basal states of attention instead of working memory while performing simple tasks. The impact of sleep deprivation on the cognitive performance depends on the moment of day when the task is applied and the complexity of the tests used to assess these mnemonic skills.
Disclosure: Nothing to disclose.

P359

Cueing emotional memories during slow-wave sleep changes subjective arousal ratings

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Objectives: Cueing replay of memories using auditory or olfactory stimuli during slow-wave sleep (SWS) has been shown to strengthen their consolidation. Moreover, there is evidence that cueing during

sleep facilitates fear extinction. This study examines the effects of auditory cueing emotional memories during SWS on memory and subjective valence and arousal.

Methods: Participants rated 36 negative and 36 neutral pictures, paired with semantically related sounds, for valence and arousal. Then, they learned the location of each picture on the screen while hearing the matching sound. Memory for the picture location was tested once in the evening and once the following morning. After the second memory test, participants again rated the stimuli for valence and arousal. Sleep was monitored with polysomnography and half of the sounds were played ~5x each during SWS. Overnight changes in memory accuracy and valence / arousal ratings were analysed using 2x2 ANOVAs, with factors cued / not cued and negative / neutral.

Results: Performance on the memory task remained the same for the stimuli that were cued during sleep, whereas it deteriorated for the non-cued stimuli ($P = 0.038$). Furthermore, we observed a cueing*emotion interaction on the change in arousal ratings, with a greater overnight decrease for cued than non-cued negative items ($P = 0.015$).

Conclusions: Our results provide evidence that cueing memory replay during SWS benefits consolidation, regardless of valence. More importantly, we show cueing memory replay in SWS increases the extent to which the subjective arousal of negative stimuli decreases overnight.

Disclosure: Nothing to disclose.

P360

Sleep and recognition memory: comparing face and scene as emotional stimuli

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Introduction: Post learning sleep is associated with improvement in recognition memory. The improvement is attributed to strengthening and stabilizing memory traces and reducing retroactive inhibition during sleep. Previous research suggests that faces irrespective of their emotional valence show better recognition memory after sleep filled nights. In the present study we aim to verify whether this result extends to natural scenes.

Objective: The objective of the current study is to compare recognition memory for emotional face and scene following one night of sleep and wake.

Method: Twelve volunteers tested twice, at learning before sleep or wake and retest the following evening. At learning subjects judged affect for 60 pictures (30 face + 30 scenes) divided equally as pleasant, unpleasant and neutral. At retest subjects performed old-new recognition test on 120 pictures (30 face + 30 scene) old & (30 face + 30 scene) new. Subject was counterbalanced across sleep and wake nights. Standard sleep monitoring was done.

Results: Split Plot ANOVA session (sleep, wake) x stimuli (face, scene) x affect (pleasant, unpleasant, neutral) on recognition accuracy (hits - false alarm) as dependent variable yielded significant main effect of sleep ($F_{1,11} = 10.23$, $P < 0.05$, $\eta^2 = 0.35$) & stimuli ($F_{1,11} = 61.93$, $P < 0.001$, $\eta^2 = 0.89$).

Conclusion: Sleep irrespective of affect consolidates recognition memory however faces show better recognition than scenes. The result can have implications in both applied and clinical research.

Disclosure: Nothing to disclose.

P361

Does bright light interfere with fear learning?

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The amygdala is involved in the processing of emotional stimuli, especially stimuli that are threatening in their nature. An fMRI study has demonstrated that blue light increases amygdala activity when compared to green light. The aim of the current study is to examine the influence of bright blue-enriched light on the processing of threatening visual stimuli. Since bright blue-enriched light may interfere with the processing of threatening stimuli, it is hypothesized that such light causes impairments in the recognition of previously presented negative visual stimuli when compared to neutral or positive pictures.

In a balanced cross-over design pictures with emotionally neutral, positive and negative contents were shown to participants ($n = 16$). A recognition task was conducted after 1 h of bright blue-enriched light exposure (or control condition), measuring accuracy and reaction times (RT).

Results showed that bright light increased RT for the recognition of neutral (-46 ± 176 ms) and positive (-56 ± 109 ms) pictures, but not for negative pictures (21 ± 148 ms). For the positive pictures there was a significantly higher decrease in the RT after bright light (relative to the control condition) than for the negative pictures (paired t-test; $P < 0.05$);

Considering that bright light not only activates amygdalic regions but also cortical networks that might be responsible for general decreased RT, current data may indicate that bright blue-enriched light interferes with processing of negative stimuli. The current study was conducted in the evening hours when light is biologically unnatural. Further research should investigate this relationship in a daytime setting.

Disclosure: Nothing to disclose.

P362

Sound asleep: processing and retention of slow oscillation phase-targeted stimuli

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Introduction: The sleeping brain retains some residual information processing capacity. Although direct evidence is scarce, a substantial literature suggests the phase of slow oscillations (SOs) during deep sleep to be an important determinant for stimulus processing. We thus examined how cortical networks respond to real-world sound stimuli as a function of SO phase.

Methods: We introduce an algorithm for predicting slow oscillations in real-time. Using this algorithm, we repeatedly presented sound stimuli directed at up and down states to sleeping subjects. By consistently targeting particular stimuli at a specific SO phase, we putatively engendered the gradual buildup of a memory trace. We evaluated brain-wide SO phase-dependent brain responses to stimuli in the time and time-frequency domain. Following sleep, subjects were exposed to the presented, as well as novel sounds; neural and behavioral indices of memory formation were explored.

Results: Sound delivery in the up state elicits a second up state that occurs earlier in time, has higher amplitude, and features more prominent fast brain oscillations, than with stimulus presentation in the down state. The robust increase in high-frequency activity

concerns the spindle/beta frequency range. However, no evidence for the formation of lasting memory traces was found during waking.
Conclusions: We show that the SO phase has a decisive influence on immediate stimulus processing. However, differential neural processing did not carry over into wakefulness or affect behavioral decisions. We speculate that while simpler forms of learning may occur during sleep, neocortically based memories are not readily established during deep sleep.
Disclosure: Nothing to disclose.

P363

Impaired consolidation of emotional memories during sleep in older adults

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Objectives: During aging, changes in sleep architecture and dysfunction of some memory-related areas may hinder sleep-dependent memory consolidation. Few studies have revealed such an impairment in older adults using declarative tasks. Here, we investigated sleep-dependent consolidation of emotional memories in older adults using functional magnetic resonance imaging (fMRI).
Methods: Nineteen older, healthy volunteers (64.9 $\pm$ 5.3 years) learned pictures with emotional (positive or negative) or neutral valence. Sleep was recorded during the post-learning night. Three days after learning, fMRI data were acquired during a recognition task. Memory performance and patterns of brain activity were compared to those obtained in 18 young subjects (22.6 $\pm$ 2 years) that followed the same procedure apart from the sleep recording.
Results: Recognition accuracy (i.e. proportion of hits – false alarms) was impaired in older adults ($P < 0.01$). However, the impairment tended to be larger for positive items. Recognition accuracy for emotional items positively correlated with time spent in REM sleep during the second half of the night (r = 0.52, $P = 0.04$). We also reported a positive correlation between memory performance for emotional items and spectral power in theta frequencies over temporal derivations (r = 0.61, $P = 0.012$). Preliminary analyses of fMRI data revealed specific activations in older adults in the left hippocampus and amygdala during recognition of positive pictures ($P < 0.001$).
Conclusions: Sleep-dependent consolidation of emotional memories is altered in aging. This impairment appears to be associated with changes during late REM sleep and subtle differences in brain activity.
Disclosure: Nothing to disclose.

P364

Neurobehavioral performance during an intensive spatial navigation task and local use-dependent changes in the wake electroencephalogram

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Recently, it has been shown the presence of *local use-dependent sleep* in awake rats during an intensive task, namely an increase in slow/theta waves (2–6 Hz) in neuronal networks associated with the task at hand, that led to a worsening of performance. The present study investigates in humans whether the local use-dependent changes during an intensive spatial navigation task are associated with errors in the task performance.
The spatial navigation task required participants (11 males, mean age 24.3 $\pm$ 2.45) to navigate in a virtual city (developed by means of a three-dimensional software, *Maze Suite*) and to learn the location of 16 *landmarks* within the city, in order to travel between different *landmarks* locations (*retrieval phase*), choosing the shortest pathway in terms of units, time and path to completion of each retrieval (analyzed by means of the mapping tool of *Maze Suite*). Before and after the *retrieval phase*, sleepiness was evaluated both using the *Stanford Sleepiness Scale (SSS)* questionnaire and 10-min of the *psychomotor vigilance task (PVT)*, recorded with video high-density electroencephalogram (hd-EEG, 128 channels) as the *retrieval phase*.
Mean reaction time and number of *lapses* (responses > 500 ms) in the *PVT* didn't differ before and after *retrieval* task. Instead, *SSS* scores showed a significant increase. Furthermore, delta and theta power (0.5–7.5 Hz) increased locally during errors with respect to both baseline and the best performance conditions.
Neurobehavioral impairment in task performance is associated with a local use-dependent slowing of EEG rhythms, beyond a generalized increase of subjective sleepiness.
Disclosure: Nothing to disclose.

Instrumentation and Methodology (Basic Sleep Science)

P365

Online wireless sleep analysis for auditory sleep stimulation

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Objectives: Recently, online phase locked sound stimulation has been used to enhance slow oscillations during sleep and to improve overnight memory recall (Ngo et al, Neuron 2013:78:1). To make such systems applicable also for home environment, we have developed online wireless sleep analysis setup that automatically evaluates the depth of sleep using self-applicable, disposable electrodes placed outside hairline and also provides phase locked auditory stimulation. In this study, we evaluated the performance of online sleep depth analysis of the developed system.

Methods: We used 15 overnight recordings from 10 subjects in sleep laboratory. Online sleep analysis detected slow oscillations based on two electrooculography signals referenced to mastoid and adaptively adjusted the sound volume to maximum of 15 dB HL depending on the depth of sleep. Sound stimulation was phase locked to slow oscillation (SO) events detected on Fpz referenced to mastoid. Offline standard AASM sleep stage scoring was performed and occurrence of sound stimulation in different sleep stages was evaluated.

Results: There were an average of 3.8 events fulfilling the criteria for triggering sound stimulation during every recorded minute both during sham and sound stimulation nights. 1.0% of stimuli occurred during W, 0.1% during R, 0.6% during N1, 12.8% during N2, and 85.4% during N3.

Conclusions: It is possible to target deep sleep phases with disposable, self-applicable electrodes and automatic analysis. Correct targeting is likely to reduce unwanted arousing effects of sound stimulation during light and REM sleep. The setup is suitable for ambulatory devices.

Disclosure: Nothing to disclose.

P366

Automatic segmentation of REM sleep into three substages

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Objectives: The research aimed to introduce and test an automatic method for segmentation of REM sleep into three substages, respectively characterized by: enhancement of rapid eye movements; selective enhancement of slow eye movements (SEMs); reduction in the amount of eye movements. This objective was suggested by two kinds of data reported in the literature: distinction between phasic and tonic REM sleep, and remarkable presence of SEMs during REM sleep.

Methods: The following signals were recorded: 19 EEG traces, submental EMG, and two EOGs (E1-A2 and E2-A2). The automatic analysis was performed on the EOG signals recorded during the REM periods that were identified by visual scoring. The method applied, which was derived from a previous method for the recognition of NREM microstructure, allowed identifying and characterizing events that consisted in transient amplitude increases in either a slower (0.2–0.6 Hz) or a faster (1–3 Hz) component of the EOG. Segmentation was obtained by means of simple queries to a database containing the features of the events.

Results: The segmentation procedure made it possible to calculate nine parameters for each REM period: the duration percentages of the three sub-stages, and the amplitude, mean frequency, and frequency variance of the two components.

Conclusions: A quantitative description of the oscillating properties of REM sleep can suggest hypotheses about currently debated issues, regarding the thalamocortical intrinsic loop active during REM sleep, the REM sleep behaviour disorder, the reduction of vulnerability during REM sleep, the mechanisms of sleep regulation, and the complex process of dream building.

Disclosure: Nothing to disclose.

P367

Translation, cross-cultural adaptation and psychometric properties of the Jenkins Sleep Scale in a sample of Portuguese shift workers

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Objectives: The aim of this study was to translate the Jenkins Sleep Scale into Portuguese, to culturally adapt it to the Portuguese culture and to assess its stability, internal consistency and convergent validity among shift workers.

Methods: The scale was validated in a random sample of 456 shift workers. The original Jenkins Sleep Scale (JSS) was translated and culturally adapted to the Portuguese Culture using recommended procedures. The psychometric methods used were confirmatory factor analysis using structural equation modeling, Cronbach's α coefficients, and intra-class correlation coefficients.

Results: The results suggest the JSS-PT has a single factor model, as the original version. The Comparative Fit Index and the Tucker-Lewis Index suggest an excellent fit. However, the relatively large sample size and the small number of items penalized Qui^2 statistics and Root Mean Square of Error Approximation. Cronbach's α coefficient was 0.839 for the extracted factor. Pearson bivariate correlations were performed on 75 participants, with an interval of 1 week for test-retest purposes with intra-class correlation of 0.989 ($P < 0.01$). Convergent validation showed significant correlations ($r = 0.570$).

Conclusions: The validity and reliability of this scale was established, enabling it to be used within the Portuguese language speakers. Nevertheless, this study should be replicated in other samples and other forms of validity might be explored.

Disclosure: Nothing to disclose.

P368

Automated sleep staging classification using a non-contact biomotion sensor

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Objective: To determine the performance of a non-contact radiofrequency biomotion sensor in estimating sleep parameters, using polysomnography (PSG) as a reference.

Methods: A dataset of 40 recordings with full PSG and non-contact biomotion signal was collected from normal healthy volunteers in a sleep-lab environment. Recordings were automatically aligned and verified by visual inspection. The dataset was split into 20 recordings for algorithm development and training and 20 recordings for independent verification. The non-contact signal was pre-processed to extract features describing gross body movement and respiration amplitude and frequency. These were used to develop an automated sleep staging classification algorithm. From the verification set, performance was determined against PSG by (i) per-epoch accuracy, where each epoch was mapped to one of four stages: Wake, Rapid-Eye-Movement (REM), Light (N1-N2), and Deep Sleep (N3), and (ii) per-subject accuracy for Sleep Efficiency and Sleep Onset Latency.

Results: For two-state Sleep/Wake classification, accuracy was 88.8% (wake sensitivity 51.2%, sleep sensitivity 95.9%, and Cohen's k 0.53). For three-state Wake/REM/non-REM classification, accuracy was 78.3% (Fleiss k 0.53). For four-state Wake/REM,/Light Sleep/Deep Sleep classification, accuracy was 63.3% (Fleiss k 0.47). The per-subject Sleep Efficiency showed correlation of 78% with an error of 4.0 $\pm$ 5.0%, while Sleep Onset Latency showed correlation of 68%, with an error of 3.0 $\pm$ 9.9 min.

Conclusions: The results suggest that a combination of movement and breathing information can detect sleep states with a good degree of accuracy. Using a non-contact sensor may allow low-cost monitoring of sleep macrostructures over successive nights in an unconstrained environment.

Disclosure: Alberto Zaffaroni, Luke Gahan, Louise Collins, Emer OHare and Conor Heneghan are employees of Resmed Ltd. The non-contact biomotion sensor was manufactured by Resmed Ltd and provided to the sleep lab at no cost. Thomas Penzel, Carmen Garcia and Ingo Fietze are affiliated to Advanced Sleep Research Gmbh. Resmed Ltd. contracted Advanced Sleep Research Gmbh to recruit volunteers, perform PSG study and expert annotations. There is no other relevant financial relationship for disclosure.

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Development of a user-friendly platform for real-time automated scoring and analysis of polysomnography data

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Introduction: The low-throughput nature of manual scoring and analysis of sleep data is a major factor preventing sleep research from reaching its full efficiency and potential. Automated approaches developed previously have generally failed to provide sufficient accuracy or 'usability' for sleep scientists without engineering expertise. Therefore, the aim of our research is to develop a user-friendly platform for real-time automated scoring of polysomnography data, known as GCSP.

Methods: We have employed a support vector machine (SVM) to classify EEG/EMG features into the various sleep stages. The SVM is adaptive and trained for each individual set of data to offset inter-subject variability in EEG/EMG traces, via a brief session of manual scoring. After teaching the overall characteristics of different sleep stages in terms of EEG/EMG features, the user has control over sequential scoring decisions and can enforce subjective decisions using the same intuitive rules employed during manual scoring, which applies a further decisional level over the purely mathematical classification of the SVM kernel. GCSP is also capable of high-throughput automated statistical analysis of the scored data.

Results: After manual training, GCSP produced automated scoring coherence with three in-house sleep experts of 94–96%, and reduced scoring times from hours to just seconds. GCSP is also capable of scoring real-time during EEG/EMG recording.

Conclusion: Our approach aims to link a sophisticated automated computational system to the empirical decisions of sleep scientists. Once fully developed, GCSP will provide accurate, reliable high-throughput scoring and analysis of polysomnography data in a range of experimental situations.

Disclosure: Nothing to disclose.

P370

Correlation of EEG slowing to cardiopulmonary coupling during sleep in chronic opioid users

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Objectives: Quantitative sleep study via polysomnography has shown heart-rate variability, respiration, and brainwaves have strong correlations. In particular, sleep-disordered breathing is associated with reduced slow EEG spectral components and increased abnormal heart-rate dynamics. This study investigates these correlations during sleep in chronic opioid users via an automated tool.

Methods: Standard polysomnography sleep study of 10 chronic opioid users (Age 35.3 $\pm$ 9.4 years, BMI 26.1 $\pm$ 4.8 kg/m^2, AHI 16.7 $\pm$ 14.9 events/h) were analysed quantitatively; Spectral analysis was applied to EEG; The RR-intervals were obtained from ECG; Breath by breath intervals and amplitudes of respirations were obtained from a Thermostat channel. Coherences between these channels were calculated to obtain cardiopulmonary coupling (CPC), cardio-cerebral (CCC), and pulmonary-cerebral couplings (PCC), and related to sleep stage scoring. The cardiopulmonary coupling was further associated with the EEG slowing, defined as ratios of delta (0.5–4.5 Hz) to alpha (8–12 Hz) spectral power, via the cross-correlation measure.

Results: CPC, CCC, and PCC increase in deeper sleep stages. However, their ability for the sleep/wake classification was limited (e.g., accuracies were 53%, 55%, 53% and for CPC, CCC, and PCC, respectively). There were significant cross-correlations between CPC and EEG for each individual (Pearson's r 0.678 $\pm$ 0.051, $P < 0.05$).

Conclusion: Greater CPC ratio of LF (0.01–0.1 Hz) to HF (0.1–0.4 Hz) during sleep in chronic opioid users correlated with EEG slowing, suggesting CPC as a candidate biomarker to identify brain functional impairment in the patient group studied.
Disclosure: Nothing to disclose.

P371

A novel sleep spindle detection method to account for intra- and inter-individual differences in spindle characteristics

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Objectives: A novel spindle detection method was developed to overcome methodological hurdles, including:

1. Extracting the signal with high signal to noise ratio,
2. Accounting for variations of spindle characteristics across the night, scalp derivations and between individuals,
3. Categorization of slow and fast spindles, and
4. Minimizing the number of user-defined parameters.

Methods: Complex demodulation was used to extract instantaneous power in the spindle band with high signal to noise ratio. To account for intra- and inter-individual differences, the signal was z-score transformed using a 60s sliding window. Spindle events were detected with a z-score threshold (e.g., 99.9th percentile). Amplitude, duration and oscillatory frequency were derived for each spindle. Rather than running separate detection passes, each spindle was categorized as slow or fast from the peak frequency of each spindle. Spindles were automatically detected in 15 young and 15 older subjects. An expert manually identified spindles from 20 min of NREM sleep from each recording. These spindles were then compared to the automated detection using 3s epochs to identify the presence of true positives (TP), true negatives (TN), false positives (FP) and false negatives (FN).
Results: Totals for TP, TN, FP and FN were used to calculate the sensitivity, specificity and FP rate, which were 85%, 90% and 10%, respectively. Preliminary results show automated detection had a high inter-rater reliability with an established method in young and older subjects ($r = 0.92$).
Conclusions: This method of spindle detection addresses many of the methodological challenges that currently plague the reliability and validity of automated spindle detection.
Disclosure: Nothing to disclose.

P372

Inter- and intraindividual variability of the pupillary unrest index (PUI)

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Objectives: The recording of slow pupillary oscillations in darkness turned out to be a promising approach for objective evaluation of sleepiness at the physiological level. Purpose of the present study was to analyse the magnitude of between and within subject variation of the pupillary unrest index (PUI) inherent in a sample of normal healthy individuals.
Methods: Present data was collected in the framework of a study which aimed to investigate possible effects of radiofrequency electromagnetic fields (RF-EMF) emitted by mobile phones on the central nervous system. Thirty (18–30 years) males participated in the study. Pupillary behavior was monitored on ten experimental days at 11 am and at 16 pm, respectively, with infrared video pupillography (Compact Integrated Pupillograph). RF-EMF had no impact on the PUI. 245 morning and 258 afternoon measurements (4–10 recordings per subject) were considered for statistical analyses.
Results: Comparisons between the individuals revealed statistically significant variations of the PUI in the morning ($P < 0.001$) as well as in the afternoon ($P < 0.001$). PUI showed an interindividual variability of more than 40% at both times of measurement. Intraindividual variation of the PUI ranged from 0.23 to 11.42 mm/min in the morning and from 0.56 to 9.41 mm/min in the afternoon.
Conclusions: The significant interindividual variability underlines that the PUI is not only a state marker. Variations may also occur within one subject with measurements under similar experimental conditions. Evaluations of such measurements should therefore also consider the PUI as possible trait to ensure comparability and correct interpretation.
Disclosure: Nothing to disclose.

P373

Quantum neural networks for predicting lane deviations from steering wheel angle

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Objectives: Driving while fatigued may cause traffic accidents. The prevalence of this condition is high among drivers. Drowsy driving increases the possibility of lane departures, and to reduce this risk, we set out to *predict* lane deviations from the steering wheel angle using Quantum Neural Networks (QNNs).
Background: Artificial neural networks (ANN) enable time series prediction through supervised learning. QNNs learn faster, are more stable, and have smaller errors than classical ANNs. QNNs handle non-linear, heavily dependable processes, and require no assumption about linearity or stationarity. Neural networks can handle both slow drifts and sudden changes, such as stock market crashes.
Methods: We use high-fidelity driving simulator data (12896 km of straight highway driving) and a Time Delay Feed Forward Neural Network with one hidden layer with qubit neurons. During supervised training the interconnecting weights were calculated from a superposition of all possible states. The superposition was achieved through a quantum rotation gate and controlled NOT gates. We compared the QNN-performance by means of mean squared error and prediction horizon to that of our previous cross-correlation method.
Results: We implemented QNNs in Matlab and will present the training phase and prediction results.
Conclusion: We expect the QNNs to produce a smaller error than our previous method.
Disclosure: Nothing to disclose.

P374

Effect of CPAP in erythrocytosis and sleep apnea hypopnea syndrome

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Introduction: Polycythemia is a finding in patients with obstructive sleep apnea syndrome (OSAS). If the hematocrit increase was due to intermittent nocturnal hypoxia, it would be interesting to analyze whether CPAP treatment produces a decrease in hematocrit, translating a correction of hypoxic events.

Material and methods: 20 patients referred from the hematology unit for respiratory sleep disorders evaluated during 2012–2013. They did study with cardiorespiratory polygraphy. Those patients diagnosed with OSAS were treated with CPAP. After 6 months of treatment, underwent a blood test. Hemoglobin levels and hematocrit were compared before and after CPAP, using the Wilcoxon test for nonparametric variables.

Results: All patients were male. The mean age was 64.5 (SD 13.6). 85% (17) patients were diagnosed with OSAS. The mean respiratory disturbance index (RDI) resulted 32.7 (SD 25.6). The minimum was 0.7 and the maximum 81. Half of the patients showed severe OSAS. The nocturnal oximetry profile presented with an average of 41% T90% (SD 35) and a middle desaturation index 34.4 / h (SD 25).
A predominance of obstructive SAHS was observed. When comparing hemoglobin and hematocrit before and after treatment with CPAP, a reduction of both parameters was observed, with a significant difference.

Conclusion: Patients with OSAS and poliglobulia show an improvement in red cell parameters after treatment with CPAP. Studies with larger series are needed to verify these results.

Disclosure: Nothing to disclose.

P375

Automatic biorhythms from actigraphy data

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Objective: Visual assessment of regular and successive sleep-wake periods derived from actigraphy is laborious, time-consuming and prone to inter-individual differences across raters. To counteract these current limitations, we developed an automatic algorithm to standardize and speed-up this procedure.

Method: We used two steps. First, we estimated regular sleep/wake periods (over at least seven successive days) with classic signal processing. This approach comprised removal of incorrectly timed data and a median filtering with subject-specific thresholding, followed by morphological opening/closing. This leads to rough estimation of final output. In the second step, data and estimations were divided into 5-min windows, labelled as either 'sleep' or 'wake'. Subsequently, a machine learning approach was applied onto these segments, and the trained machine was used to improve sleep/wake detection periods. Finally, we compared these results with expert's visual assessment, considering four major criterions: agreement rate, sensitivity (periods correctly assessed as wake over all periods assessed as wake), specificity (periods correctly assessed as sleep over all periods assessed as sleep), and Cohen′s kappa.

Result: Successive and regular 7-day actigraphy sleep-wake recordings from 25 young healthy subjects were analyzed by an expert and the automatic algorithm. Overall, we obtained an agreement rate of 97.4%, sensitivity of 98.1%, specificity of 96.3% and Cohen′s kappa of 94.2%.

Conclusion: Our automatic actigraphy analyzes was as good as the manual visual assessments, as indexed by the high agreement rate and sensitivity/specificity ratios. Importantly, the automatic assessment worked much faster, and is robust and reproducible.

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P376

Nightmare′s effects on daily functioning – the nightmare effects questionnaire (NEQ)

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Objectives: Nightmares usually occur during childhood and adolescence. Frequency and intensity of nightmares decrease with increasing age. The existing literature shows that frequent nightmares are associated with psychological stress and daily impairments. Until now age-oriented questionnaires gathering specific information about the effects and consequences of nightmares in adolescents are sparse. We developed the Nightmares Effects Questionnaire (NEQ) to close this gap.

Method: A list of six expert generated questions concerning the frequency of dreams and nightmares, and a list of 35 possible daytime impairments after having a nightmare was composed. In a pilot study 216 adolescents (aged 14–18 years) filled out the Nightmares Effects Questionnaire (NEQ). Out of this data a first check on psychometric properties was performed.

Results: A factor analysis was conducted to extract the underlying subscales. The 35 daytime impairment items were assigned to five subscales; these are 'anxiety/depression', 'concentration and attention problems', 'aggression', 'antisocial behavior', and 'bodily symptoms'. The overall reliability of the Nightmares Effects Questionnaire (NEQ) was high with $\alpha = 0.904$. Data for assessing retest-reliability are collected.

Discussion: The Nightmares Effects Questionnaire (NEQ) for adolescents shows high reliability and can be conducted to assess adolescent's psychological stress and impairment caused by nightmares. The questionnaire can also be used in research context to better understand and explore the impact of nightmares on adolescents well being.

Disclosure: Nothing to disclose.

P377

Confirmatory factor analysis of sleep model's questionnaires

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Objectives: The present study aims to test the factor structure of two sleep questionnaires and their internal consistency in a sample of adolescents and their respective parents and to evaluate the validity

and robustness of a three-dimensional model about sleep, addressing nine subcategories related to sleep habits, personal and environmental factors (Rebelo-Pinto, Pinto, Rebelo-Pinto, & Paiva, 2014).

Methods: Participants were 654 adolescents from Portuguese schools, who completed 'My Sleep and I' questionnaire, and 664 parents who completed 'My child's sleep' questionnaire; to them confirmatory factor analysis was applied.

Results: Confirmatory factor analysis indicate that a nine-factor model has better fit indices compared with the others tested models for both samples (Adolescents: χ^2/df (chi-square/degrees of freedom) = 2.59, CFI (Comparative Fit *Index*) = 0.82, GFI (Goodness-of-Fit *Index*) = 0.92, RMSEA (*Root Mean Square Error of Approximation*) = 0.049, ECVI (Expected Cross-Validation *Index*) = 1.416; Parents: χ^2/df = 2.89, CFI = 0.85, GFI = 0.91, RMSEA = 0.053, ECVI = 1.528). Moreover, the comparison of the models through $\Delta\chi^2$ index (chi-square difference between rival models) indicates a better fit for this model, $\Delta\chi^2$ (24) = 186.5, $P < 0.001$ for adolescents and $\Delta\chi^2$ (24) = 209, $P < 0.001$ for parents. Also, the three second-order factors have good internal consistency, convergent and discriminant validity for all factors in both samples.

Conclusions: Results postulate that the three factors and their nine subcategories account for correlations between sleep habits, self-perceptions and knowledge about sleep.

Disclosure: Nothing to disclose.

P378

Pilot study: blood pressure response to withdrawal of positive airway pressure treatment in patients with hypertension and obstructive sleep apnea

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Objectives: The aim of this pilot study was to assess the feasibility of PAP therapy withdrawal in obstructive sleep apnea (OSA) patients to detect a blood pressure (BP) effect.

Methods: Recruited subjects were patients using positive airway pressure (PAP $\geq$ 4 h/night for >1 year), diagnosed with hypertension and using antihypertensives. They underwent 24-h BP measurements on PAP at baseline, after 14 and 30 days without PAP and after 14 days on PAP again. Subjects measured their BP twice daily at home. They underwent screening for OSA after 6 and 30 days without PAP.

Results: The three OSA patients were two males and one female (mean age = 54 years, mean body mass index = 30 and mean apnea-hypopnea index = 20 [untreated]). The BP increased already over the first days of withdrawal for all the individuals but was very variable between days, both on and off PAP (mean morning systolic and diastolic difference of 31 and 27 mmHg during withdrawal). To assess OSA severity, 6 days PAP withdrawal was not sufficient as all subjects had higher OSA indices after 30 days withdrawal. All described increasing levels of fatigue and sleepiness during the study period.

Conclusion: Future PAP withdrawal studies should consider high BP variability and perform frequent BP measurements. The actual OSA severity does not appear after only 1 week of PAP withdrawal so a longer period is needed for full effects. No complications were observed but ethics need to be considered of a study where a patient on successful treatment is prevented from their medical care.

Disclosure: Erna Sif Arnardottir -a part time consultant for Nox Medical Iceland.

P379

A critical analysis of electronically equipped beds used in sleep medicine

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Objectives: Different electronically equipped beds that can be used to detect the health status of a patient during sleep exist. But so far quite little has been said about the advantages and disadvantages of different types of these beds when used in sleep medicine. The objective of this article is to give a systematic analysis of the electronically equipped beds used in sleep medicine, and about their usability in hospital and in home care with diagnostic or therapeutic aims.

Methods: In the paper these beds are analysed and classified according to the data acquisition method used in them. Each method is described in details of it's design principle, it's place in the practice of using, and it's ability to measure different physiological signals.

Results: In the field of electrically equipped beds there can be found at least seven different measurement methods used for detecting the health state of a sleeping patient, and at least five physiological parameters are measured. Pressure measurement is found to be the most effective data aquisition method for detecting of heart rate and breathing rate. Other methods were found to be more sensitive to artefacts and environmental influences.

Conclusion: Comparison of different data aquisition methods showed that the physiological parameters and signals, which are better determinable are the heart rate, the breathing rate and the body movement signals. The measurement of air flow and volume of lungs are difficult to conduct and sensitive to artectacts. A noticable tendency of moving towards electronically equipped mattresses exists.

Disclosure: Nothing to disclose.

P380

Beneficial effect of morning light after one night of sleep deprivation

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Exposure to artificial light improves subjective well-being, mood, cognitive performance and supresses melatonin secretion; relative to light administration and exposure time. This photic influence might be especially useful to counterbalance the impact of prolonged wakefulness on sleepiness and performance. Here, we seek to evaluate the effect of early morning light on performance, mood, alertness, and melatonin, after one night of total sleep deprivation.

Twenty four healthy young underwent a balanced cross-over design. The participants followed their habitual life rhythms prior to their admittance to the research laboratory to undergo one night sleep deprivation. During the sleep deprivation, cognitive performance was assessed every 2 h.

The bright light exposure lasted for 30 min starting at 5 am. The three following lightening conditions were applied Luminette®

(Lucimed, Belgium), Philips Energy-Light and control condition with dim light exposure.

We observed a significant ($P < 0.05$) light-enhanced performance by the number of right answers on the PVSAT and the reaction time to the PVT, and decreased sleepiness characterized by the KSS. Preliminary salivary Melatonin levels (four participants, on-going analyses), after light exposure were reduced but are not significant as compared to dim light ($P = 0.09$).

These results are of relevant not only for ergonomica and societal reasons, but medical investigations as well. The demonstration that light administration through light-emitting glasses is as efficient as conventional bright light therapy boxes may have direct societal and medical applications, most notably for shift workers.

Disclosure: Nothing to disclose.

Sleep Disorders – Breathing 1

P381

Polysomnographic evaluation of sleep disordered breathing after lung transplantation

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Objectives: A limited number of studies showed a high prevalence of sleep disordered breathing (SDB) in patients after lung transplantation (LTX) ranging from 36% to 100%. This variation in prevalence is influenced by different definitions of SDB and a variable time-frame after transplantation. This study aimed to examine timing of onset, pattern and associated clinical factors of SDB after LTX.

Methods: Fifteen patients (12 males/three females, mean age: 52.3 years) underwent a polysomnography before, 1 month and 1 year after LTX. SDB was defined as an apnea/hypopnea index (AHI) >15. If >50% of events were central, SDB was classified as central. Follow-up with lung function and biochemistry was also performed.

Results: Mean AHI before transplantation was 5.8 with two patients having obstructive SDB. One month after LTX, mean AHI was 12.4 (SDB in two patients). One year after LTX, mean AHI was 23.9 with 9/15 patients having SDB (three obstructive to six central). Patients with SDB had significantly less REM sleep, a significantly higher arousal/awake index, lower minimal saturation and lower diffusion capacity. Body mass index was not different. In patients with central SDB, diffusion capacity was lower and prevalence of diastolic heart failure was higher compared to patients without SDB.

Discussion: This prospective study shows a high prevalence of SDB in patients 1 year after LTX in contrast to a lower prevalence 1 month after LTX. This suggests that SDB after LTX develops rather late and is probably not a consequence of lung denervation or (short-term) use of immunosuppressive drugs.

Disclosure: Nothing to disclose.

P382

Continuous positive airway pressure (CPAP) impact on abdominal fat redistribution in obstructive sleep apnea patients

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Objectives: The aim of our study was to evaluate the long-term effect of continuous positive airway pressure (CPAP) treatment on intra-abdominal fat distribution in obstructive sleep apnea (OSA) patients.

Methods: Eighty five patients with OSA diagnosed by polysomnography, (50 with and 35 without CPAP treatment criteria) were followed-up for 2.1 (1.6–2.4) years by the Sleep Unit of our Hospital. Visceral and subcutaneous adipose tissue (VAT and SAT) and preaortic intraabdominal fat (PIF) were assessed by abdominal sonography methods, at the beginning and at the end of the study, in both CPAP and non-CPAP treated groups.

Results: BMI and weight didn't change significantly after the follow-up period in any group. In the non CPAP treated group, SAT and VAT mean values didn't change [(11.41 $\pm$ 4.77 vs. 11.78 $\pm$ 5.55 mm, $P = 0.288$) and (16.91 $\pm$ 4.22 vs. 15.93 $\pm$ 3.59 mm, $P = 0.211$), respectively], while a significantly PIF growth was observed (55.19 $\pm$ 23.44 vs. 63.45 $\pm$ 23.94 mm, $P = 0.021$). In the CPAP treated group, VAT and PIF mean were not significantly changed [(15.74 $\pm$ 5.79 vs. 15.45 $\pm$ 6.73 mm, $P = 0.603$) and (70.89 $\pm$ 19.64 vs. 74.51 $\pm$ 25.38 mm, $P = 0.264$), respectively], while SAT decreased significantly (11.29 $\pm$ 5.69 vs. 10.47 $\pm$ 5.71 mm, $P = 0.012$).

Conclusions: The long-term CPAP treatment produces an intraabdominal fat redistribution in OSA patients. CPAP treatment prevented PIF increase and was associated to SAT reduction. These changes could contribute to the reported CPAP mediated metabolic effects.

Disclosure: Nothing to disclose.

P383

Influence of nasal mask choice for continuous positive airway pressure (CPAP) therapy in patients with obstructive sleep apnoea (OSA)

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Objectives: Relatively few trials have investigated the influence of mask on CPAP therapy for OSA. This multicentre study compared outcomes during CPAP therapy using different first-line nasal masks in OSA patients.

Methods: Newly-diagnosed OSA patients were randomised to receive CPAP via different nasal masks (Group 1, ResMed Mirage FX®; Group 2, Fisher&Paykel Zest® or HC407®; or Philips Easy-Life®). Mask acceptability (defined as patients' continued use of randomised mask), CPAP compliance, and Home Care Provider (HCP) interventions were compared at 3-months in the intent-to-treat (ITT) and on-treatment (OT; CPAP adherent) populations. Logistic regression analysis was used to determine factors associated with nasal mask acceptance.

Results: Two hundred and eighty five patients were enrolled; 90 required a full-face mask due to mouth leaks and were excluded. 195 (ITT) and 151 (OT) patients were included in the analyses. More patients in group 1 vs. group 2 showed mask acceptance (ITT 79% vs. 68%, $P = 0.067$; OT 90% vs. 76%, $P = 0.022$). Compliance with CPAP was better in group 1 vs. group 2 (5.9 $\pm$ 1.8 vs. 5.1 $\pm$ 1.6 h/night, $P = 0.011$). The number of HCP visits as a result of nasal mask issues was lower in group 1 vs. group 2 (3% vs. 17%, $P = 0.006$); time for initial training was similar. Nasal mask acceptance was significantly associated with fewer mask leaks (OR 0.85, 95% CI 0.76.0.94, $P = 0.002$) and higher pressure therapy (OR 1.21, 95% CI 1.01.1.44, $P = 0.042$).

Conclusions: This study suggests that acceptance of various nasal masks is not equivalent, and that initial nasal mask choice may influence compliance and subsequent CPAP therapy management.

Disclosure: ResMed employees.

P384

Hyoid bone in obstructive sleep apnea syndrome patients according the craniofacial growth

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Background: Cephalometry is a reproducible method for analyzing craniofacial structures and for diagnosing UA obstruction. The hyoid bone (HB) doesn't articulate with any other bony structure. Position of the HB is determined by the muscular coordination of the geniohyoid, genioglossus, sternohyoid, thyrohyoid muscles. But plays an important role in OSAS and their treatment.

The objective of our study is to classify OSAS patients according to their craniofacial morphology and to describe the position of the hyoid bone.

Methods: This was a descriptive study. These patients had a baseline PSG to diagnose OSAS with RDI $\geq$ 10 and a lateral cephalometric radiograph was obtained from each patient. We studied the HB position at the horizontal plan (HHRgn): it's the distance between the upper point of the HB (UHH) and most posterior point of the mandibular symphisis (RGn). The vertical one (mph) is analyzed like the distance between the mandibular plan and HB. The OSAS patients were classificate by cephalometric Rx in three groups: brachyfacial (BF), mesofacial (MF) and dolichofacial (DF)

Results:

N = 46 Male: 34 Female: 12 Age: 57 (12) years old IMC: 26BF, 27MF, 28DF
RDI/h 28 $\pm$ 18 (BF) 18.7 $\pm$ 9 (MF) 18 $\pm$ 10 (DF)
Desaturation Index/h 70 $\pm$ 6 (BF) 31 $\pm$ 3 (MF) 46 $\pm$ 4 (DF)
Arousals index/h 107 $\pm$ 5 (BF) 97 $\pm$ 8 (MF) 67 $\pm$ 4 (DF)
MPH 22 $\pm$ 5 (BF) 19 $\pm$ 6 (MF) 27 $\pm$ 7 (DF)
Rtrog 44 $\pm$ 8 (BF) 41 $\pm$ 4 (MF) 43 $\pm$ 8 (DF)

Conclusions: Brachyfacial pattern have more severe OSA than the others patients.Vertical growth pattern patients have the farthest position of the hyoid bone to the mandibular plane than the other patients (bracyfacial and mesofacial). It could have implications in SAHS treatment with oral devices.

Disclosure: Nothing to disclose.

P385

In moderate to severe obstructive sleep apnea, sleepy patients do have higher apnea-hypopnea índex than nonsleepy patients

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Objective: To compare clinical and polygraphic study data of sleepy vs. nonsleepy, moderate to severe obstructive sleep apnea (OSA) patients, according to the Epworth Sleepiness Scale (ESS).

Methods: Data were obtained from 124 consecutive moderate to severe (apnea-hypopnea index or AHI >15) OSA patients who underwent sleep study in our sleep disorders unit. After excluding other sleep disorders, or comorbidities that could influence sleep study results, we selected 100 patients. 24 patients were sleepy (ESS > 10 $\leq$ 16) and 76 were nonsleepy (ESS $\leq$ 10).

Results: Sixty seven patients were male and 33 female, median age 62.5 years. 66 patients were obese, and morbid obesity was identified in 33.

Fifty eight polysomnographic and 42 polygraphic studies were analyzed. 49 patients had moderate OSA and 51 were severe.

Comparing moderate to severe OSA patients, the severe group had lower minimal arterial oxygen saturation ($mSaO_2$) ($P < 0.0001$) but no differences were found related to BMI or medium age.

Sleepy patients have higher apnea-hypopnea índex (AHI) than nonsleepy (median 42.1 vs. 28.5; $P < 0.033$), but there were no differences in age, BMI or $mSaO_2$.

In multivariable analysis, neither AIH nor $mSaO_2$ were significantly associated with the severity of sleepiness; the higher AHI was associated in logistic regression to less $mSaO_2$ and to male sex; lower $mSaO_2$ was associated in linear regression with higher AHI and higher BMI.

Conclusions: In this group of moderate to severe OSA patients, sleepy patients have higher AHI than their nonsleepy counterparts. However, OSA severity is associated mainly to higher BMI and male sex.

Disclosure: Nothing to disclose.

P386

Relationship between smoking and obstructive sleep apnoea and hypopnoea syndrome

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Objective: To investigate the relationship between smoking and obstructive sleep apnoea and hypopnoea syndrome (OSAHS).

Methods: We performed a retrospective chart-review of patients who underwent polysomnography at a Sleep-Disordered Breathing Center over 3 years. Patients were classified into an OSAHS (apnoea-hypopnoea index [AHI] > 15 events/h) and a non-OSAHS group (AHI < 5 events/h);patients with AHI between 5–15 events/h were excluded. Smoking historywas obtained using retrospective questionnaires, and its association with OSAHS was analysed.

Results: The OSAHS and non-OSAHS groups included 929 and 411 patients respectively, with a 47.1% and 25.5% smoking prevalence, respectively. Logistic regression analyses showed that after adjusting for age, gender, body mass index (BMI), smokers were 1.446 times more likely to have OSAHS than never smokers (95% CI: 1.079–1.939, $P = 0.013$). Smokers with $\geq$30 pack-years were more 2.382 times likely to have OSAHS than never smokers (95% CI: 1.127-4.375, $P = 0.012$). Compared to non-smokers with OSAHS, OSAHS smokers showed hypoxemia (SaO_2 < 90%) for a greater percentage of total sleep time (TST) [(20.5 $\pm$ 23.1)% vs. (15.6 $\pm$ 18.8)%, $P = 0.004$] and lower average SaO_2 during sleep [(69.4 $\pm$ 10.3)% vs. (73.2 $\pm$ 9.7)%, $P = 0.000$]. Moreover, OSAHS smokers with $\geq$30 pack-years were 1.893 times more likely to have SaO_2 < 90% for >5% of their TST than non-smokers with OSAHS (95% *CI*: 1.046–3.423, $P = 0.035$).

Conclusion: Smoking significantly increases the risk of OSAHS and nocturnal hypoxia.

Disclosure: Nothing to disclose.

P387

Continuous positive airway pressure therapy reduces mortality in Chinese patients with obstructive sleep apnea

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Objectives: Severe obstructive sleep apnea (OSA) is a major risk factor for mortality. The ability of continuous positive airway pressure (CPAP) therapy to mitigate this increased risk of death is not studied in diverse populations. We performed an observational study in China to compare mortality in simple snorers, patients with untreated OSA, and OSA patients treated with CPAP.

Methods: We recruited adults with OSA or simple snoring from our sleep clinic. OSA was determined with standard polysomnography. Participants were followed-up at least annually for a mean of 8.9 years (SD 1.9). CPAP compliance was checked with the built-in meter. We then assessed all-cause mortality.

Results: Five hundred and fifty simple snorers, 257 with untreated mild OSA, 316 with untreated moderate OSA, 457 with untreated severe OSA, and 235 with OSA treated with CPAP were included. Simple snorers had a much lower mortality rate (2.98 per 1000 person-years [95% CI, 2.93–3.02]) than the untreated severe OSA group (11.07 per 1000 person-years [95% CI, 10.86–11.29]; $P < 0.0001$). Compared with simple snorers, fully adjusted mortality was highest in the untreated, severe OSA group (Hazard Ratio [HR], 3.51 (95% CI, 1.93–6.39); intermediate for the untreated, mild and moderate OSA groups (HR, 1.76 [95% CI, 0.86–3.60]; HR, 1.86 [95% CI, 0.96–3.60], respectively); and lowest in the OSA treated with CPAP group (HR, 0.81 [95% CI, 0.36–1.86]).

Conclusions: Severe OSA significantly markedly increases the risk of death in Chinese patients and CPAP treatment reduces this risk.

Disclosure: Nothing to disclose.

P388

Uncontrolled hypertension and obstructive sleep apnoea hypopnoea syndrome among adult snorers in South China

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Objective: To investigate the prevalence of hypertension among obstructive sleep apnoea hypopnoea syndrome (OSAHS) patients and factors associated with hypertension and uncontrolled hypertension in South China.

Methods: A total of 1982 patients (1635 male and 347 female) from South China were enrolled in this study. The patients first completed a questionnaire consisting of a medical history interview regarding sleep apnoea, history of antihypertensive use, and blood pressure control. In addition, the questionnaire explored the presence of risk factors for hypertension and causes of uncontrolled hypertension, which included smoking, BMI, family history of hypertension, and nationality. This was followed by an in-hospital polysomnography (PSG). The patients were classified into an OSAHS and a non-OSAHS group based on PSG results.

Results: The prevalence of hypertension was 48% in the OSAHS group, 25.6% in the non-OSAHS group, 47.5% in smokers, and 41.4% in non-smokers, with a significant difference among the groups. The prevalence of hypertension was 82.1% and 27.3% in the groups with and without a family history of hypertension, respectively ($P < 0.05$). The prevalence of hypertension increased with an increase in apnoea/hypopnoea index (AHI), BMI, and excessive daytime sleepiness (EDS). OSAHS, BMI, age, and family history of hypertension were independent risk factors for hypertension. In individuals who had been previously treated with antihypertensives, OSAHS, alcohol intake, EDS, and AHI were associated with uncontrolled hypertension.

Conclusions: The prevalence of hypertension in subjects with OSAHS was higher than that in patients without OSAHS. OSAHS is a risk factor for hypertension and uncontrolled hypertension.

Disclosure: Nothing to disclose.

P389

Rates of CPAP mask initial acceptance and switching

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Objectives: Considerable development has been recently achieved in alleviating problems related to CPAP masks. We report the initial mask acceptance and the effects of mask switching on mask-induced symptoms.

Methods: We prospectively collected all cases of mask switching in our Sleep Unit for a period of 14 months. The nurse predicted the usefulness of the mask switching with a visual analogue scale (0 = useless, 100 = useful). The hospital uses ResMed™ CPAP devices and masks. Mask switching was defined as replacing a mask, used for at least a 1 day, with another mask type. Changing to a different size but keeping the same type was not considered mask switching.

Results: The size of the patient pool was 2577. Mask switching occurred in 287, of which 96 (33.4%) were due to poor fit/uncomfortable mask, 86 (30%) were leak-related, 69 (24%) due to outdated mask, 21 (7.3%) due to nasal stuffiness and 15 (5.2%) were related to other reasons. Of the 566 new CPAP initiation patients, 93 had mask switching, yielding an initial acceptance rate of 84%. Mask switching resolved mask problems in 71% of poor fit/uncomfortable cases, 64% of leak-related cases and 67% of nasal stuffiness cases. The mean $\pm$ SD of the usefulness score in symptoms-resolved and unresolved groups was 76 $\pm$ 28 and 76 $\pm$ 25, respectively.

Conclusions: The initial CPAP mask acceptance rate was good. Mask switching has reduced mask-related symptoms in about two-thirds of cases. Even experienced sleep nurses were not able to predict the usefulness of mask switching.

Disclosure: Nothing to disclose.

P390

Influence of sleep apnea on type of myocardial infarction. The Sleep Apnea in Post Acute Myocardial Infarction Patients (SAPAMI) study

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Background: Sleep apnea (SA) is associated with intermittent hypoxemia leading probably to ischemic preconditioning in the myocardium. This potential cardioprotective effect of SA may play

role in the development of non-ST-elevation myocardial infarction (NSTEMI) rather than ST-elevation myocardial infarction (STEMI) during acute ischemia. There is limited evidence about the occurrence of NSTEMI and STEMI on dependence of having SA. We therefore prospectively investigated the prevalence of these two types of myocardial infarction (MI) in different SA categories among acute MI patients.

Methods: We prospectively studied 782 consecutive patients admitted to the hospital with the diagnosis of acute MI. All subjects underwent sleep evaluations using a portable diagnostic device after at least 48 h post-admission, provided they were in stable condition.

Results: SA was present in 65.7% and NSTEMI in 30% of patients. Increasing severity of SA was associated with increasing incidence of NSTEMI and conversely with decreasing incidence of STEMI ($P < 0.001$). Relative frequency of NSTEMI in the moderate to severe SA group (AHI $\geq$ 15 events/h) was 40.6% while STEMI 29.9% ($P = 0.01$).

Conclusion: There was an increasing incidence of NSTEMI associated with increasing severity of SA. There was also a significant difference between relative frequency of NSTEMI and STEMI in the group of moderate to severe SA patients. It may suggest a cardioprotective role of SA during acute MI trough ischemic preconditioning. Outstanding issue remains at what point do the risks associated with SA outweigh the benefits of ischemic preconditioning.

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P391

Relationship between neck circumference and polysomnography parameters in obstructive sleep apnea syndrome

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Introduction: Physical assessment hasn't shown a very strong predictive severity diagnostic value in the obstructive sleep apnea (OSA). Polysomnography is the gold standard diagnostic tool, but it is expensive and difficult to get it in some cases. Therefore it is important to find other diagnostic studies that may give us an approximation to the severity of OSA.

Objective: To establish the relationship between neck circumference and polysomnography parameters.

Methods: This was a longitudinal – observational and analytic study in a population-based prospective and prolective cohort. We collected the patients with suspicion of OSA, in the Otolaryngology clinics; they were assessed with the neck circumference measure and diagnostic Polysomnography. We determined the Independent samples T- Test, and the descriptive parameters in the statistical analysis.

Results: We evaluated 141 patients, 95 males (67.4%), neck circumference (NC) range: 30–59 cm; minimal oxygen saturation range: 35–91% with a mean of 72%; mean oxygen saturation range: 65–96% with a mean of 88.9%; apnea hipopnea index (AHI) range: 0.6–173 events/h with a mean 52.6 events/h. There is a statistical significance p value lesser than 0.05 between the NC greater than 43 cm and NC lesser than 43 cm group, in these parameters: minimal saturation, mean saturation and AHI.

Conclusion: The NC greater than 43 cm was associated with the worse results in the following polysomnography parameters: minimal saturation, mean saturation and AHI. These findings may give us an association between NC and the severity of the OSA.

Disclosure: Nothing to disclose.

P392

Correlation between supine and sitting position, in the physical and endoscopic evaluation of the airway in patients with obstructive sleep apnea suspicion

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Introduction: It is very important to establish the site of obstruction in the airway, in patients with obstructive sleep apnea (OSA) suspicion. All these events occur in the supine position while the patient is sleeping; therefore the evaluation in the supine position would give a better assessment of the airway obstruction?

Objective: Establish the correlation and difference between supine and sitting position evaluation of the physical and endoscopic assessment of the airway.

Methods: This was a longitudinal, observational, prospective, analytic study and prolective cohort. We collected 63 patients with suspicion of OSA, they were assessed with the Friedman tongue position, Müller maneuver and endoscopic evaluation of the airway in supine and sitting position. We evaluate the correlation and differences of each one.

Results: There is no statistical significance between sitting and supine position findings in the physical and endoscopic evaluation, without influence by sex or BMI. With correlation coefficient >0.8 with a statistical significance $P =< 0.001$ between sitting and supine evaluation.

Conclusion: No difference in the evaluation of the airway in sitting and supine position, but with a significance correlation between the findings. For this reason is not necessary to do the airway evaluation in the supine position.

Disclosure: Nothing to disclose.

P393

Body Mass Index as a prognosis factor of collapse in the upper airway in adults with obstructive sleep apnea syndrome

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Objectives: The objective of this study is to evaluate the Body Mass Index (BMI) as a prognostic factor to collapse in the upper airway in adults with Obstructive Sleep Apnea Syndrome (OSAS).

Methods: We prospectively enrolled 54 patients, with signs and symptoms of OSAS. All patients underwent a thorough history and physical examination including fiberoptic endoscopic of the upper airway with Müller maneuver (MM) to evaluate collapse, and nocturnal polysomnography study to confirm the OSAS diagnosis. We divided our population in two groups according to the BMI: group over 30 kg/m^2, and group under 30 kg/m^2. Statistical coefficient Kendall Tau test was used to analyze correlation of collapse in the MM in both groups.

Results: 38.9% presented in the group of BMI > 30: 61.9% of them collapsed vs. 38.1% did not collapse. 61.1% presented in the group of BMI < 30: 66.7% of them collapsed vs. 33.3% did not collapse. The correlation coefficient was from 0.042, with a value of $P = 0.710$.

Conclusions: We didn't find correlation between an elevated BMI and the presence of collapse in the upper airway in adults with diagnosis of OSAS. The patient must be evaluated with OSAS, prior to starting treatment, searching for presence of collapse regardless of BMI; since they all have the same probability of collapsing.

Acknowledgments: Clínica de Trastornos del Sueño de la UNAM.

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Disclosure: Nothing to disclose.

P394

Automated scoring system for the diagnosis of obstructive sleep apnea in level 2 portable monitoring device Embletta X-100

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Objectives: We verified the reliability and validity of level 2 portable device Embletta X-100 automated scoring system compared to manual scoring for the diagnosis of obstructive sleep apnea.

Methods: One hundred nineteen patients with suspected OSA received portable polysomnography (PSG) of Embletta X-100. All PSG data was analyzed by both automated and manual method. Manual scoring is scored according to the new scoring manual of the American Academy of Sleep Medicine (AASM, 2012) criteria. Automated scoring is analyzed by the automatic algorithm (updated by AASM 2012 criteria). Each parameters are evaluated statistically by the correlation analysis and paired t test between automated scoring and manual scoring of Embletta X-100 for assessing reliability and validity of automated scoring system.

Results: There was a moderate correlation of apnea-hypopnea index (AHI) ($r = 0.76$, $P < 0.001$) between the automated scoring and manual scoring of Embletta X-100. But a poor agreement (Bland-Altman Plot, $\kappa = 0.34, 0.33, 0.26$; Cut off value is 5,15,30) was found between the automated scoring and manual scoring, respectively. AHI data was excessively tended to underestimate by diagnostic agreement and disagreement criteria. There was a no good concordance of severity of AHI (Kendall tau-b = 0.60) between the automated scoring and manual scoring

Conclusion: Automated scoring results of Embletta X-100 are statistically moderate related to manual scoring results. But automated scoring results excessively tend to underestimate compare to manual scoring results. So manual scoring by sleep expert is considered essentially for diagnosis of obstructive sleep apnea (OSA) with Embletta X-100.

Disclosure: Nothing to disclose.

P395

Comparison between body mass index, sleep architecture and severity of obstructive sleep apnea syndrome in morbid obese women

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Introduction: Obesity is the major modifiable risk factor for the development of chronic diseases and obstructive sleep apnea syndrome (OSAS). Due to the high prevalence of obesity in Mexico, it has become a health problem. The study objective is to compare the body mass index (BMI) and sleep architecture between severity groups of OSAS in women with morbid obesity.

Method: A Retrospective, observational, cross-sectional analytical study. The sample was composed of 121 patients. Inclusion criteria were female patients being evaluated for bariatric surgery with BMI > 35 kg/m^2 with a complete polysomnographic study in the Clínica de Trastornos del Sueño UNAM.

Results: We found 121 women with a mean age of 41.07 years (t.d. 11.12), BMI 45.84 kg/m^2 (35–86 kg/m^2, $\pm$ t.d. 10.27), in the group of patients with severe OSAHS was a statistically significant increase in BMI ($F = 21.6$, $P < 0.001$) and the number of awakenings ($F = 8.697$, $P < 0.001$) and a decrease of saturation average oxygen ($F = 13.694$, $P < 0.001$) and sleep efficiency ($F = 3.849$, $P < 0.012$), this group also had the lowest oxygen saturation value ($F = 1.795$, $P < 0.001$).

Conclusions: According to the literature we found that patients with higher rates of sleep apnea had higher BMI, number of awakenings, and decreased oxygen saturation and sleep efficiency. So it would be important in morbidly obese patients make early detection of OSAHS for treatment.

Disclosure: Nothing to disclose.

P396

APAP-adherence depends on device technology

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Objectives: Adherence to the prescription of APAP-therapy was compared with the results of a bench-test of different APAP-devices.

Methods: A computer-driven bench-test with the simulation of the characteristics of the human pharynx and the lung (ALOSI) was applied to six different commercially-available APAP devices. Obstructive and central events together with changes in respiratory patterns were simulated. Correlations between bench test results and adherence to the APAP-therapy was determined, using health insurance data.

Results: Due to different technical algorithms the answer of the APAP-devices to obstructive and central events varied considerably. A significant dependence of health insurance adherence data to the type of the APAP-device was found.

Conclusions: A link between the technological characteristics of APAP devices and adherence to the therapy was found. The bench test allowed a reproducible analysis and comparison of pressure modification algorithms of APAP devices. These methods have potential usefulness for predicting patient adherence to APAP therapy before treatment is started.

Disclosure: Nothing to disclose.

P397

Continuous positive airway pressure treatment reduces mortality in elderly patients with moderate to severe sleep apnea: a cohort report

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Background: Continuous positive airway pressure (CPAP) treatment is the first-line therapy for obstructive sleep apnea (OSA), and improves its clinical symptoms such as daytime sleepiness, but its long-term effects remain unclear, especially the consequence of not treating elderly patients with OSA.

Methods: A prospective cohort study was carried out to explore the survival rate and incidence of cardiovascular events in elderly patients with moderate to severe OSA who underwent or did not underwent CPAP treatment.

Results: A total of 124 elderly patients with moderate to severe OSA were selected as subjects, among whom 36 patients underwent CPAP treatment and 88 patients did not. The average follow-up was (4.03 $\pm$ 2.54) years. Among 21 cases of death, two were observed in CPAP group with mortality of 5.6% (2/36), which was significantly different from 21.6% (19/88) in untreated group ($P < 0.05$). Kaplan-Maier survival analysis showed that the survival rate in CPAP group was 94.44%, which was distinctly higher than 78.41% of untreated group ($P < 0.05$). The incidence of cardiovascular events was 13.9% in the CPAP group and 55.7% in the untreated subjects ($P < 0.001$).

Conclusions: CPAP reduced the mortality and enhanced the survival rate as well as had good long-term prognosis in elderly patients with moderate to severe OSA.

Disclosure: Nothing to disclose.

P398

Prevalence of excessive sleepiness and insomnia in patients with obstructive sleep apnea syndrome

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Objectives: The aim of the study was to address the prevalence of excessive sleepiness and insomnia in patients with obstructive sleep apnea syndrome (OSAS).

Methods: The sample comprised 1119 patients referred to Haukeland University Hospital on suspicion of OSAS between 2011 and 2013. Mean age was 48.4 $\pm$ 12.4, body mass index was 29.5 $\pm$ 5.2 and 29.2% were women. All patients underwent polygraphic sleep studies. OSAS was diagnosed and classified according to the apnea-hypopnea index (AHI) as normal (<5), mild (5–14.9), moderate (15–29.9) or severe ($\geq$30). Excessive sleepiness was measured using Epworth Sleepiness Scale (ESS), a score $\geq$11 indicating excessive sleepiness. Insomnia was measured using the Bergen Insomnia Scale (BIS), which allows identification of insomnia according to the DSM-IV criteria. Both questionnaires are validated in Norwegian.

Results: Normal AHI was found in 40.7% of the patients whereas 29.8% had mild OSAS, 16.2% had moderate OSAS and 13.3% had severe OSAS, yielding a prevalence rate of OSAS of 59.3%. Excessive sleepiness was reported by 40.9% of patients with normal AHI, 46.4% of patients with mild OSAS, 52.0% of patients with moderate OSAS and 58.0% of patients with severe OSAS, χ^2 (3, $n = 1070$) = 15.28, $P = 0.002$. Insomnia was reported by 78.9% of patients with normal AHI, 79.4% of patients with mild OSAS, 74.3% of patients with moderate OSAS and 76.3% of patients with severe OSAS, χ^2 (3, $n = 1041$) = 2.13, $P = 0.545$.

Conclusions: The prevalence of excessive sleepiness increased with increasing OSAS severity. Insomnia was more prevalent than excessive sleepiness, but was not associated with OSAS severity.

Disclosure: Nothing to disclose.

P399

Effects of a very low energy diet on cardiometabolic markers in mechanically treated and untreated obese obstructive sleep apnea patients: a stratified open-label cohort study

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Objectives: We investigated the body composition and cardiometabolic effects of a very low energy diet (VLED) combined with lifestyle modification in patients with obstructive sleep apnea (OSA). This novel study examined whether the VLED approach was effective in both treated and untreated OSA.

Methods: Obese adult OSA patients (BM $\geq$ 30 kg/m^2, AHI $\geq$ 5/h) were stratified according to whether they were on mechanical treatment (MT) or not (nMT). MT included continuous positive airway pressure or mandibular advancement splint. Patients received 2 months VLED then 4 months maintenance diet. Outcomes were measured at baseline, 2 and 6 months. Sleep studies were undertaken in nMT patients at baseline and 2 months. Outcomes reported mean $\pm$ SD and mean change (95% confidence interval).

Results: Forty-four patients were recruited and two withdrew from VLED. Twenty-four patients were on MT (weight = 115.2 $\pm$ 18.0 kg, age = 51.9 $\pm$ 7.2 years) and 18 patients were not (110.5 $\pm$ 21.26 kg, 46.3 $\pm$ 10.5 years; AHI = 29.4 $\pm$ 24 events/h). Following 2-months VLED, a significant reduction in body composition parameters and cardiometabolic markers was observed. Reductions were sustained at 6 months: weight loss ($P < 0.0001$): MT = $-$13.4 kg ($-$15.6 to $-$11.3), nMT = $-$13.5 kg ($-$15.9 to $-$11.1), body fat via bioelectrical impedance analysis ($P < 0.005$): MT = $-$3.3 kg ($-$5.5 to $-$1.1), nMT = $-$7.1 kg ($-$9.6 to $-$4.7). Sleep apnea severity was reduced in the nMT group: AHI = $-$12.5 events/h ($-$20.9 to $-$4.0) $P = 0.006$. Triglycerides and fasting glucose improved in all patients ($P < 0.005$). Systolic blood pressure, high density lipoprotein cholesterol and fasting insulin improved in the MT group ($P < 0.05$). Diastolic blood pressure and resting pulse improved in nMT ($P < 0.05$).

Conclusions: VLED in MT and nMT obese OSA patients significantly improves body composition and cardiometabolic markers at 6 months.

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Disclosure: Nothing to disclose.

P400

Randomised controlled trial of mandibular advancement devices for obstructive sleep apnoea (TOMADO): one year follow-up

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Objectives: Mandibular advancement devices (MADs) are used to treat obstructive sleep apnoea-hypopnoea syndrome (OSAHS). The previously reported TOMADO study (ISRCTN02309506) compared clinical and cost-effectiveness of a range of MADs against no treatment in mild to moderate OSAHS. Here we present follow-up data at 1 year.

Methods: The original open-label, randomised, controlled, crossover trial recruited 90 adults with Apnoea-Hypopnoea Index (AHI) 5-<30/h and Epworth Sleepiness Scale (ESS) score ≥9 to undergo 6 weeks of treatment with three non-adjustable MADs: self-moulded (SP1); semi-bespoke (SP2); fully-bespoke (bMAD); and 4 weeks no treatment. Outcomes recorded 1 year after trial exit included ESS, treatment satisfaction and compliance, quality of life (QoL) and health care usage.

Results: Sixty of the 74 (81%) patients who completed the trial continued treatment with a MAD at trial exit. At the end of the trial, all devices were cost-effective compared with no treatment at a willingness to pay (WTP) of £20 000/quality-adjusted life year (QALY). After 1 year, 40 of 58 (69%) patients completing follow up continued on the same treatment, with 32 (55%) still using a MAD (SP1 $n = 6$; SP2 $n = 9$; bMAD $n = 17$). Patient reported MAD compliance averaged 7 h/night for 88% of nights. Treatment satisfaction and sleepiness (ESS) had not deteriorated.

Conclusions: Non-adjustable MADs achieve clinically important improvements in mild to moderate OSAHS and are cost-effective in the short term. Compliance remains good and symptomatic improvement is sustained at 1 year. QoL data at 1 year is being fed into the economic model to evaluate long term cost-effectiveness.

Disclosure: Mr Cameron provides the bespoke device service at Addenbrookes Hospital.

P401

On the way to a personalised self-management program in continuous positive airway pressure therapy

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Objective: Lack of adherence in Continuous Positive Airway Pressure (CPAP) therapy is a considerable problem and associated with severe impairment of daily functioning, and premature mortality. Improving adherence is a major challenge for all healthcare providers. It has become evident that especially psychological predictors of adherence are auspicious. Recent studies have shown that the distinction of personality types in the CPAP therapy provides a promising individual approach to improve adherence. The personality system interaction theory (PSI) has proved to be particularly suitable for developing a new personalised self-management-program in CPAP therapy. In the PSI theory, the different psychological predictors of adherence can be equally integrated, and it is possible to derive concrete interventions for the patients from the theory.

Method: By utilising Ward's method for a comprehensive questionnaire battery, 187 Obstructive Sleep Apnea Syndrome (OSAS) patients aged 27–83 years have been allocated to three personality clusters.

Results: The three types 'strategic-integrative', 'indifferent' and 'anxious-avoidant' have different characteristics with regard to the following variables: daytime sleepiness, side effects of therapy, specific therapy-related cognitions, anticipated interventions and other relevant personality dimensions of the PSI theory.

Conclusions: The results of the study will be used to develop personalised interventions that improve adherence in CPAP therapy.

Disclosure: Nothing to disclose.

P402

Obstructive sleep apnea and erectile dysfunction: new possibilities of sleep medicine

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Objectives: The aim of this study was to determinate polysomnographic nocturnal penile tumescence (NPT) features in males with obstructive sleep apnea (OSA).

Methods: The sample included 51 males without complains of erectile dysfunction (ED): 37 – OSA patients and 14 – healthy males aged 46–55 years. Polysomnography (PSG) was carried out with the use of GRASS-TELEFACTOR Twin PSG (Comet) with amplifier As 40 with integrated module for sleep SPM-1 (USA) with amplifier for mercuric NPT-sensor. Statistics was developed using STATISTICA 6.1 (Stat-Soft, Inc., USA). All differences were considered significant at $P < 0.05$.

Results: PSG data confirmed altered pattern of NPT in OSA patients. All episodes of NPT in OSA patients was significantly below than in healthy males ($P < 0.05$). There was increase T_{up} period (beginning of erectile episode) with decrease both T_{max} period (maximum of erectile episode) and T_{down} period (diminution of circumference of the penis) with respect the control ($P < 0.05$). It is known that episodes of NPT are associated with rapid eye movement (REM) sleep. In OSA patients the ratio T_{max}/R (R – duration of all REM periods) was decrease and the ratio T_{up}/R was increase ($P < 0.05$) relative to thus in healthy males.

Conclusions: ED is a finding in OSA patients. Using the modern equipment allows to identify novel pathogenetic pathways for formation of ED, to diagnose it's at preclinical stage and timely start pathogenetic justified therapy in OSA patients, that will significantly improve the quality of life of males and prevention of cardiovascular diseases.

Disclosure: Nothing to disclose.

P403

Contribution of mandibular morphology to residual obstructive sleep apnea after adenotonsillectomy in children: a preliminary study

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Objectives: Pediatric obstructive sleep apnea (OSA) is frequently associated with adenotonsillar hypertrophy, and the fact that about 30 percent of affected children continue to show OSA after adenotonsillectomy (AT) suggests the presence of some other predisposing factor(s). We hypothesized that an abnormal maxillofacial morphology may be a predisposing factor for residual OSA in pediatric patients.

Methods: A total of 13 pediatric OSA patients {nine boys and four girls, age [median (interquartile range)] = 4.7 (4.0 / 6.4) y, body mass index (BMI) *z* score = −0.3 (−0.8/0.5)} who had undergone AT were recruited for this study. Maxillomandibular size was measured using an upright lateral cephalogram, and correlations between size and the apnea hypopnea index (AHI) values obtained before (pre AT AHI) and about 6 months after AT (post AT AHI) were analyzed.

Results: AHI decreased from 12.3 (8.9 / 26.5) /h to 3.0 (1.5 / 4.6) /h after AT ($P < 0.05$). Residual OSA was seen in 11 of the 13 patients (84.6%) and their AHI after AT was 3.1 (2.7 / 4.7) /h. The mandible was smaller than the Japanese standard value, and a significant negative correlation was seen between maxillomandibular size and post AT AHI ($P < 0.05$).

Conclusions: These findings suggest that the persistence of OSA after AT may be partly due to the smaller sizes of the mandible in pediatric patients. We propose that the maxillomandibular morphology should be carefully examined when a treatment plan is developed for OSA children.

Disclosure: Nothing to disclose.

P404

International scientific communications in the field of the diagnosis of obstructive sleep apnea

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Objectives: The purpose of this scientometric investigation is to examine the recent dramatic growth of the publication activity devoted to the multidisciplinary field of of the diagnosis of obstructive sleep apnea.

Methods: On April 15, 2014, a retrospective problem-oriented search was performed in *Scopus* and in *Web of Science* (*WoS*) for the period from 2009 till 2013. The following scientometric parameters were analyzed: number of abstracted publications; names and countries of authors; languages and types of primary documents, and titles and number of journals.

Results: In *WoS*, there were 7388 items by authors from 72 countries and in *Scopus* – 1449 ones by authors from 62 countries from all over the world. In *WoS*, most papers were abstracted in 2012 (1374) and in 2010 (1140) but in *Scopus*, there were 352 papers in 2013 and 320 ones in 2012, respectively. There were 85 papers by A. Malhotra abstracted in *WoS* but 15 ones by S. Tufik abstracted in *Scopus*. In *WoS*, primary publications were in 22 and in *Scopus* in 21 languages. In *WoS*, the journals *Sleep* and *Sleep & Breathing* dominated while in *Scopus, Sleep & Breathing* and *Sleep Medicine* did. In *WoS*, the papers received 17648 citations without self-citations by 10123 citing articles without self-citations. H-index was 50. The paper by D. R. Flum *et al.* (*N Engl J Med*, 361, 2009, 445–454) already received 325 citations.

Conclusions: The files with abstracts analyzed through this constellation of scientometric indicators could contribute to further improvement of international collaboration.

Disclosure: Nothing to disclose.

P405

Institutionalization of research on the applications of oral appliances in the treatment of obstructive sleep apnea

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Objectives: We examined the scientometric characteristics of the dynamic institutionalization of research focused on the applications of oral appliances in obstructive sleep apnea.

Methods: On April 15, 2014, a comparative, retrospective problem-oriented search was performed in *Scopus* as well as in *Web of Science* (*WoS*) and *MEDLINE* of *Web of Knowledge (WOK)* for a 15-year period (1999–2013). The analysis covered the number of abstracted publications; names and countries of authors; languages and types of primary documents; titles, number and thematic profile of journals, and nominations, thematic profiles and countries of authors' institutions.

Results: In *WoS*, there were 699 items by authors from 37 countries; in *Scopus* – 524 by authors from 36 countries while in *MEDLINE* (*WoK*) – 431 papers only. Most papers were abstracted in these data-bases in 2013 (69, 64 and 53, respectively). A.A. Lowe and P.A. Cistulli presented with most publications in *WoS* and *Scopus*. In *Scopus*, primary publications were in 15, in *WoS* – in 14 and in *MEDLINE* (*WoK*) – in 13 languages. The journals *Sleep & Breathing* and *Sleep* dominated in *Scopus* and *MEDLINE* (*WoK*) but *Sleep and Sleep & Breathing* did in *WoS*. The University of British Columbia was the leading institution. In *WoS*, these papers received 4040 citations without self-citations by 2617 citing articles without self-citations. H-index was 44. The paper by L.J. Epstein *et al.* (*J Clin Sleep Med*, 5, 2009, 263–276) already received 247 citations.

Conclusions: The improved research institutionalization promoted high-quality publication and citation activity in this interdisciplinary field.

Disclosure: Nothing to disclose.

P406

Two new parameters: obstruction length and height in predicting outcome of upper airway surgery in obstructive sleep apnea patients

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Study objective: To measure obstruction length and height using drug-induced sleep endoscopy (DISE) in obstructive sleep apnea syndrome (OSA) patients and to evaluate their association with outcomes of upper airway surgery.

Design: Prospective, non-randomized study.

Setting: University medical center.
Methods: Forty-three patients diagnosed by polysomnography (PSG) with mild to severe OSA were evaluated by DISE using dexmedetomidine, and obstruction sites were documented. The two new parameters, obstruction length (defined as the distance from the most superior point of the collapse to the most inferior point of the collapse) and obstruction height (the distance from the posterior border of the nasal septum to the most proximal point of the collapse) were measured by both DISE and a pressure transducer catheter method.
Results: Twenty-six (60.5%) patients were responders, and 17 (39.5%) were non-responders. The mean obstruction length and obstruction height was 1.3 ± 0.5 (range was 0.4–2.2)cm, and 3.4 ± 0.9 (range was 1.1–5.0)cm, respectively. Non-responders had a longer obstruction length and a shorter obstruction height. Multivariate logistic regression analysis revealed that among surgery type and sleep endoscopy findings, obstruction length >1.4 cm (odds ratio [OR], 0.21; 95% confidence interval [CI], 0.04–0.98; $P < 0.05$) and obstruction height $\geq$3.2 cm (odds ratio [OR], 9.35; 95% confidence interval [CI], 1.79–48.80; $P < 0.05$) were the only independent predictors of upper airway surgery success.
Conclusions: Accurate measurement of obstruction length and height can be performed with both DISE and a pressure transducer catheter method. The two parameters can predict the outcome of upper airway surgery.
Disclosure: Nothing to disclose.

P407

Achyrocline satureioides (LAM) D.C. would improve sleep quality and oxidative stress in patients with obstructive sleep apnea syndrome: a pilot study

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Achyrocline satureioides ('*Marcela*') is a plant belonging to the family Asteraceae, with a high content of flavonoids, which justifies its antioxidant and anti-inflammatory properties. Since flavonoids have beneficial effects on patients with Obstructive Sleep Apnea Syndrome (OSAS), our aim was to investigate the influence of '*Marcela*' on sleep and concentration of peroxides in plasma in these patients. Eight patients suffering mild OSAS diagnosed by polysomnography were studied with a double-blind protocol during 3 months: five treated with '*Marcela'* (extract containing 3 mg/mL of flavonoid quercetin, measured by HPLC) and three with placebo. Another polysomnography was performed at the end of the study. Three blood samples were taken (before starting with the treatment, at the middle and at the end). The blood samples were centrifuged and 10 μL of plasma were extracted. Using the kit Oxystat (Biomedika gruppe, Austria) plasma concentration of peroxides was quantified by a colorimetric reaction.

Peroxide levels in the plasma of patients treated with the *Marcela*'s extract decreases after a month and a half of treatment related to patients treated with placebo. Sleep showed a statistically significant increase of REM (Stage R, 125% increase) and an increasing trend in N2 (stage with spindles) and N3 (slow wave sleep) in patients treated with '*Marcela'*. The Epworth Sleepiness Scale decreased significantly. Patients treated with placebo showed random results.

The sleep and wakefulness improvement and decrement of peroxide levels in plasma in patients suffering OSAS, could be justified by the antioxidant and anti-inflammatory actions described for polyphenols contents in *Marcela*'s preparations.
Disclosure: Nothing to disclose.

P408

Comparison of portable monitoring devices and polysomnography for the diagnosis of obstructive sleep apnea syndrome

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Background: Although it has been estimated that the prevalence of obstructive sleep apnea syndrome (OSAS) in Japan is about 2 million, existence of many patients who are not yet diagnosed is suspected.

Portable monitoring devices (PMDs) are easier and widely used for the diagnosis of OSAS in Japan. However it has been reported that reliability of PMDs for evaluating OSAS is inferior to polysomnography (PSG).
Purpose: To compare the analysis results of PMDs and PSG for the diagnosis of OSAS.
Method: We compared the analysis results of PMDs and PSG among all the patients who performed both PMDs and PSG in our hospital from January 1, 2012 to September 30, 2013.
Result: Two hundred and ten PSG analyses were conducted in the period, and among them 155 cases were conducted PMDs prior to PSG.

According to the results of analysis in the 155 cases, the correlation coefficient of between AHI measured by PMDs and PSG is 0.56, and the number of patients showed a large difference between the results of PMDs and PSG was not a little. PMDs analyses tended to show lower AI and AHI than PSG analyses.
Conclusion: Careful consideration is needed to diagnosis the patient as mild or non OSAS by using only PMDs, because PMDs tend to estimate lower AHI than the actual condition.
Disclosure: Nothing to disclose.

P409

Factors affecting the intention and decision to be treated for obstructive sleep apnea disorder

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Background: Using the Continuous Positive Airway Pressure (CPAP) device effectively lessens OSA. Only few studies have used the Health Belief Model (HBM) to explain patients' decision to purchase or use a CPAP.

The purpose was to examine the factors affecting OSA patients' intention and actual decision to get CPAP treatment.
Methods: The study consisted of two parts:

1. Questionnaires were distributed among 633 participants suspected of having OSA and naïve to CPAP treatment, before their sleep test.
2. Telephone survey: 6 months later, 194 OSA patients were contacted to verify whether they had purchased CPAP.

Results: On average, individuals who intend to purchase CPAP, were significantly higher than those who do not intend in:

susceptibility, benefits, and cues-to-action. The barriers category was significantly lower for the 'intend to purchase'.
The main reason for purchasing the CPAP device was: 'Based on the results of my sleep laboratory test' – 97%. However, the main reason for not purchasing CPAP was: 'I tried the device and it was not comfortable to use' – 54%. Other significant factors positively affecting the actual decision to purchase a CPAP were: higher index of AHI, greater number of titration days, age, and living in the periphery.
Conclusions: Patients' attitudes and health beliefs prior to diagnosis may predict their intention to be treated for OSA, and in turn, affect their actual decision to get treatment. To the best of our knowledge, these results are new, since previous studies did not compare intention and actual decision to get CPAP.
Disclosure: Nothing to disclose.

P410

Contributing factors to obesity as predictors for obstructive sleep apnea syndrom

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Objectives: Analysis of association between obesity indicators, fat distribution and gender in subjects suspected of obstructive sleep apnea syndrome (OSAS) from the 'Victor Babes' Sleep Laboratory, Timisoara, Romania.
Methods: Between October 2005 and April 2013, 1277 subjects suspected of OSAS were antrophological evaluated, including body – mass index (BMI), neck and abdominal circumference (NC and AC), waist-hip ratio (W/HR) and performed polysomnography (PSG). Multiple linear regression analysis (stepwise regression model) was performed using apnea – hypopnea index (AHI) as a dependent variable and variables of interest as independent variables.
Results: 797 (62.41%) were obese (median age 54 years) and 480 (37.59%) had normal BMI (median age of 52). Obese had higher AHI: 41.25/h (25.5–61.3) vs. 26.8/h (15.3–39.9) ($P < 0.001$. Age ($\beta = 0.191$, $P < 0.001$) and W/HR ($\beta = 0.104$, $P = 0.043$) at females and AC ($\beta = 0.16$, $P = 0.025$) at males have a higher influence on AHI. Positive correlation of AHI with NC (r = 0.389, $P < 0.001$), and AC (r = 0.371, $P < 0.001$). The risk of having OSAS is 7.7 higher for obese female vs. normal weight (OR = 7.74, 95% CI 3.52–17.02) and 6.1 higher for obese male vs. normal weight (OR = 6.12, 95%CI 2.66–14.1), with no significant difference between genres (Breslow-Days Test, $P = 0.69$). Snoring had a 7.51 increased risk of having OSAS (OR = 7.51, 95% CI 4.29–13.15).
Conclusion: Obesity indicators and body fat distribution are strongly correlated with AHI. Obese females have a higher risk of OSAS then obese males. Associated snoring is the most powerful predictor for OSAS.
Disclosure: Nothing to disclose.

P411

Does sleep disordered breathing in women promote heart failure? A population based cohort study

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Objectives: An association between obstructive sleep apnea and the incidence of heart failure has been reported in men but not in women. The objective of this study was to investigate whether a combination of snoring and excessive daytime sleepiness, the two main symptoms of obstructive sleep apnea syndrome, was able to predict incident heart failure in a population-based sample of women.
Methods: We used the population-based cohort study, Sleep and Health in Women (SHE; $n = 5998$ women born 1901–1980), with baseline questionnaire data from April 2000 relating to snoring, excessive daytime sleepiness and covariates. The follow-up of incident heart failure continued until 31st of December 2011 using data retrieved from the Swedish National Patient Register and Cause of Death Register.
Results: Among women with both snoring and excessive daytime sleepiness at baseline 5.3 percent ($n = 13$) developed heart failure during follow-up compared with 0.9% ($n = 36$) in the reference group with neither snoring nor excessive daytime sleepiness. After adjustment for age, waist circumference, smoking, alcohol, hypertension, diabetes and previous myocardial infarction, women with the combination of snoring and excessive daytime sleepiness had a two-fold increase in the risk of incident heart failure (HR 2.3 95% CI 1.2–4.4).
Conclusions: Symptoms of obstructive sleep apnea, i.e. the combination of snoring and excessive daytime sleepiness, are associated with an increased risk of developing heart failure in women.
Disclosure: Nothing to disclose.

P412

Quantitative analysis of mandible movements during obstructive sleep apnoeas

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Objectives: To delineate the contribution of the mandible to obstructive sleep apnoeas (OSA).
Methods: Five OSA patients underwent concomitant night polysomnography (PSG) and electrognathography (EGG). The last was based on the measurement of the Hall Effect by displacements of a permanent magnet, glued on the anterior surface of the lower incisors. Two sets of four antennae tied to a cranial strap recorded the movements of the magnet. Maximal amplitudes of movements reached in different recording sessions were compared in the median plane: OM represented the voluntary maximal capacity; OC, the counting test and OA, the maximum opening during OSA.
Results: During inspiratory efforts of OSA, downward and backward movements of the mandible occurred. These movements were partially reversed during expiratory phase. They determined a recoil angle towards the vertical axis drawn from the occlusion point in the median plane.

This recoil angle was greater in every patient than during their voluntary maximal opening (OA angle: 36.9 ± 4.65 degrees vs. OM angle: 25.9 ± 4.65 degrees; $P = 0.005$). At peak amplitude of the last breathing effort during OSA, a forward propulsion movement was concomitant of the arousal, reflecting an intervention of higher centres in the nervous system (CNS), in order to free the upper airway.

Conclusions: The movements of the mouth during OSA show that the mandible plays an occlusive 'clock anchor effect' on the pharynx during OSA. A suppression of this obstructive contribution implies an activation of the CNS on the mandible.

Disclosure: Nothing to disclose.

P413

Reduction of mandibular movements associated to obstructive sleep apnea after adenotonsillectomy in children

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Mouth-breathing is a common clinical feature of respiratory efforts (RE) during sleep in children with adenotonsillar hypertrophy. Mandibular movements (MM) can be activated during the respiratory cycle when RE occurs and /or precipitated by cortical arousals (CA) which terminate the obstructive sleep hypopnea -apnea (OAH).We hypothesized that MM would decrease after surgery.

Patients, material and methods: Eleven children (3–12 years of age) consecutively recruited over a period of 2 months for polysomnography before tonsillectomy were analyzed .All the children were habitual snorers and mouth-breathers. A midsagittal mandibular movement magnetic sensor (Brizzy® Nomics, Liege, Belgium) measured the distance in mm between two parallel, coupled, resonant circuits placed on the forehead and on the chin. The mandibular positions during each respiratory cycle were recorded in the breathing frequency band of 0.25–0.6 Hz. MM were measured as a change of peak to peak distance during periods of OAH and at arousal and reported as the rate per hour (respectively MOVi and MOSi), before and 3 months after adenotonsillectomy .

Results: Before surgery OAHi, MOVi and MOSi (mean ± SD in h^{-1}) were: 23.4 ± 8.8, 32.4 ± 12.5 and 33.1 ± 21.5 respectively. Mean changes after tonsillectomy were respectively: −20.1 ($P < 0.001$), −17.1 ($P < 0.001$) and −23.0 ($P < 0.001$) .

Conclusion: Adenotonsillectomy decreased the incidence of MM accompagnying OAH in children with tonsil hypertrophy. This strongly suggests that MM are determined by RE during periods of OAH.

Disclosure: Nothing to disclose.

P414

The impact of weight reduction in the prevention of the progression of obstructive sleep apnea – explanatory analysis of a 4-year observational follow-up trial

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Introduction: Obstructive sleep apnea (OSA) is a chronic, progressive disease, and it is well-documented that severe OSA is associated with an increased cardiovascular morbidity and mortality. In the first randomized study on the topic we have previously shown that weight reduction improves OSA, however, there is definitely need for further evidence whether it may prevent the progression of OSA in long-term. The aim of the study was to assess the impact of weight change during a 4-year observational follow-up of an original 1-year randomized, controlled trial.

Methods: The participants were arranged into the two groups according to the weight change at 5-year follow-up using the 5% weight loss as a cut-off point [later referred to as successful ($n = 20$) or unsuccessful groups ($n = 27$)]. The change in apnea-hypopnea index (AHI) was the main objective outcome variable.

Results: Fifty-seven patients participated in the 4-year follow-up. At 5 years from the baseline, the change in AHI between the groups was significant; in the successful group (−3.5, 95% CI −6.1 to −0.9) compared with the unsuccessful group (5.0, 95% CI 2.0–8.5), ($P = 0.002$). Successful weight reduction achieved an 80% reduction in the incidence of progression of OSA compared to the unsuccessful group (log-rank test $P = 0.016$).

Conclusions: This study provides first time long-term evidence that even modest weight reduction can result in marked improvements of OSA and metabolism in obese patients, and these positive changes are sustained even 4 years after cessation of the active intervention, and the progression of the disease is thus prevented.

Disclosure: Nothing to disclose.

P415

Impairments of frontal lobe-related cognitive functions in sleep related breathing disorder in the elderly

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Objectives: The prevalence of sleep related breathing disorders (SDB) increased with aging, and decline of cognitive function is another serious problem in the elderly. However, there were few studies for association between SDB and neurocognitive function of old population in representative samples.

Methods: We recruited 476 elderly subjects (≥60 years) from community and a sleep clinic. SDB was diagnosed using laboratory-based polysomonography, and clinical assessments were also conducted. The neurocognitive function test was performed using the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease Neuropsychological Assessment Battery (CERAD-K).

Results: Subjects were divided into three groups by severity of SDB; AHI < 15 (control, $n = 227$), 15 ≥ and 30 < (mild to moderate, $n = 128$), and 30 ≥ (severe, $n = 121$). Significant differences were observed among three groups in the Digit Span Forward ($P = 0.004$) and Backward ($P < 0.001$). There were modest correlation between AHI and hypoxic variables, and Digit Span (DS), Frontal Assessment Battery (FAB) and Stroop Test (ST) after adjusting for age, educational level, sex and depression. Stepwise multiple regression analysis showed that AHI and hypoxic variables contribute to impairments of DS, FAB and ST.

Conclusions: SDB were modestly associated with decreased neurocognitive function in elderly population mainly through hypoxia. Affected cognitive domains were working memory, attention and executive function which are known to be related with frontal lobe vulnerable to hypoxic insults.

Disclosure: Nothing to disclose.

P416

Sleep-disordered breathing after acute ischemic stroke and transient ischemic attack: long-term clinical/vascular outcome and effect of a randomized CPAP treatment – the SAS-CARE 2-study

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Background/objectives: Few studies suggested a negative impact of sleep-disordered breathing (SDB) on stroke outcome. SAS-CARE 2 is an ongoing study assessing the long-term effect of SDB on outcome after stroke/transient ischemic attack (TIA), and the effect of continuous positive airways pressure (CPAP) treatment.

Patients/methods: Patients from five centers were studied within 3 months after stroke/TIA by conventional polysomnography. Stroke characteristics, cardiovascular variables (24-h blood pressure, heart rate variability, endothelial function), clinical and vascular outcome were assessed at baseline and again after 2 years.

Patients with significant obstructive SDB (>50% of respiratory events of obstructive type, AHI ≥ 20) and Epworth Sleepiness Scale (ESS) ≥ 10 were put on CPAP (sleepy oSDB, Group 1). Patients with oSDB, AHI ≥ 20 and ESS < 10 (non-sleepy oSDB) were randomized to CPAP treatment (Group 2) or not.

Results: The enrollment in the study was completed in April 2014 with a total of 240 patients (73% males, mean age 61 years, 83% strokes). A SDB (AHI ≥ 10) was found in 51% of patients. A total of 12 sleepy OSD and 23 non-sleepy oSDB patients were put on CPAP. A total of 17 non-sleepy oSDB and 105 patients without SDB serve as control groups. At 3/≥6 months the CPAP compliance was so-far 80%/86% in Group 1 and 57%/62% in group 2 patients.

Data collection will be completed by April 2016.

Conclusions: Preliminary data of this large, prospective study suggest a good compliance of sleepy and (to a less extent so far) non-sleepy patients with significant obstructive SDB after stroke/TIA.

Disclosure: The main investigator of this study (Prof. C.L. Bassetti) received financial support for this study also from ResMed Inc. and Respironics Inc.

P417

High risk sleep apnea on the Berlin Questionnaire is associated with hypertension in South Africans of Black Ancestry

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Sleep apnea has been previously associated with hypertension. Forty percent of people of Black Ancestry in South Africa are hypertensive however there is currently no access to sleep apnea detection/treatment in the healthcare public sector. This cross-sectional study investigated the association between sleep apnea and hypertension in a population of South Africans of Black Ancestry.

Two hundred and four participants (82% female, average age ± SD = 49.5 ± 17, all of South African Black Ancestry) were recruited from random households in Soweto, South Africa. We collected blood pressure, waist circumference, body mass index (BMI) and Berlin Questionnaire scores. We compared hypertensives (controlled treated, resistant treated and untreated hypertensives) and non hypertensives (n = 101). We also examined the unadjusted and adjusted odds of high risk sleep apnea in those two groups.

One hundred and three study participants were hypertensive. Their age (average ± SD = 59 ± 12 vs. 39 ± 14), BMI (average ± SD = 31 ± 8 vs. 26 ± 6 kg.m^{-2}) and waist circumference (average ± SD = 99 ± 15 vs. 86 ± 15 cm) were significantly higher compared to the non hypertensives (all P < 0.0001). Fifty-six percent of hypertensives vs. 19% of the non hypertensives were classified as high risk sleep apnea (P < 0.0001). When adjusting for BMI, age and waist circumference, hypertensives had higher odds to be classified in the high risk sleep apnea group (Wald OR = 3.34, [95%CI] = [1.4–7.6]).

In this South African population of Black ancestry, hypertension was positively associated with scoring high risk sleep apnea on the Berlin Questionnaire. These results suggest that offering sleep apnea detection/treatment in the healthcare public sector may be useful in the prevention/treatment of hypertension in South Africa.

Disclosure: Nothing to disclose.

P418

Peculiarities of arterial stiffness in middle-aged male patients with arterial hypertension, obesity and severe sleep apnea

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The objective: Preliminary results of the study investigating features of inflammatory response, endothelial function and arterial stiffness in patients with arterial hypertension (AH), obesity and obstructive sleep apnea syndrome (OSAS).

Materials and methods: We included 11 male middle-aged (39.6 ± 9.1 years) pts with AH – blood pressure (BP) 153.7 ± 8.9/95.1 ± 13.0 mmHg, severe OSAS (AHI 57.4 ± 28.7), min SpO2 75.5 ± 13.2, mean SpO2 87.7 ± 11.5 and obesity (BMI 35.7 ± 5.1). Pts were otherwise healthy (in terms of chronic heart disease, diabetes mellitus, chronic kidney disease, manifested autoimmune or inflammatory disease).

BP, CAVI (Cardio-Ankle Vascular Index), ABI (Ankle-Brachial index), baPWV (brachial-ankle pulse wave velocity) and delta PWV were measured by Vasera VS-1000.

EPCs (endothelial progenitor cells) – CD34 + CD133^{+}CD309(VEGF-2/KDR^{+}) were isolated and quantified from peripheral blood samples by flow cytometry.

Results: CAVI – 6.81 ± 1.27, baPWV 12.7 ± 1.3, ABI 1.08 ± 0.09, delta PWV 8.79 ± 9.72.

EPC (mean ± SD): absolute count EPC/10 mL – 262.6 ± 320.8, % CD34 – 1.18 ± 0.95.

In correlation analysis by Spearman (P < 0.05):

BMI vs. AHI (r = 0.77), HR (r = 0.75), SBP (r = 0.78).

AHI vs. CAVI (r = −0.76), HR (r = 0.94), deltaPWV (r = 0.90).

Age vs. CAVI (P < 0.05, r = 0.71).

Mean SpO2 vs. % CD34 (r = −0.80), absolute count EPC/10 mL (r = −0.89).

Conclusion: The inverse correlation between AHI and CAVI could be explained by the adaptive mechanisms that are still active in middle-aged pts with AH, but free of other cardiovascular diseases. This statement would be tested on the bigger population together with further evaluation of arterial stiffness, endothelial function and inflammation.
Disclosure: Nothing to disclose.

P419

Impaired autoregulation with increasing apnea-hypopnea index – a case-control study

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Objectives: Obstructive sleep apnea (OSA) is an independent risk factor for stroke. Hypercapnia occurs in apneas and hypopneas. A reduced cerebral vasodilatatory response to CO_2 could compromise the cerebral blood flow (CBF). Therefore, we wanted to evaluate OSA patients' cerebrovascular response to CO_2 using fMRI.
Methods: We performed a case-control study of 11 OSA patients and 16 controls. The cerebrovascular response was assessed using arterial spin labelling (ASL) and blood oxygen level dependent (BOLD) scans. We measured the change in BOLD signal and CBF (ASL) during exposure to 5% CO_2. We also imitated apneas (breath holding task) and measured the BOLD-response.
Results: There was a trend towards a lower CBF response to CO_2 in the OSA group (grey and white matter: unadjusted $P = 0.065$). We tested the CBF against the apnea hypopnea index (AHI) and found the CBF response to CO_2 impaired with increasing AHI [$P = 0.018$ (total), 0.038 (grey matter) and 0.045 (white matter)]. The BOLD-response to CO_2 and the breath holding task (BOLD) did not show any significant group-related differences.
Conclusions: We found a significantly impaired autoregulatory response to CO_2 with a higher degree of impairment with higher AHI. These findings may add to the understanding of the increased stroke risk in OSA patients.
Disclosure: Nothing to disclose.

P420

The prevalence of high risk of obstructive sleep apnea among iranian commercial drivers

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Objectives: Obstructive sleep apnea (OSA) syndrome is an important cause of excessive daytime sleepiness in drivers and may cause road traffic accidents consequently. In our study we aimed to assess the prevalence of OSA syndrome among Iranian drivers.
Polysomnography is the gold standard test for diagnosing this syndrome but is expensive. So we used 'STOP-Bang questionnaire' to find the prevalence of high risk of OSA among the drivers.
Methods: The population of our study was the drivers who participated in drivers educational program($n = 550$) or those who were evaluated in drivers qualification exams($n = 2043$).Demographic, anthropometric and historical data was obtained and the participants completed the STOP-Bang questionnaire .
Results: 13.4% of the participants were detected as high risk for OSA and the related factors were: the category of the drivers (qualification vs. education), history of cardiac problems, history of pulmonary diseases, cigarette smoking, hours of work per day,and job satisfaction.
Conclusion: Being concerned about unemployment may affect the drivers' answers to the questions.
Disclosure: Nothing to disclose.

P421

Polysomnographic predictors of mortality in stroke patients

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Objectives: To assess the polysomnographic predictors of mortality in patients with a transient ischemic attack (TIA) or stroke.
Methods: We set up polysomnographies in 63 patients with an acute TIA or stroke. After a follow-up period of 19–37 months, we performed a search in a national database for deaths within our study population.
Results: Of the 63 stroke/TIA patients, nine patients died. All nine patients (100%) had moderate or severe sleep-related breathing disorders (SRDB) – 2 (22%) had severe obstructive sleep apnea (OSA), 5 (56%) moderate OSA, and 2 (22%) had severe Cheyne-Stokes respiration. In comparison, in the total stroke/TIA population 71% had moderate or severe SRBD, and 14 (22%) had severe OSA, 17 (27%) moderate OSA, and 9 (14%) severe Cheyne-Stokes respiration. No patients with an AHI or arousal index (AI) < 15 died during follow-up. For every one point increase in AHI or AI, the probability of death increased 1% [hazard ratio: 1.01 (95% confidence limits: 0.997–1.024)] and 1.5% [hazard ratio: 1.015 (95% confidence limits: 0.995–1.036)], respectively. No TIA patients were among the non-survivors.
Conclusions: The stroke patients, who died during follow-up, all had moderate or severe SRBD. Increased awareness should be addressed to SRBD in stroke patients.
Disclosure: Nothing to disclose.

P422

Nocturnal blood pressure fluctuations – a risk factor for heart attack and stroke during sleep

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Objectives: Obstructive sleep apnea syndrome (OSAS) is highly correlated with cardiovascular diseases. Noninvasive blood pressure (BP) measurements using the pulse transit time (PTT) enable a continuous BP measurement during sleep and show that apneas/hypopneas are often followed by transient BP increases. The sum of rapid BP fluctuations can lead to an increase of the BP baseline (superposition) and to high BP values, which imply a high risk of heart attack and stroke. In the present study BP measurement based on the PTT was used to investigate underlying factors leading to an increase of the BP baseline during sleep.
Methods: 25 polysomnographic recordings of patients suffering from OSAS were analysed. Recording of data and continuous BP was performed using SOMNOscreen ® (SOMNOmedics). Increases of

the BP baseline >10 mmHg/20 min were considered as 'superposition' for analysis.

Results: A total of 55 superpositions were detected. The average increase of the BP in these areas was 15.91 mmHg (±8 mmHg) with a range from 8 to 49 mmHg. Average duration of 'superposition' was 17 min (±8 min). Superpositions were characterized by an increase of time spent in apnea as well as a decrease of the SpO2 value. Superposition occurs more often during REM (73%) or in supine sleeping position (64%).

Conclusion: This study shows that frequent BP fluctuations during sleep may present risk factor for heart attack or stroke. The fact that transient BP increases cannot be detected by cuff-based methods indicates the significance of PTT based BP measurements during sleep.

Disclosure: Dr. Gert Küchler is CEO of SOMNOmedics GmbH

Sleep disorders – Circadian rhythms

P423

Pattern of highway crash accidents in Tehran, Iran: it relates with circadian rhythm of sleepiness

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Objective: Motor vehicle collisions are a major cause of morbidity and mortality in Iran. Multiple factors cause traffic accidents and one of the most important factors is sleepiness.

Methods: In this cross-sectional study, all road traffic accidents which were reported by police to have been caused due to sleepiness were studied in Tehran's province.

Results: The risk of road traffic accidents due to sleepiness, which were reported by police, increased by more than sevenfold (Odds ratio = 7.33) in low alertness hours during circadian rhythm (0–6 A.M) compared to other hours during the day. The risk of road traffic accidents due to fatigue and sleepiness decreased 0.15-fold (Odds ratio = 0.15) in hours with maximum of alertness (18–22 h.) of circadian rhythm compared to other times during the day.

Conclusion: The occurrence of road traffic accidents caused by sleepiness had significant statistical relation with driving during lowest point of alertness of circadian rhythm.

Disclosure: Nothing to disclose.

P424

Clock pathway deregulation and clonogenic properties of human skin & hair follicle keratinocytes

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In mammalians, desynchronized circadian rhythm leads to various biological symptoms. With regard to skin and hair, human epidermal stem cell function (ie. skin homeostasis maintenance) in vitro is regulated by circadian oscillations. Its deregulation may contribute to aging. In mice, circadian arrhythmia of hair follicle stem cells contributes to age-related hair follicle cycling defect. Despite the well-described impact of circadian oscillation (through a feedback loop involving CLOCK pathway) on hair and skin stem cells function in vitro; little is known about changes in clonogenic potential of human Hair Follicle (hHF) and skin epidermal (hEpi) keratinocytes after a long term alteration of the circadian rhythm in vivo. The present study aims to assess hHF and hEpi precursor cells properties through a CLOCK pathway alteration due to long term deregulated circadian rhythm. A clinical study protocol was designed to correlate the impact of a deregulated circadian rhythm upon hHF and hEpi keratinocytes clonogenic potential: #ANSM2012-A00964-39 'Comparison of CLOCK pathway proteins expression and hHF and hEpi keratinocytes properties in two groups of women: shift workers and diurnal workers.' After informed consent, a 3 mm fresh punch biopsy was performed on each donor. Cell cultures, characterisation, measurement of colony area and immuno-staining were processed. Our results demonstrate that long term circadian rhythm deregulation affects CLOCK pathway protein expression and is correlated with hHF and hEpi keratinocytes clone-forming efficiency alterations. Our study provides, for the first time in humans, evidences that in vivo alterations of the CLOCK pathway affect skin and hair precursor cells clonogenic properties.

Disclosure: Nothing to disclose.

P425

Sleep patterns and predictors of daytime sleepiness in Korean adolescents students

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Objectives: Various sleep patterns may be shown in Korean adolescents to be busy for studying. The aim of study was to investigate sleep pattern of them and to evaluate predictors of affecting on daytime sleepiness in sleep related problems.

Methods: Among one thousand eleven high school students living in Cheonan-si, self-reported questionnaires, demographic variables including items about menstruation, morningness-eveningness questionnaire (MEQ), Beck depression inventory(BDI), Pittsburgh sleep quality index (PSQI) and Epworth sleepiness scale (ESS) were admitted.

Results: A total of 839 students (male = 453, female = 386) completed questionnaires. Significant differences were showed in sleep pattern, categorized by score of MEQ ($P = 0.004$), ESS ($P < 0.001$) and BDI ($P = 0.013$) between male subjects and female subjects. Logistic regression analysis showed that the presence of excessive daytime sleepiness was predicted by female ($OR = 2.207$, $P = 0.022$) and sleep quality ($OR = 1.284$, $P = 0.004$). In the regression analysis of female students, dysmenorrhea ($\beta = 0.108$, $P = 0.029$), eating of caffeine drink ($\beta = -0.114$, $P = 0.019$), sleep pattern ($\beta = -0.108$, $P = 0.027$), insomnia ($\beta = 0.180$, $P = 0.002$) and depression ($\beta = 0.116$, $P = 0.029$) might be associated with daytime sleepiness.

Conclusions: Korean adolescent students showed more evening type of significant daytime sleepiness and depressive symptoms. Daytime sleepiness was known to be related with cognitive dysfunction. Therefore, education program for improving of sleep quality in these adolescents should be considered for mental health.

Disclosure: Nothing to disclose.

P426

Sleepiness and behavioural circadian rhythm period lengths of delayed sleep phase disorder patients and controls

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Objectives: The objective was to compare sleepiness and behavioural rhythm period lengths (i.e., *taus*) of Delayed Sleep Phase Disorder (DSPD) patients and healthy control sleepers. The aim was

to consider the possibility that these behavioural rhythms, in addition to the physiological circadian rhythms, may be contributing to DSPD.
Methods: Nineteen patients meeting ICSD-3 criteria for DSPD (age: $M = 22.0 \pm 5.41$, 13 m) and 16 healthy control sleepers (age: $M = 24.06 \pm 5.21$, 8 m) participated in an 80-h modified constant routine. A forced-desynchrony ultradian protocol of 1-h 'days' in dim light, controlled conditions alternated 20-min sleep opportunities with 40-min enforced wakefulness. Subjective sleepiness ratings were recorded prior to every sleep opportunity and median reaction time was measured hourly, 20-min into intervals of enforced wakefulness. Sleep onset latency was derived from 20-min sleep opportunities to quantify hourly objective sleepiness. Rhythm data was curved using the 2-component cosine model.
Results: DSPD patients exhibited significantly longer subjective sleepiness rhythm *taus* (M = 24h 33 m $\pm$ 52 m) compared to both the controls (M = 23h 35 m $\pm$ 57 m) $P < 0.01$, and the 24-h Earth cycle, $t(18) = 2.795$, $P = 0.01$. Differences between groups were of a large effect size according to Cohen's criteria, $d = 1.06$. Reaction speed and objective sleepiness rhythm *taus* did not show differences between groups.
Conclusions: Feelings of sleepiness tend to cycle significantly slower in DSPD patients compared to control sleepers and the conventional 24-h Earth day. Results suggest this component could contribute to the sleep and thus biological rhythm delays in DSPD. Therefore, both cognitive and behavioural treatment approaches may be necessary for successful long-term outcomes.
Disclosure: Nothing to disclose.

P427

Nocturnal melatonin profiles in delayed sleep phase disorder compared with normal sleepers

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Objectives: A significant delay in the timing of endogenous circadian rhythms has been associated with Delayed Sleep Phase Disorder (DSPD). However, more recently other mechanisms have been proposed to account for the delay in the timing of patients' sleep. To further explore the aetiology of DSPD, this prospective study compared nocturnal melatonin profiles of 11 DSPD patients and nine normally timed sleepers in a time-free, dim-light, laboratory environment.
Methods: A 22-h modified constant routine with alternating 20-min sleep opportunities and 40-min of enforced wakefulness was used to measure the endogenous melatonin circadian rhythm. Salivary melatonin was sampled half-hourly between 1820 h-0020 h and then hourly from 0120 h until 1620 h.
Results: DSPD patients showed significantly later timed melatonin profiles compared to control sleepers. Dim light melatonin onset (DLMO) occurred significantly later in DSPD patients (M = 23h 01 m $\pm$ 3h 17 m) relative to controls (M = 20h 37 m $\pm$ 1h 40 m), $P = 0.018$. Though less consistent, the timing of dim light melatonin offset ($DLMO^{ff}$) was also later in DSPD patients compared to controls. There were no notable differences in the relative duration of secretion between groups. However melatonin release between DLMO and initial 5-h of secretion was significantly less robust in DSPD patients ($M = 252.16 \pm 138.90$) compared to good sleepers ($M = 476.49 \pm 215.64$) who showed a more prominent initial surge of melatonin following the DLMO ($P = 0.011$).
Conclusions: These results suggest that in addition to a delayed endogenous circadian rhythm, a diminished initial surge of melatonin secretion following DLMO may contribute to the aetiology of DSPD.
Disclosure: Nothing to disclose.

P428

Predictors of core temperature and melatonin circadian phase timings

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Objectives: This study assessed circadian rhythm timings, their correlation with lifestyle factors, sleep quality/disturbance, subjective sleep reports and objective sleep parameters in patients with Delayed Sleep Phase Disorder (DSPD). Our aims were to identify best predictors of circadian rhythm timing to enhance diagnosis of Circadian Rhythm Sleep Disorders, specifically DSPD.
Methods: Nineteen DSPD patients (age: $M = 22.0 \pm 5.41$, 13 male) answered a battery of tests, underwent interviews, kept sleep diaries and wore actigraphy monitors prior to a laboratory-based investigation. The laboratory study was an ultradian (20-min sleep opportunity alternating with 40-min enforced wakefulness) modified constant routine protocol that recorded minute core temperature and sampled half-hourly salivary melatonin. Pre-lab data were correlated with timing of in-lab Dim Light Melatonin Onset and first temperature minimum (Tmin).
Results: Actigraphic sleep measures were best predictors of circadian timing, particularly, bedtime, get-up time, time in bed, sleep efficiency and sleep latency ($r = 0.58 - r = 0.71$, $P < 0.05$). From subjective sleep diary reports, only sleep onset and wake up time were accurate predictors of circadian timing ($r = 0.58 - r = 0.67$, $P < 0.05$). Between the Munich Chronotypes Questionnaire (MCTQ) and the Morningness-Evening Questionnaire (MEQ), the MCTQ better predicted DSPD patients' Tmin ($r = 0.84$, $P < 0.002$) and DLMO ($r = 0.47$, $P < 0.001$). The MEQ did not significantly predict phase timing of Tmin ($r = -0.36$, n.s) or DLMO ($r = -0.26$, n.s).
Conclusions: Results highlight the importance of actigraphy for DSPD diagnosis to determine the severity of sleep delay. The MCTQ best predicts circadian timing in DSPD patients and should be used in diagnosis.
Disclosure: Nothing to disclose.

P429

Light therapy in a sighted man with a non-24-h sleep-wake disorder (N24SWD): a case study

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Objective: The N24SWD is a very rare condition among sighted individuals. Here we describe the case of a 40-year old sighted patient who reported to have a free-running sleep-wake cycle with a

period length of 25.5 h for more than 3 years after having successfully completed lymphoma chemotherapy.
Methods: After clinical assessment, his sleep-wake cycle was objectively measured by actimetric recordings over 4 months. Saliva was collected in two hourly intervals to determine circadian melatonin phase. The patient underwent a melatonin suppression test by bright light to quantify non-visual photic response, as well as a polysomnography. The therapeutic approach was light therapy (10 000 lux, 30 min) after rise time.
Results: Actimetry yielded a clear N24SWD (period length: 25.3 h) with a concurrent free-running melatonin profile synchronized with the sleep-wake rhythm (phase angle: 3 h 38 min $\pm$ 2 h 27 min). The patient's melatonin suppression to bright light and his polysomnographic sleep were both normal (PSQI score = 2). He did not report daytime sleepiness (ESS = 0), but felt inattentive. Light therapy led to synchronization to the 24 h- day during the first treatment week, but returning to a free-running pattern thereafter. The patient continued with light therapy because he felt more active during wakefulness.
Conclusions: Light therapy of 30 min duration after rise time may not be enough to consistently improve free-running sleep-wake and melatonin rhythms in a sighted N24SWD patient with normal non-visual photoreception and sleep. Prolonged light treatment durations are probably required, since his endogenous tau is more than 60 min longer than 24 h.
Disclosure: Nothing to disclose.

P430

Altered light sensitivity in a mouse model for Smith-Magenis syndrome

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Smith-Magenis syndrome (SMS), is a multiple congenital anomalies/mental retardation disorder associated with a deletion on chromosome 17p11.2 or, rarely, with point mutations in a gene located within this deletion, *Rai1* (*Retinoic acid induced 1*). The most constant phenotype in all SMS patients is a circadian misalignment of sleep coupled with an abnormal melatonin rhythm, with maximum melatonin levels during daytime. Since light is known to suppress melatonin, the latter observation suggests an impaired circadian light perception in SMS. RAI1 is believed to be a transcription factor involved in chromatin remodelling and could affect circadian rhythms at a molecular level. We here aim to determine whether an altered circadian time keeping system or problems related to entrainment by light contribute to the SMS phenotype.
We studied circadian rhythms in locomotor activity under light-dark (LD12:12) and constant dark (DD; >20 days) conditions in mice heterozygous for *Rai1* deletion (*Rai1*$^{+/-}$) in C57Bl/6J (B6) and C3H/HeJ (C3H) genetic background. EEG and EMG signals were recorded to evaluate the regulation of sleep.
In B6-*Rai1*$^{+/-}$ mice, under LD12:12, locomotor activity is strongly suppressed by light ($P < 0.001$) while an increased contribution of delta activity to the waking EEG is observed ($P < 0.05$). Under DD active phase expanded more in B6-Rai1$^{+/-}$ mice compared to wild type littermate ($P < 0.005$). These phenotypes did not occur in C3H background.
B6-*Rai1*$^{+/-}$ mice present an increased light sensitivity phenotype,with an intension of the light-induced negative masking,but,evinces a drowsy behaviour during the light period similar to the daytime sleepiness described in SMS patients.
Disclosure: Nothing to disclose.

P431

The impact of bilateral anophthalmia on sleep and mood: a case series study

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Objectives: To compare sleep and mood in relation to the ocular deficits of patients with congenitally and acquired anophthalmia and sighted control subjects.
Methods: Ten clinically and bilaterally anophthalmic adult subjects were recruited: five congenital and five acquired [eyes removed 4–20 years ago] and seven sighted controls. Subjective sleep quality was rated using the Pittsburgh Sleep Quality Index with a cut-off point of above 5/21 indicating 'poor' sleep. The level of anxiety and depression was assessed using the Hospital Anxiety and Depression Scale with a cut-off point of 8/21 for anxiety or depression. Actigraphy ($N = 7$) and MRI data ($N = 6$) were also collected in this on-going case study.
Results: Four congenital subjects reported good sleep and showed entrainment. MRI scans in these four subjects revealed tiny ovoid structures in the eye socket suggestive of vestigial eye tissue; the single congenital subject without any evident ocular tissue did not show entrainment. All acquired subjects reported significant sleep disturbance. Those recently enucleated showed entrainment, but the subject who was 20 years post-enucleation did not. There was no increased prevalence of anxiety and depression in either the congenital or acquired anophthalmic groups compared to the group of sighted controls.
Conclusion: Entrainment in congenital anophthalmia may relate to the presence of vestigial tissue with a sufficient yet small number of photosensitive ganglion cells. The amount of time one has been enucleated has an impact on rest/activity patterns but not mood.
Disclosure: Nothing to disclose.

P432

Characteristics of the selective and unique binding profile of tasimelteon, a circadian regulator of the master body clock

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Objectives: Tasimelteon is a structurally unique molecular entity that functions as a circadian regulator of the master body clock and was developed for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24). The goal of the studies presented here was to investigate the in vitro binding affinity of tasimelteon to a large panel of pharmacological relevant receptors including the MT_1 and MT_2 melatonin receptors.
Methods: The specific affinity of tasimelteon for the MT_1 and MT_2 receptors was evaluated in two independent experiments using human recombinant receptors and radioligand binding assays; the downstream changes in intracellular cyclic adenosine monophosphate (cAMP) were measured by the inhibition of forskolin-stimulated cAMP accumulation in NIH-3T3 cells stably expressing the melatonin receptors. The binding selectivity was further evaluated by deter-

mining the affinity for more than 190 other receptors and molecular targets.

Results: Results indicate that tasimelteon is a Dual Melatonin Receptor Agonist (DMRA) with 2.1–4.4 times greater affinity for the MT_2 receptor than for the MT_1 receptor. Tasimelteon potently inhibits forskolin-stimulated cAMP accumulation in cells expressing MT_1 or MT_2. Tasimelteon had no significant interaction with all other commonly screened receptors or enzyme binding sites tested, including receptors of neurotransmitter systems such as dopamine, norepinephrine, serotonin, gamma-aminobutyric acid (GABA), acetylcholine, opioid, N-methyl-D-aspartate (NMDA), and cannabinoid.

Conclusions: The very selective and unique receptor binding profile of tasimelteon supports its pharmacological properties of a circadian regulator, including in particular its ability to phase advance and entrain circadian rhythms as demonstrated in healthy volunteers and in patients with Non-24.

Disclosure: Both authors are employed by Vanda Pharmaceuticals.

P433

A multicenter open-label safety study of tasimelteon for the treatment of non-24-hour sleep-wake disorder in blind individuals with no light perception

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Objectives: HETLIOZ™ (tasimelteon) is approved in the United States for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24). A multicenter, open-label study was conducted in France to evaluate the long-term safety and tolerability of tasimelteon 20 mg in Non-24.

Methods: Blind individuals with no light perception and sleep complaints received 20 mg tasimelteon before bedtime for 52 weeks, and for up to three additional years in an optional extension. Safety evaluations included collection of adverse events, suicidal ideation or behavior, vital signs, laboratory evaluations, electrocardiograms, and physical examinations. Efficacy evaluations included scales of Clinical Global Impression-Change (CGI-C), Patient Global Impression of Change (PGI-C) for nighttime sleep, and PGI-C for daytime sleep.

Results: As of 31 October 2013, 35 (70.0%) of 50 enrolled patients completed the 52-week main study, and 24 of 28 patients who entered the extension phase (85.7%) remained active. Mean duration of exposure (N = 48) was 481.9 days (range 25–1023). There were no deaths or serious adverse events.

The most frequent treatment-emergent adverse events were headache (22.9%) and bronchitis (10.4%). There were no persistent changes in mean laboratory parameters over time, no clinically relevant changes in vital signs or ECGs values, and no treatment-emergent suicidal ideation or behaviour.

Most patients showed improvement of their symptoms as measured by CGI-C (88.6%), PGI-C for nighttime sleep (84.1%), and PGI-C for daytime sleep (61.4%).

Conclusions: Consistent with previous studies, results indicate that tasimelteon was generally safe and well-tolerated in individuals with Non-24, and that most patients showed improvement in global functioning.

Disclosure: M. Dressman, C. Perry and C. Lavedan are employees of Vanda Pharmaceuticals. Pr. Léger is the Principal Investigator and Dr. Quera-Salva is a clinical investigator in Study 3202 and both have clinical trial service agreements for this work.

P434

Nocturnal shift work is associated with reduced stage N3 and REM sleep in adults

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Objective: To assess how shiftwork might be related to objectively recorded sleep quality and timing alterations.

Methods: The current study comprised 29 workers aged 22–59, 19 females and 10 males, working in nocturnal and diurnal shifts of different job segments. The shift workers were recruited through different forms of media (electronic, newspapers, radio and magazines) from the general population of Sao Paulo city. The sleep pattern of the shift workers was evaluated by one night polysomnography (PSG) exam, on a night off work, and by Epworth Sleepiness Scale (ESS). The night workers were on this schedule for at least 6 months. The significance level was set at $P < 0.05$. T-test was used to compare the groups. The measures of correlation among the sleep pattern features were obtained by Pearson′s correlation.

Results: The mean (Standard Deviation) age of the shiftworkers was 37.1 ± 10 years and the body mass index was 26.6 ± 5.2 kg/m^2. There were no significant differences between night workers and day workers regarding the somnolence (ESS score) evaluation: night workers 11.6 ± 4.1 vs. day workers 10.4 ± 4.1. However, night workers showed decreased N3 stage (night workers 70.7 ± 30.2 min vs. day workers 92.3 ± 25.4; P = 0.04) and REM sleep time (night workers 78.8 ± 25.5 vs. day workers 98.2 ± 20.3; P = 0.03). Indeed, the N3 stage time were negatively correlated with the IAH index (P = 0.001; r = −0.6).

Conclusions: Nocturnal shiftwork is associated with reduced N3 stage and REM sleep time in adults.

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P435

Explore the impact of circadian rhythm patterns for nurses′ sleep under the influence of the shift system

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Introduction: Shift work has great impact on circadian rhythm to alter nurses' sleep. This study investigated the impact of circadian rhythm on nurses' sleep under the influence of the shifts system.

Methods: One hundred ninety-three nurses were recruited from the medical center in Taiwan. Grouping into day shift (DS, n = 73), evening shift (ES, n = 64) and night shift (NS, n = 56). Participants filled out the Pittsburg Sleep Quality Index (PSQI), the Morningness-Eveningness and personal characteristics questionnaire.

Results: There were 53.1–71.4% of nurses reported their sleep as poor (PSQI ≥ 5). Sleep quality in ES group was the worst. The ES group has the most evening type of circadian rhythm (48.4 vs. 13.7%). The ES group significantly has longer than 7 h sleep duration (40.6 vs. 17.9%). Use of sleeping medication significantly happened in most of the DS group (12.3 vs. 1.6%). Daytime

dysfunction happened in the ES groups were significantly more than DS and RS groups (85.7 vs. 75.3%). Moreover, analyzed the sleep quality associate with working shift (A) and circadian rhythm (B), there were significant differences among working shift groups ($F = 3.37$, $P = 0.036$), but no significant interaction (A*B) ($F = 0.877$, $P = 0.479$) and differences among circadian rhythm ($F = 2.18$, $P = 0.116$).

Conclusion: More than half of nurses perceived their sleep as poor, nurses' sleep in the evening shift has the most evening type of circadian rhythm and the worst sleep quality. Working shift may play a role to disturb their circadian rhythm. Findings in this study provide information for nursing scheduling to better adapt their shift work.

Disclosure: Nothing to disclose.

P436

Sleeping disorders among Dutch visually impaired persons: an investigating study

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Objectives: A majority of visually impaired individuals (VIP's) reports severe complaints of daytime fatigue and sleepiness. Both VIP's and caregivers frame these complaints as caused by compensatory effort needed to fulfil daytime activities in the (partial) absence of vision. An alternative explanation for this complaint could be the presence of a sleep disorder (Lockley et al., 2007; Warman et.al 2011). The present research aims to quantify the occurrence of a sleep disorder by having VIP's fill out validated questionnaires.

Methods: Respondents were asked to fill out an online questionnaire, which included two validated questionnaires, i.e. the Holland Sleep Disorder Questionnaire (HSDQ), the Epworth Sleepiness Scale and additional questions about demographics, daytime activities and ophthalmic disease. The HSDQ differentiates between types of sleeping disorder.

Results: VIP's have a higher score on the question about fatigue than the general Dutch population (respectively 3.16 vs. 2.81)*. A General Sleep Disorder has a higher incidence within this group of respondents than within the general Dutch population (Kerkhof, 2014) (respectively 54% vs. 32.9%)*.

Conclusions: The reported daytime fatigue might be caused by a sleep disorder rather than by the strain caused by the visual impairment, as commonly is assumed. This may be caused by a deregulation of the sleep-wake cycle.

* $P < 0.05$

References: Lockley, S.W. et a.l (2007), Dialogues Clin Neurosci.
Warman, G.R., et al. (2011), PLoS One
Kerkhof, G.A. (2014), Article in preparation.

Disclosure: Nothing to disclose.

P437

A placebo controlled study of the effects of blue light therapy on sleep and performance in late chronotypes

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Objectives: We present a placebo controlled home-study, with morning blue light pulses to treat a delayed sleep phase and check daytime performance.

Methods: 42 participants (21.4y ± 6.5, 23f/19 m) were randomly assigned to a sleep phase advancing protocol with 14 baseline days, nine treatment days with 30-min light pulses in the morning: either blue light (BL: 470 nm, 2306 m-lux, 300 lux), or amber light (AL: 590 nm, 6 m-lux, 250 lux; Philips Consumer Lifestyle, The Netherlands) and seven post-treatment days. Saliva samples were taken to calculate Dim Light Melatonin onset (DLMO), sleep was monitored with Actiwatch Spectrum (Philips Respironics Inc., USA) and reaction time was measured four times daily.

Results: DLMO showed a significantly larger phase advance after BL, 81 min. ± 12, compared to after AL, 47 min ± 10. Wake-up time in post-treatment period was earlier compared to baseline in BL group (−16 min ± 9) and later (+10 min ± 10) in the AL group. Sleep quality (number of sleep bouts) was significantly worse in the AL group during treatment, while not significantly different in the BL group. Performance was worse in the AL group during treatment at noon and at noon as well as evening during post-treatment, while not significantly different at any time point in the BL group.

Conclusion: Morning blue light therapy supports a sleep advancing protocol by phase advancing circadian rhythms including sleep timing and compensates for the sleep quality and performance decrement that was observed in the AL condition.

Disclosure: The study was financially supported by- and GoLite Blu devices and adapted amber light devices were made available by Philips Consumer Lifestyle, Drachten, The Netherlands. Vanja Hommes is an employee of Philips Consumer Lifestyle, Drachten, The Netherlands.

P438

Delayed sleep phase syndrome

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Our Biological Clock runs a little slower than 24-h, likely around 24.3 h. Most people are able to adjust their rhythm to synchronize with their community's daily chores and activities.

Youth between 16 and 22 years old have a tendency for Eveningness, resulting in Circadian Rhythms that are in disharmony with education and employment.

Optimal sleep time for humans in general varies between 6.5 h and 8.5 h/night. If a person no longer feels sleepy and do not fall asleep before long after after he/she wants to fall asleep, a condition called Delayed Sleep Phase Syndrome (DSPS) develops.

Until recently, it has been difficult to diagnose DSPS, as it has been dependent on Anamnesis and Sleep Diary. These tools are subjective, and may be subject to uncertainty. Single night PSG may give an indication, but deviations could also be First Night Effect.

Our centre has for 6 months utilized actigraphy as a tool to diagnose patients with DSPS. It registers movement patterns and wavelengths of light and scores sleep-wake-rest intervals. Actigraphy is well validated against Sleep Diary and PSG.

This abstract present the difference between normal actigraphy (female 1955), with stabile a sleep phase 23:00–07:00, and seven patients that suffers from DSPS. Five male 18–30 y.o, and two female 26–45 y.o.

Treatment of DSPS is primarily Melatonin tablets 3–6 mg 1–2 h before ideal sleep onset, and the use of a daylight-lamp in the morning, assisting the patient in adapting good Sleep Hygiene and treating comorbidity.

Disclosure: Nothing to disclose.

P439

Job strain and vagal recovery during sleep in female shift workers

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Objectives: We explored the association between high job strain (combination of low job control and high job demands) and heart rate variability (HRV) before and during sleep in a sample of health care professionals in three shift work.

Methods: Female nurses and nursing assistants (n = 95) were recruited from wards belonging to the top (high strain group, HJS, n = 42) or bottom quartiles on job strain (low strain group, LJS, n = 53) based on a survey of the Finnish Public Sector Study. The 3-week field measurements included sleep diaries and actigraphs to study the participants' sleep patterns. A subset of three pre-selected, circadian rhythm and recovery controlled measurement days, one morning shift, one night shift and a day off, included HRV measurements, where 30 min before sleep and 30 min of sleep with lowest heart rate were analyzed.

Results: The average sleep duration during the whole measurement period and during the subset of measurement days was similar in both job strain groups. The HJS group had a shorter sleep length than the LJS group after morning shift, among those who had another morning shift on the next day (6:18 vs. 7:32 h, $P < 0.03$). The bootstrapped HRV parameters (heart rate, high and low frequency power, high-to-low-frequency power and the square root of the mean square of successive differences of successive inter-beat-intervals) before and during sleep revealed no statistically significant job strain group differences (p-values ≥ 0.32).

Conclusion: Within a sample of female shift workers, no association was found between job strain and HRV.

Disclosure: Nothing to disclose.

Sleep disorders – Insomnia 1

P440

Preliminary evidence for quality of life improvements after acceptance and commitment therapy in primary insomnia

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Background: Cognitive behavior therapy for insomnia (CBT-I) improves subjective and objective parameters of sleep in patients with primary insomnia (PI). However, the perception of poor sleep and an impaired quality of Life (QoL) often persists despite treatment. This study aimed to provide first evidence that Acceptance and Commitment Therapy (ACT), an intervention including mindfulness and value-based changes of behavior, can improve subjective sleep quality and QoL in patients with chronic PI.

Methods: Eleven patients with chronic PI who were non- or partial responders to CBT-I were included. Data were collected 6 weeks prior to the intervention (T_{-1}), directly before (T_0) and after the intervention (T_1), and at 3-months follow-up (T_2). The intervention consisted of six ACT sessions in an outpatient group setting. Primary outcomes were sleep-related QoL (Glasgow Sleep Impact Index), global QoL (World Health Organization Quality of Life scale) and subjective sleep quality (measured by sleep diaries).

Results: Ten patients completed the study, one dropped out due to scheduling problems. All measures remained stable between T_{-1} and T_0. Significant improvements after the intervention were observed for sleep-related QoL, global QoL, and subjective sleep quality (ANOVA with factor Time, post-hoc contrasts T_1 and T_2 vs. T0, all *P*s< 0.05, large effect sizes). Subjective total sleep time, sleep onset latency and wake time after sleep onset did not significantly change across the study.

Conclusions: The findings provide preliminary evidence that ACT might improve subjective sleep quality and the QoL in patients with PI.

Disclosure: CN has received speaker honoraria from Servier. DR has received a consulting fee from Abbvie Germany. The other authors indicate no financial conflicts of interest.

P441

The mediating role of anxiety and depression on the association between perfectionism, sleep-disturbances, and insomnia severity

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Individuals with sleep-disturbances, specifically insomnia, often exhibit aspects of perfectionism, and symptoms of anxiety and depression, however the investigation of these factors together has been diminutive. The present study examined the mediating role of anxiety and depression on the associations between sleep-disturbances, insomnia-severity and aspects of perfectionism.

Eighty six participants (Age: M = 25, SD = 10.02; 80% female) were assessed using the Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI). Participants also completed two Multidimensional Perfectionism Scales (F-MPS; HF-MPS), and the Hospital Anxiety and Depression Scale (HADS).

Poor-sleepers demonstrated significantly higher scores on the F-MPS subscale *doubts-about-action* compared to normal-sleepers (t (84) = 2.54, $P = 0.01$). Additionally, global PSQI scores were significantly associated with *doubts-about-action* (r = 0.22, $P = 0.04$). Insomnia-severity was significantly associated with the F-MPS subscales of *doubts-about-action* (r = 0.32, $P = 0.01$), *concern-over-mistakes* (r = 0.26, $P = 0.02$), and *parental-criticism* (r = 0.30, $P = 0.01$). Hierarchal multiple-regression analyses, separately examining the global PSQI and insomnia-severity scores, demonstrated that when anxiety and depression were controlled for, none of the previous associations remained significant.

The results indicate that:

1. both increased sleep-disturbance and insomnia severity appear to be associated with increased *doubts-about-action*;
2. increased insomnia-severity also appears to be associated with increased *concern-over-mistakes,* and *parental criticism*; and
3. these associations are mediated by anxiety and depression.

These results could suggest that treatments for sleep-disturbance and insomnia should address anxiety and depressive symptoms, with the prospect of alleviating aspects of perfectionism, specifically *doubts-about-action, concern-over-mistakes*, and *parental criticism,* that may perpetuate pre-sleep arousal, consequently disturbing sleep.

Disclosure: Nothing to disclose.

P442

Sublingual flumazenil for the residual effects of hypnotics: zolpidem and brotizolam

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Background: Residual morning drowsiness is a frequent side effect of hypnotics which limits optimal treatment in Insomnia.

Purpose: To study the safety and efficacy of sublingual Flumazenil (GABA-A antidote) in reversing the residual hypnotic effect.

Methods: A double blind, placebo controlled, randomized cross over study with twenty healthy subjects who slept for 1.5 h following sleep induction (Zolpidem $n = 10$; Brotizolam $n = 10$). Upon awakening, they underwent neurocognitive tests including immediate word recall test (iWRT), Digit Symbol Substitution Test (DSST), and mood/performance questionnaires. They were then treated by Flumazenil or placebo ($n = 20;20$) and were re-evaluated after 20 and 60 min. A week later, the same procedures were performed (Placebo/Flumazenil accordingly).

Results: All 20 volunteers completed the study. Flumazenil was superior to placebo by 59–93% ($P < 0.05$–0.001) in improving performance in the various neurocognitive tasks. Subjects reported a significant improvement in vigilance with Flumazenil, both at 20 min (3.0 ± 0.6 cm vs. 1.3 ± 0.6 cm, $P < 0.02$) and 60 min (4.7 ± 0.6 cm vs. 2.8 ± 0.7 cm, $P < 0.03$). iWRT improved with Flumazenil vs. placebo at 20 min (4.2 ± 0.8 vs. 1.3 ± 0.9 words, $P < 0.005$) and 60 min (5.4 ± 1.1 vs. 1.2 ± 1.2 words, $P < 0.02$).

Conclusions: Sublingual administration of Flumazenil is safe and effective in reversing the hypnotic effects of Zolpidem and Brotizolam. This may offer a comprehensive and safer treatment for insomniac patients.

Disclosure: Prof Peled is the founder of Coeruleus which developed the sublingual flumazenil. He was not involved in the reseaerch .He saw the results only after the study was finished.

P443

Don't worry, sleep well

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Objective: To explore the relationship between sleep quality/quantity, chronotype, pre-sleep arousal, arousability, stress, coping, neuroticism, extraversion mood/affect, perceived health and sleep loss due to worry in university students.

Method: Four hundred and sixty seven females and 247 males, students (mean age 19.29 years; SD = ±1.256), completed a series of questionnaires that assessed sleep loss over worry (item from the General Health Questionnaire), other sleep-wake aspects (e.g. habitual sleep duration, sleep needs, sleep depth, subjective sleep quality, sleep latency, night awakenings, daytime sleepiness, sleep flexibility, sleep reactivity to stress), pre-sleep arousal (cognitive/somatic arousal), arousability, coping, neuroticism, extraversion, perceived physical/mental health, academic stress, and positive/negative affect.

Results: Sleep disturbance due to worry was reported by 40.6% of females (Quite often=34%, Almost always=6.6%) and 19.2% of male students (Quite often=17.7%, Almost always=1.6%). Regression models showed that cognitive arousal (b = 0.353; $P = 0.000$); perceived academic stress (b = 0.129; $P = 0.005$), arousability (b = 0.127; $P = 0.006$); worry tendency (b = 0.153; $P = 0.000$); gender (b = 0.118; $P = 0.001$) and perceived physical health (b = −0.093; $P = 0.008$) all were significant predictors of sleep loss over worry. Together these variables accounted for 40.3% of the variance in sleep disturbance due to worry scores.

Conclusion: Sleep loss over worry is highly prevalent among students, especially females. Our findings suggest that cognitive arousal, academic stress, arousability, tendency to worry, gender and perceived physical health may be important determinants of sleep loss over worry. These results may have important implications for prevention and intervention to improve sleep quality in young adults.

Disclosure: Nothing to disclose.

P444

Factors associated with self reported insomnia and sleep loss over worry in young adults

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Objective: To describe the prevalence of insomnia and sleep loss over worry and its associations with sleep quality/quantity, chronotype, pre-sleep arousal, arousability, stress, coping, neuroticism, extraversion mood/affect, and perceived health in a sample of university students.

Method: Seven hundred and thirteen students (65.6% females), mean age 19.29 years (SD = 1.256), completed a series of questionnaires that assessed sleeplessness (item from the Eysenck Personality Inventory) sleep loss over worry (item from the General Health Questionnaire), other sleep-wake aspects, pre-sleep arousal, arousability predisposition, coping, neuroticism, extraversion, perceived physical/mental health, academic stress, and mood/affect.

Results: Insomnia was reported by 10.5% of females and 9.8% of male students. Sleep disturbance due to worry was reported by 40.6% of females and 19.2% of male students. Regression analysis performed separately by type of sleep complaint revealed that cognitive arousal (b = 0.372; $P = 0.000$); perceived physical health (b=−0.075; $P = 0.057$) and tendency to worry (b = 0.086; $P = 0.051$) were all significant predictors of both insomnia and sleep disturbance due to worry. Neuroticism/NEO-PI-R facet, Anxiety (b = 0.085; $P = 0.061$), somatic arousal (b = 0.099; $P = 0.023$) and positive affect (b = −0.085; $P = 0.051$) were all significant predictors of only insomnia, whereas perceived academic stress (b = 0.129; $P = 0.005$) arousability (b = 0.127; $P = 0.006$) and gender (b = 0.118; $P = 0.001$) were all significant predictors of only sleep disturbance due to worry.

Conclusion: Although differences were found in the factors associated with the two sleep complaints, tendency to worry, cognitive arousal and perceived physical health were all predictors of both self-reported insomnia and sleep loss over worry.

Acknowledgements: The co-operation of the Professors and Students is gratefully acknowledged.

Disclosure: Nothing to disclose.

P445

Correlates of self reported insomnia in young adults

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Objective: The aim of this study was to examine the factors associated with self reported insomnia in a sample of university students.

Method: Four hundred and sixty seven females and 247 males, medical students (mean age 19.29 years; SD ± 1,256), completed a series of questionnaires that assessed insomnia (item from the Eysenck Personality Inventory «*Do you suffer from sleeplessness/insomnia*?», responses ranging from Almost never to Almost always), other sleep-wake aspects (habitual sleep duration, sleep needs, sleep depth, subjective sleep quality, sleep latency, night awakenings, sleep inertia, daytime sleepiness, sleep flexibility, chronotype, sleep reactivity to stress), pre-sleep arousal (cognitive/somatic arousal), arousability predisposition, coping, neuroticism, extraversion, perceived physical/mental health, academic stress and mood/affect.

Results: Insomnia was reported by 10.5% of females (Quite often = 9.2%, Almost always=1.3%) and 9.8% of male students (Quite often = 7.8%, Almost always=2.0%). No significant differences were found between genders. Regression models showed that cognitive arousal, (b = 0.372; $P = 0.000$); Neuroticism/NEO-PI-R at the facet level N1.Anxiety (b = 0.085; $P = 0.061$), perceived physical health (b = −0.075; $P = 0.057$); tendency to worry (b = 0.086; $P = 0.051$); somatic arousal, (b = 0.099; $P = 0.023$) and positive affect (b = −0.085; $P = 0.035$) and were all significant predictors of insomnia. Together these variables accounted for 29.8% of the variance of insomnia scores.

Conclusion: In this sample of young adults pre-sleep cognitive/somatic arousal, trait anxiety, perceived physical health, tendency to worry and positive affect were associated with self-reported insomnia.

Acknowledgements: The co-operation of the Professors and Students is gratefully acknowledged.

Disclosure: Nothing to disclose.

P446

Greater general repetitive negative thinking directly predicts more severe insomnia in males: in females it is all about depression

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Objectives: Harvey's (2002) cognitive model of insomnia suggests that Repetitive Negative Thinking (RNT) about sleep and the consequences of sleep loss leads to distress which, among other factors, leads to insomnia. The current study tested whether this pathway held true for general rather than sleep related RNT, and sought to establish any age or gender differences in these relationships.

Methods: We used mediation analysis conducted using Structural Equation Modeling (community sample, $N = 483$, age 18–91 years). RNT was a latent variable of the Ruminative Response Scale's Reflection and Brooding subscales, and the Penn State Worry Questionnaire total. Psychological distress was measured using the Short Depression Anxiety and Stress Scale (DASS-21). Insomnia Severity was measured using the Insomnia Severity Index (ISI). The model explored whether the relationship between RNT and ISI is via DASS-21.Two multi-group moderated mediations (comparing the mediation model for older and younger adults, and males and females) were then conducted.

Results: General RNT was a significant predictor of insomnia severity. While this effect was fully mediated by psychological distress for females, it was entirely direct for males. Age did not moderate the pathways.

Conclusions: General RNT, not just that which is sleep-related, is an important contributing factor to insomnia. Depression plays a different role in the relationship between RNT and insomnia for men and women. Such information, if replicated, has the potential to inform formulation and treatment strategies for individuals with insomnia.

Disclosure: Nothing to disclose.

P447

The effectiveness of mindfulness meditation with cognitive behavioral therapy in patients with chronic insomnia

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Objectives: The aim of this study is to investigate the effectiveness of mindfulness mediation on pre-sleep arousal and dysfunctional belief by comparing the patients who received mindfulness meditation and cognitive behavioral therapy for insomnia with the patients who received only cognitive behavioral therapy for insomnia.

Methods: Twenty patients with chronic insomnia were recruited at the Sleep Center of St. Vincent's hospital. The patients were allocated to the cognitive behavior therapy (CBTi) group and mindfulness meditation and cognitive behavioral therapy (MCBTi) group. CBTi group received total four sessions of cognitive behavior therapy for insomnia once a week and MCBTi group received six sessions of mindfulness meditation program additional to the four sessions of CBTi program once a week. We used Insomnia Severity Index, Sleep Diary, Pre-Sleep arousal Scale, Dysfunctional Belief and Attitudes about Sleep Scale, Kentucky Inventory of Mindfulness Skills.

Results: Results indicated that both physical arousal and cognitive arousal of pre-sleep arousal score of MCBTi group significantly decreased compared to CBTi group. Insomnia Severity Index of MCBTi group showed significantly greater decrease compared to CBTi group. There were no significant differences between groups in dysfunctional beliefs related to sleep.

Conclusion: MCBTi group showed significant decrease in pre-sleep arousal score and Insomnia Severity Index, although there were no significant differences between groups in dysfunctional beliefs related to sleep. Mindfulness meditation has additional therapeutic effects on arousal and insomnia severity, which could help patients have a better sleep quality with higher sleep efficiency.

Disclosure: Nothing to disclose.

P448

Clinical characteristics of patients with primary insomnia in Korea: comparing the misperception group and non-misperception group

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Objectives: The purpose of this study was to identify the differences of clinical characteristics between primary insomniacs with and without sleep state misperception (SSM) in Korea.

Methods: A total of 250 consecutive primary insomniacs without other comorbid sleep disorders, aged 18 or older whose objective total sleep time (TST) was more than 120 min were enrolled. We divided these subjects into a misperception group and non-misperception group. SSM is defined as those whose objective TST was more than 6.5 h, sleep efficiency was at least 85%, as well as underestimating one's TST by more than 60 min in subjectively reported TSTs, compared to the objective TST of the PSG. All subjects underwent an over-night PSG and completed sleep related and psychiatric measurements.

Results: The prevalence of the SSM was 26.4%. The misperception group was significantly younger than the non-misperception group (47.48 ± 12.63 vs. 54.24 ± 11.32, $P < 0.001$). Thus we adjusted age as a covariate in the data. There were no significant differences in sleep related and psychiatric measurement results between the misperception group and non-misperception group but the scores of both groups were abnormal compared with the norm. Comparing the PSG variables, the misperception group showed significantly longer TST, shorter sleep latency, and better sleep efficiency.

Conclusions: Although the subjects with SSM were almost normal in objective sleep variables, they subjectively complain of insomnia and poor quality of sleep. In the misperception group there were some psychiatric problems, including mild depressive and anxiety symptoms.

Disclosure: Nothing to disclose.

P449

Perfectionistic tendencies in insomnia patients′ behaviour during psychometric testing

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Objectives: According to self-report questionnaire studies, insomnia patients differ from healthy controls with respect to several personality traits. The current study aimed at exploring how these personality traits may translate into behaviour.

Methods: Insomnia patients′ behaviour during psychometric testing (n = 163) was investigated in comparison to healthy controls (n = 81), patients with other sleep disorders (n = 80) and patients with obsessive-compulsive disorder (n = 36).

Results: In line with our hypotheses, insomnia patients made more additional comments than healthy controls and more corrections than patients with other sleep disorders during sleep-related questionnaire completion. Furthermore, insomnia patients calculated the sum score of a depression questionnaire more frequently than both healthy controls and patients with other sleep disorders.

Conclusions: These findings further support the assumption of an altered personality profile in patients with primary insomnia. Future work should aim to elucidate what personality factors these novel behavioural markers may reflect.

Disclosure: Nothing to disclose.

P450

Slow dissolving of emotional distress contributes to hyperarousal

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Insomnia is highly prevalent and a major risk factor for depression. Understanding the mechanisms of a key symptom common to both disorders, hyperarousal, would provide opportunities to develop better treatment and prevention of depression. Emotion regulation is facilitated by unperturbed REM sleep. It was hypothesized that the fragmented REM sleep that is typical of insomnia interferes with the overnight resolution of emotional distress and that its accumulation results in chronic hyperarousal. Participants (N = 1221) completed questionnaires on insomnia, hyperarousal, nocturnal mental content – an indicator of REM sleep fragmentation – and emotional distress after experiencing shame, a relevant self-conscious emotion in psychiatry. Mediation analyses investigated whether fragmented REM sleep contributed to hyperarousal by leaving emotional distress unresolved. Specifically the frequency of experiencing distress lasting overnight increased with insomnia severity (β = 0.21; $P < 0.001$), whereas distress lasting less than a day did not (β = 0.03; P = 0.38). Confirming previous studies, insomnia severity was associated with hyperarousal (β = 0.46; $P < 0.001$) and with the frequency of recalling nocturnal mental content, an indicator of REM sleep fragmentation (β = 0.09; $P < 0.001$). Notably, 47.4% of the association between these key characteristics of insomnia was mediated specifically by reduced overnight resolution of emotional distress. The findings demonstrate reduced overnight resolution of emotional distress in association with insomnia severity, which may in part result from REM sleep fragmentation, and contribute to the characteristic chronic hyperarousal. The finding adds clinical relevance to the role of REM sleep in emotion regulation and calls for studies on sleep interventions for emotionally distressed patients.

Disclosure: Nothing to disclose.

P451

Blood lead levels and sleep quality in workers of lead- zinc companies

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Objectives: Effects of lead on creating a variety of sleep disruption is not well understood and there are conflicting reports of relationship between sleep disorder and blood lead levels (BLL).

This study assessed the relationship between BLL and sleep quality.

Methods: It was a Cross- sectional study. All personnel of some lead companies in zanjan city were studied . BLL concentrations were evaluated, blood samples storage at -20 ° C and analyzing with Atomic absorption spectrophotometry in baharloo hospital.

Sleep quality assessed with standardized sleep questionnaires. These questionnaires were Insomnia Severity Index (ISI), Epworth Sleepiness Scale (ESS) and Pittsburg Sleep Quality Index(PSQI).

Statistical analyses were performed with using SPSS 16 software.

Results: Four hundred and fifty eight workers were studied. 425 person complete the questionnaire. Responsive rate was 92%.

Mean of BLL was 34.7 $\pm$ 16.7 μg/dL.

Association between BLL and questionnaires scores shows that Increasing BLL was associated with higher odds of abnormal ISI score, ESS score and PSQI score (p for trend 0.000).

High BLL was associated with Difficulty falling asleep, Difficulty Staying sleep, Waking up too early and shorter duration of sleep.

Conclusion: Lead increase risk of sleep disorder. It can cause initial insomnia, excessive daytime sleepiness and may disturb sleep quality. We should select ways to further reduce environmental and occupational lead exposures.

Disclosure: Nothing to disclose.

P452

The role of emotion dysregulation in insomnia: longitudinal findings from a large community sample

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Objectives: The purpose of this longitudinal investigation was to examine the association between emotion regulation processes and future insomnia (incidence and persistence).

Methods: A survey was sent out to 5000 individuals in the community. To those who returned the baseline questionnaire (n = 2327), two follow-up surveys, 6 and 18 months later, were sent out and then completed by 1887 and 1795 individuals, respectively. The survey contained information about demographic factors, insomnia symptomatology, and the Difficulties in Emotion Regulation Scale (DERS; five subscales).

Results: Among those with no insomnia at previous assessments, more dysfunctional scores on one of the DERS dimensions (goals) and change over time towards more dysfunctional scores on four of the DERS subscales (goals, non-acceptance, impulse, and strategies) increased the risk for incident insomnia. Among those with

insomnia at prior assessments, more dysfunctional baseline scores on three of the DERS subscales (goals, non-acceptance, and awareness) increased the risk for persistent insomnia, relative to developing normal sleep, and that one of the DERS dimensions (goals) increased the risk for persistent insomnia, relative to developing insomnia remission. Among those with insomnia at prior assessments, change over time towards more dysfunctional scores on two of the DERS subscales (awareness and strategies) increased the risk for persistent insomnia.

Conclusions: This study points towards an association between on the one hand emotion dysregulation and on the other hand incident and persistent insomnia over time. This might have implications for the conceptualization and management of insomnia as well as for future research.

Disclosure: Nothing to disclose.

P455

Prevalence, associated factors and management of insomnia in prison populations: an integrated review

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Objectives: The aim of this review was to identify existing evidence concerning insomnia in a prison population.

Methods: An exploratory integrative review was utiltised to collate, describe and discuss the prison-sleep literature by exploring potential themes and study quality. Cochrane Library, EMBASE, MEDLINE, Evidence Based Medicine Reviews and PsycINFO databases were examined against appropriate search operators for insomnia (e.g. sleep disturbance, sleep problems, hypnotic) and prison (e.g. incarceration, jail, inmate) terms. Several key comorbidity reports were also included.

Results: The review identified 33 articles that explored sleep in a prison establishment. A thematic analysis identified five key themes: the prevalence of sleep problems, the comorbidity of sleep problems, psychiatric disorder and substance misuse, the influence of the prison environment on sleep, reliance on hypnotic medication and the effectiveness of sleep management. An estimated insomnia prevalence rate ranged from 10.9% to 81.0% depending on sex, age, sentencing type or insomnia criteria used. Non-pharmacological treatments such as meditation and relaxation techniques were also identified as a means of improving sleep.

Conclusions: Insomnia seems to be a common condition in a prison setting. There is some consistency between country in terms of insomnia prevalence, associated factors and general management. However, the criteria, measure and method used to identify insomnia or sleep difficulties differed across these themes. This makes it difficult to ascertain clarity and certainty in the results. More research is needed to identify exactly how problematic insomnia is in the world prison estate.

Disclosure: Nothing to disclose.

P456

Sleeping difficulties remain chronic over 9 years in young Australian women

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Objectives: Young women are especially at risk of poor sleep but the extent to which their poor sleep remains chronic is unknown. Here we investigated self-reported sleeping difficulties over 9 years in a large sample of young women, who commenced the study with no reported depression or anxiety.

Methods: Data was from the Australian Longitudinal Study on Women's Health (n = 9683). Information on self-reported sleeping difficulties was obtained from four questionnaires in 2000 (aged 21–25y), 2003, 2006 and 2009. Generalized estimating equations (unadjusted) were conducted to calculate odds ratios (OR) for the likelihood of women who reported sleeping difficulties 'never', 'rarely', 'sometimes' and 'often' during the previous 12 months in 2000, to continue to report sleeping difficulties at the subsequent three surveys. Women who, in 2000, reported a diagnosis in the past 4 years or symptoms in past 12 months of depression or anxiety, or used antidepressants, were excluded.

Results: Over the 9 years reported sleeping difficulties 'often' was relatively consistent at 9.1% to 10.9%. Women who reported sleeping difficulties 'often' in 2000 had a markedly increased risk of also reporting sleeping difficulties 'often' over the subsequent 9 years (2003: OR [95% CI] = 9.96[7.16–13.84]; 2006: 10.96[7.85–15.31]; 2009: 9.61[6.76–13.67]. This risk of chronicity was highest for those with sleeping difficulties 'often'.

Conclusions: Self-reported sleep difficulties 'often' in non-depressed young women strongly predicted a continuation of this level of sleeping difficulty, with a nearly 11-fold risk over the next decade. The poor sleep perpetuating factors need to be identified.

Disclosure: Nothing to disclose.

P457

Beliefs about the 'shape' and continuity of healthy sleep as a function of age

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Objectives: Treating sleeping difficulties includes challenging unrealistic beliefs which may contribute to anxieties and wakefulness. This study explored beliefs about the shape and continuity of healthy adult sleep across the night at different adult ages.

Methods: Younger (n = 113, M = 21.4(2.4) years) and older adults [n = 110, M = 72.3 (7.7)] plotted their conceptualization of the 'shape' of normal sleep (showing depth of sleep and awakenings) for both a healthy 18 and 65 year old. Plots were scored as ratings of sleep depth (0 = awake and 3 = very deep sleep) across 15 time periods. Frequency counts were also conducted of plots that were

1. U-shape
2. Non-U shape with no wake, and
3. Non-U shape with wake shown.

Results: The average of all 434 plots was found to be a clear U shape. A two way mixed MANOVA indicated a significantly deeper U

shape for the sleep plots of an 18 year old compared to a 65 year old, regardless of the age of the respondent. About 70% of all plots were U shaped. Importantly, more than nine out of ten younger adults and about three quarters of older adults believe that healthy sleep includes no awakenings, whether a sleeper is 18 or 65 years old.
Conclusion: Since awakenings are the norm in typical sleep patterns, the mismatch of awakenings with conceptualized healthy sleep may cause anxiety about these awakenings and contribute to the development or perpetuation of insomnia. Therefore these results have clinical implications for the use of sleep education in the treatment of insomnia.
Disclosure: Nothing to disclose.

P458

Correlates of improvements in daytime impairments during cognitive behavioural therapy for primary insomnia

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Objectives: Insomnia patients experience daytime impairments including feelings of fatigue, poor mood and irritability. Although daytime impairments improve during Cognitive Behavioural Therapy for Insomnia (CBTi), the factors driving these improvements are poorly understood. The current study aimed to examine associations of treatment-related changes in daytime impairments with objective and subjective sleep, sleep misperceptions and hyperarousal symptoms to better understand their etiology and positive treatment response.
Methods: Participants included 83 older adults with primary insomnia treated with CBTi. For each symptom, participants' 'follow-up' scores were subtracted from 'baseline' scores to calculate 'change' scores. Correlational analyses were undertaken to examine relationships between these 'change' scores.
Results: From baseline to 3-month follow-up, participants' subjective, objective, and sleep misperceptions, hyperarousal symptoms and daytime impairments showed significant moderate – large improvement ($P = < 0.05$, *Cohen's* $d = 0.38–1.03$). Correlational analyses indicated that improvements in daytime impairments were consistently positively related to improvements in symptoms of hyperarousal (86% of 35 analyses' $P = <0.05$), however were unrelated to the majority of improvements in measures of sleep (14% of 63 analyses' $P = <0.05$).
Conclusions: The current study suggests that improvements in daytime impairments are related to reductions in hyperarousal symptoms during treatment, and mostly unrelated to improvements in sleep parameters. This is consistent with the proven efficacy of behaviour therapies which reduce total sleep time and hyperarousal symptoms. Future studies may also attempt to improve daytime impairments in insomnia by treating symptoms of hyperarousal with educational and cognitive interventions.
Disclosure: Nothing to disclose.

P459

Structural and functional changes in the mesolimbic system in primary insomnia patients: an fMRI and DTI study

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Epidemiological studies have suggested that chronic insomnia increases the vulnerability to mood disorders. In this study, we investigated the brain response to emotional stimuli as well as the changes in functional and structural connectivity between brain regions involved in the mood regulation in primary insomnia patients by fMRI and diffusion tensor imaging. Ten patients and ten age-gender-matched healthy controls participated in the study. Using fMRI, we investigated the brain responses to conscious and non-conscious (backwardly-masked) emotional faces stimuli. Under the non-conscious condition, a happy or fearful facial expression was presented for 26 ms, followed by a neutral facial expression of the same person for 174 ms. Also all participants underwent diffusion tensor imaging.
Comparison of the happy vs. neutral contrasts for the non-conscious condition revealed larger activity of the left striatum in the patients group compared to the control group ($P < 0.05$, voxel-level FWE corrected). In functional connectivity analysis, the patients group tended to show lower connectivity between the left striatum and the ventral tegmental area(VTA) of the midbrain ($t[18]=1.98$, $P = 0.06$). Furthermore, in diffusion tensor analysis, the patients group showed significant smaller fractional anisotropy, which reflects integrity of the neural fibers, in the white matter between left ventral striatum and the VTA ($t[18]=2.26$, $P < 0.05$).
These results suggest that primary insomnia patients have structural and functional changes in the mesolimbic system which is related to the processing of enforced learning, reward, motivation and pleasant emotions. These changes may be associated with a higher risk of depression in chronic insomnia.
Disclosure: Nothing to disclose.

P460

Does mindfulness have an impact on hyperarousal in participants with insomnia complaints?

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Objectives: The Mindfulness-Based Stress Reduction program (MBSR – Kabat-Zinn) is a group intervention that has shown promising results for people with insomnia. One possible explanation is that regular practice of mindfulness meditation may reduce hyperarousal, one factor that has been shown to play a pivotal role in maintaining insomnia. However, to date, little is known regarding this specific relation.
Methods: This study included participants with sleep complaints. Twenty-two participants were assessed before and after the 8-week MBSR program (MBSR group; mean age 47.5 ± 13.8; 77% female), and compared to 23 controls that did not participate to an MBSR group (mean age 51.8 ± 11.1; 70% female). Hyperarousal was assessed with the Pre-Sleep Arousal Scale (PSAS) and the Dysfunctional Beliefs About Sleep Scale (DBAS). MBSR participants completed a daily meditation log during the 8-week group.

Results: Cognitive pre-sleep arousal score (PSAS) and worries about sleep (DBAS) were significantly reduced after 2 months in MBSR participants compared to controls [repeated measures ANOVA 2(groups)x2(pre-post), cog-PSAS: interaction $P < 0.01$, worry-DBAS: interaction $P = 0.06$]. However, there was no impact of MBSR on the somatic pre-sleep arousal (interaction $P = 0.11$). The decrease of cognitive pre-sleep arousal after MBSR was further shown to be correlated with the duration of formal meditation practice during the 8-week period ($r(20) = -0.46$; $P < 0.05$).
Conclusions: Our findings suggest that MBSR has an impact on cognitive hyperarousal in people with sleep problems. This effect could, in part, be determined by the amount of meditation practice in which participants engaged during the 8-week intervention.
Disclosure: Nothing to disclose.

P461

Experiences of insomnia patients from specialist clinics compared to a community sample: how different are they?

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Self-treatment is common practice among patients with insomnia and often takes place prior to seeking conventional medical care. These initial experiences may have a role in shaping patients' subsequent help-seeking behaviours and treatment beliefs. The current study maps out and compares the insomnia experiences from a general community based sample and a specialist clinic population.

A series of semi-structured interviews were conducted with insomnia patients recruited from general community venues ($n = 28$) and specialist sleep/psychology clinics ($n = 20$). Interviews were audio recorded, transcribed verbatim and analysed for emergent themes using 'Framework Analysis'.

A wide range of insomnia experiences was described across both patient groups. Complementary medicines or passive sleep-inducing strategies were often initiated in response to insomnia. Health care for the community patient group was limited to medication and basic sleep hygiene advice whereas clinic patients implemented a broad range of behavioural strategies as part of their treatment program. The community patient group also reported more maladaptive bedtime routines and greater vulnerability to the effects of psychosocial stressors. Whilst both groups interacted with similar interpersonal networks (e.g. friends, family, colleagues and health professionals), participants attending clinics appeared to have acquaintances with greater knowledge about insomnia treatment options.

This is the first Australian study exploring the insomnia experiences between two distinct patient populations. Delineating clearer insomnia treatment pathways for the public and delivering targeted interventions within primary care which address maladaptive sleep beliefs and behaviours appear important in the early stages of the treatment-seeking process.

Disclosure: Nothing to disclose.

P462

Acute and chronic effects of electroacupuncture on daytime vigilance in primary insomnia: placebo-controlled EEG topography/tomography and psychometric studies

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Objectives: While interest in treating insomnia with acupuncture is high, controlled clinical sleep studies are scarce and objective data on daytime vigilance lacking. Thus, one aim of this sham-controlled polysomnographic, psychometric and electrophysiological neuroimaging trial was to study the immediate and chronic effects of electroacupuncture on daytime vigilance in primary insomnia.
Methods: Twelve patients (9 f, age: 21–58 years, mean: 39.5 years) with primary insomnia (DSM-IV-TR 307.42) were included in the study. QEEGs were evaluated after acute electroacupuncture/placebo and chronic 10-week treatment (one 30-min electroacupuncture session/week) utilizing EEG mapping and EEG tomography (low-resolution brain electromagnetic tomography = LORETA). Psychometry included various noo- and thymopsychic measures.
Results: EEG mapping of the acute effects of electroacupuncture compared with both baseline and sham acupuncture demonstrated a significant decrease in absolute and relative delta and theta power as well as an increase in alpha power, specifically fast alpha-2. Chronic electroacupuncture induced similar EEG changes, with an additional increase in absolute beta power and an acceleration of the delta/theta and total centroid over the right occipitotemporal region. Spatial distribution will be described on the basis of the LORETA data. Psychometrically, some variables improved after sham acupuncture and remained on this level thereafter.
Conclusions: As compared with baseline and sham acupuncture, both acute and chronic electroacupuncture induced QEEG changes indicative of improvements of daytime vigilance. On the behavioural level, this vigilance increase induced partial thymo- and noopsychic improvements, which also became obvious after sham acupuncture and subsequently remained on this level, suggesting a placebo effect.
Disclosure: Nothing to disclose.

P463

Acute and chronic effects of electroacupuncture in primary insomnia: placebo-controlled clinical and polysomnographic studies

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Objectives: Exploratory, placebo-controlled, clinical and polysomnographic studies evaluated acute and chronic effects of electroacupuncture on sleep and awakening in primary insomnia patients over 10 weeks.
Methods: Twelve patients (9 f, 38.6 ± 11.1 years) were investigated in five sleep laboratory nights (pre-treatment, acute placebo and

electroacupuncture nights [randomized], two nights after 10-week treatment 1x/week). Observer ratings (CGI/DOTES) and self-ratings (QOL, PSQI, ISI, SAS, SDS, ESS, IRLSSG, AS, SSA) were performed pre and post treatment. A total of 10 needles were applied to specific acupuncture points, which were subjected to randomized real or sham stimulation by an electric generator.

Results: The CGI-S improved from moderate (4 ± 0.6) to borderline disturbance (2.1 ± 1.0) ($P < 0.05$, Wilcoxon). The PSQI, ISI and SAS improved on the 1%, subjective sleep and awakening on the 5% level. PSG showed a reduction of sleep latency to S1, wake-time within TSP, WASO and awakenings and improvements of SE from 81.2 ± 9.4 to 89.7 ± 6.7% ($P < 0.05$) from pre-treatment to placebo. The following treatment nights did not differ from placebo, except for a further latency decrease after chronic acupuncture. S1 decreased from pre-treatment to placebo, S2, S3 + S4 and REM increased. Respiratory and PLM parameters did not show any significant changes, except for an improvement of the oxygen desaturation index.

Conclusion: Clinical ratings improved significantly after 10-week electroacupuncture. In the PSG, even sham acupuncture induced significant improvements of sleep initiation, maintenance and efficiency, a decrease in S1, an increase in S2, S3 + 4 and SREM, and an improvement of the desaturation index, with values remaining on this level thereafter.

Disclosure: Nothing to disclose.

P464

Cognitive training improves sleep quality and cognitive function among older adults with insomnia

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Objectives: Insomnia is a sleep disorder frequently observed in older persons. In view of the findings showing that sleep during the night is critical in the consolidation of previously acquired memory traces, we hypothesized that intensive new learning experience provided by cognitive training will act as a catalyst to change sleep architecture and by doing so will improve sleep quality among older adult insomniacs. The present study examined the impact of cognitive training on sleep quality and cognitive performance among older adult insomniacs.

Methods: Fifty-one older adult insomniacs (22M/29F; mean age: 72.13 ± 5.1) were randomized into two groups: a cognitive training group ($n = 34$) and an active control group ($n = 17$). The participants in the cognitive training group completed an 8-week, home-based, personalized, computerized cognitive training program, while the participants in the active control group completed an 8-week, home-based program involving computerized tasks that do not engage high-level cognitive functioning. Before and after training, all participants' sleep was monitored for 1 week by an actigraph and their cognitive performance was evaluated.

Results: Mixed models for repeated measures analysis showed between-group improvements for the cognitive training group on both sleep quality (sleep onset latency and sleep efficiency: $F_{1,51} = 5.49$, $P < 0.05$; $F_{1,51} = 6.86$, $P < 0.05$, respectively) and cognitive performance (avoiding distractions, working memory, visual memory, general memory and naming). Moreover, hierarchical linear regressions analysis indicated correlation between the improvement in cognitive function and those in sleep quality.

Conclusions: Cognitive training may be beneficial in the initiation and maintenance of sleep among older adult insomniacs.

Disclosure: Nothing to disclose.

P465

Quality of sleep and quality of life in patients with primary insomnia treated with a prolonged-released melatonin

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Objectives: We evaluated the effect of prolonged-released (PR) melatonin on the quality of sleep (QoS) and quality of life (QoL) in patients with primary insomnia in routine practice.

Methods: Patients with primary insomnia aged 55 years or more who gave written informed consent were included in this multi-centric, open, prospective study. Patients were treated with PR melatonin in accordance with the SPC and were asked to complete the 'Pittsburgh Sleep Quality Index' (PSQI) and 'World Health Organization Well-Being Index' (WHO-5) just before and 3 weeks after initiation of the treatment.

Results: At baseline, 93.7% of the patients rated their QoS as fairly/very bad according to the PSQI; the median WHO-5 score of 10 indicated a bad QoL (<13 points).

One thousand nine hundred and seventy nine patients were included in the intention to treat group; PSQI score was available for the two visits for 1069 (54%) patients; WHO-5 values for 1654 (83.6%) patients.

969 (90.6%) patients improved their PSQI score after treatment, 79.6% had a clinically relevant (≥3 points) improvement. Remission (score after treatment <6) was present in 40.1% of the patients.

The QoL was bad (WHO-5 < 13 points) in 70.6% of the patients before treatment, but 19.5% after treatment. 1285 (77.7%) patients showed a clinically significant improvement.

7 (0.35%) patients reported adverse drug reactions, all non serious.

Conclusions: This study confirms the relationship between the QoS and the QoL in primary insomnia.

PR melatonin improved both qualities in patients ≥55 years with primary insomnia with a good safety profile.

Disclosure: Prof. Poirrier has received honoraria or research grants from Takeda Belgium and has been on the advisory board for Takeda Belgium.

P466

Is a poor night of sleep followed by a bad day?

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Objectives: Those suffering insomnia symptoms generally report daytime impairments. However, research has not assessed whether this relationship holds on a nightly basis despite the strongly held belief that a night of poor sleep impairs mood and functioning the following day. The objective of this study was to test this relationship in a group of older insomniacs compared with good sleepers.

Methods: This study utilised a within subjects design to investigate day-to-day subjective daytime functioning and it's relation to the prior night's sleep. Seventeen older individuals (mean age = 67.5 years) were selected with retrospective questionnaire and 2-weeks of sleep/wake diary to have primary insomnia. Seventeen good sleepers (mean age = 67.8 years) were selected using the same measures. Participants reported their beliefs about sleep and

daytime functioning on the Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS-16). One-week later they commenced sleep-wake diaries and concurrent daytime experience scales for a period of 14-days.

Results: There was significant night-to-day co-variation between sleep efficiency and daytime functioning for individuals with insomnia but not for good sleepers. Those insomniacs who held this co-variation belief most strongly were those who subsequently showed this night-to-day relationship the most strongly. This was not true for good sleepers.

Conclusions: These findings demonstrate the belief held by most insomniacs, that a poor sleep is followed by an impaired daytime, is consistent with their experience. This has implications for the use of cognitive therapy in the treatment of insomnia.

Disclosure: Nothing to disclose.

P467

Factors affecting therapeutic responsiveness to eszopiclone in adult patients with chronic insomnia: a post hoc analysis of a double-blind phase III study in Japan

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Objectives: To identify whether baseline demographic factors or sleep variables are associated with responsiveness to eszopiclone using data from a recent randomized controlled trial of 78 Japanese subjects with insomnia who were treated with 2 mg eszopiclone per day.

Methods: We performed a post hoc analysis of factors including sleep latency (SL), wake time after sleep onset (WASO) and several demographic variables. Subjects with a SL or WASO >30 min at baseline and with evaluable SL/WASO data at Week 4 were included in SL and WASO responder analyses, respectively; those with a SL or WASO $\leq$30 min at Week 4 were defined as SL or WASO responders, respectively. Threshold baseline SL and WASO values for identification of responders were determined.

Results: No relationships between therapeutic responsiveness and demographic factors were identified. Patients with shorter SL and lower WASO values at baseline were more responsive to treatment with eszopiclone in terms of SL and WASO responses, respectively. Baseline SL of 75 min and baseline WASO of 80 min were selected as arbitrary cut-off values for determination of SL and WASO responders/non-responders, respectively.

Conclusions: These findings may help clinicians to predict their patients' responses to standard doses of eszopiclone in clinical practice.

Disclosure: Leadership position / advisory role for: HISAMITSU PHARMACEUTICAL CO.,INC. Honoraria(lecture fee) from: Nippon BoehringerIngelheim Co.,Ltd., Philips Respironics GK, Alfresa Pharma Corporation, Takeda Pharmaceutical Company Limited, MSD K.K., Pacific Medico Co.,Ltd., Otsuka Pharmaceutical Co., Ltd, Eisai Co., Ltd., Mitsubishi Tanabe Pharma Corporation., Glaxo-SmithKline K.K., sanofi-aventis K.K., Yoshitomiyakuhin Corporation. Honoraria(manuscript fee) from: Takeda Pharmaceutical Company Limited.

P468

Work time control and sleep disturbances

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Objectives: Employee control over work times has been associated with favourable psychosocial and health-related outcomes, but the evidence regarding sleep quality remains inconclusive. We examined cross-sectional and prospective associations between work time control and sleep disturbances in a large working population, taking into account total hours worked.

Methods: The data were from a full-panel longitudinal cohort study of Finnish public sector employees who responded to questions on work time control and sleep disturbances in years 2000–2001, 2004–2005, 2008–2009, and 2012. The analysis of cross-sectional associations was based on 129 286 person measurements from 68 089 participants (77% women) aged 17–73 years (mean 43.1). Data from 16 503 participants were used in the longitudinal analysis. Log-binomial regression analysis with the generalized estimating equations method was used.

Results: Consistently in both cross-sectional and longitudinal models, less control over work time was associated with greater sleep disturbances in the total population and among those working normal 40-h weeks. Among participants working more than 40 h/week, both very high (cross-sectional prevalence ratio compared to intermediate work time control [PR] 1.32, 95% confidence interval [CI] 1.05–1.65) and very low (PR 1.23, 95% CI 1.08–1.39) work time control were associated with sleep disturbances, after adjustment for potential confounding factors.

Conclusions: These data suggest that having few opportunities to influence the duration and positioning of work time may increase the risk of sleep disturbances among employees. For persons working long hours, very high levels of control over working times were also associated with increased risk of sleep disturbances.

Disclosure: Nothing to disclose.

P469

Maladaptive beliefs and sleep quality in adults with insomnia symptoms

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Objectives: To evaluate the role of beliefs on sleep quality in adults.

Methods: Until now, eighty seven participants (86.7% women), aged 25.6 $\pm$ 7.8 years, completed a battery of tests that evaluate irrational beliefs (Shortened General Attitude and Belief Scale-GABS), emotion regulation style (Difficulties in Emotion Regulation Scale-DERS), automatic thoughts (Automatic Thoughts Questionnaire-ATQ- and Automatic Thoughts Questionnaire-positive), as well as sleep quality (Sleep Condition Indicator), maladaptive sleep behaviours and thoughts (Sleep Hygiene Index and Dysfunctional Beliefs and

Attitudes towards Sleep) and sleep knowledge (Sleep Beliefs Scale). The completion was online (SurveyGyzmo platform).

Results: Based on sleep quality (cut-off score 5), we divided participants in bad and good sleepers. The former (N = 29; 33.3%) reported significantly more irrational beliefs (GABS score: 71.8 ± 17.1 compared to 63.8 ± 15.6; t(85)=2.15, P = 0.035) and negative automatic thoughts (ATQ score: 41.9 ± 16.5 compared to 27.3 ± 13.5; t(83)=4.35, P < 0.001), as well as more difficulties in regulating their emotions (DERS score: 85.6 ± 22.0 compared to 74.5 ± 16.3; t(85)=2.67, P = 0.009). Sleep quality was significantly and inversely linked with ATQ (r = −0.552, P < 0.001), DERS (r = −0.365, P = 0.001) and GABS scores (r = −0.369, P < 0.001). Poor sleep hygiene and dysfunctional beliefs towards sleep were also significantly linked with ATQ (r = 0.498, P < 0.001; r = 0.626, P < 0.001), DERS (r = 0.404, P < 0.001; r = 0.351, P = 0.001) and GABS (r = 0.357, P = 0.001; r = 0.345, P = 0.001). Positive automatic thoughts were not linked with these variables and were almost similar in the two groups.

Conclusions: Automatic negative thoughts, irrational beliefs and emotion regulation style were significantly worse amongst bad sleepers and linked with sleep quality, sleep hygiene and dysfunctional sleep beliefs.

Disclosure: Nothing to disclose.

P470

Transcraneal magnetic stimulation as therapeutic option in patients with diagnose of idiopathic insomnia

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Objective: To evaluate the effect of Repetitive Transcraneal Magnetic Stimulation (rTMS) on sleep architecture and self-reported in 20 patient with idiopathic insomnia.

Method: 10/20 polysomnographic study was performing to 20 patients with idiopathic insomnia. After 10 Low Frequency rTMS (<1 Hz) sessions, during 15 min each day, we made a second PSG-10/20 study. The results of both studies were compared.

Results: Reduction of sleep latency (P = 0.04), increments in total sleep time (P = 0.019) as well as sleep efficiency were observed. There were not differences in each sleep stage proportion. All the patients reported subjective improvement.

Conclusions: Slow rTMS seems to be effective as a therapeutic option for idiopathic insomnia, without the collateral effects that produce some pharmacological treatment, such as changes in sleep stages (increase in stages I and II with reduction of REM sleep and slow wave sleep), generating a worsened in sleep perception.

Disclosure: Nothing to disclose.

P471

The effect of support on internet-delivered treatment for insomnia: does baseline depression severity matter?

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Introduction: Internet-delivered cognitive-behavioral treatment (CBT) is effective for insomnia. However, little is known about the beneficial effects of support. Recently we demonstrated that motivational support moderately improved the effects of internet-delivered treatment for insomnia. In the present study, we tested whether depressive symptoms at baseline moderate the effect of support on internet-delivered treatment for insomnia.

Methods: The current presentation reports on a secondary data analysis of a trial in which people with insomnia were randomly assigned to an internet-delivered treatment with support (n = 129) or without support (n = 133). We performed an intention-to-treat multilevel regression analysis to test for within-group (time: baseline vs. post-treatment, baseline vs. 6-month follow-up) and between-group (support, depression, and depression × support) effects.

Results: We found that baseline depressive symptoms moderate the effect of support on sleep efficiency, total sleep time, and sleep onset latency (but not on wake after sleep onset, number of nightly awakenings and the Insomnia Severity Index). This means that for these variables, people with high levels of depressive symptoms benefit from support, whereas people with low levels of depressive symptoms improve regardless of support.

Conclusions: The data show that baseline depression severity plays an important role in the way internet treatments need to be delivered. These findings open up opportunities to personalize the support offered in internet-delivered treatments. Furthermore, support seems to enhance the benefit of treatment. In a stepped care model, providing support to internet-delivered treatment may be the first step up after pure online self-help treatment.

Disclosure: Nothing to disclose.

P472

Standardization of laboratory diagnostic of insomnia

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Objectives: The goal of this study was to standardize the Protocol of the determination of main melatonin derivatives excretion and to determine the reference ranges of this parameter in the framework of this Protocol.

Methods: The concentrations of 6-Sulfatoxymelatonin (6-SMT) in day and night portions of urine was defined in 39 patients with insomnia and 40 healthy volunteers using enzyme-linked immunosorbent assay ELISA (Buhlmann Laboratories AG, Switzerland).

Results: As a result of research the Protocol of pre-analytical phase of 6-SMT definition was designed. We suggested that the night portion of urine should include all portions of urine collected over night and morning urine portion, and the day portion of urine – all other portions collected regardless of the time. We consider this approach is essential. Thus, we have found that not only reducing peak of melatonin synthesis was significant for insomnia, but the pronounced shifting peak with night on the evening. The received data indicate reduced synthesis of nocturnal melatonin in patients

with insomnia. We have found the link between nighttime melatonin synthesis and characteristics of sleep also. We believe that this result can be associated with change of pre-analytical phase of urine collection proposed by us.

Lower limits of the reference intervals identified in our study are 5.8 μg per night and 13.5 ng/mL (1st quartile).

Conclusions: Standardization of pre-analytical phase of the determination of metabolites of melatonin in the urine should be required when using this test for diagnostic purposes.

Disclosure: Nothing to disclose.

Sleep disorders – Parasomnias

P473

Expert evidence on forensic parasomnias: a qualitative study of expert witnesses

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The provision of expert evidence was studied by qualitative semi-structured interviews of forensic sleep experts in the UK and North America. The data were analyzed by grounded theory and various themes emerged, most notable the difficulties of the law on automatism, the issues raised by alcoholic intoxication, and the limitations of the assessment of forensic sleep disorders. The conclusions were that the law needs reform to accommodate advances in the diagnosis and management of neuropsychiatric disorders and to provide appropriate disposal for those absolved of criminal responsibility due to a parasomnia.

Disclosure: Nothing to disclose.

P474

Spectral analysis of polysomnography in narcolepsy

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Objective: We performed a whole-night polysomnography and analysed its electroencephalographic contents to evaluate detailed pathophysiology of narcoleptic patients' sleep.

Methods: Seven drug-naive narcoleptic patients and their age-sex matched healthy controls underwent whole-night polysomography and multiple sleep latency tests. All the participants' night polysmonographies were analized with using Fourier transform.

Results: REM sleep latency in narcolepsy was significantly shorter than controls. Delta power in 1st NREM sleep was also significantly lower than controls. In contrast to delta power, theta powers in 1st and 2nd NREM sleep were significantly higher in narcolepsy than controls. In analysis of delta power according to sleep progression, delta powers were significantly decreased in controls, but none in narcoleptics.

Conclusion: These results indicate that narcoleptic patients have inefficient sleep because of inefficient delta and theta power in early phase of NREM sleep. Physiological abnormality of Brain which both produce delta and theta activity could be related to narcolepsy.

Disclosure: Nothing to disclose.

P475

Mirtazapine-induced sleep related eating behavior

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Objectives: Mirtazapine is an atypical antidepressant with noradrenergic and specific serotonergic activity.

Methods: We report a case of mirtazapine-induced sleep related eating disorder (SRED).

Results: A 24-year-old woman admitted psychiatric ward with her parents with depressed mood and suicidal gesture. She reported that she had experienced depressed mood, volition loss and sleep disturbance for several years and has been treated her symptoms with fluoxetine 40 mg/day, trazodone 75 mg/day and zolpidem 10 mg/day at a local psychiatric clinic from a year ago. We stopped her medications and replaced it to mirtazapine 30 mg/day and clonazepam 0.25 mg/day. Her depressive mood, suicidal ideation and insomnia were improved, and night binge eating episodes were disappeared. After 2 weeks of admission, she discharged from psychiatric ward with markedly improved states. However, she reported weight gain and night binge eating episodes again after 2 weeks of discharge. She usually received her medications around 11 PM and went to bed. Approximately, 1–2 h after sleep-onset, she woke up and ate large amounts of foods. But she couldn't remember her unusual eating behavior in the next morning. Despite of reducing mirtazapine dose to 15 mg/day, her abnormal eating behaviors were repeated. Finally, we discontinued mirtazapine. Binge eating behavior disappeared after mirtazapine was stopped.

Conclusions: This was the first case of mirtazapine-related SRED. The use of mirtazapine should be considered as a possible precipitating factor for developing SRED.

Disclosure: Nothing to disclose.

P476

Agomelatine in idiopathic REM sleep behavior disorder

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Objectives: To assess the effects of agomelatine, a melatonin receptor agonist, on behavior and sleep of patients with idiopathic REM sleep behaviour disorder (iRBD).

Methods: Videopolysomnography (vPSG) of 10 drug-naïve patients with iRBD were obtained, before and after (2.2 ± 0.4 months) treatment with agomelatine 25 mg at bedtime. The Clinical Global Impression scale (CGI) and the REM sleep behavior disorder severity scale (RBDSS) were used, as well as vPSG, assessing sleep structure and the REM sleep atonia index.

Results: None of the patients reported side effects. The RBDSS scale showed no significant effects of treatment on both motor events (1.67 ± 0.7 vs. 1.89 ± 0.60) and vocalizations (0.78 ± 0.44 vs. 1.00 ± 0.2). Also CGI (3.78 ± 0.83 vs. 3.55 ± 0.72) and sleep parameters showed no significant changes. difference between the two recording nights. There was a trend towards a decrease in REM sleep percentage (21.5 ± 5.7 vs. 18.2 ± 6.5) and an increase in PLMS index (20.1 ± 16.7 vs. 26.1 ± 23.1). REM sleep atonia index indicated an altered EMG atonia during REM sleep in both vPSG recordings. Only two patients reported a subjective improvement of episodes during the night.
Conclusions: This short-term study shows no substantial objective-effect induced by agomelatine in iRBD patients, although two of them reported subjective improvement in the frequency and intensity of their nocturnal episodes. Agomelatine may be a safe choice as an antidepressant drug in iRBD patients in whom other antidepressants (i.e pure serotoninergic agents) may have deleterious effects on sleep and nocturnal behavior.
Disclosure: Nothing to disclose.

P477

Objective daytime sleepiness in somnambulism/sleep terrors: a case-control study

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Objective: To measure objectively daytime sleepiness and to assess for clinical and polysomnographic determinants for mean sleep latency in adult patients with somnambulism (SW)/ sleep terrors (ST) compared to controls.
Methods: Thirty drug-free adult patients with primary SW or ST, and 30 age- gender- BMI-matched healthy controls participated in a standardized clinical interview, completed a battery of questionnaires including Epworth Sleepiness Scale (ESS), and underwent one night of video polysomnography followed by the Multiple Sleep Latency Test (MSLT).
Results: A complaint of excessive daytime sleepiness defined as ESS >10 was reported in 66.7% of patients, higher than 6.7% in controls. The temporal pattern of sleep latencies on individual MSLT trial differed between patients and controls, with progressive increased sleep latency in patients across the trials in contrast to a 'U curve' for controls. No between-group differences were found regarding the mean sleep latency on the five MSLT trials, but reduced sleep latencies were found in patients for the first two trials. Despite higher slow-wave sleep disruption found in patients (i.e. higher micro-arousals and hypersynchronous high-voltage delta waves arousals), no polysomnographic characteristic differences were found between sleepy patients with either subjective or objective daytime sleepiness on MSLT compared to alert patients.
Conclusions: EDS is a common complaint in subjects suffering from somnambulism/sleep terrors with increased objective daytime sleepiness in the morning. Despite an increased slow-wave sleep fragmentation found in these patients, we could not identify any association with the level of daytime sleepiness.
Disclosure: Nothing to disclose.

P478

REM sleep behavior disorder and sleep-related eplepsy

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Objectives: REM sleep behavior disorder(RBD) reveals mimic symptoms of sleep-related eplepsy, namely frontal lobe or temporal lobe epilepsy.
The aim of study is to identify the diagnosis of cases with REM sleep without atonia(RSWA) and violent behavior without corresponding to dream enactment.
Method: Ten patients with idiopathic RBD (male 6, female 4, mean age 68.4 ± 8.1 years) and six patients with sleep-related temporal lobe epilepsy (male 5, female 1, mean age 56.5 ± 19.6 years) were diagnosed by clinical symptpm, PSG and clinical EEG.
Results: All patients with RBD had history of dream enhanced abnormal behavior while sleep and suffered injury such as laceration on face, clavicular fracture.
In patients with RBD, PSG revealed RSWA and did not epileptic discharges.
Six patients with sleep-related temporal lobe epilepsy had violent abnormal behavior without corresponding to dream enactment and revealed epileptic discharges, predominantly, anterior temoral and midd temporal lesion. In two of six patents with temporal lobe epilepsy, PSG revealed RSWA, but the violent abnormal behavior was not documented during PSG monitoring.
Conclusion: RBD accoding ICSD-2nd criteria is as follwed:

1. Presence of RSWA
2. Sleep related injurious behavior with corresponding to dream enactment
3. Absence of epileptic discharge during REM sleep.

It is speculated that two patients with temporal lobe epilepsy in whom there is RSWA is comorbidity of subclinical RBD.
Disclosure: Nothing to disclose.

P479

Clinical manifestations and polysomnographic findings in patients with REM sleep behavior disorder

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Objectives: To establish polysomnographic characteristics and clinical correlation in a cohort of patients with REM Sleep Behavior Disorder (RBD).
Methods: We revised polysomnography study (PSG) and clinical history in all consecutive RBD patients diagnosed and followed- up in our Sleep Disorder Unit from January of 2012 to January 2014. The clinical diagnosis of RBD was based on the second edition of International Classification of Sleep Disorders. A descriptive analysis was performed. The correlation between quantitative and qualitative variables was performed with different statistical analysis according to the results.
Results: We evaluated 30 patients with an average age at diagnosis of RBD of 66 years, an average of evolution time of RBD of 7.5 years and an average delay in diagnosis of 4.9 years. Nineteen patients presented an idiopathic RBD and 11 presented neurodegenerative disease (six with Parkinson disease, four with dementia with Lewy bodies and one with Multiple System Atrophy). In PSG study, 29

patients had REM sleep without atonia and 19 patients had also abnormal REM sleep behavior documented. 69.23% of the patients had another disturbance in REM sleep. We analysed different data and there are differences, but not statistically significant, between PSG characteristics in patients with and without neurodegenerative disease.

Conclusions: It is important to detect and study RBD early in a Sleep Disorder Unit. It is necessary to know specific characteristics of RBD because it is an early pathological event in the synucleinopathies and it is relevant to design potential interventions with neuroprotective agents.

Disclosure: Nothing to disclose.

P480

New data on psycho-behavioral and polysomnographic profiles of patients affected by night eating syndrome

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Objectives: Nocturnal eating behavior is shared by patients affected by a parasomnia the Sleep related Eating Disorder and an eating disorder, the Night Eating Syndrome, but characteristics of these patients have been poorly studied, so this maintains the difficulties in defining the borders between the two syndromes. Aim of this study was to evaluate polysomnographic and personality characteristics of nocturnal eaters.

Methods: All subjects underwent a full night video-PSG study and a psychometric assessment including the Eating Disorder Inventory (EDI-2), the self-rating Bulimic Investigatory Test-Edinburgh (BITE), the temperament and character inventory and the Barratt Impulsivity Scale (BIS). For 6 months, consecutive patients complaining of nocturnal eating were asked to participate wenty-four patients who were found to eat during the PSG study and gender-matched control subjects were included in the study.

Results: We found a mild reduction in sleep efficiency and duration due to a moderate sleep fragmentation, while the percentages of the single sleep stages were not significantly affected. NES scored higher on many subscales of the EDI-2, on the BITE, symptoms subscale and on BIS attentional impulsivity subscale.

Conclusions: Psychological characteristics of NES are typical of patients affected by eating disorders, further sustaining the hypothesis that their nocturnal behavior is due to an eating disorder, moreover specific traits allowing to further differentiate NES from Binge Eating Disorder have been found.

Disclosure: Nothing to disclose.

P481

Effects of clonazepam and pramipexole on REM sleep behavior disorder

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Objectives: REM sleep behavior disorder (RBD) is often associated with neurodegenerative diseases, especially Parkinson's disease. While recent studies suggest that RBD involves a dopaminergic deficiency, clonazepam (CZP) is currently the medication of choice for managing RBD. The purpose of this study is to investigate the effect of CZP and pramipexole (PPX), a dopaminergic D2-3 receptor agonist, on sleep variables with idiopathic RBD.

Methods: Nine patients (58–78 years) participated in the study. They were treated with CZP (0.5–1.0 mg, six patients) or PPX (0.25 mg, three patients) for more than 6 months, and the following PSG recording was performed. Sleep stages were visually scored by 20-s epoch according to the criteria of Rechtschaffen and Kales.

Results:

1. Clinical effects: All patients showed a reduction in the intensity of RBD symptoms.
2. Effects on sleep variables (% of sleep period time): Five patients treated with CZP showed a decrease in stage 1 sleep and an increase in stage 2 sleep. Four patients with CZP (67%) showed an increase in REM sleep, whereas all patients treated with PPX showed a decrease in REM sleep. REM sleep without atonia decreased after CZP treatment (67%) and PPX treatment (33%).
3. Effects on PLMS: Eight of all patients had a PLMS index >15 at a baseline. Four patients with CZP and two patients with PPX showed no change of PLMS index after the treatment.

Conclusions: In our study, CZP improved sleep quality and decreased the proportion of REM sleep without atonia.

Disclosure: Nothing to disclose.

P482

Investigating the role of cortical 'off periods' on the EEG theta power with a Jansen and Ritt's model

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Objectives: EEG theta power is often considered as a reliable marker of homeostatic sleep pressure buildup during wakefulness (Finelli et al., 2000). The neural correlates of human cortical theta rhythm during wakefulness is still unknown but seems related to synchronous arrests of firing in large cortical neuronal populations ('off-periods') (Vyazovskiy et al., 2011). We hypothesized that 'off periods' could play a significant role in the EEG theta power buildup throughout wakefulness.

Methods: We developed a model based on a Jansen and Ritt's model of cortical activity known to emulate waking EEG signal. This model includes two components. The first one simulates the temporary drop of pyramidal cells excitability when 'off periods' occur. The second takes into account the influence of time spent awake and circadian phase on the cortical connectivity. The model provides emulated EEG signals depending on an 'off periods' density and on the clock time. Model outputs have been compared to EEG data acquired during a sleep deprivation protocol.

Results: Simulations show that theta power in the emulated signal is increasing with the density of 'off periods'. They also show that 'off periods' influence on the power spectrum depends on both time spent awake and on circadian phase. It particularly shows an important theta enhancement after the wake maintenance zone, when the circadian oscillation switches brain oscillatory behavior to sleep conditions.

Conclusions: Theta power buildup throughout wakefulness could reflect the homeostatic increase in 'off period' density at the local level of neural activity.

Disclosure: Nothing to disclose.

Medical Disorders and Sleep

P483

Obstructive sleep apnea in patients with fibromyalgia – report from a fibromyalgia clinic

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Objectives: To determine the prevalence and incidence of obstructive sleep apnea (OSA) in patients with fibromyalgia.

Methods: Chart review of 500 patients seen at a Fibromyalgia Clinic between 12/2010 and 10/2011. Data abstracted: results of Berlin Sleep Questionnaire (BSQ), overnight-oximetry, polysomnography. From a pool of 21 944 patients seen in a General Medicine Division during the same time period using a random algorithm 1 control was selected for each case matched by sex, year of birth and body mass index (BMI). Charts were reviewed for a diagnosis of OSA. Basic statistics were used for analysis.

Results: Four hundred and fourty one of 500 fibromyalgia-patients were females. Median age was 48 years, median BMI 29.6 (range 15.6–64.3). 104 (20.8%) patients carried the diagnosis of OSA at time of presentation. Of the 396 remaining patients 340 (85.8%) completed the BSQ. Using this instrument 191 (56.2%) patients were found to be at high risk for OSA. 146/396 (36.9%) patients underwent oximetry with abnormal results in 63 (43.2%). 47/396 (11.9%) patients underwent polysomnography and 32 (68.1%) were diagnosed with OSA. 78/500 (15.6%) patients were advised to undergo polysomnography based on a high risk BSQ or an abnormal overnight oximetry but were unable to stay for this evaluation. The prevalence of OSA in our fibromyalgia patient population was 27.2%, the incidence 6.4%. The prevalence of OSA in the control group was 10.8%.

Conclusion: The prevalence of OSA in patients with fibromyalgia is significantly higher ($P < .0001$) than in patients presenting to a General Medicine Division without the diagnosis of fibromyalgia.

Disclosure: Nothing to disclose.

P484

Restles legs syndrome (RLS): another intestine related disorder! Increased prevalence of RS in Crohn's disease

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Objectives: To compare the incidence and severity of RLS in Crohn's Disease (CD) patients with controls.

Methods: Cross-sectional study using validated questionnaires in 144 CD patients and 80 controls, assessing presence and severity of RLS and severity of CD.

Results: Prevalence of RLS was 25.7% (37/144) in CD patients compared to 12.5% (10/70) in the control group. *(P = 0.02)*. CD patients with arthralgias had a higher risk for RLS. A higher score on the Harvey Bradshaw Index and CD-related surgery were also associated with a higher risk for RLS. CD-related surgery was also associated with a more severe course of RLS.

Conclusion: Prevalence of RLS is increased in CD patients compared to healthy subjects and severity of CD correlates with severity of RLS. Consequently RLS may be considered as an extraintestinal manifestion CD.

Clinical implications: An explanation for the association between CD and RLS may be an increased permeability of the intestine dependent of the rate of inflammation. Recently several central nervous system disorders with unknown etiology, including migraine, autism and depression, were found to be associated with intestinal diseases characterized by increased intestinal permeability. Further studies are needed to confirm the relationship between intestinal permeability and RLS and this may offer new possibilities for treatment (with medication or probiotics).

Disclosure: Nothing to disclose.

P485

Sleep disordered breathing in coronary heart disease patients with mild and moderate heart failure

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Objectives: The relationship between sleep apnoea and degree of heart failure in coronary heart disease (CHD) patients was studied.

Methods: A total of 3017 CHD patients (77.4% men and 22.6% women; mean age 59.7 $\pm$ 9.9 years) were analyzed. All patients had clinical cardiovascular examination, including echocardiography. Heart failure (HF) was determined according to the New York Heart Association (NYHA) functional classification. Sleep data were recorded using standard polysomnography. The total number of obstructive (OSA), central (CSA), and mixed sleep apneas and hypopneas per hour was evaluated.

Results: Multivariate logistic regression analysis adjusted for all covariates revealed that patients with NYHA functional class II had 1.41 (95% CI=1.04–1.91) times increased odds of having moderate AHI (15.1–30.0 events/h). Patients with NYHA functional class III demonstrated the highest odds for moderate (OR=1.81; 95% CI=1.29–2.53) and severe (OR=2.19; 95% CI=1.47–3.27) AHI. Oxygen desaturation index was associated with increased odds for severe desaturation (OR=1.24; 95% CI=1.24–2.63) for all covariates only in NYHA functional class III. The prevalence of CSA against OSA was observed in patients with mild and moderate HF.

An increase of stage 1 and wakefulness after sleep onset and a decrease of stages 3–4 and REM sleep and diminution of sleep efficiency with worsening of HF were observed.

Conclusions: Sleep disturbed breathing is more common in CHD patients with higher NYHA functional class. The number of CSA was strongly related to the severity of HF.

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Disclosure: Nothing to disclose.

P486

Excessive daytime sleepiness in obstructive sleep apnea and upper airways resistance syndrom – disturbed sleep microarchitecture by CAP-subtypes A2/A3 as a result of extraesophageal reflux

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Objectives: Excessive daytime sleepiness (EDS) is key symptom both in Obstructive Sleep Apnea (OSAS) and Upper Airways Resistance Syndrom (UARS). Even with successful CPAP-therapy sleepiness will often persist.

The Cyclic Altrernating Pattern (CAP) correlates with sleepiness in adults with UARS (1)

There is a high coincidence of 'silent' (extraesophageal) reflux disease and sleep apnea. A high proportion of CAP is also written at reflux (2)

Sleep fragmentation by CAP-subtypes A2/A3 results in a reduction of the cognitive perrformance (3)

We examined the relationships between sleepiness, sleep microarchitecture – especially CAP – and extraesophageal reflux.

Methodes and patients: Eleven patients with OSAS and persisting sleepiness despite effective CPAP-ventilation and 20 patients with UARS.

Full polysomnography corresponding to the criteria according to AASM, disturbance of daytime vigilance (ESS, pupillometry), long-term laryngo-pharygeal pH-metry (ResTech).

Results: In the sleep microstructure we found in excessive frequency specific changes in the EEG particularly in the form of the CAP-subtypes A2/A3. These occurred at reflux events with measured pH-drops. Reflux events were independent of flow limitations.

Conclusions: In OSAS- and UARS-patients with persisting daytime sleepiness despite intensive therapy more sensitive measures such as CAP analysis are required in addition to the traditional diagnostic scoring systems. In the presence of CAP-subtypes A2/A3 is essential to think of the possibility of an extraesophageal so-called silent reflux. For confirmation the laryngo-pharyngeal longterm pH-metry is required.

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Disclosure: Nothing to disclose.

P487

Sleep-wake abnormalities in patients with cirrhosis

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Liver cirrhosis is the end result of chronic liver injury of any origin (i.e. viral hepatitis, alcohol misuse etc.). Up to 70% of patients with cirrhosis complain of disturbed night sleep, delayed sleep habits and excessive daytime sleepiness. These are not as common in other chronic diseases, such as kidney or heart failure. Sleep-wake abnormalities in cirrhosis have been variously attributed to impaired hepatic melatonin metabolism and/or cirrhosis complications (for example hepatic encephalopathy, a neuropsychiatric syndrome due to impaired disposition of neurotoxins of gut origin). However, their pathophysiology remains poorly defined, and their treatment problematic. Based on a series of studies we have performed over the last few years (large sets of well-characterised patients with varying degrees of liver failure studied in the lab and in the field), we propose a comprehensive model for the interpretation of sleep-wake abnormalities in cirrhosis.

1. Circadian regulation. The phase of the melatonin rhythm is delayed by 60–90 min due to a combination of impaired sensitivity to light and reduced melatonin clearance. This leads to a jet-lag East-type sleep disorder, which contributes to the observed difficulties in commencing/maintaining sleep.
2. Homeostatic regulation. Hepatic encephalopathy-related daytime sleepiness compromises the homeostatic build-up of sleep pressure during the daytime hours (inefficient wakefulness), contributing to a reduction in slow wave, restorative sleep.

The above produce a significant misalignment between the circadian and homeostatic regulatory systems. Based on this model, we have started two trials of aetiological treatment (morning light administration and vigilance enhancement) and pilot data are available.

Disclosure: Nothing to disclose.

P488

Sleep disturbances compared to traditional risk factors for incident diabetes: systematic review and meta-analysis

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Sleep disturbances have been linked to increased risk of incident diabetes but their effect size relative to that of the traditional risk factors is unknown. Therefore, a systematic review and meta-analysis were performed to compare the relative risk of incident diabetes associated with sleep disturbances to traditional risk factors. Studies were identified from Medline and Scopus. Meta-analysis was performed using a random effects model to pool risk ratios (RR) for sleep duration, sleep quality, misaligned sleep associated with shift work and obstructive sleep apnea (OSA). The effects of traditional risk factors were retrieved from systematic reviews and meta-analyses that pooled the RRs for family history of diabetes, overweight, and physical inactivity.

For sleep variables, we included 35 cohort studies with a total of 1 055 168 subjects. Individuals sleeping $\leq$ 5 h, 6 h, and >8 h/day were respectively 1.48(95% CI: 1.25, 1.76), 1.18(1.10, 1.26) and 1.36 (1.12–1.65) times more likely to develop diabetes in comparison to those sleeping 7–8 h/day. Poor sleep quality and shift work were associated with incident diabetes with a pooled RR of 1.35(1.19, 1.53) and 1.44(1.18, 1.75), respectively. OSA had the largest estimated impact on diabetes risk, with a pooled RR of 2.24(1.84, 2.73).

When considering traditional risk factors for diabetes, the pooled RRs were: physical inactivity 1.52(1.30, 1.78), family history of diabetes 2.33(1.79, 2.79), and being overweight 2.99(2.42, 3.72).

The risk of developing diabetes associated with various sleep disturbances are comparable to traditional risk factors. Sleep disturbances, potentially modifiable factors, should be considered when screening for diabetes.

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P489

Sudden cardiac death in patients with systolic heart failure, Cheyne-Stokes breathing and amiodarone-induced thyrotoxicosis: a case report

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We would like to report a case of a 50-years old man who suddenly died.

We have been observing him for the last 3 years and performed an echocardiography and a 24-h multifunctional monitoring using portable monitors annually. According to his medical history, he was suffering from a systolic heart failure after a Q-myocardial infarction in 2011; 1 year later he survived a paroxysm of a sustained polymorphic ventricular tachycardia and ventricular fibrillation. After defibrillation he was administered amiodarone (200 mg).

During the observation period (February 2011–February 2014) we have detected an increase in the size of the left atrium (from 46 to 51 mm), as well as an increase in the end-diastolic size (65–71 mm) and the left ventricular ejection fraction (18–41%); furthermore we observed an occurrence of supraventricular extrasystoles (>30 per hour), a prolongation of the corrected QT-interval (up to 625 ms), an increase in the duration of periodic Cheyne-Stokes phases during the sleep (47–59% of total sleep time), an increase in the central apnea index (28–36 per hour of sleep), a reduction of the average duration of the periodic cycle length (from 68.0 $\pm$ 5.2 to 46.8 $\pm$ 4.4 s) and an increase in the index of hypoxemia (from 30 to 44); the minimal oxygen saturation decreased from 84.6% to 78.0%.

In February 2014 the patient was diagnosed with an amiodarone-induced thyrotoxicosis, therefore an antithyroid agent was prescribed. One month later the patient died.

Disclosure: Nothing to disclose.

P490

Increase apnea-hypopnea index and lengthening of QT_c interval closely correlated in newly diagnosed untreated patients with obstructive sleep apnea and arterial hypertension

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To assess whether duration lengthening of QT-corrected interval (QTc) is correlated with apnea-hypopnea index (AHI).

Fifty-seven male (age 38.0 $\pm$ 7.4 years; body mass index 33.8 $\pm$ 5.4 kg/m^2) with untreated arterial hypertension underwent a 24-h multifunctional monitoring ($S_3C_1O_1P_2E_4R_2$) using 'Kardiotekhnika 07' portable monitors (Incart, St. Petersburg). Within sleep, at 39 patients (68%) were five or more episodes of apnea duration of 10 s or more.

The average observation period was 21.32 h, including 7.7 h of sleep. AHI from 5 to 15 had 17 (30%) of patients, 8 (14%) had AHI from 15 to 30 and 14 (25%) had AHI $\geq$ 30 events/h. Diurnal systolic and diastolic blood pressure (150 $\pm$ 13.5 mm Hg and 87 $\pm$ 9.8 mm Hg accordingly), nocturnal systolic and diastolic blood pressure (135 $\pm$ 16.4 mm Hg and 74 $\pm$ 11.2 mm Hg accordingly) were observed increase. The mean value diurnal heart rate was 89.4 $\pm$ 9.6 beats per minute, nocturnal heart rate was 66.1 $\pm$ 8.2 beats per minute. Lengthening QTc interval more than 450 ms was detected in 30 male (53%), including 6 (20%) this prolongation was noted for 50% or more during the observation period. The other at six participants (11%) was shortening QTc interval. The statistically significant direct correlation was revealed between duration lengthening of QTc interval and AHI (r = 0.40; $P < 0.01$).

The increase of value AHI (or apnea severity) closely correlated to increases lengthening QTc interval, which leads to risk of cardiac arrhythmias, in particularly fatal.

Disclosure: Nothing to disclose.

P491

Predictors of excessive daytime somnolence

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Objectives: The Epworth Sleepiness Scale is a simple, self-administered questionnaire which provides a measurement of the subject's general level of daytime sleepiness.

The aim of this study was to investigate the factors that can predict daytime sleepiness in patients with sleep apnea.

Methods: Fifty consecutive patients with suspected obstructive sleep apnea were enrolled into the study. Age, gender, anthropometric and polygraphic data were thoroughly analysed. In all subjects daily sleepiness was assessed by Epworth Sleepiness Scale.

Results: The mean age of the subjects was 54.7 $\pm$ 12.8 years, 82% males. The mean BMI was 31.9 $\pm$ 6 kg/m^2. Pearson correlation coefficient analysis demonstrates a significant positive correlation between the Epworth Sleepiness Scale and the desaturation index (r = 0.31, $P < 0.01$) and arterial hypertension (r = 0.32, $P < 0.01$). The forward stepwise regression analysis shows that the apnea hypopnea index and desaturation index are important predictors of daytime sleepiness in patients with obstructive sleep apnea which explains 40% of the Epworth Sleepiness Scale score.

Conclusion: The Epworth Sleepiness Scale is a useful instrument for clinical assessment of obstructive sleep apnea. The apnea hypopnea index and desaturation index in patients with obstructive sleep apnea are independent risk factors for daytime sleepiness.

Disclosure: Nothing to disclose.

P492

The role of effective CPAP therapy in patients with idiopathic pulmonary fibrosis and obstructive sleep apnoea

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Background: Recent literature shows an increased incidence of obstructive sleep apnea (OSA) in patients with idiopathic pulmonary fibrosis (IPF). Our aim was to assess the effect of CPAP on sleep and overall life quality parameters in IPF patients with OSA after 1 year of effective OSA therapy.

Methods: Ten patients, with newly diagnosed IPF and moderate to severe OSA, confirmed by overnight attended polysomnography, were included. CPAP therapy was initiated after a formal in-lab CPAP titration study. The patients completed the Epworth Sleepiness Scale (ESS), the Pittsburgh Sleep Quality Index (PSQI), the Functional Outcomes in Sleep Questionnaire (FOSQ), the Fatigue Severity Scale (FSS), the SF-36 quality of life questionnaire, and the Beck Depression Inventory (BDI) at CPAP initiation and 1 year after effective CPAP therapy.

Results: A statistically significant improvement was observed in the FOSQ ($P = 0.008$), PSQI ($P = 0.01$), parameters of Social Functioning ($P = 0.04$) and Role-Emotional ($P = 0.03$) after 1 year of effective CPAP treatment. Trends towards improvement, although without statistical significance, were noted in the rest of the used questionnaires.
Conclusion: OSA is common co morbidity in IPF and its early recognition and treatment is crucial. Effective CPAP treatment in these patients results in a significant improvement in daily living activities based on the FOSQ, an OSA specific follow-up instrument. In addition statistically significant improvement was noted in the PSQI, namely a specific questionnaire for sleep quality. In the absence of any effective treatment for IPF, the improvement of quality of life and sleep should be a primary therapeutic goal.
Disclosure: Nothing to disclose.

P493

Obstructive sleep apnoea syndrome and comorbidities

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Objectives: Patients with obstructive sleep apnoea syndrome are at increased risk for a broad range of cardiovascular (systemic hypertension, pulmonary arterial hypertension, coronary artery disease, cardiac arrhythmias, heart failure, stroke and motor vehicle crashes) and metabolic comorbidities (insulin resistance, diabetes, and metabolic syndrome). The aim of this study was to evaluate the relationship between comorbidities and severity of obstructive sleep apnoea syndrome.
Methods: 50 consecutive patients with suspected obstructive sleep apnea were enrolled into the study. Age, gender, anthropometric, overnight cardio-respiratory monitoring data and comorbidities were analysed.
Results: The mean age of the subjects was 54.7 $\pm$ 12.8 years, 82% males and 18% females. The mean BMI was 31.9 $\pm$ 6 kg/m^2. Spearman correlation coefficient analysis demonstrates a significant positive correlation between the hypertension and the apnea hypopnea index ($r = 0.55$, $P < 0.05$), the desaturation index ($r = 0.6$, $P < 0.05$). Obesity and diabetes mellitus correlated weaker with these indexes. The forward stepwise regression analysis shows that the hypertension and diabetes mellitus are important predictors of severity of obstructive sleep apnea which explains 40% of the apnea hypopnea index.
Conclusion: The hypertension and diabetes mellitus in patients with obstructive sleep apnea are independent risk factors for severity of obstructive sleep apnea.
Disclosure: Nothing to disclose.

P494

Sleep disturbances and risk of myocardial infarction among men aged 25–64 years (WHO MONICA -psychosocial)

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Objective: We sought to examine the relationship between sleep disturbances (SD) and the risk development of myocardial infarction (MI) among men ages 25–64 years.
Methods: Within the framework of program, WHO MONICA-psychosocial was examined representative sample of men 25–64 years old (1994 year). Total sample was 657 persons. SD were measured at baseline with the use of the Jenkins' questionnaire. Incidence of news cases of MI was revealed at 14-year follow-up. Cox- proportional regression model was used for an estimation of hazard ratio (HR).
Results: Only 1/3 of the 25–64 -year old male subjects with the first MI referred to their sleep as 'good', whereas 2/3 had SD (63.1%). The risk of development of MI within 5 years at group of men with SD was 2.43 (95%CI 1.27–8.59) times higher than without it. For the following 10 years, risk of development of MI was 2.6 (95%CI 1.35–9.41) times higher in men with SD. Within 14 years HR=2.3 (95%CI 1.1–4.6); ($P < 0.05$) Most frequently of MI occurred in men with SD and higher negative psychosocial factors, i.e. widowers, divorced, those with primary and not-completed secondary school education and those engaged in hard and moderate manual labor and head, with low index social network.
Conclusions: The results demonstrate that SD present a social problem and contribute greatly to the risk of MI in men. The highest frequency of MI occurred in men with SD and negative social gradient. Supported by Grant of Russian Foundation for Humanities №140600227.
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P495

The optimal dose of midazolam for sleep in critically Ill patients: pilot study

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Objectives: Many critically ill patients treated in the intensive care unit (ICU) experience sleep disruption. For the sedation of critically ill patients, midazolam is commonly used. This pilot study was undertaken to identify the optimal dose of midazolam for the sound sleep in critically ill patients.
Methods: This prospective study was conducted in medical ICU of a tertiary referral hospital. Polysomnography (PSG) recording was performed over 24 h to assess the quantity and quality of sleep in patients who sedated with midazolam.
Results: Total nine patients were enrolled. However, the PSGs of three patients could not be interpreted because of artifact or coma at electroencephalography. Therefore, six patients were analyzed. Median total sleep time was 510.0 (IQR: 142.8–865.0) min. The majority of sleep was stage 1 (median 223.5 [IQR 70.8–388.0] min) and stage 2 (median 216.0 [26.0–528.0] min) with scant REM (median 9.5 [2.3–35.3] min) and absent stage 3 (0.0 min) sleep. The wake index and microarousal index were median 14.3 (IQR: 8.0–25.6) and 16.5 (IQR: 9.9–24.9), respectively. The dose of midazolam showed positive correlation with total sleep time ($r = 0.931$, $P = 0.011$). Midasolam dose of 0.05 and 0.01 mg/kg/h showed more than 19 h and <3 h sleep, respectively.
Conclusions: The quantity of sleep in critically ill patients was met with continuous infusion of 0.02–0.03 mg/kg/h midazolam. However, the quality of sleep was poor. Further study is required for the promotion of quality of sleep in these patients.
Disclosure: Nothing to disclose.

P496

The effect of age, gender, BMI and hypertension on the oxygen desaturation index

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Objectives: To examine the factors associated with increased oxygen desaturation index (ODI).

Methods: The study population included patients with one or more symptoms of sleep apnoea, referred to pulmonary physician consultation during 2004–2012. Data was collected by use of the standard questionnaire and limited ambulatory sleep investigation (three channels). Body mass index (BMI) was calculated based on direct measurements. The diagnosis of hypertension was verified using medical databases. The effect of age, gender, BMI and hypertension on the likelihood of ODI ≥ 15 was evaluated using multivariate logistic regression.

Results: The analysis included 3640 patients. In a multivariate model including age, gender and BMI, the risk of ODI ≥ 15 was significantly elevated for all age groups compared with patients age < 40 (OR 2.06, 95% CI 1.62–2.61 among patients age 40–49; OR 3.41, 95% CI 2.68–4.34 among patients age 50–59; OR 5.31, 95% CI 4.17–6.77 among patients age ≥60). Women had significantly lower risk than men (OR 0.29, 95% CI 0.24–0.35). Compared with patients with BMI< 25, the OR was 2.08 (95% CI 1.49–2.91) for patients with BMI 25–29, 5.68 (95% CI 4.09–7.91) for patients with BMI 30–34 and 17.32 (95% CI 12.32–24.33) for patients with BMI≥35. We also observed elevated risk of ODI ≥ 15 among patients with a diagnosis of hypertension (OR 1.87, 95% CI 1.61–2.18) after adjusting for age and gender.

Conclusions: The risk of increased ODI was significantly elevated among patients of older age, male gender, higher BMI and those with diagnosis of hypertension.

Disclosure: Nothing to disclose.

P497

Lifestyle considerations and type 2 diabetes risk: sleep quality and habitual caffeine consumption

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Objectives: Epidemiological evidence suggests that short, low-quality sleep may increase type-2 diabetes (T2D) risk, whereas long-term high coffee consumption may reduce T2D risk (Friedman et al., *NEJM*, 2012). We aimed at investigating potential roles for these lifestyle factors in T2D.

Methods: In an ongoing case-control field study, 78 T2D patients (72% male; mean age: 64.5 ± 10.2 years) and 127 non-diabetic (ND) participants (38% male; 67.3 ± 7.1 years) of European descent completed validated questionnaires regarding health and lifestyle, quality of life (World Health Organisation-5), daytime sleepiness (Epworth Sleepiness Scale), subjective sleep quality (Pittsburgh Sleep Quality Index), habitual caffeine consumption, and sleep timing (Munich Chronotype Questionnaire).

Results: The T2D report lower quality of life, greater daytime sleepiness, worse sleep quality ($p_{all} < 0.05$), and higher caffeine consumption than ND (340 vs. 250 mg per day; $P < 0.01$). The higher caffeine intake stems from 80 mg more coffee-based caffeine, equivalent to 1–2 extra cups of coffee per day. The T2D and ND report similar sleep length and sleep timing on free days: 7.1 ± 1.1 and 7.2 ± 1.2 h mean sleep duration and 3.06 ± 0.9 and 3.20 ± 0.9 a.m. mean mid-sleep point, respectively ($p_{all} > 0.09$). Both groups describe their chronotype as 'slight early type'.

Conclusions: These preliminary results challenge epidemiological evidence possibly indicating that caffeine contained in coffee may decrease T2D risk. Data from a larger sample will be needed, to corroborate the present findings.

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Disclosure: Nothing to disclose.

P499

Impact of nasal obstruction on sleep quality – a community based study of women

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Objective: To analyse the impact of self-reported nasal obstruction on sleep quality in women.

Methods: A community-based sample of 400 women underwent a full night of polysomnography. Airway diseases and sleep-related symptoms were assessed by questionnaires. Women with subjective nasal obstruction were subdivided into three groups: persistent nasal obstruction (PNO, $n = 46$), hay fever ($n = 88$) and nasal obstruction at night (NON, $n = 30$).

Results: Sleep problems and related daytime symptoms were most prevalent among women with NON. After adjusting for age, BMI, smoking and asthma, NON was an independent predictor of 'Difficulties inducing sleep due to nasal obstruction' [adjusted odds ratio (95% CI): 89.5 (27.0–296.7)], 'Snoring' [4.2 (1.7–10.2)], 'Sweating at night' [2.6 (1.1–6.1)], 'Difficulties maintaining sleep' [2.7 (1.2–6.2)], and 'Waking up hastily gasping for breath' [32.2 (8.7–119.1)]. 'Dry mouth on awakening' [7.7 (3.2–18.4)], 'Waking up unrefreshed' [2.7 (1.2–6.0)], 'Excessive daytime sleepiness' [2.6 (1.1–6.0)], and 'Daytime nasal obstruction' [12.2 (4.8–31.2)] were also associated with NON. PNO and hay fever were both associated with some sleep problems due to an overlap with NON. When women with NON were excluded, only 'Daytime nasal obstruction' was still significantly associated with PNO, while hay fever was associated with 'Daytime nasal obstruction' and 'Waking up hastily gasping for breath'. There were no significant differences in objectively measured sleep variables between any of the three subgroups and the study cohort.

Conclusion: Self-reported nasal obstruction at night in women has a significant effect on several subjective day- and night-time symptoms, but it does not appear to affect objectively measured sleep quality.

Disclosure: : Nothing to disclose.

P500

An association between intestinal microflora changes and sleep efficiency in chronic fatigue syndrome: a pilot open-label trial of the antibiotic erythromycin

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Objectives: Chronic Fatigue Syndrome (CFS) is a multisystem illness, associated with disabling fatigue, cognitive dysfunction and sleep disturbances and this may be associated with imbalances in gut microbiota (dysbiosis). This pilot study is the first systematic research to determine whether CFS patients who were colonized predominantly with gram-positive faecal organisms at baseline and responded to antibiotic treatment had resulting improvements in sleep.

Methods: To date, 21 patients with CFS, diagnosed according to the Canadian criteria, have completed a 22-day open-label trial. Stool sample analysis was performed at baseline and again at the end of the trial. Actigraphy and sleep diaries were used to monitor sleep, symptoms and mood. During week 1, baseline measures of sleep and mood were recorded, during week 2, all patients were administered erythromycin 400 mg b.d., and post-intervention changes were assessed during week 3.

Results: At baseline higher *Enterococcus* counts were associated with higher ratings of anger and confusion (ps < 0.02). After treatment lower *Streptococcus* counts were associated with higher ratings of vigour, while lower *Lactobacillus* was associated with lower ratings of CFS symptoms and depression, and higher subjective sleep ratings (*P*s < 0.03). Eleven patients showed improvements in gut dysbiosis after antibiotic treatment. In these patients, actigraphic sleep efficiency improved across the 3 weeks (baseline: 73.6%; intervention: 79.2%; post-treatment: 78.9%).

Conclusion: The finding that reducing the levels of gram-positive gut microbiota is associated with some improvement in sleep efficiency in CFS patients is encouraging. Further study of possible links between gut microorganisms and sleep disturbances is warranted.

Disclosure: Henry Butt is the director of Bioscreen.

P501

Independent associations of low 25 hydroxy vitamin D and high parathyroid hormonal levels with OSA and NAFLD in Asian Indians residing in north India

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Objectives: To look for any associations of 25 hydroxy vitamin D [25 (OH) D] and parathyroid hormone (PTH) levels with clinical, anthropometric and biochemical parameters in obese Asian Indians with obstructive sleep apnea (OSA) and non alcoholic fatty liver disease (NAFLD).

Methods: A total of 160 overweight/obese subjects [body mass index (BMI > 25 kg/m^2)], 69 with OSA and NAFLD (group 1), 30 with OSA and without NAFLD (group 2), 37 without OSA and with NAFLD (group 3) and 24 without OSA and without NAFLD (group 4) were evaluated. Clinical, anthropometric, biochemical parameters, overnight polysomnography and liver ultrasound was done. Fasting serum 25(OH) D and PTH levels was measured by *chemiluminescence method*.

Results: Subjects with OSA and NAFLD had lower serum 25(OH) D [12.9 $\pm$ 3.8 (group 1), 15.1 $\pm$ 7.6 (group 2), 19.4 $\pm$ 8.5 (group 3), and 27.8 $\pm$ 9.4 ng/mL (group 4), $P = 0.005$] and higher serum PTH [61.9 $\pm$ 12.5 (group 1), 59.6 $\pm$ 20.6 (group 2), 54.9 $\pm$ 19.5 (group 3) and 41.5 $\pm$ 18.3 pg/ml 9group 3), $P = 0.006$] levels. We observed significantly high values of systolic blood pressure ($P = 0.0003$), diastolic blood pressure ($P = 0.0003$), BMI ($P = 0.003$), waist circumference ($P = 0.001$), serum triglycerides ($P = 0.01$), total cholesterol ($P = 0.02$), alanine transaminase ($P = 0.03$) and fasting insulin ($P = 0.001$) in the OSA and NAFLD group as compared to other three groups. Multivariable-logistic regression showed that low serum 25(OH) D [OR (95%CI): 4.31 (2.25–6.90), $P = 0.0001$] and high PTH [OR (95%CI): 2.65 (1.59–3.40), $P = 0.0001$] level was independently associated with OSA and NAFLD.

Conclusions: Low serum 25(OH) D and high PTH levels are independently associated with the presence of OSA and NAFLD in Asian Indians.

Disclosure: Nothing to disclose.

P502

Sleep dysfunction in patients with panhypopituitarism

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Objectives: Craniopharyngioma and pituitary macroadenomas are the most prevalent intracranial tumors. Invasion of nearby anatomical structures and late effects of treatment may cause significant neurological, neurocognitive and endocrinological complications including hypothalamic damage and sleep dysfunction.

The goal of this study was to evaluate sleep disorders in patients diagnosed with this pathology.

Methods: Prospective descriptive study of 17 patients who were referred by the endocrinology department; three denied sleep evaluation.

Clinical data, resection, treatment, comorbidity, sleep questionnaires, polysomnography and Multiple Sleep Latency Test (MSLT), actigraphy and sleep diaries were evaluated.

Results: Fourteen patients were reported (9:5 women:males, range of age 23 to 61) with panhypopituitarism due to craniopharyngioma (9), pituitary adenoma (4) and aracnoidocele (1). 12/14 had Body Mass Index (BMI) greater than 25.

13/14 reported daytime sleepiness (DS) or fatigue with Epworth Sleepiness *Scale* greater than 10 in 9/14.

In 9/14 subjects we documented obstructive sleep apnoea (OSA), one was diagnosed before our test. The mean Apnoea Hipoapnoea Index (AHI) was 38 (range 13–98). BMI and age was significantly greater in OSA patients ($P < 0.05$).

We performed MSLT in 9/14; in 7 we confirmed DS, 3 patients had normal AHI. None of them had more than 1 SOREMPs.

We found no difference between types of tumours.

Conclusions: Somnolence is common in our patients and in the majority this is a consequence of obstructive sleep apnoea. No patient was found with narcolepsy.

These results suggest that formal sleep evaluations should be considered in all patients with craniopharyngioma and pituitary tumors.

Disclosure: Nothing to disclose.

P503

Effect of sleep modulation on trauma-induced cognitive impairment and histological trauma marker in a rat model of closed, diffuse traumatic brain injury

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Objectives: Traumatic brain injury (TBI) is a major cause of death and disability worldwide. Memory impairment is the most prevalent residual and chronic deficit following TBI, with no treatment options available. The aim of present investigation was to examine posttraumatic cognitive impairment and effect of acute sleep induction and sleep deprivation as possible outcome modulators for posttraumatic memory performance and amyloid precursor protein (APP-1) expression level, a trauma-induced histological marker.

Methods: We used a novel rat model of closed diffuse TBI, based on the classical weight-drop model to induce the trauma, in which posttraumatic cognitive impairment was assessed using Novel Object Recognition test. For acute sleep induction, rats received a 5 days GHB treatment (415 mg/kg, i.p.), whereas sleep deprivation was performed using gentle handling method (5 days $\times$ 6 h/day).

Results: Our results show that milder TBI severities caused mild memory abnormalities and that higher TBI severities caused severe persistent memory impairment. On the other hand, both sleep induction and deprivation acutely after TBI resulted in reduced memory impairment in high TBI severity in the long term, suggesting an important role of pharmacologically-induced sleep and sleep rebound in posttraumatic cognitive outcome. Moreover, both sleep deprivation and sleep induction resulted in reduced APP-1 trauma index in the cortex, suggesting a neuroprotective role of sleep after TBI.

Conclusions: In summary, our rat TBI model recapitulates posttraumatic memory impairment, and our results suggest acute sleep modulation as a potential treatment option for posttraumatic cognitive impairment.

Disclosure: This work was partially supported by drug manufecturer UCB.

P504

Sleep structure and cardiometabolic disorders in the general population: the Hypnolaus study

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Objectives: Previous studies using subjective assessments have reported associations between sleep quantity and quality and cardiometabolic disorders, but little is known regarding the associations with objective sleep characteristics. The purpose of this study was to evaluate the association between objective sleep measures and metabolic syndrome (MS), hypertension, diabetes and obesity.

Methods: 2162 subjects (51.2% women, mean age 58.4 $\pm$ 11.1) from the general population were evaluated for hypertension, diabetes, overweight/obesity and MS, and underwent a full polysomnography (PSG). PSG measured variables included: Total sleep time (TST), percentage and time spent in slow wave sleep (SWS) and in rapid eye movement (REM) sleep, sleep efficiency and arousal index (ArI).

Results: In univariate analyses, MS was associated with decreased TST, SWS, REM sleep, sleep efficiency and increased ArI. After adjustment for age, gender, smoking, alcohol, physical activity, drugs that affect sleep and depression, the ArI remained significantly higher, but the difference disappeared in subjects without significant sleep disordered breathing (SDB). Differences in sleep structure were also found according to the presence or absence of hypertension, diabetes and overweight/obesity in univariate analysis. However, these differences were attenuated after multivariate adjustment and after excluding subjects with significant SDB.

Conclusions: In this population-based sample we found significant associations between sleep structure and MS, hypertension, diabetes and obesity. However, these associations were cancelled after multivariate adjustment. We conclude that normal variations in sleep contribute little if any to MS and associated disorders.

Disclosure: Nothing to disclose.

P505

Effect of sleep disordered breathing on postural stability

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Objective: Postural stability depends on the coordination of the central nervous system with visual sense, proprioceptive and vestibular information. Sleep deprivation has been shown to affect this function. The objective of this study was to assess the effects of sleep disordered breathing (SDB) on postural stability.

Methods: 158 subjects referred for suspected SDB had an overnight sleep study and were placed on a posturographic platform in late afternoon. This platform measures the oscillations of the center of pressure (*CoP)* and calculates: total displacement of *CoP* in X and Y axis, mean surface and speed of CoP displacement, and the LFS ratio (length of CoP displacement x surface of CoP trajectory).

Results: 98 men and 60 women were included. Mean age $\pm$ SD was 45.4 $\pm$ 5.5 y.o., BMI 27.5 $\pm$ 5.6 kg/m^2 and apnea-hypopnea index (AHI)13.6 $\pm$ 16.1/h. AHI was < 5/h in 65 (41%) subjects, 5–15/h in 43(27%), 15–30/h in 30(19%), and >30/h in 21(13%). In patients with an AHI > 5/h vs. AHI < 5/h, we observed an important increase in LFS (+21%, $P < 0.001$), in XY length (+23%, $P < 0.001$) and in mean speed (+ 23%, $P < 0.001$). After controlling for age and BMI in linear regression models, there was a positive association between AHI and LFS($P = 0.04$) and negative associations between mean SaO2 and LFS ($P < 0.007$), mean speed ($P = 0.01$), and XY length ($P = 0.01$), and a trend toward an association between LFS and % time with a Sao2 < 90% ($P = 0.07$).

Conclusion: The severity of SDB and the related decrease in nocturnal SaO_2 seem to affect significantly daytime postural stability.

Disclosure: Nothing to disclose.

P506

Obstructive sleep apnea syndrome (OSAS) and erythrocytosis

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Introduction: Polycythemia is characterized by an increase in the number of red blood cells and / or the amount of hemoglobin per volume unit of blood. Polycythemia is characterized by increased erythropoiesis stimulating factor (EPO), being normal erythrocyte precursors in the bone marrow. OSAS is characterized by intermittent hypoxia during sleep and can cause secondary polycythemia. Several studies have examined this phenomenon.

Objective: Evaluate patients referred from the Hematology department with polycythemia and suspected OSAS in the Sleep Disorders Unit, having discarded polycythemia vera.

Methods: We analyzed data from 20 patients referred by Hematology with secondary polycythemia and suspected OSAS during 2012–2013.

Results: All patients were male. The mean age was 64.5 (SD 13.6). The mean body mass index was 33 (SD 4.6). The average hematocrit (HCT) was 52 (SD 2.5) and the mean hemoglobin 18 (SD 0.6).

OSAS was diagnosed in 85% of patients studied. The mean respiratory disturbance index (RDI) resulted 32.7 (SD 25.6). The minimum was 0.7 and the maximum 81. Half of the patients had severe OSAS. The nocturnal oximetry profile presented with an average of 41% T90% (SD 35) and a middle desaturation index 34.4 / h (DT 25). Functionally 3 patients (20%) had COPD, with a degree of obstruction and phenotype II A.

Conclusion: In patients referred from hematology with no primary polycythemia, is confirmed OSAS in most cases, which are predominantly obstructive with impact in nocturnal oximetry. It is essential to rule out OSAS in patients with secondary polycythemia.

Disclosure: Nothing to disclose.

P507

High rates of medical comorbidity in narcolepsy: findings from the burden of narcolepsy disease (BOND) study of 9312 patients in the United States

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Objective: To evaluate medical comorbidity patterns in patients with a narcolepsy diagnosis in the United States.

Methods: Truven Health Analytics MarketScan® Research Databases were accessed to identify individuals ≥18 years of age with at least one diagnosis code for narcolepsy ± cataplexy (ICD9 347.0, 347.00, 347.01, 347.1, 347.10 or 347.11) continuously insured between 2006 and 2010, and controls without narcolepsy matched 5:1 on age, sex, region, and payer. Extensive sub-analyses were conducted to confirm the validity of the narcolepsy definitions.

Narcolepsy and control patients were compared for frequency of comorbid conditions, identified by the appearance of ≥1 diagnosis code(s) mapped to a Clinical Classification System (CCS) level 1 category any time during the study period, and on recognized narcolepsy comorbidities of obstructive sleep apnea (OSA) and depression.

Results: The final study group included 9312 narcolepsy patients and 46 559 controls (each group, average age 46.1 years; 59% female). Compared with controls, narcolepsy patients demonstrated a statistically significant excess prevalence of comorbid diagnoses in all CCS multilevel categories, the only exceptions being conditions originating in the perinatal period and pregnancy/childbirth complications. The greatest excess prevalence in the narcolepsy cohort was seen for mental illness (31.1% excess prevalence; OR 3.8, 95% CI 3.6, 4.0), followed by diseases of the digestive system (21.4% excess prevalence; OR 2.7, 95% CI 2.5, 2.8) and nervous system/sense organs [excluding narcolepsy], (20.7% excess prevalence; OR 3.7, 95% CI 3.4, 3.9).

Conclusions: Narcolepsy is associated with a significant burden of medical comorbidity.

Disclosure: Dr. Black is a part-time employee of, and holds stock options in Jazz Pharmaceuticals.

P508

Nocturnal intermittent hypoxemia: utility for the evaluation of severity sleep apnea and cardiovascular comorbidity

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Introduction: Sleep apnea-hypopnea syndrome (SAHS) is a complex public health problem causing increased risk of cardiovascular diseases. Traditionally, evaluation of the severity of the disease is based on Apnea-Hypopnea Index (AHI). Oxygen desaturation index (ODI) could be a good parameter for the evaluation of the severity of SAHS and its potential cardiovascular consequences.

Objectives: The aim of the present study was to examine the relationships between the overnight oxygen desaturation index (ODI), parameters sleep study and cardiovascular events in a sample of patients evaluated in the Unit Respiratory Sleep Disorders.

Materials and methods: We performed a retrospective study collecting data from 105 patients evaluated in the Unit Respiratory Sleep Disorders. It was studied the correlation of ODI with AHI and the presence or absence of comorbidity, defining this as the presence of ischemic heart disease and / or arrhythmias and / or acute stroke.

Results: Among the 105 studied patients, 17 (16%) had comorbidity. ODI values were correlated with AHI with a correlation coefficient of 0.87. There was a significant relationship between the severity of ODI and the presence of comorbidity (p 0.038), and also a significant association between the AHI and the presence of comorbidity (p 0.024).

Conclusions: ODI appears a good parameter to estimate the severity of OSA and may be associated with more prevalence of ischemic heart disease, arrhythmias and acute stroke.

Disclosure: Nothing to disclose.

P509

Impact of continuous positive airway pressure (CPAP) on chronic cough in obstructive sleep apnoea (OSA) – a randomized controlled trial

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Objective: To investigate the effect of CPAP on cough in patients with OSA and chronic cough in a randomised controlled trial.

Methods: Consecutive patients with OSA confirmed on polysomnography (respiratory disturbance index (RDI) > 15/h) and chronic cough > 2 months were recruited. All patients underwent a CPAP titration study. The patients were randomised to receive sham CPAP (4 cm H_2O) or CPAP determined by the titration study. The primary outcomes were objective 24-h cough count via the Leicester Cough Monitor (LCM), subjective cough severity via the visual analogue scale (VAS, in mm) and cough related quality of life via the Leicester Cough Questionnaire (LCQ, score out of 21) after 1 month.

Results: 13/15 patients received sham CPAP and completed the protocol. 10/16 received titrated CPAP and completed. There were no significant differences between groups in sex, age, BMI), RDI, baseline 24-h cough count(, VAS and LCQ. After 1 month there were no significant changes in 24-h cough count in the sham CPAP group [(317.5(64.6) vs. 251.5 (76.0). $P = 0.36$]) but there was significant improvement in the treatment group [(229.8(50.1) vs. 58.2 (17.0), $P = 0.006$)]. There were no significant changes in VAS in the sham CPAP group [54.7(6.1) vs. 40.5 (6.7) $P = 0.19$] or in the treatment group [54.4(5.9) vs. 32.9 (8.4) $P = 0.09$]. There were no significant changes in LCQ in the sham CPAP group [14.4(0.9) vs. 15.6(1.4), $P = 0.57$] or treatment group [14.2(1.1) vs. 15.9(1.1), $P = 0.26$].

Conclusions: CPAP may reduce objective cough severity in patients with cough associated with OSA.

Disclosure: Nothing to disclose.

P510

Interrelationship of sleep quality with fatigue, neuroticism and global health in unexplained chronic fatigue: the validity of current fatigue scales

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Objective: The interrelationship of different dimensions (fatigue, neuroticism, sleep quality, global mental and physical health) in unexplained chronic fatigue and the validity of current fatigue scales was explored.

Methods: Patients with unexplained chronic fatigue filled out two fatigue scales (Fatigue Questionnaire, FQ and Checklist Individual Strength, CIS), NEO-Five Factor Inventory (NEO-FFI), Pittsburgh Sleep Quality Index (PSQI) and Medical Outcomes Study 36-item Short Form Health Survey (SF36). Exploratory and confirmatory path analyses were performed.

Results: In the first path analyses, 203 subjects were included (mean age 39.0 years, SD 10.37, 89% female). Using FQ for assessment of fatigue, night-time PSQI sleep quality had a direct effect on SF36 physical health quality of life (PHQL) and no effect on FQ. This was confirmed by a subsequent path analysis with CIS. These unexpected results raised the question whether FQ or CIS sufficiently reflects fatigue. For both scales, the introduction of a latent variable into the model resulted in a significant improvement of fit, with an indirect effect of PSQI sleep quality on SF36 PHQL through this latent variable. Furthermore, this variable had a direct effect on FQ or CIS, respectively, and on the two SF36 variables. The results of these exploratory analyses were confirmed within 81 patients (mean age 38.47 years, SD 10.314, 88% female).

Conclusions: The use of current fatigue questionnaires do not sufficiently show the presumed role of fatigue as a mediator between sleep and quality of life measures. A latent variable was needed as missing link in this relationship.

Disclosure: Nothing to disclose.

P511

The effect of one year CPAP therapy on blood pressure values in obstructive sleep apnea patients with severe resistant hypertension-an on going study

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Objectives: Few studies showed the effect of CPAP on blood pressure (BP) values in patients with obstructive sleep apnea syndrome (OSAS) and resistant hypertension (RHT), most of them reporting a small BP reduction comparing with a control group. We analyzed the BP variation measured with 48 h ambulatory blood pressure monitoring in CPAP treated OSAS patients, comparing values from baseline with those at 3, 6 and 12 months.

Methods: We excluded patients with secondary RHT, mild OSAS, central SAS, hypercapnia, insomnia, restless legs syndrome, manual PSG titration failure, modifying HT medication during the study, poor CPAP compliance.

Results: 10 patients using CPAP completed 12 months: 7 men (70%), mean age=58.50 $\pm$ 7.81 years, Epworth score=10.80 $\pm$ 5.75, IAH=69.26 $\pm$ 13.16/h, arousal index=51.76 $\pm$ 13.02/h,baseline SBP=166.80 $\pm$ 20.28 mmHg and DBP=90.80 $\pm$ 11.67 mmHg, diagnosed with HT for 12.10 $\pm$ 11.24 years, average CPAP compliance=5.35 $\pm$ 1.7 h/night (increased in time). The only significant difference was an increase of nocturnal maximum SBP from 3 to 6 months (181.60 $\pm$ 18.82 to 203.80 $\pm$ 27.02 mmHg, $P = 0.047$). Although no significant differences were recorded regarding the dipper pattern, mean/diurnal/nocturnal SBP and DBP values or sphygmomanometer values from baseline to 3, 6 or 12 months, a decreasing trend was observed regarding mean SBP (Δ=16.10 mmHg) and DBP(Δ=7.50 mmHg) from baseline to 12 months.

Conclusions: This is the first study enrolling patients with uncontrolled severe HT, evolving for a long period, reporting an important trend in BP reduction obtained only at 1 year and compared with baseline. This results can be explained by increasing compliance in time, by accommodation with the psychological burden of disease and by myocardial and vascular remodeling.

Disclosure: Nothing to disclose.

P512

Napping and risk of type 2 diabetes in adult humans

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Objectives: There are few cross-sectional studies indicating an association between napping and increased risk of type 2 diabetes (T2D). We studied this in a sample representative of general population.

Methods: A questionnaire was administered to the Finnish Twin Cohort in 1990 (response rate 77%, age 33–60 years), giving 12.351 subjects replying to the question 'Do you sleep during daytime (take naps)?' with alternatives

1. No need;
2. I would like to but I cannot sleep during the daytime;
3. On 2 days weekly or more seldom;
4. On 3–5 days weekly; or
5. Every or almost every day.

Information on incident cases of diabetes was obtained by linkage of nationwide registers. Logistic regression models were used to obtain Odds ratios (95% confidence intervals) for incident T2D risk in 1991–2004 by napping category.

Results: 32% had no need for napping, and 15% did so on ≥3 days weekly. There were 229 incident T2D cases during the follow-up. The risk of T2D was significantly increased only among those napping most frequently [1.86 (1.29–2.67), age- and sex-adjusted]. After adjusting for work, working time, use of alcohol, sleep length, sleepiness in the morning, insomnia or snoring the results were essentially the same, but decreased (about 1.5, non-significant) when adjusted for BMI or sleepiness during the day.

Conclusion: There is an association between daily or almost daily napping and increased future risk of T2D, which, however, is largely explained by the higher proportion of obese subject among frequent nappers.

Disclosure: Nothing to disclose.

P513

Co-Morbidities in a Portuguese sample of obstructive sleep apnoea patients

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Objective: Co-morbidities are frequent in Obstructive Sleep Apnoea Syndrome (OSAS). Characterization of co-morbid condition in OSAS patients is necessary for adequate treatment. Our objective was to analyse the association of co-morbidities in a specific sample of OSAS patients from Northern of Portugal.

Methods: A cohort of 324 Sleep Disordered patients was consecutively evaluated. OSAS was confirmed after night sleep video-polygraphic recording (EEG/EOG/EMG/ECG/Nasal and Thoracic Respiration/ O2Saturation/ Movement/ Behaviour) in 141 patients (124 Males/17 Females) Aged (mean): 54.6 (54.4/55.7) years. Co-morbidities: obesity and dyslipidaemia, hypertension (HTA), cardiovascular (CV) disorders, diabetes, psychiatric, neurological/neuromuscular, ENT disorders, were also analysed as a function of OSAS severity (AHI).

Results: From 141 OSAS patients, 96 (68%) (80-M/16-F) have co-morbidities. OSAS was Severe (S:AHI > 30) in 31 patients, Moderate (M:AHI-16–30) in 24, Mild (ML: AHI > 5–15) in 41. Most common co-morbidities were: obesity in 45 patients (21 S; 6 M; 18 ML) and dyslipidaemia in 10 (1S; 4M; 5ML), HTA in 33 (11S; 6M; 16 ML), diabetes in 20 (6S; 3 M; 11ML), cardiovascular diseases in 17 (7S; 1M; 9ML). Psychiatric disorders in 8 (depression was most frequent). Neurological disorders in 13
(5 neuromuscular). ENT/upper airway respiratory disorders in 8. Tumours in 7.

Conclusions: Present work confirms that at the time of sleep disorder diagnosis co-morbidities are commonly associated to OSAS independently of disease severity. The finding of this common association in non-severe cases of OSAS has strong implications on definition of best strategy of treatments in order to avoid patient health deterioration namely on metabolic status.

Disclosure: Nothing to disclose.

P514

Sleep disorders in patients with fatigue-related problems

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Objectives: To evaluate sleep disorders with questionnaires and polysomnography (PSG) in patients with fatigue-related problems.

Methods: Patients were referred to Myalgic Encephalomyelitis(ME)/Chronic Fatigue Syndrome(CFS)-rehabilitation for suspected diagnosis of ME/CFS. Criteria for further referral to lab for full night PSG were: often or always daytime or morning tiredness and/or Epworth sleepiness scale (ESS) ≥10.

Results: Sixty four consecutive patients underwent PSG, 55 women and 9 men, mean age 45.8 ± 9.5, mean BMI 25.3 ± 4.3. Diagnosis of ME/CFS was given to 47 patients, while 17 patients had other disorders explaining fatigue. According to the Apnea-Hypopnea Index (AHI), 27(42.2%) patients were diagnosed with Obstructive Sleep Apnea(OSA); 9 of them had mild, 15 moderate and 3 severe OSA; 6 of those 27 patients had supine related OSA. The mean ESS score was 8.4 ± 6.1, and 22(34.4%) patients had ESS score ≥10. There was no significant correlation between OSA severity and ESS score. 27 (42.2%) patients fulfilled the criteria of Restless Legs Syndrome(RLS). Periodic Limb Movement Index (PLMI) ≥10 was detected in 13 patients (7 with RLS); and PLM Arousal Index ≥10 in 5 patients (2 with RLS). Scores of Hospital Anxiety and Depression scale, Short Form-36 Health Survey and various scales for fatigue did not correlate with AHI, PLMI, PLMAI, ESS and RLS scores. 21(32.8%) patients had normal PSG, among them 16 diagnosed with ME/CFS.

Conclusions: In patients with fatigue and suspected ME/CFS sleep disturbances such as OSA and RLS are quite common, however, it seems difficult to explain subjectively expressed physical and emotional fatigue with these sleep disorders.

Disclosure: Nothing to disclose.

P515

Health complaints across age and gender: the impact of sleep variables

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Objectives: To measure the association across age/gender of a set of sleep variables upon reported health complaints.

Methods: Data from a national survey: n = 3706, 18–79 years. Sleep variables were: Sleep efficiency (SE) < >85%, duration< >5 h and time in bed< >10 h. Age groups were: Young adults(18–29y); AdultA(30–49y); AdultB(50–65y); Elderly(>66y). The health issues were: diabetes (DIA), hypercholesterolemia(CHO), hypertension(BP), cardiac disorders(HEART), respiratory disorders(RESP), depression(DEP), medication use(Med). Odds/ratio analysis used a 2X2 matrix; age groups were compared with AdultA, disorders were coded yes/no; sleep variables as normal/abnormal and gender as male(M)/female(F). Pearson chi square analysis, used z transformation and Bonferroni adjustment of p values; the Odds ratios and 95%CI were computed.

Results: All the prevalence increased with age. Low SE increased the prevalence of: depression in F young adults; cardiac disease for M and medication for F in AdultB; Sleep <5 h increased the prevalence of: RESP and MED in young M; DIA and BP in AdultB and Elderly for M and RESP for F in the same groups. In young adults Bed >10 h increased the prevalence of: RESP for both genders and DIA, DEP and MED for F; of DIA, BP, and MED for both genders and of DEP and cardiac disorder in F in AdultB; of DIA, BP for males, DEP for females and MED for both genders in elderly.

Conclusions: In spite of significant increases of medical and sleep disorders with age, the influence of sleep seems to tune such increased prevalence in subtle ways, which differ also with gender.

Disclosure: Grant Sanofi-Aventis.

P516

Sleep disturbances and quality of life in symptomatic patients with stable chronic cbstructive pulmonary disease

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Background: Sleep disturbances and poor quality of life (QoL) are common but underestimated in patients with Chronic Obstructive Pulmonary Disease (COPD). Purpose of the study was to assess, with questionnaires, sleep characteristics and QoL of COPD patients with severe dyspnea and poor disease control.

Methods: Included were 60 consecutive patients with stable COPD, whose scores in the Medical Research Council Dyspnea Scale (MRC) and COPD Assessment Test (CAT) were indicative of severe dyspnea (MRC ≥ 2) and poor COPD control (CAT score ≥ 10). Additionally, the following questionnaires were answered: Athens Insomnia Scale (AIS; for insomnia), Epworth Sleepiness Scale (ESS; for daytime sleepiness), Pittsburg Sleep Quality Index (PSQI; for sleep quality) and WHO-5 Well-Being Index (for QoL).

Results: Patients were all males, aged 74.4 ± 7.3 years, with a BMI of 28.2 ± 2.7 kg/m^2 and impaired respiratory function (FEV_1 40.8 ± 13.5% pred, FVC 57.4 ± 14.3% pred, FEV_1/FVC 54.7 ± 9% pred). In 52 patients (86.7%) the WHO-5 questionnaire was indicative of poor quality of life. Overall, 83.3% of patients (n = 50) reported poor sleep quality (PSQI score > 5). Additionally, insomnia (AIS score ≥ 6) was reported by 93.3% (n = 56) of the patients, while daytime sleepiness (ESS score > 10) only by four patients (6.7%).

Conclusions: In symptomatic COPD patients with poor disease control, prevalence of insomnia, poor sleep quality and poor QoL is significantly high, while daytime sleepiness is not prevalent.

Disclosure: Nothing to disclose.

P517

Sleep quality and cytokine expression in adults with and without irritable bowel disease

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Objectives: Plasma cytokine levels vary as a function of disease status in those suffering from Irritable Bowel Disease (IBD), of which Crohn's disease (CD) is a main type. Some of the same inflammatory markers have been associated with sleep problems. This study sought to establish whether patient sleep quality, disease status and cytokine levels are related.

Methods: Fifteen patients with CD and 30 healthy age- and IQ-matched control participants were examined (Visit 1) and followed prospectively over a 6 month period (Visit 2). Pittsburgh Sleep Quality (PSQI) and plasma levels of interleukin (IL)-6, IL-8, and tumour necrosis factor (eTNF)-α were determined at both visits.

Results: At Visit 1 Overall Sleep Quality was higher for Healthy Controls (P = 0.08), and significantly so at Visit 2 (P < 0.01). CD patients' level of TNF was associated with PSQI-Daytime Dysfunction (P < 0.01) and PSQI-Subjective Sleep Quality (P < 0.05), and well as Overall PSQI (P < 0.05) at that first visit. Healthy controls showed neither this, nor any other pattern of relationships between sleep quality and inflammatory markers. At Visit 2, despite the fact that PQSI scores were highly correlated with those from Visit 1, there were no statistically reliable relationships between inflammatory markers and sleep quality.

Conclusions: These data show that while sleep quality and inflammatory markers differ between IBD and healthy controls, relationships between levels of plasma cytokines and reported sleep quality are inconsistent. These inconsistencies are discussed in terms of the mediating roles of disease status, HPA-axis function and changes in cytokine concentration.

Disclosure: Nothing to disclose.

P518

The wake-up bus sleep study: falling asleep at the wheel in 19 European countries

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Background and objectives: The European Sleep Research Society conducted a survey of European drivers aiming to estimate

the prevalence and determinants of falling asleep at the wheel, as well as the consequences of drowsy driving.

Methods: Data from 19 countries were collected using an anonymous online questionnaire that collected demographic data, driving behavior, history of sleepiness and accidents and the wheel, and sleep-related problems. Associations between sleepiness at the wheel and its determinants were quantified using multivariate logistic regression (odds ratios and 95% confidence intervals).

Results: Overall, 12 434 questionnaires were submitted. The median prevalence of falling asleep at the wheel in the previous 2 years was 17%. Among respondents who had fallen asleep, the median prevalence of accidents was 7.0%;1% of them involved hospital care and 3.6% involved fatalities. The most frequent reasons for falling asleep were poor sleep in the previous night (42.5%) and poor sleeping habits in general (34.1%).

After adjustment for country of residence, age, gender and distance driven, falling asleep was associated with: younger age [OR (95% CI): 1.68 (1.14; 2.47) in drivers under 30 years]; male gender [1.78 (1.61; 1.98)]; driving $\geq$20 000 km/year [2.06 (1.79; 2.39)]; higher daytime sleepiness [3.20 (2.75; 3.65) for ESS $\geq$10]; and higher risk of OSA [3.52 (2.83; 4.38) in men].

Conclusions: We found a high prevalence of drowsy driving. Estimates were similar between 11 countries, after adjustment for individual characteristics. The main determinants of falling asleep were male gender, driving exposure and obstructive sleep apnea risk.

Disclosure: Nothing to disclose.

P519

Impact of sleep quality and clinical outcome in the ICU patients: Central Asian study

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Objective: Survivors of ICU patients frequently report sleep deprivation and it may impact on clinical outcome. Therefore, the careful study of sleep in ICU is essential. However, sleep disturbances in ICU have not been investigated in detail. We sought to quantify polysomnographic (PSG) findings to evaluate sleep quality and investigate the factors that may effect on it.

Method: Sleep measurements were conducted in surgical and internal medicine ICU for 6 months in Tongji Hospital in China.182, critically ill patients were underwent continuous PSG, for 1 night. The patients also completed the Richards-Campbell Sleep Questionnaire (RCSQ).

Results: A mean age was 48.1 $\pm$ 12.3 years. 32.6% were mechanically ventilated, and 56.3% received intravenous sedatives/analgesics. Sleep-awake abnormalities were found 86% of patients; the most frequently cited reasons were pain, light, intravenous catheters, and noise. No significant correlations were found between perceived sleep quality and illness severity or mechanical ventilation. Patients were receiving sedatives reported better sleep quality ($P < 0.001$). RCSQ sleep quality ratings did not reach statistical significance, but improvements in secondary ICU outcomes did reached. The patients who reported better sleep had a shorter ICU stay and less mortality ($P < 0.03$).

Conclusion: ICU environmental factors, medications, stress and other treatments all contributed to sleep deprivation. It may continue months after discharge from ICU and lead to emotional distress, delirium and increased mortality, even further impact on quality of life, and rehabilitation. A multidisciplinary approach is necessary to reduce the sleep disturbances in ICU patients. The ICUs should implement a sleeping protocol.

Disclosure: Nothing to disclose.

P520

Predictors of self-reported sleep quality in university students

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Objective: To examine the relationship between pre-sleep arousal, arousability, coping, academic stress, affect, neuroticism, extraversion, self-esteem, sleep reactivity to stress and sleep quality, in university students.

Method: Seven hundred and thirteen medical students (468; 65.6% females), mean age 19.29 years, (SD = 1.256; range = 17–24) completed a series of questionnaires that assessed pre-sleep cognitive/somatic arousal, arousability predisposition, tendency to worry/ruminate, sleep reactivity to stress, neuroticism, extraversion, perceived academic stress, positive affect (PA)/negative affect, self-esteem and a multi-dimensional measure of sleep quality, including sleep depth, subjective sleep quality, sleep latency (min) and night awakenings (nr.).

Results: In females, the regression models showed that sleep reactivity to stress (β=0.170; $P = 0.002$), pre-sleep cognitive arousal (β=0.340; $P < 0.001$) and pre-sleep somatic arousal (β=0.126; $P = 0.020$) were all independent significant predictors of sleep quality. Mediation analysis revealed that somatic arousal (95%CI 0.0010–0281) and cognitive arousal (95%CI 0.0009–0421) both are significant partial mediators of the relationship between sleep reactivity to stress and sleep quality

In males the regression models revealed that pre-sleep cognitive arousal (β=0.311; $P < 0.001$), sleep reactivity to stress (β=0.176; $P = 0.023$) and PA ($\beta = -0.214$; $P = 0.001$) were all independent significant predictors of sleep quality. PA was a significant partial mediator of the relationship between pre-sleep cognitive arousal and sleep quality (95%CI 0.0014–0373) and between sleep reactivity to stress and sleep quality (95% IC 0.0090–0623).

Conclusion: Our findings suggest that sleep reactivity to stress and pre-sleep arousal may be key determinants of overall sleep quality, in young adults.

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Disclosure: Nothing to disclose.

P521

Association between sleep quality and computer use among university students

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Objectives: To investigate associations between sleep quality and computer use among university students.

Methods: This cross-sectional study was performed on 312 students of Tehran University of Medical Sciences, Iran. Data was collected using Pittsburgh Sleep Quality Index (PSQI) and a background and computer use questionnaires. SPSS software was used for statistical analyses. Descriptive statistics, independent samples test, analysis of covariance (ANCOVA), and chi square test were used to analyze data.

Results: The final sample was composed of 164 (52.6%) male and 148 (47.4%) female students aged 17–30 years. The mean of PSQI final score was not significantly different between the male (7.27 $\pm$ 3.41) and female (6.72 $\pm$ 2.79) groups ($P > 0.05$). From all of participants, 81.1% were poor sleepers (PSQI $\geq$ 5). There was significant association between computer work (h/day) and poor sleep quality ($P < 0.05$). We found significant association between headache associated with computer use and poor sleep quality ($P < 0.05$).

Conclusions: Poor sleep quality was common among university students. The prevalence was more prevalent among prolonged computer users. Also, the headache associated with computer use deteriorates the quality of sleep. Longitudinal and interventional studies on larger populations are recommended to determine more clearly the effects of computer use and its health-related problems on sleep quality.

Disclosure: Nothing to disclose.

P522

Survery for sleep of neurology residents

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Objectives: For evaluating the work load for medical residents, it is important to search the work hours and sleep status. The purpose of this study was to evaluate the sleep status of residents in neurology department in Korea.

Methods: We recruited neurological residents of 12 university hospitals. They completed questionnaires including their sleep and work hours, sleep habit, Stanford Sleepiness Scale (SSS), Epworth Sleepiness Scale (ESS), and health problems.

Results: We excluded the residents who were previously diagnosed with sleep disorders. One hundred and three residents (male 67, female 36) were analyzed. Average sleep duration on off duty days was 5.8 $\pm$ 0.9 h, on duty days was 4.6 $\pm$ 1.3 h and mean work hours was 14.6 $\pm$ 2.3 h. Average SSS score was 2.6 $\pm$ 1.0 and ESS was 10.6 $\pm$ 5.1. Group analyzed by training years showed short sleep duration in first and second years of training. ESS score was higher in first and second years compare to other years.

Conclusions: Most neurological residents were suffering from sleep deprivation especially first and second years of training. They also reported more sleepiness and drowsiness during the daytime.

Disclosure: Nothing to disclose.

P523

Pets in the bedroom: a survey of American patients

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Pet ownership and the number of pets per household are at the highest level in two decades (2012 American Pets Products Association data). The American Veterinary Medical Association in 2012 reported that dogs are the most popular pets (36.5% of households) followed by cats (30.4%) and birds (3.1%). These trends raise questions of where pets sleep and whether they disturb their owners' sleep. A 2002 study published in abstract form reported that 52% of patients seen at the Center for Sleep Medicine had pets, 58% of which slept on the bed. Only 1% of pet owners perceived their companion animals to cause inconvenience at night. (Shepard, 2002).

Methods: One hundred and fifty consecutive patients provided information about pets at night as a part of a comprehensive sleep questionnaire. Questions were incorporated into sleep environmental section asking the type and number of pets. During the subsequent sleep interview, additional information was collected about where the companion animals slept, any notable behaviors and whether the patient was disturbed.

Results: Pet ownership was similar at 46% (74 patients). Households with multiple pets increased markedly at 42% (31). A larger number of patients (10%) in 2013 reported annoyance that their pets sometimes disturbed their sleep.While the majority of patients did not view their pets intolerably disturbing their sleep, in 2012 a higher percentage of patients experienced irritation. This may be related to the larger number of households with multiple pets. Sleep specialists should inquire about companion animals and help patients problem seek methods to optimize their sleep.

Disclosure: Nothing to disclose.

Normal Physiology of Sleep and Normal Variants

P524

Association between insulin and leptin levels and sleep duration in general population

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Objectives: To assess lipid metabolism in subjects with different sleep duration in a random cohort from Russian epidemiologic study (ESSE-RF).

Methods: A random age and sex stratified sample included 1600 St Petersburg citizens aged 25–65 years; 1552 subjects were included in analysis: mean age 50 (21–68) years, 570 males [mean age 47 (21–65) years] and 1027 females [mean age 52 (25–68) years]. All participants underwent a survey, including questionnaires about sleep duration in last month; fasting blood samples were taken during the visit, lipids and insulin were analyzed. Six groups were formed depending on sleep duration: ≤5 h (group 1), 6 h (group 2), 7 h (group 3), 8 h (group 4), 9 h (group 5) and ≥10 h (group 6).

Results: There were no statistical differences in age or body mass index between groups. One-way ANOVA demonstrated significant differences in insulin and leptin levels between groups. Post hoc analysis (Bonferroni test) showed differences in insulin level between groups 1 (73.5 pmol/l), 2 (59 pmol/l) and 3 (56 pmol/l) ($P = 0.008$) and in leptin levels between groups 4 (13 ng/ml) and 6 (17 ng/ml) ($P = 0.027$).

Conclusions: These epidemiological data suggest that sleep duration ≤5 h is associated with the higher insulin levels, while sleep duration ≥ 10 h is associated with the higher leptin levels. However, the consequences of these hormonal changes and their relation to metabolic disorders in general population need further investigation.

Disclosure: Nothing to disclose.

P525

Stage 1 sleep: 'no man′s land' between the opponent driving forces for wake and sleep

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Objectives: Wakefulness is separated from a well-established sleep by an onset period. This is characterized by dramatic changes in scores on the first and second principal components of the electroencephalographic (EEG) spectrum, which reflects the kinetics of sleep- and wake-promoting processes. The present analysis examined whether significant buildups and declines of the first and second scores can occur throughout stage 1 ('drowsy') sleep, or only on its boundaries with stage 2 and wakefulness.

Methods: Twenty-seven adults participated in multiple 20-min attempts to nap in the course of 24-h wakefulness after either deprivation, restriction or ad lib night sleep. Power spectra were calculated on 1-min intervals of 251 EEG records.

Results: Irrespective of accumulated sleep debt and duration of stage 1 sleep (from < 2 to >5 min), the first principal component score was permanently attenuated across this stage as well as during preceding wakefulness. It showed rapid buildup only on the boundary with stage 2. The second principal component score always started its decline earlier, on the wake-sleep boundary. It did not show further decline throughout the following intervals of stages 1 and 2. It seems that stage 1 sleep occurs due to a delay of the buildup of the sleep-promoting process relative to the decline of the wake-promoting process which coincide with initiation of stage 2 sleep and termination of wakefulness, respectively.

Conclusion: Stage 1 or 'drowsy' sleep can be regarded as occupying 'no man′s land' between the opponent driving forces for wake and sleep.

Disclosure: Nothing to disclose.

P526

Estimating individual optimal sleep time and potential sleep debt

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Objectives: Although insufficient sleep has been known to cause many health problems, estimation skill for individual optimal sleep time (or sleep debt) remains to be developed. We hypothesized that saturated sleep time under sufficient sleep opportunities would reflect the individual's optimal sleep time (OST) and that differences between OST and habitual sleep time (HST) represent individual's potential sleep debt (PSD).

Methods: After in-home recording, 15 healthy young men with no subjective and PSG-based sleep problems were enrolled 12-h, 9-night sleep extension protocol followed by 39-h total sleep deprivation and recovery sleep. OST was estimated from the asymptotic values of exponential curves fitted to the total sleep times under the sleep extensions for each individual. PSD was estimated from the differences between OST and HST.

Results: On the first extended night, the mean sleep time (10.59 ± 0.19 h, MEAN±SEM) showed a 3-h rebound from HST (7.37 ± 0.27 h). Total sleep time subsequently showed a gradual decrease toward OST (8.41 ± 0.18 h) across the extension period. The mean PSD (1.07 ± 0.90 h) correlated to the rebound on the first extension night (r = 0.770, $P = 0.001$). Moreover, PSD showed a stronger relationship with objective sleepiness than HST when individual differences of sleep homeostasis were adjusted.

Conclusions: The present findings suggest the existence of a modest sleep debt in the healthy young subjects without any subjective or objective symptoms. The fact that PSD had a stronger relationship with objective sleepiness than actual sleep time strongly claimed the individual variations of sleep needs should be considered to establish appropriate sleep hygiene.

Disclosure: Nothing to disclose.

P527

Mechanisms underlying the association between anxiety and sleep architecture in healthy good sleepers: the role of pre-sleep arousal

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Objectives: Whilst clinically significant sleep disturbances are often comorbid with anxiety disorders, less extreme sleep disturbances are also associated with anxiety in the general population. However, understanding of the mechanism underlying this association is unclear. Associations between sleep architecture and anxiety, and the extent to which these associations were mediated by pre-sleep arousal, were examined in healthy, good sleepers.

Methods: Eighty five healthy, good sleepers (50.1% female; Age: M = 26.8 years, SD = 10.3 years) completed a 2-night in-lab polysomnographic study, the Hospital Anxiety and Depression Scale, and the Pre-Sleep Arousal Scale. Hierarchical linear regressions were performed to examine mediation models.

Results: Both increased anxiety and pre-sleep arousal were associated with decreased time in N1 (% of total sleep time) ($r = -0.25$, $P < 0.05$; and $r = -0.29$, $P < 0.01$, respectively); but increased time in REM (% of total sleep time) ($r = 0.21$, $P = 0.05$; and $r = 0.24$, $P < 0.05$, respectively). Hierarchical linear regressions indicated that these associations were reduced to non-significance in the presence of pre-sleep arousal.

Conclusions: Individuals with higher levels of state anxiety appear to spend more time in REM at the expense of stage 1 sleep – relationships which are mediated by heightened arousal. Such individuals may exhibit a greater REM requirement; or heightened arousal may continue throughout the night, manifesting in increased REM sleep. Decreased stage 1 sleep may thus be an artefact of subsequent increased REM. Alternatively; such individuals may exhibit more discrete transitions from wake to sleep, to some extent bypassing stage 1 sleep. Further analyses aim to determine whether such arousal is somatic, cognitive or cortical.

Disclosure: Nothing to disclose.

P528

Sleeping towards or against earth electromagnetic field?

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Objectives: Built environment conditions have some effects on sleep quality. Orientation is a key factor in built environment designing. Solar radiation, wind, climate and etc. are considered for orientation in designing.

For designing bedroom, bed orientation can arrange by any reason but what about the effects of earth electromagnetic field? What is the difference between sleeping towards North-South or East-West? In this research we examine the effects of bed orientation towards and against earth electromagnetic field on sleep's EEG signals.

Methods: Twenty seven healthy participants slept for 2 following naps, in Sleep Clinic in two rooms with the same interior designing but different bed orientation towards and against earth electromagnetic field. EEG signals were divided into five sub-frequencies with Discreet Wavelet Transform that includes; delta (0–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), $beta_1$ (16–24 Hz), $beta_2$ (24–32 Hz), Moreover Spindle and K-complex frequency ranges (8–16 Hz) has considered to calculate the energy signals to find out the significance with two sided t-test validation. For five frequencies range the differences considered between two different bed orientations.

Results: Delta, Theta and Alpha differences had significance results in t-test. The p-values for Delta, Theta and Alpha were 0.006, 0.007 and 0.01, respectively. Also, only Alpha energy ratio over whole signal energy was significance ($P < 0.05$). The average energy of Delta, Theta and Alpha frequencies were increased in the North-South bed's positions vs. East-West positions.

Conclusions: Study shows that bed orientation has some effects on sleep's EEG signals and sleeping towards North-South can have more benefits.

Disclosure: This work was supported by Baharloo hospital and all data recording was performed in the Sleep Clinic of Baharloo hospital in Tehran.

P529

The alerting effects of ad-libitum daytime naps

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Objectives: Laboratory studies have established the beneficial effects of daytime naps taken at experimenter-set times. However, this effect may be underestimated particularly if participants are not sleepy at this time. The present study compared the benefits of a 10-min nap taken at a self-selected and an experimenter-set time.

Methods: Fifteen good sleepers aged 18–35 years (mean age=23.64, SD = 3.61, 40% male; 73% regular-nappers) participated in a repeated-measures counterbalanced design with four experimental conditions; 10-min nap at a self-selected (14:00 h–15:00 h) or experimenter set time (14:00 h), and corresponding no-nap control (90-s of sleep) at either the self-selected or experimenter-set time. Subjective alertness (Stanford Sleepiness Scale), cognitive performance (Symbol Digit Substitution Task, Psycho-motor Vigilance Task), and objective sleepiness were measured pre-and post-nap in a controlled laboratory environment. Post-nap testing began immediately after waking and continued for 3-h.

Results: Preliminary results demonstrate significant improvements in measures of subjective and objective sleepiness, and cognitive functioning following a 10-min nap taken at an experimenter-set or self-selected time when compared to no-nap. Improvements in subjective sleepiness emerged approximately 20-min post-nap, followed by improvements in objective sleepiness and cognitive functioning from 40-and 70-min post-nap, respectively. Greater improvements in subjective sleepiness were observed following naps taken at a self-selected compared to an experimenter-set time. Despite a lack of statistical significance, this effect is reflected in measures of cognitive functioning with medium/large effect sizes in this limited sample.

Conclusions: The effects of a 10-min nap are enhanced when the nap is taken at a self-selected rather than an experimenter-set time.

Disclosure: Nothing to disclose.

P530

Physiologic effects of non-awakening electrocutaneous stimulation of palm during slow wave period of nap

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Objectives: Resent research revealed the possibility to influence slow wave activity during sleep as well as learning process by means of magnetic electric and afferent stimulation. Previously we observed physiologic and therapeutic effects of non-awakening electrocutaneous stimulation of palm during slow wave night sleep. The purpose of current research was to confirm those effects for the case of daytime sleep, using similar stimulation method.

Methods: Eighteen good sleepers (nine male and nine female, aged 20–30 years) participated in the study. Each subject took part in 3 control experiments the 4th one with stimulation. Subjects had to take a nap at 12:30 or 14:30 on a weekend.

Sub-threshold rhythmic low frequency (1.0 Hz) palm electric stimulation was applied to subjects during slow wave (stage 3) periods of nap. Stimulation switched on automatically when certain quantity of EEG delta waves appeared and turned off 30 s later. Stimulation off period lasted for 20 sec and then it could resume.

Results: Experimental data has shown the sub-threshold low frequency electrocutaneous stimulation of palm during slow wave period of nap to produce positive effect on sleep structure resulting in significant increase of EEG delta wave (0.5–2.0 Hz) power.

Conclusions: We suppose that the result obtained is determined by hypothetical mechanism sustaining and deepening the sleep process. That mechanism also counteracts arousing effects of afferent stimulation. Future studies should test the possibility to use such techniques to support functional recovery in neuropsychological patients.

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Disclosure: Nothing to disclose.

P531

Involvement of the amygdala in blood pressure fluctuation during REM sleep

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In addition to rapid eye movement, a variety of changes in autonomic nervous system occur during REM sleep, including sudden fluctuation of heart rate, respiration or blood pressure. Such phenomena are considered to reflect the emotional changes during REM sleep. Brain imaging studies in human have revealed that activity of amygdala increases during REM sleep. In rats, considerable number of the amygdala neurons increase their activity during REM sleep. Therefore, it is hypothesized that the autonomic changes during REM sleep would be triggered in amygdala. In the present study, (1) single neuronal activity in amygdala was recorded in unanesthetized, head-restrained rats under sleep-waking cycles, and (2) effect of electrical lesion in amygdala on blood pressure fluctuation during REM sleep was examined. About 40% (18/48) of amygdala neurons demonstrated activity closely correlated with blood pressure fluctuation during REM sleep. Blood pressure fluctuation during REM sleep is composed of single peak increase (4.2 counts/h), multi peaks increase (15.5 counts/h) and single peak decrease (5.9 counts/h). After electrical lesion (500 μA, 30sec) to the amygdala, these fluctuations almost disappeared. These results suggest that amygdala has closely involved in blood pressure fluctuation during REM sleep. Further studies are required to identify the amygdala subnucleus involved in this phenomenon.

Disclosure: Nothing to disclose.

P532

The European Portuguese version of the children chronotype questionnaire (CCTQ): reliability and raw scores in a large continental sample

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Objectives: To study the psychometric properties, and to obtain raw scores, of the European Portuguese version of the Children ChronoType Questionnaire (CCTQ – Werner, LeBourgeois, Geiger and Jenni, 2009) in a large sample aged 4–11 yr.-old from Continental Portugal.

Methods: A cluster sample was recruited in all educational regions of Continental Portugal. Questionnaires for 3166 (51.1% boys) kindergarten and school aged children were retrieved. Based on parents/tutors answers, three chronotype measures were computed: morningness/eveningness scale score (M/E); corrected midsleep point on free days (cMSF); five-point chronotype score (CT).

Results: Chronbach alpha for the M/E scale was 0.73. Corrected item-total correlations ranged from 0.27 to 0.49, average of 0.40. Scores on the M/E scale showed a Gaussian distribution with a mean of 29.0 ($\pm$ 5.16); cMSF mean was 3:34 ($\pm$ 42 min); CT median score was 3. Associations between the chronotype measures ranged from moderate (r_s = 0.38) to large (r_s = 0.58).

Conclusions: Our results for the European Portuguese CCTQ in a Continental sample were similar to the ones obtained on the original questionnaire for the M/E scale, but our children showed later schedules as expressed by cMSF. The CCTQ [PT] M/E scale appears to be a reliable tool. At the moment, its validity is being studied using actigraphy.

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P533

Efficacy of Japanese sake yeast on the sleep quality: a double-blind randomised controlled clinical trial

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Objectives: We searched for a new food materials to improve the quality of sleep and found Japanese sake yeast (Kamada *et al.*: Journal of Sleep Research, 21 (Suppl. 1), p276, 2012). In this study,

we examined the effects of Japanese sake yeast on the quality of sleep in a clinical trial.

Methods: In a double-blind placebo-controlled cross-over study, 68 healthy participants were selected by the Pittsburgh Sleep Quality Index score, which is equal to or higher than 5 points. They took the tablets containing 500 mg of Japanese sake yeast or the placebo about an hour before sleep for 1 week, respectively. An electroencephalogram (EEG) was recorded during sleep, and a subjective evaluation using the MA version of the OSA sleep questionnaire was surveyed.

Results: The EEG power spectral analysis showed that Japanese sake yeast significantly increased EEG delta power in the first slow wave cycle as compared with placebo ($P < 0.05$). In subjective evaluation, sleepiness and fatigue in the morning were significantly improved by taking of Japanese sake yeast, although the feelings of initiation-maintenance of sleep, frequent dreaming and sleep length were not changed significantly.

Conclusion: Japanese sake yeast improved the quality of sleep in terms of the delta power in the first slow wave cycle and feeling of the sleepiness and fatigue in the morning.

Disclosure: Nothing to disclose.

Instrumentation and Methodology

P534

Sleep estimation based on respiratory analysis

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Objectives: Analysis of heart rate variability (HRV) is the most common alternative to polysomnography (PSG) method of sleep structure detection. In some works HRV analysis is combined with respiratory analysis (RA). The purpose of this study is sleep estimation based on RA only.

Material and methods: Data from 21 subjects (mean age 36.76 $\pm$ 14.57 years, 11 females) without sleep breathing disorders (SDB) were used. Full-night polysomnography (PSG) including registration of respiratory movements by respiratory inductance plethysmography (RIP) was performed. PSG records were scored by a physician expert. Features for classification were extracted from RIP signal, inter-breath interval and tidal volume. Automatic sleep stage classification based on the features was performed and obtained results were compared with physician estimation.

Results: Sleep scoring by RA is consistent with results of PSG and in general hypnograms were similar. Bland Altman plots showed agreement between sleep efficiency and total sleep time obtained by PSG and RA.

Conclusions: The results demonstrate that RA is potentially able for sleep estimation. Although the method is less accurate than HRV analysis and not appropriate for people with SDB, it seems to be a promising research direction and useful in for the development of long-term home sleep monitoring systems.

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P536

Investigating novel variables based on a probabilistic model of sleep microstructure for characterizing hypnotic drug effects

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Objectives: To analyze novel descriptions of sleep microstructure with respect to characterizing the effects of the orexin receptor antagonist almorexant.

Methods: Polysomnographic data from 36 insomnia patients receiving placebo and 400 mg almorexant in a random crossover fashion were subjected to a probabilistic sleep model (1), which describes sleep in terms of probability curves, corresponding to classical sleep stages, with a 1s resolution. Besides variables corresponding to classical sleep variables such as percentage of each stage, novel variables were derived. These include a novel form of 'sleep latency' in terms of percentiles, and various types of 'hidden states', the extent of one probabilistic sleep stage hidden under another stage. The differences of all variables between placebo and almorexant were tested (paired t-test). A Benjamini-Hochberg procedure was applied to correct for multiple testing.

Results: All continuous variables akin to classical variables confirmed the main known effects of 400 mg almorexant (2), which can be considered validation of the probabilistic model. The novel variables revealed interesting additional information about the drug effects. While the relative amount of the continuous 'REM' stage increases under almorexant (19% vs. 16%, $P = 0.035$), the percentiles, i.e., the latencies to different amounts of 'REM' – remain the same. Under probabilistic stage 2 the amount of 'hidden' SWS increases by about 15% ($P = 0.013$), pointing to interesting sleep stabilizing effects.

Conclusions: This study shows that continuous sleep models reveal additional information about drug effects.

(1) Lewandowski et al., Comp Meth Prog Bio 2012, 108(3):961–72.
(2) Hoever et al., Clin Pharmacol Ther 2012, 91(6):975–85.

Disclosure: Nothing to disclose.

P537

Could a virtual human be used to explore excessive daytime sleepiness in patients?

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Objectives: Sleep disorders and Excessive daytime somnolence (EDS) are very common in the general population. It is therefore very important to be able to screen patients for this symptom in order to obtain an accurate diagnosis of sleep disorders.

Methods: Embodied Conversational Agents (ECA) have been used in the field of affective computing and human interactions but up to now no software has been specifically designed to investigate sleep disorders. We created an ECA able to conduct an interview based on the ESS and compared it to an interview conducted by a sleep specialist. 32 consecutive patients and a group of 30 healthy volunteers free of any sleep complaints were recruited.

Results: The best results (sensibility and specificity of the interview conducted by the ECA >98%) were obtained for the sleepiest patients (ESS $\geq$ 16) but very good scores (sensibility and specificity > 80%) were also obtained for alert subjects (ESS < 0). ESS scores obtained in the interview conducted by the physician were significantly correlated with ESS scores obtained in the interview ECA-conducted. 65% of the participants felt that the virtual doctor could significantly help real physicians.

Conclusions: Our results show that a virtual physician can conduct a very simple interview to evaluate EDS with very similar results to those obtained by a questionnaire administered by a real physician. The expected massive increase in sleep complaints in the near future likely means that more and more physicians will be looking for computerized systems to help them to diagnose their patients.

Disclosure: Nothing to disclose.

P538

Automatic sleep classification using a data-driven approach reveals six latent sleep states

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Objectives: The golden standard for sleep classification uses manual scoring of polysomnography, which is criticised for oversimplification, low inter-rater reliability and the standard being designed on young and healthy subjects. To meet the criticism, this study used a data-driven approach.

Methods: A general and automatic sleep classifier, which evaluates sleep using latent sleep states, was optimized. The model used spectral EEG and EOG measures and eye correlation in 3 s windows with one second resolution. Each thirty seconds epoch was expressed as mixture of probabilities of the latent sleep states. To test the model application, control subjects and patients with periodic leg movements represented a non-neurodegenerative group and patients with idiopathic REM sleep behavior disorder and Parkinsons Disease represented a neurodegenerative group. The model was optimized using 50 subjects and validated on 73 subjects.

Results: The optimized model used six latent sleep states indicating that sleep contains six diverse latent sleep states and the state transitions were expressed as continuous processes. Statistics of the latent sleep states showed accordance to the spectral EEG and EOG content as well as eye movements in the AASM stages. The sleep model performed similar across the four groups and the overall subject-specific accuracy reached (%) 68.3 $\pm$ 7.5.

Conclusions: Analysing sleep using a data-driven approach and inclusion of only EEG and EOG revealed six latent sleep states. The model is general applicable on subject groups and may contribute to the research in neurodegenerative diseases.

Disclosure: Nothing to disclose.

P539

Feasibility of sleep apnea detection using a single piezo snoring sensor

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Obstructive sleep apnea (OSA) is a most common sleep-disordered breathing with high prevalence and more than 80% of patients with suspected OSA are undiagnosed. Although, polysomnography (PSG) is currently regarded as the gold standard for OSA diagnosis, it is high cost, inconvenience for patients and immobility. Thus, a low cost, portable and convenient OSA screening technique is required urgently.

We investigated the possibility of developing a novel method for OSA screening technique by using a single channel piezo snoring sensor. Pulse rate variability (PRV) was induced from snoring sensor signals and then time domain and frequency domain analysis of PRV were performed. To detect OSA, we have extracted eight features (NN, SDNN, RMSSD, NN10, NN50, LF, HF and LF/HF ratio) from PRV analysis. The performance was evaluated using snore recordings from 13 subjects (ages: 52.1 $\pm$ 9.5 years, body mass index: 72.6 $\pm$ 2.0 kg$\times$m^{-2}, apnea-hypopnea index: 25.8 $\pm$ 2.0 h^{-1}). The sensitivity and specificity were 78.8 $\pm$ 0.9% and 78.9 $\pm$ 0.9% for training set and 77.8 $\pm$ 10.9% and 79.0 $\pm$ 2.8% for test set, respectively. This study demonstrated the feasibility of implementing a snoring piezo snoring sensor based on portable device as a simple and cost-effective solution for contributing to the OSA screening and other breathing disorders.

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Disclosure: Nothing to disclose.

P540

Polish adaptation of Holland Sleep Disorders Questionnaire – first impression from pilot study

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Sleep disorders are among the most common health problems of contemporary society. In order to identify sufferers an easy to administer self-report measure can be very useful. One of such measures is the Holland Sleep Disorders Questionnaire (HSDQ) based on International Sleep Disorders Classification-2 (Kerkhof et al., 2013). Aim of the study was to adapt this questionnaire into Polish.

The HSDQ was translated into Polish and back-translated to English using the standard procedure recommended for adaptation. After author of questionnaire accepted the translation 103 students aged from 18 to 24 years were tested. Additionally 87 participants were reevaluated after 2 weeks to assess the test-retest stability. The obtained data were analyzed with exploratory factor analysis (extraction method: *maximum* likelihood, rotation: oblimin).

Factor structure of Polish version is similar to original version of HSDQ representing six diagnostic groups. Internal consistency was assessed by Cronbach's α coefficient, which was satisfactory for all scales (ranging from 0.49 to 0.87) with exception for Sleep Related Breathing Disorder scale (SRBD; 0.03) However only few students were found to suffer from SRBD, what makes the assessment of Cronbach α for this scale unreliable. Test-retest reliability, assessed by Pearson correlation coefficient, was good (r = *0.*89). The most common disorder was insomnia (14.56%), further was restless leg syndrome (9.71%) followed by circadian sleep disorder (6.80%).

Results from healthy sample are promising. We have found a six-factor solution. This study suggest that HSDQ has good psychometric properties. Further study would require clinical sample to assess diagnostic accuracy.

Disclosure: Nothing to disclose.

P541

Automatic artifact detection for whole-night polysomnographic sleep recordings

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Objective: Detecting of bad channels and artifacts for whole-night polysomnographic recordings is very time consuming and tedious. We therefore developed an automatic procedure.

Method: The method uses temporal and spectral parameters estimated from the data, and thresholds that are systematically adapted to the recording analyzed. First, bad channel detection proceeds per individual channel per scoring window (of 20 or 30 s), leaving usable episodes available for further processing. Afterwards artifacts are searched for over 1-s epochs and across all channels: 'slow undulation' linked to breathing and sweating, 'rapid transient activity', and 'movements and arousals'. Automatic artifact detection is compared to manual detection, using four criteria: inter-rater reliability (S), sensitivity (Se), overlap of detected artifacts (C) and False Discovery Rate (FDR).

Results: Forty three recordings (from 23 different subjects) were rated by one expert and our automatic method. By considering the manual detection as the gold standard, we obtained: S = 93.8%, Se=78.2%, C = 71.9% and FDR=51.7%. Inter-expert variability was tested by comparing the automatic detection with that of six different experts on four sleep recordings (7 scoring for each recording) from a single subject: S_{auto}=97.7% vs. $S_{experts}$=98.4%, Se_{auto}=86.2% vs. $Se_{experts}$=72.7%, C_{auto}=73.2% vs. $C_{experts}$=90.3% and FDR_{auto}=54.7% vs. $FDR_{experts}$=27.5%. Post hoc checks showed that automatic detection usually found artifacts that had been overlooked by the experts.

Conclusion: Tests performed over different datasets show that our automatic method is robust and reproducible, as well as more reliable than different experts between them. Moreover it works (on a standard PC) much faster than manual detection

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P542

Efficacy of the mandibular advancement device in patients with sleep apnea syndrome

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Introduction: The high efficacy of continuous positive airway pressure (CPAP) in treating obstructive sleep apnea (OSA) is limited by poor compliance often related to pressure intolerance. Mandibular advancement devices (MAD) as a medical non- continuous positive airway pressure (CPAP) treatment have proven to reduce respiratory disturbances.

Objetives: The present study investigated the effectiveness of an intra-oral mandibular advancement device in the treatment of patients with OSA who could not tolerate or who had failed to comply with CPAP.

Methods: A total of 27 OSA patients treated during 2011–2012, who do not tolerate CPAP, participated in the study. The clinical, analytical and sleep apnea recordings were evaluated before and after application of MAD.

Results: Of 27 patients, 20(74.1%) were men with a middle age of 53.15 and 7 were women(25.9%) with a middle age of 60.43. The median initial Epworth's scale reduced from 11.13 $\pm$ to 7.67 $\pm$ 3.9, $P < 0.05$. The mean disturbed respiratory index (RDI) statistically decreased with MAD (16.8 $\pm$ 23 vs. 27.1 $\pm$ 16, $P < 0.05$. In addition, oxygen desaturation index (ODI) improved with MAD (19.84 $\pm$ 21.2 with MAD vs. 26.42 $\pm$ 19 before MAD; $P < 0.05$). The percentage of time spent below 90% saturation improved from 24.9 $\pm$ 31.21% to 14.75 $\pm$ 21.12, $P > 0.05$).

Conclusion: MAD may be considered for patients not compliant with CPAP treatment or those who refuse to use it. Even though CPAP is the more effective treatment modality, in the individual case, the better compliance seen in some patients with the MAD may be advantageous.

Disclosure: Nothing to disclose.

P543

RemLogic® plug-in enables calculation of apnea-hypopnea index adjusted for severity of individual obstruction events

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Objectives: Obstructive sleep apnea (OSA) is diagnosed based on apnea-hypopnea index (AHI) [1] neglecting severity of individual obstruction events. However, long apnea and hypopnea events and deep desaturations are related to increased mortality rate [2]. We have previously introduced *adjusted AHI* parameter incorporating morphology, duration and number of the events [3]. *Adjusted AHI* is calculated using custom-made MATLAB® (Mathworks, Natick, MA) functions and is not clinically available. RemLogic™ (Embla, Thornton, CO) is widely used clinical polysomnography software. Presently, we introduce and test a house-made RemLogic™ plug-in for determination of *adjusted AHI*.

Methods: The plug-in was written in C++ using Somnologica™ (Flaga, Reykjavik, Iceland) Software Development Kit and compiled with Microsoft Visual C++® 6.0 (Microsoft, Redmond, WA). The plug-in was tested by comparing *adjusted AHI* values calculated with RemLogic™ and MATLAB® with twenty-five patients from normal, mild, moderate and severe OSA categories (n_{total}=100) based on polygraphy.

Results: The values of *adjusted AHI*, calculated with RemLogic™ and MATLAB®, were strongly correlated (r = 0.999, $P < 0.01$). Mean ($\pm$SD) difference between the values was 0.7 $\pm$ 1.2%.

Conclusions: *Adjusted AHI* improves recognition of OSA patients with especially high risk of cardiovascular morbidity or mortality [3]. The present RemLogic™ plug-in allows clinical use of *adjusted AHI*. This may greatly help the individual assessment of the severity of OSA.

Acknowledgements: Financial support from Seinäjoki Central Hospital and Kuopio University Hospital is acknowledged.

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Disclosure: Nothing to disclose.

P544

Effect of different oxygen desaturation threshold criteria used for defining hypopneas on conventional and adjusted apnea-hypopnea indices and classification of sleep apnea severity

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Objectives: To examine the effect of different oxygen desaturation threshold (ODT) criteria on apnea-hypopnea index (AHI) and our recently introduced parameter, adjusted AHI [1]; and to clarify the impact of the different criteria on the classification of obstructive sleep apnea (OSA) severity.
Methods: Ambulatory polygraphic recordings of 67 patients (18F/49M, 51.2 ± 9.2 yrs, AHI≥5) were reviewed retrospectively. The AHIs and adjusted AHIs were calculated using AASM 2012 rule for apneas; and ≥30% drop in airflow for ≥10 s associated with ≥2% oxygen desaturation for hypopneas (ODT2%), and then utilizing stricter criteria (ODT3%-ODT15%). Subsequently, the patients were divided into different OSA categories based on the AHIs and adjusted AHIs.
Results: Compared to ODT4%, the ODT3% resulted in 48.5%±19.6% higher conventional AHI. Instead, adjusted AHI increased only 9.7%±6.6%. A significant rearrangement of patients into severity categories took place when using different ODTs. When assessing with ODT3% instead of ODT4%, the portion of the patients with AHI≥15 raised from 28.4% to 73.1% using AHI, but only marginally, from 73.1% to 77.6%, using the adjusted AHI.
Conclusions: Conventional AHI was found to be very sensitive to minor changes in ODT which may lead to substantial variability in classification of disease severity. Since the adjusted AHI comprises information on severity of individual obstruction events, it is less sensitive to events with minor desaturations. This may be advantageous as the most severe events cause greatest stress to the patient and have been shown to be particularly hazardous [1].
[1] Muraja-Murro et al, Sleep Breath, doi: 10.1007/s11325-013-0927-z
Disclosure: Nothing to disclose.

P545

The new therapy of sleep disturbances and depression by using the non-awakening electrostimulation during SWS

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Objectives: The purpose of our present investigation was to check the possibility to improve the sleep quality by using non-awakening electrostimulation during sws.
Material and methods: Sixteen subjects (nine men and seven women) aged 30–60 years. These subjects were selected for the investigation according to their reduced emotional tone accompanied by complaints on sleep disturbances. Polysomnography was performed during the 4 consecutive nights: 1st night – adaptation, 2nd night -sleep background, without stimulation, 3 and 4 – with stimulation in SWS stage. Stimulation started automatically of sustainable delta EEG rhythm and was stopped after a significant reduction of delta rhythm. Pauses between the continuous stimulations were 20–40 s.
Results:

1. It was shown that low-frequency electric sub-threshold stimulation of the inner side of the human hand palm during delta-sleep phase has a positive impact on the sleep structure, increased the duration SWS in the first half of sleep and significantly increased the power of delta waves.
2. REM sleep normalized, and this normalization displayed itself in the growth of intensity of eye movements in successive cycles of sleep.
3. Stimulation caused the improvement of the overall structure of the sleep which became more cyclical.
4. Subjective assessment of one night sleep after stimulation reliably became more positive compared to the estimate for the nights without stimulation.

Conclusions: We suppose that the result obtained is determined by hypothetical mechanism sustaining and deepening the sleep process.
Disclosure: The work is supported by RFBR grant 14-07-00580

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FASST, 'fMRI artefact removal and sleep scoring toolbox'

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Objective: FASST, 'fMRI Artifact rejection and Sleep Scoring Toolbox', was developed to analyze sleep EEG data (possibly acquired alongside fMRI) and help handling long continuous multichannel M/EEG recordings.
Method: The toolbox has the following functionalities:

1. Cleaning of EEG-fMRI data from the MR induced artefacts (gradient and ballistocardiogram);
2. Reviewing, appending and chunking of continuous multichannel recordings, including channel selection, temporal zoom, online filtering, re-referencing;
3. Manual sleep scoring by multiple users; including scoring comparison and fusion;
4. Marking of specific events, artefacts and bad channel episodes;
5. Automatic detection of sleep slow waves and spindles;
6. Power spectrum calculation and display.

Result: For sleep scoring, users simply browse through the data and add a score with a single key press. Other operation are interfaced through a user friendly GUI. FASST is implemented in Matlab and relies on SPM8/12 (Welcome Trust Centre for Neuroimaging, UCL, London, UK) data format. Some data formats (BrainAmp, EGI, EDF)

are directly converted by FASST, others can be imported with SPM. This ensures that data can be further processed with any of the SPM8/12 tools and all the saved information (sleep scoring, events, artefacts) is directly available for further analysis.

Conclusion: This could be a valuable tool for the reviewing, processing and analysis of multichannel M/EEG recordings, in particular for paradigms where no stimuli are administered to the subject and the spontaneous fluctuation of brain activity is studied. The toolbox is available for free download here: http://www.montefiore.ulg.ac.be/~phillips/FASST.html

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Heart rate variability evaluation of sleep mattress breathing categories

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Objectives: Sleep has its own internal structure in which autonomous nervous system regulation is very dominant. Heart rate variability (HRV) analysis of obstructive sleep apnea patients reveals an increase in sympathetic activity. In addition to polysomnography, nocturnal breathing can be assessed with sleep mattress sensors. Sleep disordered breathing (SDB) diagnostics can be performed with mattress sensor by dividing the signal into different breathing categories. In addition to normal breathing (NB), and periodic apneas/hypopneas (POB), the mattress sensors unveil a breathing category consisting of sustained partial obstruction (increased respiratory resistance, IRR). The aim of our study was to evaluate HRV during these three breathing categories.

Methods: 53 patients with suspected SDB underwent an overnight polysomnography with an Emfit mattress sensor. The mattress signal was scored visually into different breathing categories in 3-min epochs according to established rules, and confirmed with oesophageal pressure measurement as a part of polysomnography. Evaluation of HRV in NB, POB, and IRR was calculated from at least 6-min epochs after combining all NB-, POB- and IRR-epochs to as long periods as possible.

Results: HRV parameters revealed an increase of sympathetic tone during POB compared to NB and IRR. There was no increase of sympathetic tone during IRR, but interestingly parasympathetic activity increased.

Conclusions: The HRV findings during POB resembled HRV results of sleep apnea patients but during sustained prolonged partial obstruction (called IRR) a shift towards parasympathetic activity was achieved. The mattress-type movement sensors are inexpensive and unobtrusive, and thus provide interesting tool for sleep research.

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P548

Evaluation of compressed tracheal sound patterns in screening of sleep-disordered breathing

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Objectives: There is an increasing need for unobtrusive and semi-automated sleep screening methods. Devices like microphone and sleep mattress do not interfere with sleep. We wanted to evaluate the suitability of the compressed tracheal sound signal for screening different sleep-disordered breathing patterns. The previous results suggest that the plain pattern in the compressed sound signal represents mostly normal, unobstructed breathing, the thick pattern consists of periodic apneas/hypopneas, and during the thin pattern, flow limitation in the nasal cannula signal is abundant.

Methods: Twenty-seven patients underwent a polysomnography with a tracheal sound analysis and oesophageal pressure monitoring. The tracheal sound data was compressed and scored visually into three different breathing patterns. The percentage of oesophageal pressure values under -8 cmH_20, the minimum pressure value and the average duration of the breathing cycles were extracted from 10-min episodes of plain, thick and thin patterns. In addition, the spectral content of the tracheal sound during patterns were evaluated.

Results: The median percentage of time when the oesophageal pressure negativity increased was highest during the thin pattern and lowest during the plain pattern. In addition, the thin pattern presented more high frequency components in the 1001–2000 Hz frequency band of the tracheal sound.

Conclusions: Both the thick and thin patterns consisted of obstructed breathing, whereas during the plain pattern the breathing seems to be unobstructed. Most screening methods for sleep-disordered breathing reveal only periodic apneas/hypopneas, but with the compressed sound signal the sustained partial obstruction can be estimated as well.

Disclosure: The study was financially supported by Tekes, the National Technology Agency of Finland and by the Competitive State Research Financing of the Expert Responsibility area of Tampere University Hospital, Grant numbers 9M014 and 9P013.

P549

Overnight pulse wave analysis in patients with suspected sleep apnea and diabetes mellitus

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Objectives: Sleep is a specific window for the investigation of cardiovascular function. We developed an oximeter-based pulse wave analysis algorithm to continuously assess autonomic, cardiac

and vascular parameters during sleep. The current study aimed to characterize pulse wave derived parameters in patients with suspected sleep apnea and diabetes mellitus (DM).

Methods: DM patients and non-DM patients matched for age, body mass index (BMI), apnea hypopnea index (AHI) were selected from five sleep centers (n = 83/83, age 62.1 ± 10/62.3 ± 10 yrs, BMI 33.2 ± 6/33.3 ± 7 kg/m^2, AHI 21.7 ± 20/21.0 ± 20 n/h, respectively). Finger pulse wave signal was derived from overnight oximeter recording and pulse wave parameters (pulse variability, vascular stiffness, pulse wave amplitude, respiratory related pulse oscillations, heart rate response to episodic hypoxia and a composite cardiovascular risk score) were computed.

Results: Pulse variability index and hypoxia induced pulse variability were reduced in DM patients compared to controls (median [IQR] 18.7[30.5]/27.9[38.5] n/h, (−11.6 [34.3]/ −4.1[33.1] n/h, Wilcoxon test P = 0.018 and 0.034, respectively). Respiratory related pulse oscillations tended to be lower in DM patients vs. controls (29.3[18.2]/32.3 [26.0], P = 0.085). Vascular stiffness, pulse wave amplitude variability and cardiovascular risk score did not differ between the groups. Usage of beta-blockers was more frequent in DM patients compared with controls (n = 37 and 24, respectively, P = 0.045).

Conclusions: Measures of cardiac variability determined by overnight oximetry were altered in DM reflecting an influence of both DM and medication on cardiac chronotropy. Pulse wave parameters during sleep may be useful to classify CV dysfunction in DM patients with sleep apnea.

Disclosure: The study was supported by Weinmann GMBH, the Swedish Heart and Lung Foundation and the University of Gothenburg.

P550

Features analysis of actigraphic recordings for sleep/wake classification

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Objective: To analyze the discrimination power of individual data and statistical features from actigraphic recordings for sleep/wake (SW) classification using an Artificial Neural Network (ANN) automatic classifier.

Methods: Actigraphic recordings were performed in 119 healthy adolescents. Actigraphic data (ACT) recorded in 1-min periods were analyzed with an 11-min moving window, considering raw data and the natural logarithm of the current minute and the previous and next five. Features considered were based on previous studies [1]. The signal was pre-processed with a noise-rejection filter. Compared statistics included feature sets applying different tools – (a) mean and standard deviation, and (b) median and median absolute deviation (MAD) – plus time of the day and current minute ACT for both, and were used as inputs to an ANN classifier.

Results: A 5 × 2 cross validation was conducted testing four ANN classifiers, trained with different feature sets. Combinations of mean and standard deviation or median and MAD calculated on the natural logarithms of different segments of the moving 11-min window on ACT data were tried. The classifier using mean and standard deviation obtained the best performance, outperforming previous studies [1].

Conclusion: Several of the tested features added information; the mean of the logarithms of ACT stood up as a powerful discriminator between wakefulness and sleep; the mean acts as a low pass filter, revealing important differences between data distributions on sleep and wakefulness classes.

Support: FONDECYT-Chile Grants 1120319 and 1110513.

P551

Previous irregular sleep pattern may influence the first night effect

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Objectives: We aimed to evaluate the sleep architectural difference between the first and second night's sleep studies and to investigate the effect of the previous sleep pattern before the sleep study on first-night effect.

Methods: Total 30 young adult male subjects were recruited for the study and total 24 subjects participated in the study. During 1 week prior to study, the subjects kept a sleep-wake diary and wore actigraphs (Actiwatch-L, Mini Mitter) to identify sleep-wake cycle. Two consecutive nights of polysomonography were conducted. The two nights were compared using paired t-test. The standard deviation of sleep onset was used as an index of irregularity of the sleep-wake cycle. A linear regression test was applied to detect correlation between sleep irregularity and the first night effect.

Results: There were significant differences in the values of sleep efficiency (p-value =0.01) and WASO (p-value=0.006) between the two nights. The sleep study of the first night showed lower sleep efficiency and higher WASO compared to the study of the second night. Sleep irregularity of the previous sleep pattern showed a negative correlation with sleep efficiency (p-value < 0.001) and a positive correlation with WASO (p-value =0.023).

Conclusions: We could confirm the existence of first-night effect in this study. Our results suggest that the previous irregular sleep pattern may influence the first night effect.

Disclosure: Nothing to disclose.

P552

Can we define a threshold for MWT sleep latencies regarding driving risk?

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Objectives: Sleepiness at the wheel is a risk factor for traffic accidents. Past studies have demonstrated the validity of the Maintenance of Wakefulness Test (MWT) scores as a predictor of driving impairment in untreated patients with obstructive sleep apnea syndrome (OSAS), but there is limited information on the validity of the maintenance of wakefulness test by MWT in predicting driving impairment in patients with hypersomnias of central origin. The aim of this study was to compare the MWT scores with driving performance in sleep disorder patients and controls.

Methods: 19 patients suffering from hypersomnias of central origin (9 narcoleptics and 10 idiopathic hypersomnia), 17 OSAS patients and 14 healthy controls performed a MWT (4 × 40-min trials) and a 40-min driving session on a driving simulator. Participants were divided into 4 groups defined by their MWT sleep latency scores: pathological (sleep latency 0–19 min), intermediate (20–33 min), alert (34–40 min) and control (>34 min). The main driving performance outcome was the number of inappropriate line crossings (ILCs).

Results: Patients with pathological MWT sleep latency scores (0–19 min) displayed statistically significantly more ILC than patients from the intermediate, alert and control groups ($F (3, 46) = 7.47$, $P < 0.001$).

Conclusions: Pathological sleep latencies on the MWT predicted driving impairment in patients suffering from hypersomnias of central origin as well as in OSAS patients. MWT is an objective measure of daytime sleepiness that appears to be useful in estimating the driving performance in sleepy patients.

Disclosure: Nothing to disclose.

Ontogeny / Aging

P553

Sleep duration and cognitive performance in older adults: a systematic review and meta-analysis

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Objectives: To estimate the risk for lower cognitive performance associated with long and short sleep in older adults.

Methods: We performed a systematic search of publications in English using MEDLINE, PUBMED, PSYINFO (1990–2013), and manual searches. We included studies that were

1. Cross-sectional or
2. Prospective with self-report sleep duration at baseline and cognitive assessment at follow-up of at least 1 year.

Sleep duration was assessed by questionnaire, and cognitive performance through neuropsychological tests. We extracted odds ratios (OR) and 95% confidence intervals (CI) and pooled them using a random effects model.

Results: The 9 cross-sectional and 6 longitudinal studies analyzed provided 21 independent cohorts (n = 54 639). Long sleep was associated with higher risk for lower cognitive performance (OR: 1.62; 95% CI: 1.46, 1.81), and so was short sleep (1.33 [1.21, 1.46]). In fact, these risks varied with cognitive domains. For long sleepers, the risk for poor working memory / executive function was 92% higher than normal sleepers (CI: 1.52, 2.43), while the risk for poor verbal memory and general cognitive performance was respectively 69% (1.31, 2.17) and 38% higher (1.17, 1.63). In contrast, for short sleepers, the risk for lower general cognitive performance were 43% (1.12, 1.82), working memory / executive function 35% (1.18, 1.55), and verbal memory 22% (1.10, 1.36) higher than normal sleepers.

Conclusions: In older adults, self-report sleep duration and lower cognitive performance have a U-shaped association. Furthermore, subjective long and short sleep does not uniformly impact all cognitive domains.

Disclosure: Nothing to disclose.

P554

Sleep across the ages: paediatric, adult, and, geriatric idiosyncrasies

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Sleep disorders (SD) are prevalent across ages: the clinical signs, symptoms, and their manifestations vary according to age. Children may display symptoms of hyperactivity and insist they are not tired. Conversely, adults may complain of persistent fatigue, while geriatric populations may erroneously assume their sleep problems are the result of normal aging.

We constructed a 116-item questionnaire to use in conjunction with Nocturnal Polysomnography studies (NPS), Multiple Sleep Latency tests (MSLT), the Epworth Sleepiness Scale (ESS), and medical chart reviews of participants referred for evaluation of SDs. Additionally, we created a 12-item questionnaire for the pediatric group to assess both the child/youth and caregiver perspectives. We categorized 990 participants into three broad age groups: pediatric (age $\leq$ 16; n = 54); adult (age 17–64; n = 728); and geriatric ($\geq$66; n = 208).

Analyses comparing these groups resulted in both significant differences and similarities across groups depending on the variable. For example, cessation of breathing during sleep increased with age, while sleep walking, sleep talking, and family history of SD decreased with aging. Adults reported more sleep complaints even though geriatrics and children had greater intensity of sleep disturbance verified by NPS. All groups complained of anxiety, headaches and acid reflux. All groups had a prevalence of abnormal sleep architecture, though the patterns of time spent in specific stages of sleep varied across groups, with children spending more time in N3 and less time in REM.

Age specific characterizations of SD conveying patterns of similarities and differences advance knowledge to ensure best treatment modalities for all.

Disclosure: Nothing to disclose.

P555

Changes in sleep across the lifespan: using mathematical models to explore hypotheses to explain sleep timing

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Objective: Experimental measurements of the Mid-Sleep on Free days (MSF) have a characteristic ′n′ shape, with a rapid shift to later times during adolescence/early adulthood and a gradual drift back towards earlier times in mid- to older age groups. Our objective is to use mathematical models of sleep-wake regulation to investigate the biological mechanisms behind published experimental results of Roenneberg et al for MSF across the human life-span.

Methods: A systematic parameter study of the Phillips-Robinson model, a physiologically-based mathematical model of sleep/wake regulation, was carried out, giving computational results for MSF. The resulting computed data was fitted to experimental measurements of MSF.

Results: Good fit to the experimentally measured MSF could be obtained with two different hypotheses:
(i) that there is a simultaneous reduction in the circadian amplitude and in the strength of the homeostatic process as we age;
(ii) that only the strength of the homeostat changes.

Conclusions: The study shows that changes in sleep timing and duration that underlie the observed MSF could be the result of changes in both circadian and homeostatic rhythms with changes to the homeostat tending to reduce sleep duration and changes in circadian rhythms changing sleep timing. However, changing the strength of the homeostat in the mathematical model also increases the likelihood of sleep fragmentation. Increasing sleep fragmentation in turn induces changes in timing of sleep. Consequently, there is no

need for changes in the circadian rhythm to explain the MSF; changing the strength of the homeostat is sufficient.
Disclosure: Nothing to disclose.

P556

Caffeine chronic consumption during early post-weaning in rats negatively affects emotional status later in life

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Objectives: We recently found that postnatal day 21 (P21)-P30 is a sensitive period for sleep maturation in rats. Caffeine is known to affect sleep-wake regulation. Present study is aimed to assess the effects of chronic caffeine consumption during early post-weaning development on cognition and emotional status later in life.
Methods: P19 rats (n = 8) were implanted with EEG/EMG electrodes. Within P20-P30, four rats were treated with caffeinated water (0.3 g/L), whereas other four rats drank non-caffeinated water. On P21/P29, all rats were recorded for baseline sleep (BSL) at Zeitgeber time (ZT, hrs after the lights-on) 1–6. On P22/P30, the rats were subjected to sleep deprivation (SD, ZT1-4) followed by recovery period (ZT4-6). On P40, the rats were subjected to measures of locomotion, exploration and anxiety in the Open Field Test.
Results: During BSL, caffeine-treated vs. control rats spent more time awake (on P21, 61 $\pm$ 2.1% vs. 37 $\pm$ 2.7%; on P29, 49 $\pm$ 1.9% vs. 30 $\pm$ 2.4%, $P < 0.001$). During recovery, caffeine-treated rats slept less compared to the controls (P22, 54 $\pm$ 2.0% vs. 82 $\pm$ 1.8%; P30, 61 $\pm$ 2.9% vs. 87 $\pm$ 1.8%, $P < 0.001$). Caffeine-treated vs. control rats showed lower numbers of crossed squares ($P < 0.001$), rearing ($P < 0.05$), and central area entries ($P < 0.05$) during the first 5 min from the beginning of the test. Caffeine-treated rats showed increased grooming frequency compared to the controls ($P < 0.05$).
Conclusions: Caffeine treatment across P20-30 disrupts normal development of sleep, and it negatively affects emotional status in young adulthood.
Disclosure: Supported by the U.S. Department of Veterans Affairs, NIH Grant MH63323, Sh. Rustaveli NSF #31/61.

P557

Associations between nocturnal sleep and daytime functioning in 206 healthy young, middle-aged and older participants

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Objectives: Sleep and cognition both change with advancing age even in healthy individuals. It is widely assumed that sleep is an important contributing factor to brain functioning. However, little is known about the extent to which individual differences in sleep are associated with variation in waking performance. The present study aimed to investigate the relationship between nocturnal sleep and daytime cognitive performance across a wide age range.
Methods: Polysomnographically assessed nocturnal sleep and next day waking performance were analysed in 206 (92 males and 114 females; age range: 20–84 y) healthy and carefully screened volunteers without sleep disorders who were resident in a Clinical Research Centre for the duration of the study.
In order to assess attention, psychomotor speed, executive function and working memory, all participants completed a computerised performance test battery five times per day.
Results: Slow-wave activity, sigma activity, REM sleep and sleep efficiency as well as 24 out of 29 indices of waking performances all diminished significantly with age.
Many sleep indices, and in particular slow-wave activity, sigma activity and sleep efficiency significantly correlated with many daytime performance measures, such as the Digit Symbol Substitution Test and the Verbal 2-back Memory Task. However, nearly all correlations fell to non-significant levels when age and sex were partialled out.
Conclusions: Sleep affects waking performance in ways that are closely associated with the ageing process. The separate independent contribution of sleep to the observed decline in cognition with age is difficult to ascertain.
Disclosure: Nothing to disclose.

P558

Neonatal sleep restriction induces pronociceptive behaviour and changes in c-Fos expression in periaqueductal gray of adolescent mice

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Objective: Sleep is a physiological event able to promote proper brain activity to the sensory systems in which development is dependent upon activity, such as the nociceptive system. Sleep loss during the critical period for development can lead to negative implications for the maturation process of nociceptive response. We tested the hypothesis that neonatal sleep restriction induces a long-term increase on nociceptive response, and that this hypersensitivity occurs due to changes in the activity of nociceptive pathways.
Methods: Neonatal mice at postnatal day (PND) 12 were randomly assigned to the following groups: control group (CTRL), sleep restriction (SR) and maternal separation (MS). The SR and MS were performed 2 h/day during 10 days (PND 12 until PND 21). The method of gentle handling was used to prevent sleep. At PND 35 or PND 90, mice were tested for nociceptive response. Mice were perfused, their brains harvested and immunohistochemically stained for c-Fos protein in anterior cingulate cortex, primary somatosensory cortex and periaqueductal gray.
Results: Neonatal SR significantly increased the nociceptive sensitivity in the hot plate test (−23.5% of pain threshold). This alteration in nociceptive response was followed by decrease in c-Fos expression, a neuronal activity marker, in the periaqueductal gray. The pronociceptive behaviour present during adolescence did not persist until adulthood with all mice showed comparable nociceptive response.
Conclusions: Repeated exposures to sleep loss during early-life period are able to induce mild-term changes in nociceptive response associated with alterations of neural activity in descending control of pain.
Disclosure: Nothing to disclose.

Chronobiology

P559

Health hazards accumulate to evening chronotype

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Objectives: Diurnal preference for eveningness predisposes to a range of health hazards. We have studied association of chronotype to life habits as well as to several health issues.

Methods: Our sample of 3696 women and 3162 men, aged 25 to 74, is based on the National FINRISK Study 2007 in Finland. Data consists of information from study questionnaires, health examination, laboratory measurements as well as information gathered from national hospital records. Chronotype was assessed based on six items from the original Horne-Östberg Morningness-Eveningness Questionnaire.

Results: In our studies, the evening chronotype associates not only with unhealthy lifestyles, but also with sleeping problems and the increased odds for depression, type 2 diabetes, hypertension, bronchial asthma and spinal diseases. Diurnal preference for morningness lowers the odds.

Conclusions: We conclude that assessment of the chronotype is important when evaluating health hazards.

Disclosure: Nothing to disclose.

P560

What could 'owls' do in our ancestral environment? Evolutionary chronotypological account for the origin of nocturnal lifestyle

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Objectives: Since evolutionary process is slow, the human brain was designed for and adapted to the ancestral rather than today's environment. Therefore, genetic predisposition of young adults, especially males, to nocturnal lifestyle requires explanation.

Methods: The questionnaire self-assessments were collected from 2054 native and non-native residents of Turkmenia, Siberia, Yakutia, Chukotka, and Alaska. They were analyzed to detect age- and sex-associated differences in the preferences for early-late wakeups and early-late bedtimes. The revealed differences in early-late bedtimes were then used for predicting age- and sex-associated differences in the 24-h time course of subjective sleepiness in healthy adults (54 males and 76 females).

Results: The pattern of age- and sex-associated differences was found to be similar in all studied linguistic and ethnic groups. The prediction of such differences was confirmed in the experimental study and through the model-based quantitative simulations of 24-h time course of sleepiness in participants with early, moderately late and extremely late bedtimes.

Conclusions: The questionnaire-based findings on age- and sex-associated differences might be regarded as cross-culturally replicated differences. The questionnaire, experimental and simulation results supported the suggestion that the preference for late bedtimes might have been the target of sexual selection. It is hypothesized that this preference evolved due to sexual division of daytime labor in ancestral societies to solve an adaptive problem of creation of a temporal (early night) lek for displaying throughout courtship various human-specific behaviors advertising high cognitive, music, gymnastic, artistic, language, and humor abilities of young male adults.

Disclosure: Nothing to disclose.

P561

Seasonal variation in human executive brain responses

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It is well established that cognition shows daily fluctuations with changes in circadian phase and sleep pressure. The physiological impact of season changes, which is well characterized in animals, remains largely unexplored in human. Here we investigated the impact of seasonal variation on human cognitive brain function.

This cross-sectional study, conducted in Liège (Belgium), spanned from May 2010 to October 2011. Following 8 h baseline night of sleep, 30 volunteers (age 20.9 ± 1.5; 15F) spent 42 h awake under constant routine conditions (<5 lux, semi-recumbent position, no time-cues). After 12 h recovery night, they underwent 15 min fMRI recording while performing a working memory 3-back task (3b) and a letter detection 0-back task (0b). Thus, fMRI data were acquired when volunteers had been in isolation under controlled conditions for 63 h. Executive brain responses were isolated by subtracting 0b activity from 3b responses (3b > 0b). Analysis tested seasonal influence on executive brain responses at the random effects level, using a phasor analysis across the year. Inferences were conducted at $P < 0.05$, after correction for multiple comparisons over a priori small volume of interest. Significant effects of season on executive responses were detected in middle frontal and frontopolar regions, insula, and thalamus, with a maximum response at the end of summer and a minimum response at the end of winter. These brain areas are key regions for executive control and alertness.

These results constitute the first demonstration that seasonality directly impacts on human cognitive brain functions.

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P563

Chronotype-dependent nap behaviour in shift workers

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Objectives: Shift-work is the most ruthless disruption of the biological clock in modern societies. Individuals frequently develop behavioural coping mechanisms (*e.g.*, napping) to overcome sleep deficits, which are common in shift-workers. Beyond compensating for acute sleep loss, napping is suggested to be a long-term countermeasure for shift-work-associated health risks. In this field study we analysed the nap behaviour in shift-workers based on employees' internal time.

Methods: Chronotype was assessed with the $MCTQ^{Shift}$ in 119 employees working forwards rotational shifts (start times: MS: 6a.m.,

ES: 2p.m., NS: 10p.m., age=20–57 years, 26.2% females). Nap times, durations, and frequencies were derived from daily sleep logs. T-tests, repeated measures ANCOVAs, and multiple regression analysis were used to explore the nap behaviour (frequency, duration, and timing) in regards to chronotype.

Results: Nap behaviour was chronotype-dependent: early types napped predominantly, longest, and most frequently on night shift days, late chronotypes on morning, and intermediate types on both extreme shift days ($P < 0.01$). Chronotype and the duration of the main sleep episode influenced nap behaviour, the shorter the main sleep episode the higher the probability of taking a nap. Chronotype and age (which highly correlate) were significant predictors for nap frequency, duration, and timing ($P < 0.05$).

Conclusions: The analysis indicates that napping behaviour is an important coping mechanism when suffering from chronotype- and shift-work-dependent sleep deprivation. These findings add to the growing body of literature that stresses the importance of considering internal time when analysing the effects of shift-work on sleep, health, and cognition.

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P564

Assessment of difference in chronotypes between patients with multiple sclerosis and healthy controls

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Background: Sleep in multiple sclerosis (MS) patients has not been extensively studied although it is known that sleep disorders and sleep disruption is a very common symptom in this population. The aetiology behind these disturbances may come from many sources.

Patients and methods: By using the Morningness-Eveningness Questionnaire (MEQ) we assessed the chronotype of 193 participants, 100 MS patients and compared them to 93 healthy controls. The questionnaire consisted of 19 items, 14 Likert-scale based and 5 with time scales, the majority of questions were preferential, thus determining the subject's preferences, not the actual timing.

Results: Through analysis with the Mann-Whitney U test we found that the MEQ scores between the MS patient group and the healthy controls was statistically significant. The MS group had a median score of 52 and the control group had a median score of 46 ($P < 0.001$).

Conclusion: Although there was a correlation between MS and the MEQ questionnaire and previous research has confirmed that MS patients are more likely to wake up earlier, further research is needed to clarify the aetiology.

Disclosure: Nothing to disclose.

P565

Individual differences in the variability of sleep times across the week

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Evening types and younger individuals have been found to adapt better to shift work than do morning types and older individuals (Åkerstedt and Torsvall, 1981). We thus hypothesised that differences in usual bedtimes and differences in usual waketimes between weekdays and weekends for a sample of young students would be negatively related to morningness and age. We also investigated the relationship of these sleep variables to extraversion.

93 participants (all students, 47 males, 46 females, mean age = 21.3, SD = 3.5) reported their usual time of going to bed and usual time of waking, on weekdays and weekends. They also completed the extraversion scale on the Eysenck Personality Questionnaire-RS, and Horne and Östberg's morningness-eveningness (Mo-Ev) questionnaire, in which higher scores indicate eveningness.

Change in bedtimes (CHB) and change in waketimes (CHW) between weekends and weekdays were calculated for each participant [positive values indicate weekend times are later; mean CHB = 1.13 hrs (SD = 0.76), mean CHW = 1.71 hrs (1.05)]. In regression analyses CHB was found to be predicted by age (standardised beta = −.190, $P < .05$), Mo-Ev (standardised beta = .196, $P < .05$) and extraversion (standardised beta = .269, $P < .01$), CHW was predicted by age (standardised beta = −.231, $P < .05$).

Even in this somewhat young sample the within-subject variation in bedtimes across the week was negatively related to age and positively related to eveningness and extraversion, and the within-subject variation in waketimes was negatively related to age.

Disclosure: Nothing to disclose.

P566

Effects of lunar phase on sleep in men and women in Surrey

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Objectives: Recently, evidence has emerged that moon cycles may modulate subjective sleep quality and sleep structure in humans. We aimed to further explore the effects of circa-lunar periodicity (~29.5 days) on subjective and electrophysiological properties of human sleep.

Methods: Sleep records of 205 (91 males and 114 females; mean age 47.47, SD = 19.01) healthy and carefully screened participants who were admitted to the Surrey Clinical Research Centre were analyzed. Sleep was recorded in windowless sleep laboratories. For each study night, we calculated the distance – in days – to the date of the closest full moon phase. We subdivided the resulting distance in three lunar classes. Multivariate analysis of variance, with factors Lunar Class, Age and Gender was applied to selected sleep parameters.

Results: No significant main effect for the Lunar Class factor was observed for any of the investigated sleep parameters but some significant interactions were observed. The interaction between Lunar Class and Gender was significant for Total Sleep Time and duration of REM sleep. In addition, the interaction between the factors Lunar Class, Age and Gender was significant for the duration of REM sleep.

Conclusions: These data provide limited evidence for an effect of the lunar cycle on human sleep and suggest that effects may depend on age and gender of the participants.

Disclosure: Nothing to disclose.

P567

Sleep habits in a representative sample of the Swiss population

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Objectives: The prevalence of short sleep (5–6 h) increased from 19.7% to 26.7% from 1977 to 2009 in the US. Here, we document Switzerland's sleep based on a representative sample of 2011 and compare it to the situation 28 years ago (1983).

Methods: The 2009 residents (age range 12–95y) were surveyed by means of a computer-assisted telephone interview. Quotas were defined for age, gender and working state in accordance with the population structure.

Results: Mean sleep duration was of 7:24 h (1.1 SD) on workdays and of 8:26 h (1.9 SD) on free days. Sleep timing (i.e. ready to sleep after lights off) was on average at 23:03 h (1.2 SD) for workdays and at 23:39 h (2.1 SD) for free days, while average rise time was 6:27 (1.1 SD) on workdays and 8:06 (1.8 SD) on free days, both significantly modulated by age and gender. Compared to 28 years ago, Swiss slept on average 40 min less on workdays and 35 min less on free days, and sleep timing was delayed by 1 h, while the percentage of short sleep (5–6 h) during workdays increased from 5.4% to 6.7%.

Conclusions: Compared to other nations (e.g. US, UK), Swiss people have on average earlier sleep/wake times and longer sleep durations. However, compared to almost 3 decades ago, a larger relative trend to shorter sleep duration was observed for Switzerland compared to the US.

The study was supported by the FOEN and the Noise Abatement Commission.

Disclosure: Nothing to disclose.

P568

Association between morningness/eveningness, addiction severity and psychiatric disorders among individuals with addictions

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Objective: Chronotype, or morningness-eveningness preference, is defined as a 'continuum' between two extremes; morning-type (MT) and evening-type (ET). Several studies have shown that ET subjects used more stimulating and sedative substances, and were more likely to present psychiatric disorders than MT subjects. However, there is a lack of data on the chronotype of patients with addiction. The aim of our study was to describe chronotype and associated factors in a sample of outpatients beginning treatment for addiction (substance and non-substance).

Methods: Subjects were recruited in an outpatient addiction treatment center. Chronotype was assessed with the morningness-eveningness questionnaire (MEQ) of Hörne & Ostberg. Associated factors (addiction severity, socio-demographic characteristics and psychiatric co-morbidities) were evaluated with the Addiction Severity Index (ASI) and the Mini International Neuropsychiatric Interview (MINI). A multivariate model was fitted with all variables that showed a significant association in the univariate model.

Results: Three hundred and thirty three dependent (use disorder) subjects were included in this study. ET (32%) was more prevalent than MT (20%). Multivariate analysis showed that lower MEQ score (Eveningness) was significantly associated with non-substance addictions (gambling, eating disorders,. . .) and mood disorders, but not with severity of addiction. Morningness was associated with antisocial personality disorder.

Conclusions: Results suggested that chronotype was not associated with addiction severity directly, but indirectly through psychiatric disorders and ET was more associated with non-substance addiction than substance addiction.

Disclosure: Nothing to disclose.

P569

Sleep and fatigue among officers on board gas tankers

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Objectives: Fatigue is a growing safety concern in the maritime industry; especially on board gas tankers, safety is of crucial importance. Therefore, this field study investigates sleep and fatigue levels on board routinely operating gas tankers.

Methods: Twenty two officers working on 2 gas tankers from a Dutch shipping company participated on a 10-day voyage through European waters, working either day work (n = 16) or on 4 h on/8 h off watch system (n = 6). Sleepiness (Karolinska Sleepiness Scale, KSS) was rated hourly, neurobehavioural performance (Sustained Attention to Response Task, SART) at the start and end of each work period. Sleep and sleep quality was assessed using actigraphy and diaries. Sleepiness ratings were also correlated to predictions based on the three-process model of alertness regulation.

Results: Sleepiness peaked around 4 AM in both watch keepers (KSS=5.5) and day workers (KSS=6.2) and correlated well with model predictions (average r = .60, P < .001). Average sleep efficiency was 88% – with no difference between watch keepers and day workers. Daily sleep duration was shortest in those working 08-12 (6 h), and longest in those working 00-04 (8 h). Day workers slept about 6.5 h/day. Errors on the SART were most frequent at night and were 35% more frequent at the end of a working period compared to the beginning.

Conclusions: Highest sleepiness is reached in line with model predictions (i.e. around 4 AM). Although no sleep on duty was observed, the fact that neurobehavioural performance declined with time at work may be of risk.

Disclosure: Nothing to disclose.

P570

Long term sleep and fatigue at sea: a field study

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Objectives: Although anecdotal reports are frequent, real field studies on long-term fatigue and sleep at sea are lacking. This will be the first such study.

Methods: Two European shipping companies participate with volunteers from the entire crew of, in total, 8 ships during their routine operations for a period of, on average, 15 weeks at sea. Sleep is assessed using weekly sleep diaries together with actigraphy. Sleepiness (Karolinska Sleepiness Scale) is rated 2-hourly during a full day every week. Fatigue (Multiple Fatigue Inventory) is measured weekly. Preliminary analysed background questionnaires of participants (n = 23) reveal what is typical sleep/wake-behaviour in the seafarer.

Results: Average working-time is 69 $\pm$ 11 h/week and 83% of seafarers do overtime work at least once a week. 50% of seafarers report having split sleep (2 sleeps of >1.5 h per 24 h). Self reported daily sleep need is 8,2 $\pm$ 1.1 h, self reported daily sleep duration 7.7 $\pm$ 1.5 h. 70% naps once a week or more. Twice as many report being morning type as compared to evening type. 43% report higher fatigue levels at the end of a journey at sea compared to the start. Coffee consumption is considerably higher during working days (2.8 $\pm$ 1.9 cups) than during days off (1.0 $\pm$ 1.2 cups).

Conclusions: Preliminary analyses give a highly interesting insight into sleeping habits at sea. Full analyses of the field studies including long term fatigue, sleep and sleepiness at sea will be carried out during the summer and presented on site.

Disclosure: Nothing to disclose.

P571

Effect of circadian thermoregulatory phase in recovery of both temperature and rest/activity rhythms after a standard physical exercise in rats

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Objective: Core temperature circadian rhythm results from both endogenous regulation factors and external factors such as physical activity. Physical exercise induces higher rise of temperature when performed during the circadian rising phase ('heatgain phase') compared to the circadian falling phase ('heatloss phase'). However, effects of thermoregulatory circadian phase on body core temperature (BCT) and rest-activity rhythms after exercise remained to be explored by further investigations.

We hypothesize that the thermoregulatory phase during which a physical exercise is performed would modulate both core temperature rhythm and activity-rest rhythm mediated by the hypothalamus. Indeed the preoptic area (POA) plays a crucial role in the regulation of BCT after thermal stress, locomotor activity and sleep initiation.

Methods: Fifteen males Wistar rats (300–320 g) performed a forced treadmill running trial (15 min, 30 $cm.s^{-1}$) during both the heatloss and the heatgain phases to induce a thermal stress. BCT and spontaneous locomotor activity were continuously monitored by telemetric pills temperature (Anipill®) and infrared actimetry boxes (Imetronic®) during 48 h before and after each exercise trial.

Results: Preliminary results suggest that exercise performed during the heatgain phase induces a higher thermal rise associated with a lower spontaneous motor activity after the exercise. Moreover, the recovery of the thermal rhythm is faster during heatloss phase.

Conclusions: This study offers a better understanding of the involvement of thermoregulatory phase of a physical exercise on BCT and rest-activity rhythms. Direct exploration of POA involvement in the relationship between thermoregulation and sleep will be further investigated.

Disclosure: Nothing to disclose.

P572

Naturalistic field study of sleep and performance in truck drivers: effects of the number of nights in the restart break between duty cycles

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Objectives: In the US, Commercial Motor Vehicle (CMV) drivers must take a 34 h restart break after each duty cycle. For nighttime drivers – who routinely experience sleep restriction – a 34 h restart break contains only one night, which laboratory studies have shown is insufficient for sleep recuperation. New US hours-of-service regulations therefore require drivers to include at least two nights (01:00–05:00) in their restart break. A naturalistic field study was conducted to investigate the effectiveness of this new rule.

Methods: One hundred and six CMV drivers (ages 24–69, 6 females) logged duty and sleep times and wore an actigraph throughout two duty periods and the intervening restart break. They performed a 3 min psychomotor vigilance test (PVT) three times a day. A lane tracking system measured lane deviation while driving.

Results: During duty cycles after restart breaks containing only one night, compared to two or more nights, drivers showed nighttime-oriented duty patterns ($P < 0.001$) and daytime sleep ($P < 0.001$). They also exhibited significantly more PVT lapses (reaction times >500 ms) ($P = 0.015$) and greater lane deviation ($P = 0.001$). Restart breaks contained predominantly nighttime sleep ($P < 0.001$).

Conclusions: CMV drivers with only one night in their restart break were primarily nighttime drivers. They showed reduced PVT and driving performance compared to drivers with more than one night in their restart break. They reverted to a predominantly nighttime sleep schedule during the restart break. Thus, adding a night to the restart break should be effective at providing greater opportunity for sleep recuperation, and may thereby mitigate performance impairment.

Disclosure: Nothing to disclose.

P573

Age-dependent non-visual effects of a moderately bright light exposure during 40-h of extended wakefulness

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Objectives: Here we examined the role of extended light exposure as a countermeasure for sleep-loss related decrements in sleepiness and cognitive performance as well as on melatonin and cortisol profiles in young and older volunteers.

Methods: Twenty-six young and twelve older participants underwent 2 or 3 times 40-h of extended wakefulness under dim light (DL: 8 lux), and either white light (WL: 250 lux) or blue enriched white light (BL: 250 lux) exposure. Questionnaires were administered hourly to assess subjective sleepiness, along with saliva collections for melatonin and cortisol assays. Cognitive tests were completed every 2 h.

Results: Moderately bright light during sustained wakefulness induced a significant alerting response in the older and the young participants (light condition $P < 0.0001$). In contrast, melatonin

suppression was only significant in the young participants during both non- and blue enriched light (light x time of day $P < 0.0001$). Contrariwise, no differences were found under WL exposure, but under BL, cortisol levels were significantly increased in the older while decreased in the young. Furthermore, no significant differences were observed in both age groups under BL exposure in the visual 3-Back test. Whereas, under WL, performance in the young was reduced after 22 h of extended wakefulness.

Conclusion: Our data indicate an age-related modulation of the non-visual response to light at 250 lux under extended wakefulness. Thus, the use of moderately bright light in night work and shift work settings, where constant light levels are very common, may have differential effects on young and older workers.

Disclosure: Nothing to disclose.

P574

Nightmares are associated with seasonal variations in mood and behavior

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Objectives: Nightmares are emotionally negative and disturbing dreams that lead to an awakening from sleep. Mood disturbances and sleep problems, as well as the use of antidepressants and hypnotics, are strongly associated with nightmares. Thus, we hypothesized that nightmares are also more frequently experienced by individuals who report seasonal variation in mood and sleep patterns.

Methods: The current study utilized data from the National FINRISK study from Finland. The surveys consist of random cross sectional population samples from adults aged 25–74 who fill in a comprehensive health questionnaire including items on sleep and mental well-being. Nightmares were assessed with self-estimated frequency during the last month and seasonality by the Global Seasonality Scale. In the current study, the additional questionnaire of the survey of 2012 was used ($N = 4\,777$).

Results: Preliminary analyses show that nightmares are significantly associated with seasonal fluctuations in mood, energy level, social activity, sleep duration, appetite, and weight (χ^2-tests, all p values < .0001, Cramer V effect sizes vary from 0.094 to 0.177). Further, there is a linear association between the frequency of nightmares and the severity of symptoms related to the seasonal variations.

Conclusions: Nightmares are associated with seasonal variations in mood and behavior, most strongly with changes in mood, social activity, and energy level. These results give rise to an intriguing possibility that there are common etiological factors behind deviated regulation of mood and emotions with seasonal variations and nightmares.

Disclosure: Nothing to disclose.

P575

Chronotype, genotype and sleep behaviours in adolescents; the effect of technology access on preferred and actual behaviour

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Objectives: There are no studies of genotype, chronotype and sleep patterns in adolescents. Adolescence is associated with a phase shift in sleep, and an increase in social interaction and other activities that may influence sleep preference and patterns. This study examined the association between the Period 3 (Per3) gene, chronotype, sleep patterns and social context in adolescents and young adults.

Methods: Adolescents ($n = 38$ [12–19 years]) and young adults ($n = 9$ [20 years and over]) completed the Morningness-Eveningness Questionnaire (MEQ), the Pittsburgh Sleep Quality Index (PSQI) and diary measures of sleep and wake behaviour (4 days). Participants also provided buccal swabs that were used for genotyping for the Per3 gene.

Results: There were 22 4/4, 20 4/5 and 5 5/5 genotypes, and the categorisation to chronotype by MEQ indicates there were 5 morning types, 14 evening types and 28 intermediate types. There was no consistent association of genotype and chronotype. Correlation analyses revealed significant association of age, chronotype (MEQ), social media use and daily sleep and activity patterns. Patterns of daytime dysfunction and subjective sleep quality were associated with evening technology use, but not chronotype.

Conclusion: The results are discussed within a development theories perspective, and with reference to the social contextual influences on sleep and reported sleep-activity preferences and behaviour that may exert greater influence during the adolescent and emerging adult period. The increased opportunity for social contact in a digital world may contribute to changes in sleep patterns and preferences during adolescence.

Disclosure: Nothing to disclose.

P576

Is chronotype associated with cardiovascular risk factors?

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Objectives: We studied the association of chronotypes with risk factors of cardiovascular diseases in a sample of workers.

Methods: Participants were 1394 employees of a Finnish airline company (55% men, average age 44.6 yrs., age-range 24–65). Risks factors and covariates were measured twice (T1 and T2) with an interval of 3 years and chronotype (morning type, intermediate type and evening type) was assessed at T2. Evening type and morning type was compared to the intermediate chronotype. Analyses were done separately for T1 and T2.

Results: After controlling for age, sex and work schedule, evening type was associated with lower HDL cholesterol (T1 $P = .002$, T2 $P = .005$), higher triglycerides (T1 $P = .015$, T2 $P = .001$) and higher BMI

(T1 $P = .007$, T2 $P = .006$) compared to the intermediate chronotype. Findings for increased diastolic and systolic blood pressure and high sensitive CRP in the evening chronotype were inconsistent (diastolic blood pressure T1 $P = .159$, T2 $P = .023$; systolic blood pressure T1 $P = .663$, T2 $P = .023$; hsCRP T1 $P = .045$, T2 $P = .482$). Glucose levels did not differ between the chronotypes.

After additional adjusting for education, smoking, alcohol use and physical activity, the associations of evening type with triglycerides at T1 and hsCRP at T1 were no longer significant ($P = .069$ and $P = .073$, respectively).

Conclusions: The results indicate that evening chronotype is associated with aspects of cardiometabolic risk profile and may therefore predispose to the development of cardiovascular diseases.

Disclosure: Nothing to disclose.

P577

Cortical excitability dynamics during extended wakefulness set PVT performance

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Objectives: Alertness and vigilance are regulated by the subtle interaction of circadian and sleep homeostasis processes. However, brain mechanisms that underlie how this interaction impacts on alertness and vigilance remain scarcely understood, particularly at the neuronal level. Here we assessed the relationship between excitability of human cortical neurons and performance to a Psychomotor Vigilance Task (PVT), which probes sustained attention and phasic alertness, during extended wakefulness.

Methods: Twenty-two healthy young men (18–30y) followed 28-h sleep deprivation under constant routine conditions. During the protocol, they underwent 8 transcranial magnetic stimulation (TMS)-EEG sessions and 12 cognitive task sessions, in which they performed the PVT. Cortical excitability was inferred from the amplitude of the first TMS-evoked EEG potentials component over the prefrontal cortex, a brain region sensitive to sleep deprivation. We computed a linear regression between cortical excitability and PVT performance [median (MedRT), mean (MRT), slowest (SRT), fastest (FRT) reaction times and intermediate reaction times (INT; between fastest and slowest)].

Results: Analyses indicate a significantly positive regression between the overnight variation of cortical excitability, i.e. changes from morning after habitual sleep to the morning after sleep deprivation (27-h of wakefulness) and global PVT measures averaged across all cognitive task sessions (MedRT, MRT, INT and SRT; $r > .18$; $P < .05$). Collectively, our data show that higher changes in cortical excitability are associated to slower reaction times across all PVT variables analyzed.

Conclusions: Our data suggest that changes cortical excitability during prolonged wakefulness modulate overall performance to a vigilance task.

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P578

Influence of artificial dusk on sleep

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Objectives: Aim of the study was to elucidate an influence of artificial dusk on sleep of healthy sleepers.

Methods: Twenty-six participants with normal 5–6-day weekly active schedule, sleeping single in bedroom and naïve to the primary aim of the study completed two consecutive arms of the study, each consisting of 7 days baseline, 13 days intervention, and 8 days follow-up. The intervention was dusk and dawn simulation (dusk) compared to the rectangular light pulse prior to sleep time and dawn simulation (non-dusk). The 30-min dusk signal was preceded by 10-min of constant light to be similar with the 17-min non-dusk in the overall light dose. Throughout the study subjects were filling sleep diary immediately before and after sleep and wore actiwatches. Saliva for melatonin ELISA and circadian phase estimation was sampled prior to bedtime at home on days 7–8, 13–14 and 20 of each arm.

Results: The circadian phase was unchanged throughout the study. Of the 13 variables analyzed, only one showed a difference: number of minutes with movements during the first 40 min of sleep episode was lower at dusk presentation compared to both non-dusk presentation and pre- and post-dusk days ($P < 0.05$). In the end evaluation, 42–45% of subjects spontaneously pointed out an improvement of falling asleep with the dusk ($P = 0.057$ or $P = 0.041$ if include 7 withdrawn subjects), corroborating objective measurements.

Conclusions: Artificial dusk helps people to fall asleep more peacefully.

Funding support: Philips Consumer Lifestyle (The Netherlands).

Disclosure: Vanja Hommes is affiliated with the Philips Consumer Lifestyle who sponsored the study.

P579

Social jetlag in Korean people

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Objectives: The presence of social jetlag might be related to poor mental and cardiovascular health due to chronic sleep loss or circadian misalignment. We aimed to explore the relationship of social jetlag with cardiovascular and mental health at the population level.

Methods: We included 1038 subjects aged 20–40 years old (mean age was 44 years $\pm$ 11(SD), 484 women) who are randomly selected from the Korean general population. Demographic variables, sleep-wake pattern on working and free days,Pittsburgh Sleep Quality Index, Golberg short screening scale for anxiety and depression, and information on medical conditions were documented. Social jetlag was defined if there is any difference between midsleep time on working and free days. Corrected midsleep time on free days was an index of chronotype. Association of social jetlag with mental and cardiovascular health was analyzed.

Results: Social jetlag was present in 52.5%.In the group with social jetlag, average sleep duration was longer due to the weekend catch up sleep. Presence of social jetlag was related to lower body mass index and lower prevalence of diabetes and hyperlipidemia, but higher prevalence of depressive mood. Presence of hypertension and cardiovascular diseases was not different between two groups.

Conclusions: Against the hypothesis, social jetlag was related to lower cardiovascular risk and longer sleep duration. It suggests that the presence of social jetlag indicates weekend catch up sleep to compensate sleep debt on working days. The role of circadian misalignment is unclear.

Disclosure: Nothing to disclose.

P580

The effect of bright light treatment via ear canals (device VALKEE™) on mood and well-being in healthy subjects

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Objectives: Bright light is very important for the regulation of melatonin synthesis, which also influences mood, well-being and tiredness. In this study, we evaluated the effect of bright light utilising the device Bright Light Headset VALKEE™ on morning mood and well-being in healthy subjects.

Methods: The VALKEE™ is a mobile device for the application of light via ear canals to photosensitive receptors of the brain. Although the neurophysiological mechanisms of light perception over non-visual pathways are still under discussion, the VALKEE™ has shown beneficial effects in treating seasonal affective disorders. In this study, 20 healthy subjects were instructed to use the VALKEE™ over two consecutive weeks for 12 min in the morning, approximately 60 min after getting up. Before and after light application subjects had to document mood and well-being by 100 mm visual-analogue scales (VAS). Over the whole study period (3 weeks) the sleep-wake rhythm was monitored by diaries and wrist-worn actigraphs.

Results: Results are based on data sets of 16 subjects (mean age: 24.5 $\pm$ 3.4; 11 females). Under bright light application a significant improvement was found in mood (feeling good/bad) and well-being (tired/alert) after getting up in the morning as compared with baseline conditions (Wilcoxon-test: $p \leq 0.01$). This effect was also present in VAS mood ratings in the evening, but not in ratings of feeling tired/alert.

Conclusions: Although bright light application utilizing the device VALKEE™ is effective, most participants criticized the device for various reasons, most of them related to discomfort when wearing the ear plugs.

Disclosure: Nothing to disclose.

P581

Ultradian rest-activity rhythm of fetal movement starts in conceptual 28-weeks

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Objectives: Fetal movement is an important biological index of fetal well-being. Further, its ultradian rhythm would become an index of fetal neurophysiological development. Ultradian rest-activity rhythm of a fetus is observed by ultrasonography; however, its process is unclear. We developed an original sensor, device and analysis system (Fetal Movement Acceleration Measurement: FMAM, Med Eng Phy 34, 2012). We examined to observe a process on ultradian rhythm of fetal movement along gestational weeks.

Methods: The subjects were eleven healthy pregnant women. All mothers gave written informed consent to the study. We asked them to record fetal movement using FMAM at night on a fixed schedule, once every 4 weeks, from 24 to 36 weeks of gestation (24, 28, 32, 36 weeks). The FMAM analysis system with a function of excluding artifacts was used to detect fetal movement. Autocorrelograms were calculated using number of fetal movement per 1 min and a lag time from 0 to 150 min. Group mean autocorrelograms for all subjects were calculated for each week, and t tests were used (Physiol & Behav 77, 2002).

Results: There was not a peak on mean autocorrelogram in 24 weeks. However, in 28 weeks, there was a significant peak with ca. 70 min lag time. Peaks in 32 and 36 weeks were unclear and not significant. They tended to be longer than 70 min. This finding seemed to be individual differences on fetal development.

Conclusion: Ultradian rest-activity rhythm of fetal movement starts in conceptual 28 weeks.

Disclosure: Nothing to disclose.

P582

Working night shifts affects surgeons' biological rhythm

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Objectives: In medical residents, chronic sleep deprivation combined with work during the night is known to affect performance, increase the risk of medical errors and compromise residents' own safety. The aim of this study was to examine markers of circadian rhythm and the sleep-wake cycle in surgeons exposed to acute sleep deprivation due to night shifts in the clinical setting.

Methods: Thirty surgeons were monitored prospectively for 4 days: pre call, on call, post call day 1 (PC1) and post call day 2 (PC2). The urinary metabolite of melatonin (aMT6s) and cortisol in saliva were measured to assess the circadian rhythm. Sleep and activity was measured by actigraphy and sleep diary. The Visual Analog Scales (VAS) for fatigue, general well-being, quality of sleep and Karolinska Sleepiness Scales (KSS) were used for assessments of the surgeons' subjective conditions.

Results: For both aMT6s and cortisol, a statistically significant difference ($P < 0.05$) was found in the measurement period. The primary difference was between the on call values and the pre call values with normalization on PC1 for aMT6s and cortisol. There was increased sleep time during the day on call prior to work start and on PC1 compared with pre call and PC2. No correlation was found between the circadian markers and the VAS scales and KSS ($P > 0.05$ for all comparisons).

Conclusion: Surgeons' circadian rhythm was affected by working night shifts and their sleep pattern on PC1 resembled that of shift workers.

Disclosure: Nothing to disclose.

P583

Chronotype and P300 amplitude after chronic sleep restriction

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Objectives: P300, an event-related potential (ERP) considered to reflect information processing connected with attentional mechanism, is correlated to some individual differences. This study looked for the effect of chronotype on P300 amplitude in saccadic reaction in sleep restriction, i.e. the possible modifying role of morning-evening orientation for the vulnerability to sleep loss.

Methods: A dense-array EEG was recorded simultaneously with eye tracking in 22 subjects (11 females; mean age 22.7 $\pm$ 1.6 years). A spatial cueing paradigm was employed to induce leftwards and rightwards saccades. Congruent and incongruent trials were analysed separately. Measurements were scheduled four times a day, in two conditions: after a week of full recovery sleep and after a week of

partial sleep deprivation by 33% of individual sleep need. Chronotype was described as morning-evening preference (subjective phase) and magnitude of circadian fluctuations (subjective amplitude) with the Chronotype Questionnaire.

Results: The congruent trials revealed P3b potential (peak at 330 ms after target onset), whereas incongruent ones showed the P3a potential (peak at 280 ms). Chronotype (median split) did not differentiate mean amplitude, nor the range of diurnal changes of those potentials. The amplitude of P3a in sleep restriction was sensitive to the chronotype × time-of-day interaction, revealing the decrease for morning types (LSD post-hoc, 22:00 vs. other times – $P < 0.05$) and a stable diurnal pattern for evening-oriented individuals (LSD post-hoc n.s).

Conclusions: Chronic partial sleep deprivation induces changes in brain ERPs in saccadic reactions. Individual morning-evening orientation is reflected in diurnal pattern of P3a amplitude.

Disclosure: Nothing to disclose.

P584

Blue blocker glasses as a countermeasure for alerting effects of evening LED-screen exposure in teenagers

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Objectives: Adolescent's sleep and wake time preferences delay considerably compared to children or adults. Concomitantly, multimedia use in the evening is prevalent among teenagers involving light exposure, particularly in the blue-wavelength range to which the biological clock and its associated arousal promotion has its greatest sensitivity. We investigated whether the use of blue-light-blocking glasses (BB) during the evening, while sitting in front of a light emitting diodes (LED) computer screen, favours sleep initiating mechanisms at the physiological, subjective, and cognitive level.

Methods: Thirteen 15–17 years old healthy male volunteers were included. The ambulatory study part comprised 2 weeks, during which their sleep-wake cycle, evening light exposure and screen use were monitored. BB or clear lenses (CL) as control glasses were worn in a counterbalanced cross over design for 1 week each, during the evening hours while using LED screens. Afterwards, participants entered the laboratory and underwent a blue-enriched-LED-screen-light exposure for 3 h prior to habitual sleep time while wearing the same glasses than during the preceding week. Salivary melatonin, subjective sleepiness and vigilant attention data were regularly collected and subsequent sleep was recorded by polysomnography.

Results: Compared to CL, BB significantly attenuated LED-induced melatonin suppression in the evening ($P = 0.006$), decreased vigilant attention ($P = 0.008$) and increased subjective sleepiness ($P = 0.027$) prior bedtime. Visually scored sleep stages and behavioural measures collected in the morning after were not significantly affected.

Conclusion: BB glasses can be used as a countermeasure for alerting effects in the evening in adolescents using multimedia technologies with LED screens.

Disclosure: Nothing to disclose.

P585

Short day forced desynchrony in C57BL/6J mice leads to arrhythmia and sleep disturbances

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Objectives: Clock gene transgenic/mutant mice have played a critical role in understanding the molecular basis of circadian rhythms generation, but such models often show a range of abnormal physiology and behaviour. These co-morbid changes confound the study of the mechanistic links between circadian disruption and sleep, and their impact upon cognitive processes. Here we induced a circadian disruption in healthy mice using a light-dark cycle outside the range of entrainment to study the effects of circadian disruption on sleep.

Methods: C57BL/6J ($n = 5$; 15–17 weeks old) were implanted with DSI-telemetry EEG/EMG/CBT transmitters on 12:12 Light-Dark (LD) cycles (T24). After surgery recovery, continuous EEG/EMG/CBT recordings were obtained under 10:10LD cycles. The 1st 10:10LD (T20) cycle started at dark-onset (ZT12 of the previous 12:12LD). The dark-onset of the 4th T20 occurred out of the phase (beginning of the subjective day based on preceding T24). Periodogram analyses were performed on the activity/temperature data. EEG data was scored per 10-s epochs.

Results: Mice were arrhythmic throughout the fourth to fifth T20 cycles. During the first and 4th T20 cycle, time spent in each vigilance state (NREMS: 1st:44.0 ± 1.3; 4th:44.5 ± 0.3; REMS: 1st:8.0 ± 0.4; 4th:8.7 ± 0.8; % of total recording time) did not differ between cycles. The Light-Dark ratio of sleep (measure of nocturnality/diurnality) was normal during the first T20 (NREMS: 1.52 ± 0.07; REMS: 2.92 ± 0.52) but highly affected during the 4th T20 (NREMS: 0.88 ± 0.07; REMS: 0.61 ± 0.12).

Conclusion: These preliminary data shows that mice under T20 become arrhythmic. Under these conditions, sleep architecture is highly disrupted with reduced sleep during the light phase.

Disclosure: Nothing to disclose.

P586

Change to higher illuminance and light colour temperature in open office, implications for sleep and sleepiness in Scandinavian winter

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The study followed a change of luminaires and affects on recovery, sleepiness and light appraisal during work in an open office.

Fifty-two office workers in two rooms were introduced to changes from use of fluorescent tubes (3000K), giving 400–500 lx at the desk, to systems (4000K) giving 700–860 lx. In one room the number of tubes were increased and in the second room an in-built LED-lighting was introduced (Philips Soundlight Comfort Ceiling). The workers were followed 1 week in winter using original fluorescent tubes, a second week after change and 1 month later. Workers gave daily ratings and wore actigraphs. For analyses, a repeated measures mixed model was used.

The new lights were found being more stimulating, inspiring, promoting readability ($P < 0.001$), giving a more favourable overall rating and appreciation of the LED solution ($P < 0.05$). Sleepiness and perceived energy ratings, given six times each day of study showed an effect of week ($P < 0.001$), showing a reduction of

sleepiness and increase of energy across weeks. Actigraph recordings from 34 workers showed an advanced start of sleep ($P < 0.001$;11 min) and sleep duration increased both at work ($P < 0.05$, m_week1 = 394 $\pm$ 8; m_week3 = 406 $\pm$ 8 min) and during weekends ($P < 0.01$, m_week1 = 440 $\pm$ 19; m_week3 = 482 $\pm$ 22 min).

A higher colour temperature in combination of a higher illuminance appears to reduce sleepiness and improve energy status among office workers compared to standard tubes and positively affect sleep. Several visual areas seem to be positively improved including readability and visual comfort.

Support: Swedish Energy Agency, Philips Lighting.

Disclosure: Researchers (van der Zande, Geerdinc) work at Philips, supplying lighting of study.

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P587

Sleep-dependent changes in learning-related magnetic evoked fields in children

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Objectives: Behavioural studies have highlighted a beneficial impact of post-training sleep on the consolidation of declarative memories in children. However, the underlying cerebral mechanisms remain barely investigated. We used magnetoencephalography (MEG) to investigate the impact of a 90-min diurnal sleep (nap) on the brain processes subtending memory retrieval after learning functional properties of novel objects, i.e. a core mechanism in the development of conceptual and declarative knowledge in children.

Methods: Twenty-one children were scanned using MEG (Elekta Oy, Finland) during three picture-definition sessions, i.e. pre-learning [session 1; S1], immediate retrieval [S2] and delayed retrieval [S3]). S2 and S3 were separated by either a 90-min nap (sleep-group; N) or a similar period of wakeful rest (Wake-group; W). Children were randomly assigned between conditions. After MEG data preprocessing, immediate (S2) vs. delayed (S3) retrieval Event Related magnetic Fields (ERFs) were compared between groups, first in sensor then in source spaces.

Results: Although similar behavioural patterns were observed in W and N participants at S2 and S3, results in sensor space disclosed a sleep-dependent ERFs modulation for newly learned non-objects, developing 450–650 ms after stimulus onset ($p^{corr} < .05$). Analyses in the source space windowed over this late temporal component of interest disclosed underlying activity in the left medial prefrontal cortex (−12.40,-12; $p^{svc} < .05$), in a location previously associated in adults with long-term overnight storage of verbal declarative memories.

Conclusions: Our results suggest that sleep in children like in adults subtend memory consolidation and a sleep-dependent functional reorganization of learning-related brain circuits.

Disclosure: Nothing to disclose.

P588

The role of rapid eye movement sleep for the consolidation of emotional stories

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Objectives: Our study aimed at delineating the role of Rapid Eye Movement (REM) sleep in the consolidation of emotional memories.

Methods: After being slightly restricted of sleep the night before the experiment, participants learned a neutral or a sad story in the morning, and were then assigned to either a short nap (44 (±13) minutes; $n = 11$) or a long nap (duration 90 (±12) minutes; $n = 11$). After the nap, they had to recall the story based on structured questions, while mood and emotional state were assessed via questionnaires and skin conductance measurements.

Results: As expected, REM sleep was more abundant in the long (19.5 (±11 min) than in the short nap (2.8 (±6 min), $P < .0001$). Preliminary results failed to disclose nap-duration related differences for the recall of the neutral story, but sad stories were better remembered after long compared to short nap ($P = .046$). Additionally, mood improved after a long but not a short nap for the sad stories ($P < .04$) whereas it remained stable for the neutral stories.

Conclusions: Altogether, our findings highlight the importance of REM sleep in the consolidation of emotional memories, and are in agreement with the Sleep to Forget and Sleep to Remember (SFSR) hypothesis (Van der Helm & Walker, 2009) which suggests that REM sleep promotes a better memorization of emotional materials, and in parallel reduces the affective tone initially associated with the memories.

Disclosure: Nothing to disclose.

P589

Insomnia treatment and cognitive functioning in adolescents

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Objectives: To examine effects of Cognitive Behavior Therapy for Insomnia (CBTI) on sleep and cognitive functioning of adolescents with primary insomnia.

Methods: Thirty two adolescents (13–19 years, M = 15.9, SD = 1.6) with primary insomnia were randomly assigned to a treatment group ($n = 18$) and a waiting list group ($n = 14$). The intervention for the treatment group consisted of 6 weekly CBTI sessions through an internet website with preprogrammed modules, guided by a trained sleep therapist with personalized feedback and a chat session. Sleep was assessed with questionnaires for symptoms of chronic sleep reduction and insomnia, and with actigraphy and sleep logs for seven consecutive days, at baseline and post treatment. Cognitive functioning was assessed with cognitive tests at baseline and post treatment.

Results: At post treatment there was more improvement for the treatment group in symptoms of chronic sleep reduction and insomnia, and of sleep onset latency, wake after sleep onset, and total sleep time from sleep logs, and sleep efficiency from sleep logs and actigraphy. Cognitive functioning improved more for the treatment group for visuospatial processing, selective attention and working memory and a trend of improvement for response inhibition and set shifting, letter fluency and sustained attention, but not for declarative memory, visuospatial working memory, category fluency and general cognitive speed.

Conclusions: These results indicate that CBTI can have positive effects on insomnia and some cognitive functions in adolescents, with a notable difference of improvement for phonological working memory but not for visual working memory.

Disclosure: Nothing to disclose.

P590

The effect of sound stimulation during sleep on procedural memory processes

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Goals: Sleep is very important in memory consolidation. Sound stimulation may increase the amount of slow oscillations and sleep spindles, which are thought to be critical to memory consolidation, and therefore improve memory consolidation during sleep. In this study the effect of sound stimulation on procedural memory consolidation was studied.

Methods: Ten subjects (1 man, 9 women) participated in the first experiment (SDS1) and 15 (8 men, 7 women) in the second experiment (SDS2). Subjects slept three nights in the sleep laboratory of FIOH. After adaptation night there were two experimental nights in random order, one with sound stimulation presented phase locked to the ÙP phase of the sleep EEG and one without. To evaluate procedural memory consolidation, subjects performed a serial finger tapping task. The morning performance was compared against the average of both evenings.

Results: Subjects performed better in finger-tapping test on the morning of the sound stimulation night compared to the control night in SDS1 ($P < 0.05$) but not in SDS2.

Conclusions: Sound stimulation during sleep may have an effect on the consolidation of procedural memory. Difference in results between the two experiments reflects large within-subject variance as compared to the effect of the stimulation. More reliable procedural memory tasks are needed to address the question if sound stimulation can excite procedural memory consolidation.

Disclosure: Nothing to disclose.

P591

Sleep-dependent memory consolidation and SMR neurofeedback – a double-blind study in primary insomnia

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Objectives: The suggested functions of sleep are manifold, involving adaptive strategies, physical recovery and more recently 'offline' information reprocessing.

Methods: Here we present an insomnia study in which the same type of declarative (word-pair learning) and procedural (finger-tapping) task was conducted four times (weeks apart) in the evening with subsequent interference manipulation the next morning. In addition 36 healthy controls spend 3 nights in the laboratory to test for (healthy) sleep-dependent memory consolidation. Twelve sessions 12–15 Hz (sensorimotor rhythm; SMR) as well as placebo 'neurofeedback' were conducted (double-blind) in the insomnia group flanked by 2 PSGs each.

Results: Overall, susceptibility to interference was more pronounced in the declarative as compared to the procedural memory domain and also more so in insomnia than healthy controls. Analyses of the sleep EEG revealed a trait-like relationship between fast spindle activity (SpA) and

(i) the initial learning levels in the declarative memory as well as

(ii) a positive association with the declarative overnight memory change.

Last but not least our neurofeedback results indicate that patients suffering from insomnia are able to enhance (training-location specific) SMR-power and (fast) sleep spindles over the 12 SMR-training sessions. Yet this SMR learning is attenuated and direct benefits on sleep quality and memory consolidation fail to appear; the (subjective) sleep complaint decreases unspecifically with time.

Conclusions: Results indicate associations of (overnight) memory performance and (fast) sleep spindle activity and show that latter can be increased using 12–15 Hz instrumental EEG conditioning.

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P592

Fragmenting sleep with auditory stimulation: preliminary findings regarding sleep dependent memory consolidation

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Objectives: Intervening sleep benefits consolidation of motor skill learning, except in patients with Obstructive Sleep Apnoea (OSA). The current study aimed to measure both the direct impact of fragmenting sleep continuity, as well as manipulation of stimulation during wakefulness on the consolidation of memory.

Methods: Participants ($n = 10$, recruitment ongoing) completed the Karolinska Sleepiness Scale (KSS), Psychomotor Vigilance Task (PVT) and the Sequential Finger Tapping Task (SFTT, a sleep dependent motor learning task) at 10.00–12:00 and were retested 7 h later at 17:00–19:00. Earlier, at 13.30 all participants had a 2 h sleep opportunity where they either had (1) a 30 min NREM nap (2) 45mins of quiet wakefulness (left in quiet room without stimulation), (3) 30 min NREM nap fragmented by audio tone induced arousals, or (4) 45 mins of wakefulness with full access to TV, movies, books and internet. All participants completed 2 conditions in a randomized order separated by at least 1 week.

Results: Motor skill performance remained stable with slight non-significant increases in typing speed following nap (1.37%) and fragmented nap conditions (2.6%). Performance was decreased following quiet wake (−3.2%) and more notably following active wake (−8.1%) conditions. A preliminary 2x2 within-between subjects ANOVA (sleep v quiet wake, fragmented sleep v active wake) shows a significant main effect of sleep ($F = 5.858$, $P = 0.023$). No significant interaction effect was found ($P = 0.427$).

Conclusions: These preliminary results suggest sleep related motor skill improvements are robust to induced disruption of sleep continuity. Further investigation into the manipulation of stimulation during wakefulness is forthcoming.

Disclosure: Nothing to disclose.

P594

Poor sleep, cognitive ability and function in early adolescence

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Objectives: We examined associations between sleep duration and quality [sleep efficiency, fragmentation, and wake after sleep onset (WASO)] and cognitive function, including cognitive ability and neurocognitive function.

Methods: A cross-sectional study in a birth cohort born in 1998, 354 participants with mean age of 12.3 years (SD = 0.5). Sleep was measured with actigraphs for 8 nights on average. Cognitive ability was evaluated with subtests from Wechsler Intelligence Scale for Children (WISC), and neurocognitive function was assessed using Developmental Neuropsychological Assessment (Nepsy), Wisconsin Card Sorting Task (WCST), Conners' Continuous Performance Task (CPT) and Trail making.

Results: In boys, poor sleep quality was associated with higher cognitive ability within several tests. In girls, poor sleep quality was associated with poor cognitive ability in one of the cognitive ability subtests. Girls' long sleep duration and low sleep fragmentation were associated with poorer memory performance. In boys, poor sleep quality was associated with better memory performance. Both sexes showed decline in various areas of executive function when sleep quality was poor. However, good sleep quality was also associated with poorer executive function performance in certain areas of testing.

Conclusions: In boys, poor sleep quality may be associated with better cognitive ability. Neurocognitive function suffers from poor sleep quality in both sexes, but poor sleep quality is also associated with better performance in some executive function domains. Sex differences in development may explain some of the contrasting results. Neural efficiency may play a part in the associations between poor sleep quality and better cognitive ability.

Disclosure: Nothing to disclose.

P595

Does unintentional learning without emotional valence still consolidate during REM-sleep?

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Objectives: Sleep has been found to preferentially consolidate information with either emotional valence or retrieval expectancy. The current study aimed to investigate whether information with neither characteristic would still be consolidated during sleep.

Methods: The sample consisted of 64 healthy adults (17–25 years, 36.5%male). Participants first completed the digit-symbol coding task (DSCT) in the Wechsler Adult Intelligence Scale, Third Edition, and were randomly assigned to either have a nap (Nap, $n = 35$) or stay awake (Wake, $n = 29$) for about 90 min. Afterwards, to their surprise, they were asked to complete the incidental memory section of the digit-symbol coding task (DCST-incidental). The accuracy and reaction time were the major measures of their incidental memory ability.

Results: The groups were matched on age, sex, body-mass-index, 5-day sleep duration measured by actigraphy (mean=7.08 h, SD = 0.9), as well as DSCT score. No participants expected the DSCT-incidental. The Nap group had significantly higher accuracy, $t(61)=2.618$, $P = .011$ and a trend of faster reaction time, $t(61)=-1.875$, $P = .066$, on the DCST-incidental than the Wake group. Among the Nap group, higher accuracy, $r(29)=.456$, $P = .013$, and faster reaction time, $r(29) = -.473$, $P = .009$, were found to correlate with more REM-sleep.

Conclusions: Our results were first to show that sleep, particularly REM-sleep, even during a 90-min nap, consolidated information learnt unintentionally and without any retrieval expectancy or emotional valence. While individuals nowadays tend to have decreasing nighttime sleep duration that potentially compromises their learning and memory ability, taking a daytime nap may be considered as a compensatory strategy.

Disclosure: Nothing to disclose.

P596

Sleep deprivation, not sleep, fosters insight in a verbal creativity task

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Objectives: Sleep after learning promotes the quantitative strengthening of new memories. Less is known about the impact of sleep on the qualitative reorganisation of memory content. This study tested the hypothesis that sleep facilitates memory reorganisation as indexed by a verbal creativity task.

Methods: Sixty healthy university students (30 f, 30 m, 20–30 yrs) participated in a randomised, controlled parallel-group study (nighttime sleep with polysomnographic monitoring, nighttime sleep deprivation and daytime wakefulness group). At baseline, 60 items of the compound remote associate task (CRA), an established creativity task, were presented for 10 s, in which the participants had the possibility to name the solution. At re-test after the experimental condition, the same items were presented again together with 20 new control items to disentangle off-line incubation from on-line performance effects. At re-test, participants had the possibility to solve each item in maximally 30 s.

Results: Sleep significantly strengthened formerly encoded memories in comparision to both wake conditions (improvement in speed of correctly re-solved items). However, off-line reorganisation was significantly enhanced following sleep-deprivation (solution time of previously incubated newly solved items). On-line performance did not differ between the conditions (solution time of new control items).

Conclusions: In contrast to our hypothesis, sleep deprivation, not sleep, fostered memory reorganisation in a verbal creativity task. Whereas there is converging evidence for quantitative strenghening of memories during sleep, future studies are needed to further determine the impact of sleep on different types of qualitative memory reorganisation.

Disclosure: Nothing to disclose.

P597

Memory is affected by sounds presented with time-locking to EEG delta

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Goals: It was recently demonstrated that trains of short sounds given during strong delta activity in the rising (up) phase of the frontal delta EEG signal could potentially help in declarative memory consolidation (Ngo et al., 2013). We wanted to investigate this effect with single sounds and two types of word-pair memory tasks.

Methods: Two sets of experiments (SDS1, $N = 10$, 1 male; SDS2, $N = 16$, 8 males) were recorded in the sleep laboratories of FIOH. After an adaptation night, the participants received sound stimulation with single sounds on one of the two experimental nights, and performed learning and recall of word pair associates in the evening and delayed recall task in the morning. In SDS1, in the evening prior to the experimental nights, the participants saw 40 pairs of word pairs selected from Ngo et al and translated into Finnish, and were tested for learning. In SDS2, the learning phase of 120 pairs included two rehearsal rounds. In both experiments, the ability to remember was again tested in the morning.

Results: The performance of the participants did not differ in SDS1 ($P > .466$), but in SDS2, the performed significantly better ($P < .011$) after sleeping with the sound stimulation triggered to their EEG delta waves when compared to sham stimulation night.

Conclusions: Sound stimulation during sleep may have a positive effect on the consolidation of declarative memory, especially when the learning phase has involved rehearsal.

Disclosure: Nothing to disclose.

P598

How to measure sleep-dependent memory consolidation? – Don't forget the within-block position effect

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Objectives: Sleep-dependent consolidation (SDC) is a widely studied phenomenon in cognitive neuroscience. However, protocols to measure SDC in memory and learning have limitations. There are several factors that can affect SDC. If we consider Within-Block-Position Effect in sleep and memory studies we might have to reconsider previous findings of SDC. In this talk we show an example of Within-Block Position Effect from a study of memory consolidation in Mild Cognitive Impairment (MCI).

Methods: Seventeen MCI patients and 17 healthy elderly controls participated in the experiment. The MCI and the control group were matched on age, years of education and gender. We used the Alternating Serial Reaction Time task (ASRT) to measure sequence learning.

Results: individuals with MCI showed weaker learning performance than the healthy elderly group. However, using the reaction times only from the second half of each learning block, we found intact learning and consolidation in MCI. Based on the assumption that the first part of each learning block is related to reactivation processes, we suggest that these processes are affected in MCI. The offline period showed no effect on sequence-specific learning in either group but did on general skill learning: the healthy elderly group showed offline improvement in general reaction times while individuals with MCI did not.

Conclusions: Our findings deepen our understanding regarding the underlying mechanisms and time course of sequence acquisition and consolidation. We suggest a new protocol for SDC studies considering the Within-Block Position Effect in sleep and memory consolidation studies.

Disclosure: Nothing to disclose.

P599

No sleep-related enhancement in consolidation of implicit skills

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Objectives: Implicit skill learning is an unconscious way of learning which underlies not only motor but also cognitive and social skills. The influence of sleep on implicit skill consolidation has been a research topic of increasing interest. Here we show two experiments investigating the consolidation of different aspects of implicit skill learning.

Methods: We used a sequence learning task that enabled us to assess sequence-specific and general skill learning separately. Healthy young adults performed the task in two sessions with a 12-h delay between them. Half of the participants were assigned to the AM-PM (no sleep-) group and the other half were assigned to the PM-AM (sleep-) group (Experiment 1). In Experiment 2 we modified the task to be able to more specifically measure consolidation of motor and perceptual aspects of skill learning. Participants were assigned to one of four groups based on whether they slept or not between the learning and the testing phase and whether they were tested on the motor or perceptual aspects of skill learning.

Results: We found no sleep-related enhancement either in sequence-specific or in general skill learning in Experiment 1. Moreover, these findings were replicated in Experiment 2 both in motor and perceptual domain, showing no differences between AM-PM and PM-AM groups.

Conclusions: Our results suggest that at least on behavioral level sleep does not benefit consolidation of implicit skills. These findings have implications for the debate concerning perceptual/motor learning and the role of sleep in skill acquisition.

Disclosure: Nothing to disclose.

P600

Effects of gentle rocking on sleep and memory

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Why do we cradle babies or irresistibly fall asleep in a hammock? In a previous nap study (Bayer et al., 2011), we showed that lying on a slowly rocking bed facilitates sleep onset and strengthens deep sleep with increased spindles and slow wave activity that are known to promote neural plasticity and memory.

In the present study, we aimed at assessing the effects of rocking on whole-night sleep and its possible effect on overnight memory consolidation using polysomnography on healthy young adults.

Therefore, 19 participants spent two experimental nights in a bed, which either remained in a stationary position or rocked gently at 0.25 Hz. To assess memory retention, participants performed a word-pair associate learning task before and after sleep in both conditions.

EEG data revealed that rocking increased the duration of deeper sleep (N3) along with boosted spindles density ($P = 0.006$) and slow wave activity ($P = 0.02$).

Memory data analysis showed that rocking yielded a significant increase in the number of word-pairs recalled in the morning ($P = 0.004$) as compared to the stationary condition.

These findings demonstrate that rocking during a whole night makes us sleep deeper with an increase in spindle density, and that these changes in sleep reinforce memory consolidation processes.

Bayer, L., Constantinescu, I., Perrig, S., Vienne, J., Vidal, P. P., Muhlethaler, M., & Schwartz, S. (2011). Rocking synchronizes brain waves during a short nap. Current Biology, 21(12), 461–462.

Disclosure: Nothing to disclose.

P601

The role of memory strength for sleep-associated memory consolidation

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Objectives: While recent findings demonstrate that processes of sleep-associated memory consolidation can stabilize memories, it is unclear whether such consolidation varies with one of the most basic features of memory representations, i.e., memories' initial strength. The aim of this study was to address this question by examining the role of memory strength for subsequent ′offline′ memory consolidation.

Methods: 26 subjects (18–28 yrs) learned 80 word-pairs in the evening (sleep-group, $n = 13$) or in the morning (wake-group, $n = 13$). Half of the word-pairs were studied twice (weak memories, SS) while the other half was studied thrice (strong memories,SSS). Recall performance was tested after a retention interval of 9 hrs. Whereas participants in the sleep-group were tested in the morning after spending a night with full polysomnography in the sleep lab, wake-group participants were tested in the evening after 9 hrs of wakefulness.

Results: A mixed-design ANOVA testing behavioral performance revealed a significant main effect for STRENGTH (SS vs. SSS, $F_{1,24} = 59.79$, $P < 0.001$) as well as GROUP (sleep vs. wake, $F_{1,24} = 31.91$, $P < 0.001$). Post-hoc tests indicate better memory performance for strong over weak memories ($t_{25} = 7.23$, $P < 0.001$) and better overall performance levels for subjects in the sleep compared to the wake-group (Sleep:SS=74.61%, SSS=85.58%; Wake:SS=35.58%, SSS=55.00%). Furthermore, there was a STRENGTH x GROUP interaction ($F_{1,24} = 4.64$, $P < 0.05$) reflecting that sleep was more beneficial for weak than strong memories.

Conclusions: Data suggest that the beneficial effect of sleep for memory consolidation varies with memories′ initial strength and is more pronounced for initially weak encoded information.

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Disclosure: Nothing to disclose.

P602

Slow oscillations during NREM sleep in adolescents are related to intellectual abilities

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Objectives: Slow oscillations are a hallmark of non-rapid eye movement (NREM) sleep, represent an electrophysiological correlate of the homeostatic regulation of sleep and seem to be critically involved in cortical plasticity. Furthermore, slow oscillations undergo remarkable changes during development: amplitude increases during childhood, reaches a maximum before puberty, and then declines rapidly during adolescence. We here investigated the association between slow oscillations and intellectual abilities in adolescents.

Methods: All-night polysomnography recordings were performed during 2 nights in a group of 18 adolescents (13 male, 5 female) aged between 12–15 years (mean=13.39 years, SD = 0.85 years). Intellectual ability was examined by the Raven′s Standard Progressive Matrices. Slow oscillations were detected during NREM sleep at Fz, Cz, Pz and related to intelligence scores.

Results: A 3-factor ANOVA (night x location x IQ-group) revealed that peak-to-peak amplitude was identical during both nights and did not differ between locations (Fz, Cz, Pz). We found a significant main effect ($F_{1,16} = 6.866$, $P = 0.019$) for IQ-group showing that subjects with lower intellectual abilities ($n = 8$; IQ ≤ 100) have reduced peak-to-peak amplitude in comparison to subjects with higher intellectual abilities ($n = 10$; IQ > 100) during both nights at all 3 locations. Correlations between peak-to-peak amplitude and intelligence scores reached significance for all 3 locations during both nights (r (18) range 0.584–0.742, p-values range 0.0004–0.011).

Conclusions: Slow oscillations during NREM sleep in adolescents show within-subject stability and may be a marker for intellectual ability: adolescents with higher peak-to-peak amplitude are showing higher intellectual abilities.

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P603

Retroactive memory interference and reconsolidation in long term memory

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Objectives: The present study aimed at studying the effect of retroactive memory interference on long-term consolidation in healthy young adults.

Methods: Subjects (18–30 years) participated in an interference ($n = 14$) or a control ($n = 15$) condition. Both groups learned 40 unrelated AB word pairs on Day 1 and their performance was retested 7 days later. In the meantime, subjects in the interference condition were tested two nights after AB learning. First, consolidation was tested on half of the AB word pairs from which 10 pairs will be subjected to interference. Then, participants learned a new list including 20 pairs for which the first words were identical to the original list AB. Following interfering learning, participants recalled the other half of the list AB, again including 10 pairs subjected to interference.

Results: On Day 3, participants recalled fewer AB word pairs after interference. This interference was generalized to all AB pairs. At variance on Day 7, participants forgot more word pairs subjected to interference than word pairs not subjected to interference. Moreover, participants in the interference group globally forgot more word pairs than the control group after 7 days.
Conclusions: We hypothesize that the interfering learning on Day 3 reactivated the entire AB list, eventually leading to a generalized retroactive interference. However, reconsolidation of the AB list during the next 5 consecutive days resulted to a retroactive interference specific to the disrupted word pairs. Finally, comparison with the control group shows that disruption of consolidated memories accelerates forgetting for declarative long-term memories.
Disclosure: Nothing to disclose.

P604

Expose to emotional stimuli change the micro structural sleep electroencephalography

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Objective: Studies show association between learning and microstructure of sleep. Our hypothesis was that emotional learning compared to neutral is accompanied by a change in the components of CAP characterized by SWA (Slow Wave Activity), i.e. its A1 subtypes.
Methods: The sleep EEG of 16 young subjects (7 males and 9 females) was studied. Age ranged from 20 to 26 years. Subjects spent two consecutive nap session in the sleep laboratory. First session is baseline and in second session they learned emotionally negative and neutral picture stimuli, selected from IAPS (International Affective Picture System) dataset. The polygraphic recording included twelve EEG derivations, EOG and EMG.
Result: All CAP A phases were detected in each recording, during NREM sleep, and classified into three subtypes (A1, A2, and A3). Results show the macrostructure sleep parameters include in two substantially nap session are same and no statistically significant differences (all p-value > 0.15). On the contrary, CAP analysis demonstrated a significant increase in the A1 index and CAP rate following the emotional stimuli, as compared to baseline (all *P*-value < 0.01). This increase was accompanied by a nonsignificant increase in CAP rate and CAP index for A2 and A3 CAP subtypes (all p-value > 0.2).
Conclusion: CAP components characterized by sleep SWA was modified by an emotional learning task during the day preceding sleep. These results also support the idea that these components may play a role in sleep-related cognitive processes favoring performance improvement after learning.
Disclosure: Nothing to disclose.

P605

The role of REM-sleep in emotional recognition bias and discriminability

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Objectives: Previous studies on sleep-dependent memory consolidation solely focused on memory measures. However, response bias, an important aspect of memory performance was often neglected. This study investigated the association between sleep stages and both emotional memory discriminability (d') and response bias (C).
Methods: Sixty-four young adults (Mean age=20.38, SD = 1.39, 63.5%male) were randomly assigned to either the Nap (n = 35) or the Wake (n = 29) condition with no significant group differences in age, sex, body mass index, habitual sleep duration and sleep quality. Participants performed an incidental recognition task of emotional pictures after either a 90-min polysomnography-monitored nap or wakefulness. Based on Signal Detection Theory, C and d' for stimuli of positive, neutral and negative valence were compared. Correlational analyses were performed to further investigate the relationship between sleep stages and major dependent variables.
Results: Significant group difference was only found in C for neutral stimuli, with nap group being more conservative, P = .023. Among the nap group, C for neutral stimuli was positively correlated with Rapid Eye Movement (REM) latency (r = .39). C for negative stimuli was associated with less REM(r = −.44). Also, d' for negative stimuli was correlated with less REM (r = −.52) and positively correlated with stage two sleep (r = .39).
Conclusions: Our results showed that increasing amount of REM was associated with more liberal response bias and decreased memory performance for negatively-valenced stimuli, whereas longer REM latency was related to more conservative response for neutral stimuli. This study provided the first evidence on relationships between REM and criterion shifting and decision-making in emotional memory.
Disclosure: Nothing to disclose.

P606

Detecting memory replay during sleep

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Objectives: Memory consolidation during sleep is thought to be mediated by spontaneous memory replay which can be intentionally triggered. Our long term objective is to develop a method to detect memory replay during sleep and determine how this influences plasticity, and the current work presents the development of a classifier for objectively identifying triggered replay responses during sleep.
Methods: Four healthy participants underwent an experiment in three stages with EEG recording throughout:
(1) performing a motor response to a sequence of visual stimuli, paired with sounds, displayed on a PC-monitor,
(2) imagining the response when the audiovisual stimuli were presented and
(3) experiencing audio presentation of the same sequence during subsequent sleep. A pattern recognition classifier was designed to classify the EEG responses to the imagined task and then used to detect the response using the sleep EEG.

Results: The correct classification rates (CCRs) for the motor response stage were: 72% (σ= 3%), 81% (σ= 3%), 74% (σ= 2%) and 60% (σ= 3%). For the imagined response the CCRs were: 55% (σ= 3%), 64% (σ= 4%), 67% (σ= 3%) and 48% (σ= 2%). Stimuli replays during sleep were detected above chance for all of the four participants with CCRs: 23% (P = 0.05), 24% (P = 0.00), 24% (P = 0.00) and 23% (P = 0.00).

Conclusion: These results show that it is possible to detect triggered memory replay during sleep using EEG.

Disclosure: Nothing to disclose.

Dreaming

P607

The effect of low-frequency repetitive transcranial magnetic stimulation (rTMS) on subjective dream experience during sleep onset period

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The research of neural correlates of dreaming has associated dreaming with the activity in the perceptual areas of the forebrain. The damage of these areas results in deficiencies in perceptual aspects of dream experience (e.g., faces or colours). However, lesions in the forebrain regions (e.g., the parieto-temporo-occipital junction [PTOj]) identified by Mark Solms lead to global cessation of dreaming. The purpose of the following study was to investigate the inhibitory effect of repetitive transcranial magnetic stimulation (rTMS) applied to the PTOj on subjective dream experience. Four healthy subjects participated in the sleep experiments where they were awakened from the sleep onset period to collect dream reports. The data indicates that the suppressed excitability of the PTOj lead to depressed visual contents in subjective dream experience, consistent with the neuropsychological results by Solms.

Disclosure: Nothing to disclose.

P608

Aggression in dreams of adolescents and young adults: further exploration of gender and within age differences

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Objectives: It is well established that males report more aggression than females in dreams. Recently, in comparison to norms of young adults, the dreams of preadolescent boys (10–12) were reported to contain more aggression than men but no such difference was found between girls and adult women. Our objective was to replicate and expand on these observations with a new sample of adolescents and young adults.

Method: Fifty male and female adolescents (ages 12–17) and fifty male and female young adults (ages 18–24) (N = 200) kept a diary of the day's events and dreams for 10 days. The first dream of each participant was scored by two independent judges, with inter-rater reliability established, using the Hall and Van de Castle (1966) scale of aggressive interactions, controlling for dream report length by dividing scores by word count. The program DreamSAT was used for statistical comparisons.

Results: A 2X2 ANOVA revealed significant main effects showing more aggression in male's than female's dreams and in adolescents compared to young adults. A significant interaction and simple effects tests clarified that there was no differences in aggression between adolescent females and young women's dreams but higher aggression in the dreams of adolescent males compared to young men.

Conclusions: Our results confirm earlier observations of gender differences and differentiated developmental trends in the presence of aggression in dreams. Further studies should document these important between and within gender differences in older age groups.

Disclosure: Nothing to disclose.

P609

Does rapid eye movement (REM) sleep prepare the brain for awakening?

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Objectives: It has been proposed that rapid eye movement (REM) sleep prepares the brain for wakefulness and that it is easier to wake up from REM-sleep than from non-rem sleep (NREM). To address this question, we investigated how waking up from different sleep stages affected cognitive functions and subjective aspects of performing and waking-up.

Methods: 31 healthy participants (mean age 25 $\pm$ 4SD year, 10 women) went through the study protocol twice. The participants carried out a test battery (*Karolinska WakeApp*), during baseline (2 h prior bedtime), and directly upon awakening from slow wave sleep (SWS), NREM stage-2 sleep (N2) and rapid eye movement sleep (REM). The test battery included five cognitive tests – each test being 2 min long – and ratings of sleepiness and effort to perform.

Results: Cognitive performance was most adverse after waking up from SWS, followed by REM and N2 (P's < .05). Performance when waking up after REM was for several cognitive functions as bad as from waking up from SWS (e.g. working memory), and in no case better than when waking from N2 (P's > .05). REM was not better with respect to sleepiness or the amount of effort to perform as compared to neither SWS nor N2 (p's >.05).

Conclusions: We found no scientific support for REM to prepare the brain for wakefulness.

Disclosure: Nothing to disclose.

Sleep Deprivation 1

P610

New findings on the link between sleep deprivation and risky behaviour in young adults

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Many adolescents and young adults are chronically sleep deprived and several studies reveal a link between sleep problems and risky behaviour in this population. The present research aimed to explore this link in the context of prevention campaigns against drunk driving. Prevention campaigns in this field commonly provide social comparison information by showing a reckless person who drives after drinking and ends up having a serious car accident. Do sleep-deprived individuals respond to such social comparison information in the same way as control subjects?

Participants (256 sleep-deprived subjects, 257 controls) watched a short video in which the main character displayed either cautious (upward standard) or reckless (downward standard) behaviour. We assessed risk-taking behaviour in potentially dangerous driving situations using the Vienna Risk-Taking Test Traffic. Participants also reported their usual alcohol consumption and completed the Positive and Negative Affect Schedule.

Results show that in control subjects the upward standard elicits higher levels of anxiety than does the downward standard. By contrast, no effect of the standard is found in sleep-deprived participants. Furthermore, control subjects exposed to the upward standard display less risky behaviour than those presented with the downward standard. This beneficial effect of the upward standard is not found in sleep-deprived subjects. We also show that sleep-deprived participants consume more alcohol than controls.

Taken together, our findings suggest that not only are sleep-deprived young adults more prone to engage in risky behaviours, but they also seem impervious to prevention messages.

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P611

Physiological and cognitive changes after total sleep deprivation

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Objective: The purpose of this study was to investigate the physiological and neurocognitive effects of total sleep deprivation by using the laboratory blood test and the Vienna test system (reaction test, vigilance test) in healthy subjects.

Methods: Sixteen healthy volunteers participated in this study. Subjects were recommended to remain awake for 48 h under continuous surveillance. Cortisol, prolactin, thyroid hormone, growth hormone, immunoglobulin(IgG, IgA, IgM, IgD, IgE), CBC, BC and the Vienna test system were performed before and after total sleep deprivation.

Results: 1. Concentration of T3 and T4 significantly increased after deprivation.

2. In immunoglobulin levels, manifested decreased IgG, IgA and IgM concentrations. But these differences were not statistically significant.

3. After total sleep deprivation, WBC counts significantly increased.

4. Level of fasting blood sugar, total protein, albumin, alkaline phosphatase and potassium significantly increased, respectively. But total bilirubin level decreased.

5. In the reaction test, distribution reaction time significantly increased, and correct reaction significantly decreased. In the vigilance test, amount of correct reaction significantly decreased, and the mean value of reaction time correct was significantly delayed.

Conclusions: The effect of total sleep deprivation on the physiological function was significant in thyroid hormone, and there were partly consistent results in the immune system, prolactin level and growth hormone. In blood chemistry, the components related with hepato-biliary system altered, it suggested that sleep deprivation may influence the metabolism of hepato-biliary system. And the cognitive impairment resulting from total sleep deprivation were markedly detected in the reactive and vigilant functions.

Disclosure: Nothing to disclose.

P612

Successful sleep extension improves basal insulin resistance in usually sleep-restricted adults

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Objectives: A link between sleep loss and increased risk for the development of diabetes is now well recognized. This study investigates whether sleep extension in healthy adults who are chronically sleep restricted is feasible and improves fasting glucose metabolism.

Methods: During 2 weeks, 16 healthy volunteers (27 $\pm$ 6 years old, 3 men) slept at their habitual bed times and then tried to extend their sleep by 1 h per day for the following 6 weeks. At the end of the 2-week and the 6-week periods, participants were requested to follow the same diet on the day preceding a morning fasting blood sample in which glucose and insulin were assayed.

Results: Sleep time successfully increased (mean weekday actigraphic data: +44 $\pm$ 34 min, $P = 0.001$; polysomnographic data: +46 $\pm$ 69 min, $P = 0.023$), without any significant change during the weekend. A large inter-individual variability in the increase of sleep time emerged without any difference in awakenings. Sleep extension tended to be associated with increases in glucose levels ($P = 0.055$) and correlated negatively with decreases in insulin levels ($P < 0.04$), resulting in improved insulin-to-glucose ratio ($P = 0.017$), a surrogate measurement of insulin resistance.

Conclusions: Our results demonstrates that sleep extension is feasible in healthy adults who are chronically sleep restricted and is associated with decreases in basal insulin resistance. Further investigation in pre-diabetic and diabetic patients who are chronically

sleep restricted is now needed to explore the possibilities of reducing the severity of diabetes by promoting sleep extension.
Disclosure: Nothing to disclose.

P613

Napping on the night-shift: do recovery benefits extend to the commute home?

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Objectives: Car accidents and near-misses are common on the commute home from night-shift. Whether napping may reduce crash risk has not been systematically studied. We investigated whether a short, night-time nap with an additional nap before the commute home reduces crash risk on a simulated driving task.
Methods: Thirty healthy subjects (21–35y; 18F) participated in a 3-day laboratory study, including one baseline night (2200–0700 h sleep opportunity) and one sleep deprivation night with random allocation to: a 10-min nap ending at 0400 h plus a 10-min nap ending at 0700 h (10-10-NAP); a 30-min nap ending at 0400 h (30-NAP); or no napping (NO-NAP). A 40-min Yorke driving task was administered at 0700 h to simulate the commute home. Generalised Estimating Equation analyses for counts were conducted to determine differences in crash count between conditions across time-on-task (eight 5-min time bins).
Results: There were significant effects of condition ($P = 0.013$), time ($P < 0.001$), and their interaction ($P = 0.008$) on crash count. Crash count was similar for NO-NAP and 10-10-NAP, with performance remaining relatively stable throughout the task. For 30-NAP, crash count increased progressively over the task and was already significantly higher than NO-NAP and 10-10-NAP after the first 5 min.
Conclusions: Crash risk was low in a driving task after a 10-min nap ending at 0400 h with an additional 10-min nap just before a simulated commute-but no better than after no napping. A 30-min nap ending at 0400 h without an additional nap before the commute, however, appeared to worsen crash risk following the night-shift.
Support: UniSA
Disclosure: Nothing to disclose.

P614

Repeated sleep extension and sleep restriction in healthy young people leads to transient homeostatic responses in sleep and wake EEG

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Objectives: Nocturnal slow-wave activity (SWA) and daytime theta activity are classical markers of sleep homeostasis as investigated in short-term (2–5 days) sleep restriction protocols. We investigated changes in SWA and theta activity over 7d of restricted and extended sleep opportunities.
Methods: Thirty-six individuals participated in this 2-way cross-over study. The electroencephalogram (EEG) was recorded during daytime cognitive tests, a baseline night [8 h time in bed (TIB)], seven condition nights (Restriction [SR:6 h TIB] or Extension [SE:10 h TIB]), and a recovery night (12 h TIB) following ~40 h total sleep deprivation. The time-course of NREM SWA and theta activity were compared with daytime theta activity.
Results: During SR, NREM SWA and theta activity initially increased above, before reverting back to, baseline. During SE, SWA and theta activity initially declined below, and then returned to, baseline. During SE, daytime theta activity initially increased and then returned to baseline, whereas during SR, theta activity remained at or just below baseline levels across the protocol. Positive correlations between changes in sleep and wake EEG activity were observed in both the SE and SR condition.
Conclusions: The return of NREM SWA and theta activity back to baseline towards the end of SR and the lack of increase in daytime theta activity may indicate that the homeostatic response to sleep loss, indicated by nocturnal SWA and theta activity, is transient. This may reflect a change in the dynamics of homeostatic processes in response to sleep restriction.
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P615

An EEG analogue of the Karolinska Sleepiness Scale based on the Karolinska Drowsiness Test

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Objectives: In order to construct and establish validity of an objective scale, one is forced to somehow calibrate it using subjective scales. In this study we tried to construct, validate, and calibrate an objective scale based on electroencephalographic (EEG) alertness measures.
Methods: The EEG records (2 and 5 min with eyes open and closed, respectively) were obtained with 2-h interval during sleep deprivation of 15 study participants. Prior to and following each of 16–25 completed EEG recordings, a participant self-measured sleepiness with the 9-step Karolinska Sleepiness Scale (KSS). Objective alertness/sleepiness score was determined from scores on the 2nd principal component of the EEG spectrum (any derivation), and from the difference between alpha and theta powers (occipital derivation). Each objective or subjective alertness/sleepiness score was expressed as a step from 5 to 0 on 6-step alertness scale (i.e., 6 reversed final steps of KSS).
Results: To correct subjective scores, each non-zero score reported after 28 h of wakefulness by any of 7 participants identified as 'sleepiness under-estimators' was lowered on one. Then, each non-zero score after 56 h of wakefulness was lowered on one in any of still waking participants. It was found that, in terms of the corrected KSS scores, 6 consecutive steps of the objective alertness scale reflected a gradual change in subjective feeling from alert rather than sleepy to extremely sleepy.
Conclusion: Steps down on objective scale from 5 to 0 reflect changes from minimal through mild, moderate, marked, and severe to disabling sleepiness.
Disclosure: Nothing to disclose.

P616

Effects of 10 min and 30 min night-time naps on sleep inertia

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Objectives: Short (≤30 min) day-time naps have been found to improve alertness without significant sleep inertia (SI). It is unknown

whether this holds true for short night-time naps as well. This study examined SI after short naps during a simulated night shift.
Methods: Thirty healthy subjects (21–35y; 18F) participated in a 3-day laboratory study including one baseline sleep opportunity (2200–0700 h) and one experimental night involving randomisation to one of three conditions: total sleep deprivation (NO-NAP), a 10 min nap (10-NAP), or a 30 min nap (30-NAP). Nap opportunities ended at 0400 h. A 3-min psychomotor vigilance test (PVT) was performed pre-nap (0300 h) and at 2, 17, 32 and 47 min post-nap. Mean reciprocal reaction times were analysed with mixed-effects ANOVA.
Results: There were significant effects of time ($P < 0.001$), condition ($P = 0.032$), and their interaction ($P = 0.002$). In the NO-NAP condition, PVT performance declined steadily over the measurement period. In the 10-NAP condition, there was a small SI effect at 2 min post-nap compared to pre-nap, but then performance remained relatively stable and was better than the NO-NAP condition by 47 min post-nap. In the 30-NAP condition, there was considerable SI post-nap compared to pre-nap, and performance remained worse than in the other conditions through to 47 min post-nap.
Conclusions: These results suggest that a 10 min nap- but not a 30 min nap- ending at 0400 h helps to mitigate performance impairment from one night of total sleep deprivation for at least 47 min post-nap, with minimal SI upon awakening from the nap. Research supported by a UniSA DRPF Seeding Grant.
Disclosure: Nothing to disclose.

P617

Effects of partial sleep deprivation on the neural mechanisms of face perception

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Introduction: This study aimed to investigate effects of partial sleep deprivation (PSD) and sleepiness on face perception, a process of great social importance.
Methods: 27 healthy young adults (*mean age* = 23.9, SD = 2.4, females= 14) participated in a within-subject PSD experiment. Subjects were monitored using polysomnography during the sleep intervention nights, and underwent an fMRI paradigm on the following evenings. During fMRI, participants viewed pictures of neutral, angry and happy faces in a block design, and rated their sleepiness using the Karolinska Sleepiness Scale (KSS). Sleepiness was also assessed using a 5-min psychomotor vigilance task (PVT). The fusiform gyri and amygdalae were chosen as regions of interest (ROI).
Results: Across sleep conditions, viewing faces caused increased fusiform gyrus and amygdala activation bilaterally ($P < 0.05$, FWE corrected). Preliminary ROI analyses on data from 22 subjects revealed no effect of PSD on neutral face perception. However, PSD was associated with reduced activation in fusiform gyri when viewing happy and angry faces compared to baseline (Happy: R-fusifrom, $P = 0.01$, $d = 0.77$, L-fusiform, $P = 0.02$, $d = 0.76$; Angry: L-fusiform, $P = 0.04$ $d = 0.64$). Furthermore, fusiform activation in response to all faces was negatively correlated to mean KSS scores(R-fusiform: $P = 0.01$, $r = -0.50$, L-fusiform: $P = 0.01$, $r = -0.56$) after PSD (*mean score*= 7.09, SD = 1.25) but not following normal sleep (*mean KSS*= 5.06, SD = 1.44). PVT responses were not correlated to BOLD activity in any ROI.
Conclusion: These results suggest that the effects of PSD on the neural mechanisms of face perception are emotion dependant.
Disclosure: Nothing to disclose.

P618

Sleep restriction impairs vigilance but not temporal attention

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Objectives: Attentional blink (AB) is inability to detect a second target (T2) presented within 200–500 ms after the first target (T1). It is thought to occur because attentional capacity bottlenecks prevent processing of T2 while still engaged with identifying T1. This study investigates if sleep restriction exacerbates AB.
Method: Twenty-four (aged 18–30y; 12 female) healthy, regular 7–8 h sleepers completed two counterbalanced experimental conditions:
(1) normal sleep,
(2) sleep restriction to 5 h.
Testing commenced at 2 pm. Participants completed an AB task followed by a 10 min psychomotor vigilance task (PVT). AB was assessed using a rapid serial visual presentation sequence (10.6 items/s) of 8 distractor letters and 2 target numbers. Lag (number of distractors) between T1 and T2 varied randomly from 1–8 letters, with each lag presented 20 times. Targets were identified immediately following sequence presentation. The Karolinska Sleepiness Scale (KSS) quantified subjective sleepiness.
Results: Following sleep restriction KSS significantly increased and vigilance reduced (PVT reaction time and lapses significantly increased). AB occurred in both conditions: T2 identification was significantly impaired at short lags. However, AB did not differ between conditions: neither maximal AB (lowest accuracy at a particular lag) nor AB magnitude (difference between accuracy at best and worst lag) significantly differed between conditions.
Conclusions: Temporal attention as measured by AB appears unaffected by sleep restriction. It is possible that the somewhat self-paced nature of the AB task may have mitigated the impact of sleep restriction. Further research is needed to determine whether AB increases following more severe sleep restriction.
Disclosure: Nothing to disclose.

P619

Association between self-reported sleep quality and metabolic syndrome among healthcare workers

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Objectives: The aim of this cross-sectional study was to examine the association between sleep quality and metabolic syndrome (MetS) and comparing them among shift-working healthcare employees and others.
Methods: 544 participants (18.2% male, 62.7% shift-worker, 59% nurse) from one hospital in Iran completed the Persian version of Pittsburgh Sleep Quality Index (PSQI). The diagnosis of MetS according to the International Diabetes Federation (IDF) as central

obesity in combination with 2 out of the following conditions were: elevated triglycerides, blood pressure, fasting plasma glucose, and reduced HDL-cholesterol (or treated hyperlipidemia or hypertension, or previously diagnosed type-2 diabetes, respectively). The number of hours of sleep were classified into three groups according to their sleep duration: short (<6), normal (6–8 h), and long sleepers (>8 h).
Results: Prevalence of MetS based on IDF criteria was 14.9% (17.2% men, 14.4% women). This study showed that the prevalence of MetS increases with increment of age and Body Mass Index (BMI). 72.8% of shiftwork nurses were poor sleepers. Diabetes and reduced HDL prevalence in this study were 15.1% and 65.6%, respectively. A u-shaped relationship between sleep duration and the prevalence of MetS (24.1%, 0% and 12.8% in short, normal and long sleepers, respectively) was found merely in males ($P = 0.03$).
Conclusions: While self-Reported Sleep Quality could not help identify individuals at risk for MetS; seeking for sleep duration can be helpful, particularly in males. In our study, no differences were seen in shift-workers and others.
Disclosure: Nothing to disclose.

P620

The relationship between sleepiness and driving ability

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Objectives: The complex task of driving requires driver vigilance, attention and ability to perceive, comprehend, react and adapt. While it appears self-evident that most, if not all, of these functions are affected by fatigue and drowsiness, little direct, concrete proof exists. The aim of the present study was to examine the relationship between objectively measured sleepiness and driving ability.
Methods: Twelve adults (6M/6F; mean age: 24.5 $\pm$ 1.4) participated in the study. During the entire study period (24 h of continuous awakening) participants were tested every 3 h with a battery of computerized tests (Vienna Test System) known to significantly correlate with accident involvement and with the Pupillographic Sleepiness Test (PST) that objectively measures sleepiness. The PST consists of an 11-min recording by infrared video pupillography of the sitting participant's pupil diameter, followed by automated data analysis. In sleepy subjects the pupil shows spontaneous oscillations with a predominantly low frequency component and amplitudes reaching several millimeters.
Results: Analysis revealed significant difference between day and night tests in mean motor reaction time [$t(11) = 3.61$; $P < 0.01$], in distribution reaction time [$t(11) = 2.89$; $P < 0.05$], and in the percentage of wrong responses [$t(11) = -1.80$; $P < 0.001$]. Likewise, analysis revealed a significant correlation between PST Index and mean motor reaction time ($r = 0.94$; $P < 0.01$), between PST Index and distribution reaction time ($r = 0.84$; $P < 0.05$), and between PST Index and percentage of wrong responses ($r = 0.80$; $P < 0.005$).
Conclusion: The results suggest that driving ability is directly and highly related to fatigue and sleepiness.
Disclosure: Nothing to disclose.

P621

Cocoa flavanols to counteract the effects of sleep deprivation on cognitive functions

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Objectives: To date it is not known whether the detrimental effects of sleep deprivation on cognitive functions can be mitigated by cocoa flavanols. In this study we investigated the effects of flavanol-rich cocoa consumption on cognitive skills in healthy subjects who underwent one night of sleep deprivation.
Methods: Thirty-two subjects (age range: 20–37 years; 16 females) underwent four testing sessions: 2 Baseline sessions performed after normal sleep at home and 2 Experimental sessions after one night of sleep deprivation. Before each session, the participants were randomly assigned to consume a dairy-based cocoa drink containing a high dose (500 mg, flavanol-rich, FR) or a placebo drink (0 mg, flavanol-free, FF). During the testing sessions all subjects performed the Psychomotor Vigilance Task (PVT) and a working memory (WM) task (2-back task).
Results: No significant effect of flavanols was observed on PVT performance. Regarding the WM task, males subjects showed a lower performance accuracy on the 2-back task when they were sleep deprived, independent of the flavanol intake. On the other hand, females showed a deteriorated performance after sleep deprivation only when they took the placebo FF drink. Instead, females showed a preserved WM perfomance accuracy when they consumed the FR drink after sleep deprivation.
Conclusions: The present data show that flavanol-rich cocoa consumption may partly counteract the negative consequences of sleep loss in females, suggesting a differential role of flavanols for preserving WM ability after sleep loss as a function of gender.
Disclosure: Nothing to disclose.

P622

Vigilance and cortical excitability after acute sleep deprivation and chronic sleep restriction

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Acute sleep deprivation (aSD) impairs vigilance and increases cortical excitability. However, chronic sleep restriction (cSR) resembles sleep loss in everyday life much better than aSD. Chronic SR and aSD result in similar vigilance impairment, but the effect on cortical excitability in cSR is unknown. We therefore aimed at investigating the changes in vigilance and cortical excitability after aSD and cSR.
Five subjects underwent one night of aSD and seven nights of cSR (5 h instead of 8 h sleep/night). We assessed vigilance using psychomotor vigilance task (PVT), where we calculated reaction speed and number of lapses, i.e. reaction times >500 ms (trans-

formed: $\sqrt{x}+\sqrt{(x+1)}$). As a measure of cortical excitability we used early evoked cortical activation (ECA) in response to single-pulse transcranial magnetic stimulation (TMS), i.e. the integrated area under the rectified curve in a time window of 30 - 80 ms after TMS-pulses.

After aSD, we found decreased speed ($-0.4s^{-1} \pm 0.3$ [mean $\pm$ SD], $P < 0.05$) and increased number of lapses (+5.3 $\pm$ 2.3, $P < 0.01$) in PVT. Similar results were found after cSR (speed: $-0.5 \pm 0.3s^{-1}$, $P < 0.05$; lapses: +2.7 $\pm$ 2.7, $P = 0.091$). ECA was increased after both cSR (+26.4 $\pm$ 8.2%, $P < 0.05$) and aSD (+32.8 $\pm$ 32.1%, $P < 0.05$).

Our preliminary results show that impaired vigilance after cSR is accompanied by increased cortical excitability, similar to aSD. This electrophysiological measure may provide the means to investigate underlying mechanisms of vigilance and cognition impairment due to shortened sleep times, common in our 24/7 society.

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Disclosure: Nothing to disclose.

P623

The sensitivity of tests measuring driving related skills to the effects of prolonged wakefulness

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Objective: Initial screening is needed to assess drug induced driving impairment. However, no consensus has been reached about which initial screening tools have to be used. The present study aims to determine the ability of a battery of psychometric tests to detect performance impairing effects of clinically relevant levels of drowsiness as induced by one night of sleep deprivation.

Methods: Twenty-four healthy volunteers participated in a 2-period crossover study in which the highway driving test was conducted twice: once after normal sleep and once after 24 h of wakefulness. The psychometric tests were conducted on four occasions: once after normal sleep (at 11 am) and three times during a single night of sleep deprivation (at 1 am, 5 am, and 11 am).

Results: On-the-road driving performance was significantly impaired after sleep deprivation, as measured by an increase in Standard Deviation of Lateral Position of 3.1 cm compared to normal sleep. At 5 am, performance in most psychometric tests showed significant impairment. As expected, large effect sizes were found on performance in the Psychomotor Vigilance Test (PVT). Large effects sizes were also found in the Divided Attention Test (DAT), Attention Network Test (ANT), and test for Useful Field of View (UFOV) at 5 and 11 am.

Conclusions: From the psychometric tests used in this study, the PVT, DAT, and UFOV seem most promising for initial evaluation of drug induced impairment based on sensitivity and short duration. Further studies are needed to assess the sensitivity of psychometric tests to benchmark sedative drugs.

Disclosure: Nothing to disclose.

P624

Sleep and sleepiness during cumulative sleep restriction and subsequent recovery sleep

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Objectives: This study investigates sleep and sleepiness during successive nights with restricted sleep and during recovery when habitual sleep length is regained.

Methods: After two baseline nights of 8 h time in bed (TIB), 14 healthy young men had 4 h TIB for 5 nights, followed by three recovery nights with 8 h TIB. Seven control subjects had 8 h TIB per night throughout the experiment. Sleep stages were scored and ANOVA used to detect changes across nights with restricted sleep and across nights with recovery sleep. Subjects rated their sleepiness (Karolinska Sleepiness Scale, KSS) 140 times throughout the experiment. Ratings were longitudinally correlated to sleepiness as predicted by the three-process model of alertness regulation (TPMA).

Results: During the 4 h TIB nights, sleep efficiency (from 0.95 to 0.98) and total sleep time (228 to 234 min.) increased, whereas stage 1 (S1) sleep (from 15 to 10 min.), time awake (11 to 5 min.) and sleep latency (6 to 2 min.) decreased. During recovery nights S1 sleep increased (from 28 to 35 min.) whereas slow wave sleep (SWS) decreased (from 72 to 57 min.) and sleep latency increased (from 3 to 7 min.). In CON, no changes were observed except reduced sleep efficiency towards the end of the experiment.

Individuals sleepiness ratings correlated to model predicted sleepiness (ranging from r = 0.20 ($P < 0.05$) to 0.72 ($P < 0.001$).

Conclusions: Sustained short sleep reduces the amount of S1 sleep without increasing SWS. The TPMA is well capable of predicting sleepiness levels under such conditions.

Disclosure: Nothing to disclose.

P625

Caffeine increases light responsiveness of the circadian pacemaker

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Objectives: Caffeine is the most used psychoactive stimulant. It reduces sleep and sleepiness by blocking adenosine receptors. Adenosine increases during sleep deprivation (SD) and is thought to induce sleepiness and initiate sleep. Light-induced phase shifts of the circadian rest-activity rhythm are mediated by light responsive suprachiasmatic nucleus (SCN) neurons. Previous studies showed that SD reduces circadian phase shifting capacity and decreases SCN neuronal activity. In addition, adenosine agonists and antagonists mimic and block the effect of SD on light-induced phase shifts in behaviour, suggesting a role for adenosine. Here, we examined the role of SD and the effect of caffeine on light responsiveness of the SCN.

Methods: We performed in vivo electrical activity recordings of the SCN in freely moving mice subjected to light pulses in combination with sleep deprivation and adenosine injections (15 mg/kg i.p.). In

additions, we undertook behavioural recordings in constant light and dark conditions with or without caffeine in the drinking water.
Results: The sustained response to light in SCN neuronal activity was attenuated by 51% (± 14% SEM) after a 6-h SD prior to light exposure. Subsequent i.p. application of caffeine was able to restore the light response. The period length in constant light during caffeine treatment in drinking water was 36 min (± 10 min) longer.
Conclusions: The data suggest that increased homeostatic sleep pressure changes circadian pacemaker functioning by reducing SCN neuronal responsiveness to light. The electrophysiological and behavioural data together provide evidence that consuming caffeinated beverages may increase clock sensitivity to light.
Disclosure: Nothing to disclose.

P626

Transcriptome analysis of sleep deprivation induced neuroprotection in a rodent model of stroke

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Objectives: Sleep deprivation (SD) performed before stroke induces ischemic tolerance as observed in other forms of preconditioning. As the mechanisms underlying this neuroprotective effect are not well understood we wanted to identify by DNA oligonucleotide microarrays, which genes are involved in the neuroprotective mechanisms elicited by SD preconditioning.
Methods: Gene expression analysis was performed at 3 days after pre-stroke SD in adult rats. Animals were assigned to four experimental groups:
i) SD.Is: total SD performed before stroke;
ii) nSD.Is: stroke without previous SD;
iii) SD.Sham: SD performed before sham surgery;
iv) Sham: sham surgery without SD.
SD was performed during the last 6 h of the light period by gentle handling and ischemia induced immediately after.
Results: Stroke induced a massive alteration in gene expression both in nSD.IS and SD.IS group. However, SD.IS group showed a general reduction in transcriptional changes with a downregulation in the expression of genes involved in cell cycle regulation and immune response with respect to nSD.IS. Moreover an upregulation of a neuroendocrine pathway including melanin concentrating hormone, glycoprotein hormones-α-polypeptide and hypocretin was observed only in SD.Is animals.
Conclusions: SD before stroke induces an alteration in gene expression specific to the condition, reprogramming the signaling response to injury. The inhibition of cell cycle regulation and inflammation have been reported for other neuroprotective preconditioning treatments whereas the third identified pathway, linked with neuroendocrine function, has never been described before. This provides a possible new insight into neuroprotective mechanisms involved during the acute phase of stroke.
Disclosure: Nothing to disclose.

P627

Effect of adenosine receptor antagonism in the blood-brain barrier disruption induced by chronic REM sleep loss

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Blood-brain barrier (BBB) maintains brain homeostasis and is localized at the brain capillaries. Previously, we found that chronic loss of rapid eye movement sleep (REM) altered BBB structure and function in the rat. Moreover, sleep recovery restablished normal BBB function; but the recovery effect varied as a function of the brain region and the period of sleep opportunity; regions such as the hippocampus and cerebellar vermis presented altered BBB function even after 2 h of sleep recovery. Independent evidence show that adenosine accumulates during prolonged waking and that adenosine receptors modulate BBB function.
Objectives: The aim of this study was to elucidate the role of adenosine receptors in the regulation of BBB function after chronic REM loss.
Methods: Male Wistar rats were subjected to chronic REM loss using the modified multiple platform method. In the last day, vehicle or an adenosine receptor antagonist were administered, 1 h later rats were anesthetized, and Evans blue or FITC-dextrans were administered. Brain was dissected and processed by optical density or spectrofotometric analyses to quantify BBB permeability.
Results: REM restriction increased BBB permeability to Evans blue and FITC-dextrans; the antagonism of adenosine receptors partially blocked the BBB increased permeability secundary to chronic REM loss; however not in all brain regions, hyperpermeability remained in the hippocampus and cerebellum but not in basal ganglia.
Conclusions: Our data suggest that adenosine effects upon its receptor might have an important role in the regulation of BBB structure and function during normal sleep.
Disclosure: Nothing to disclose.

P628

Homeostatic regulation of REM sleep in narcoleptic mice

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Objective: The symptomatology of narcolepsy suggests an impaired REM Sleep (REMS) regulation, as seen by the presence of cataplexy, sleep paralysis and sleep-onset into REMS (SOREM). Only one study conducted with six narcoleptic patients has looked at REMS homeostatic regulation (Vu and al., 2009) and none were done on narcoleptic mice. Here, we studied orexin Knockout narcoleptic mice (KO), by REMS depriving them for 48 h using platforms-over-water technique.
Methods – results: During the recovery period, KO mice showed a REMS rebound similar to wild type mice (WT) indicating that REMS homeostatic regulation is maintained in KO. However, REMS latency during recovery is much shorter in KO (20 ± 4.2 min) than WT (113 ± 5.6 min). As it could be due to a higher REMS pressure, we used our newly developed automatic REMS deprivation method to objectively evaluate it. When REMS is detected, a TTL-signal is sent by the computer to the cage floor to move it up and wake-up the mouse.

Interestingly, KO were stimulated more often (782.3 ± 60.7) than WT (367.6 ± 42.0) revealing a stronger need to enter REMS, a stronger REMS pressure. WT mice had a higher REMS pressure during the light phase than dark phase in accordance to REMS circadian distribution. KO mice however accumulated REMS pressure similarly during light and dark phases and similarly to WT during the light phase.

Conclusion: These findings may reflect a lack of inhibition of REMS during the dark phase in KO mice.

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P629

EEG topography during sleep inertia after recovery from sleep deprivation

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Objectives: The EEG substratum of sleep inertia (SI) following normal sleep has been recently identified. After recovery sleep following sleep deprivation (SD) several behavioural and physiological markers of higher SI have been found, but the waking EEG topography associated with SI has never been investigated. The objective of the present study was to evaluate the effect of SD on post-recovery SI.

Methods: Twenty-four healthy subjects participated in a SD protocol across four consecutive days and nights. Subjects slept during the first night (adaptation), the second night (baseline) and the fourth night (recovery). After awakening from baseline sleep, a period of 40 h SD started at 10:00 a.m. In both baseline and recovery conditions 12 subjects were awakened from stage 2 NREM sleep, while the others from REM sleep. The 5-min eyes-open waking EEG was recorded from 19 derivations immediately after awakening from baseline and recovery sleep. EEG power spectra were calculated across the following bands: delta (1–4 Hz), theta (5–7 Hz), alpha (8–12 Hz), beta1 (13–16 Hz), and beta2 (17–24 Hz).

Results: after awakening from REM sleep, post-recovery wakefulness was characterized by an increase of delta and theta bands in anterior areas and an increase of alpha, beta1 and beta2 bands in centro-posterior regions. No significant differences between recovery and baseline were observed after awakening from NREM sleep.

Conclusions: after recovery from SD, the waking EEG topography is characterized by regional changes when subjects are awakened from REM sleep, mostly affecting the low-frequency bands.

Disclosure: Nothing to disclose.

P629a

Orienting attention after sleep-loss: is it disengagement that makes the difference?

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Objectives: Posner and Raichle (1994) define three attentional networks: alerting, orienting, and executive control. Within the spatial orienting network they identify three sub-components: disengagement of attention from a focus, shift of attention, and engagement of attention on a target position. The research on relations between sleep deprivation and covert orienting of attention have produced evidence indicating either a negative or a null impact of sleep loss on orienting. Moreover, whether, following sleep deprivation, there is a general impairment of orienting processes or a selective one is still unclear. Aim of the present study is investigating the effects of sleep deprivation on the three sub-components of orienting of attention.

Methods: Thirty participants (22 female and 8 male, age 20–26). The ANT-R (Fan et al. 2009) was administered at 9:00 a.m following two sleep conditions: Baseline - a regular night of uninterrupted sleep in their own homes under actigraphic control; and Deprivation - 24 h of total sleep deprivation. The two conditions were counterbalanced across participants with an interval of one week between the two.

Results: We found a significant slowing down of the disengagement component (13.60 msec), while engagement and shift components were virtually unaffected by sleep deprivation (−6.45 and −6.20 msec. respectively).

Conclusions: Our data show that sleep deprivation selectively affects the three subcomponents underlying covert orienting of attention. Hence, they suggest that performance deficits following sleep curtailment should no longer be accounted for in terms of a general reduction of alertness or global attentional deficits.

Disclosure: Nothing to disclose.

Sleep disorders - Breathing 2

P630

Didgeridoo therapy for Korean patients with obstructive sleep apnea

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Objectives: Previous Swedish trial showed that didgeridoo therapy reduces severity of obstructive sleep apnea (OSA). We conducted this study to assess the effects of didgeridoo therapy on severity of OSA and related conditions in Korean patients.

Methods: We enrolled 19 patients aged from 18–64 years with an apnea-hypopnea index (AHI) ≥15/h who does not want or could not tolerate CPAP therapy. Patients received a standardized didgeridoo and regular lesson for playing them during the 16-week treatment period. Patients had played didgeridoo ≥5 days a week with ≥20 min each day. Polysomnography was undertaken two weeks after the treatment period. Visual analogue scale (VAS) for snoring, Epworth sleepiness scale, Pittsburgh Sleep Quality Index, and Short form 36 were measured before and after the treatment period.

Results: Fifteen patients completed the therapy. Patients practiced didgeridoo playing for 42.9 ± 9.4 h. Their weight remained unchanged. VAS for snoring, which measures severity of snoring subjectively by their bed-partners, was significantly improved (7.27 ± 1.2 to 4.8 ± 1.9, $P = 0.004$). AHI, however, did not changed and apnea index was even worsened after the treatment (11.4 ± 13.9/h to 14.3 ± 14.7/h, $P = 0.043$). Except improved mental health score of the SF-36 (75.5 ± 13.7 to 68.7 ± 14.5, $P = 0.048$), no variables were changed significantly.

Conclusions: We failed to reproduce positive effect of didgeridoo therapy on the severity of OSA in Korean patients. This may partly due to anthropometric differences between Korean and Swedish population.

Disclosure: Nothing to disclose.

P631

Sleep apnea in diabetic patients with macular oedema

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Introduction: Obstructive sleep apnea syndrome (OSA) is frequent amongst diabetic patients. We conducted a randomized multicenter study to compare the evolution of macular oedema in two groups of diabetics: conventional treatment or intensified intervention on OSA and blood pressure (clinical trial NCT00970723). We studied clinical characteristics and compared patients with or without OSA.

Methods: Diabetic patients with macular oedema were consecutively randomized to benefit or not from a polysomnography (PSG). PSG were centrally and blindly scored, using ASDA 2012 criteria. Quantitative data expressed as mean ± SD were compared with ANOVA, qualitative data (%) with Chisquare, with significant P value ≤ 0.05 (GraphPad Prism, San Diego CA USA).

Results: Fifty-five patients were included, 38 were randomized to have PSG, 14 were female. 32 (86%) had hypertension. 32 (86%) presented an apnea hypopnea index (AHI) >5 events/h, 25 (65%) an AHI > 15/h and 15 (41%) an AHI > 30/h. BMI was 29.8 ± 5.2 kg/m^2, HbA1c 7.5 ± 1.2%, Epworth score 7.0 ± 4.5, systolic BP 144 ± 21 mmHg, diastolic BP 78 ± 13 mmHg. No differences were found between patients with or w/o OSA, no matter the AHI cut-off (5, 15 or 30/h) except for a higher diastolic BP in patients with OSA (86.1 ± 16.1 mm Hg vs. 76.3 ± 12.2 mmHg).

Conclusion: Prevalence of OSA is high in diabetics with macular oedema. Neither symptoms nor clinical characteristics distinguish diabetic patients with OSA from those without. Screening should therefore be performed systematically.

Disclosure: Nothing to disclose.

P632

Sleep apnea and autonomic profile in patients undergoing coronary artery bypass grafting surgery

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Introduction and aim: Myocardial revascularization by coronary artery bypass grafting surgery (CABG) is an effective measure for treating severe coronary artery disease. Hypoxic stress due to obstructive sleep apnea (OSA) and imbalance in autonomic cardiovascular function has been linked with coronary artery disease and outcome from CABG surgery. The aim of this study is to evaluate hypoxic stress and autonomic dysfunction in patients undergoing CABG and correlate their effects on the surgical outcome.

Methodology: Patients with ischemic heart disease and posted for CABG were recruited for the study. Sleep study, echocardiography and autonomic functions using task force monitor were performed one day before surgery, 6 days and 30 days post surgery.

Results: Thirty-two patients agreed to participate in the study (28 men and four women). Twenty patients completed three stages of the study. There was no significant difference in sleep apnea parameters in all stages of the study ($P > 0.05$). Central sleep apnea (CSA) has been reduced post surgery (12 ± 17 pre CABG compared with 6 ± 12 six days and 27 ± 66 thirty days after surgery but $P > 0.05$).There was trend of correlation at day six post surgey between baroreflex sensitivity and CSA ($P = 0.07$) but the correlation disappeared at day 30 ($P = 0.7$). There was significant difference among autonomic parameters in three stages of the study (Low Frequency (LF), &very low frequency (VLF) with $P = 0.001$).

Conclusion: OSA has no significant role in autonomic modulation post CABG surgery and changes in autonomic indices are due to heart manipulation and re-perfusion of the myocardium.

Disclosure: Nothing to disclose.

P633

Sleep loss and sleep disorders and their impact on the short- and long-term outcome of stroke

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Objectives: Project 1 investigates whether adaptive-servo-ventilation (ASV) used to treat sleep disordered breathing (SDB; apnea-hypopnea-index (AHI) $\geq$ 20) immediately after stroke is beneficial for stroke outcome. Project 2 assesses the frequency of sleep-wake-disorders following stroke and their impact on stroke outcome.

Methods: For project 1, 150–200 patients with acute ischemic stroke will be recruited over 2.75 years. Following respiratory polygraphy, SDB-patients will be randomized to treatment with ASV or no treatment. The evolution of the ischemic penumbra within the first week and of the lesion volume from days 1 to 4–7 and 90 following stroke will be compared between the two treatment groups using Perfusion and Diffusion Weighted Imaging. Further, the resting brain's functional connectivity, blood pressure variability, endothelial integrity and inflammatory blood markers are assessed. These measurements will be compared between the two treatment groups and patients without SDB.

For project 2, ~1000 patients with stroke will be recruited over 2–3 years. During the acute phase and after 3 and 12 months, assessments will include stroke outcome and sleep-wake/psychiatric questionnaires. Actigraphy will be obtained in every 5th patient. The sample will be stratified according to stroke severity and sleep-wake-disorders to assess stroke evolution and new cardiovascular events over the three time points.

Conclusion: Evidence for better stroke outcome due to ASV treatment and a deeper understanding of the frequency of sleep-wake-disorders following acute stroke and of their impact on stroke outcome would change clinical practice and improve patients' well-being.

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P634

Plasma homocysteine in sleep apnea: a cardiovascular risk marker and the study of its relationship with respiratory parameters of sleep

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Objectives: To study the possible relationship between plasma homocysteine (HC) and the respiratory parameters of sleep.

Methods: Included 61 patients with SAS. The patients' respiratory parameters of sleep were measured, as well as their blood HC, hemoglobin, hematocrit levels and cardiovascular risk factors (CRF).

Results: Significant correlations were found between HC levels and age (r = 0.303), hemoglobin levels (r=−0.479) and hematocrit levels (r=−0.467).

We also found a correlation with the mean duration of the apnea-hypopnea (DAH) (r = 0.409) and with the mean heart rate (r= −0.262) but not with apnea-hypopnea index (AHI), desaturation index, rate of fall in desaturation or the mean value of the desaturations.

We found differences when comparing the HC values between the patients with and without cardiovascular disease (15.7 $\pm$ 14.9 vs. 10.1 $\pm$ 3.5 μmol/L; $P < 0.023$), but not when differentiating according to the presence or absence of CRF.

For each sleep parameter, we differentiated three subgroups from lesser to greater severity. The differences were only significant among the subgroups in the DAH variable (8.7 $\pm$ 2.2; 10.7 $\pm$ 4.5; 15.5 $\pm$ 14.0 μmol/l; $P < 0.04$). Using linear regression analysis: significant relationship between HC and DAH ($P < 0.001$).

Conclusion: 1) We found a positive association between HC levels on the one hand and DAH and age on the other, and a negative association between HC levels on the one hand and heart rate, hemoglobin levels and the hematocrit levels on the other.

2) The patients with cardiovascular diseases had higher levels of HC.

3) The longer the apnea or hypopnea, the higher the plasma HC levels.

Disclosure: Nothing to disclose.

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Planetary habitat simulation: interactions between bedrest, hypoxia and confinement on sleep and breathing

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Objectives: Environmental conditions of future space habitats are anticipated to be hypoxic (~4000 m equivalent). Both acute and prolonged exposures to high altitude (>3000 m) can cause poor sleep quality, resulting in central sleep apneas and periodic breathing. The aim of this study was to assess the separate and combined effects of bedrest and hypoxia on sleep-breathing parameters.

Methods: Eleven subjects completed this cross-over study, comprising of three 31-d campaigns, each separated by a 20-week washout period: hypoxic ambulatory confinement (HAMB, 4000 m equivalent altitude), hypoxic bedrest (HBR, 4000 m equivalent), and normoxic bedrest (NBR, 990 m). Sleep polysomnography (PSG) occurred on seven nights: 1. BL-baseline night 2. NBR1-1st night NBR, 3. NBR21- 21st night NBR, 4. HBR1-1st night HBR, 5. HBR21-21st night HBR, 6. HAMB1-1st night of HAMB, 7. HAMB21- 21st night of HAMB. All recordings were performed and scored following the American Association of Sleep Medicine guidelines.

Results: Objective PSG measures indicate that although there were no differences in total sleep time relative to baseline night, sleep macrostructure demonstrated an increased light sleep and decreased slow wave sleep with exposure to both hypoxia and bedrest. Sleep fragmentation (increased number of awakenings, stage shifts and sleep latency) and clinically-significant increases in apnoea-hypopnea index (AHI) occured in both hypoxic scenarios.

Conclusion: Subtle, chronic sleep disturbances and respiration persist when exposure to hypoxic environments consistent with lunar and/or planetary habitats occur.

Disclosure: Nothing to disclose.

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Is obstructive sleep apnea in older adults is associated with changes in the characteristics of sleep slow waves?

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Introduction: Slow waves (SW) are low frequency (<4 Hz) and high amplitude (>75 μV) waves that are affected by aging and play a role in synaptic plasticity and the restorative function of sleep. As SW seem to arise from coherent neural activity, brain dysfunctions secondary to obstructive sleep apnea (OSA) could also influence their morphology. This study aims to determine if changes in SW characteristics are observed in older adults with OSA and whether they are associated with clinical characteristics, respiratory variables and subjective sleep quality.

Method: Ninety-seven subjects (23 female; mean age: 64,2 ± 6,7 years) with a mean apnea-hypopnea index of 19,8 ± 18,2 (range from 0,2 to 84,8) were included. All subjects underwent an overnight polysomnography and filled out sleep quality questionnaires. The following SW characteristics were measured on F3 lead: density, amplitude, frequency, negative/positive phase duration and slope. Associations between SW characteristics, and other variables were assessed using Pearson partial correlations with age as a covariant.

Results: No correlation was observed between SW characteristics and apnea-hypopnea index or subjective sleep quality. However, a steeper SW slope was associated with higher oxygen saturation during sleep (r = 0.26; $P = 0.01$). Higher neck circumference was associated with lower SW density, amplitude, and slope (r=−0.30 to −0.37; $P < 0.01$) and with longer positive phase duration (r = 0.33, $P = 0.002$).

Conclusion: Lower oxygen saturation during sleep and higher neck circumference were associated with changes in SW characteristics, reflecting lower neuronal synchronisation. How these modifications influence daytime functioning and cognitive functions should be investigated in aging population with OSA.

Disclosure: Nothing to disclose.

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Efficacy of oral appliances for treating obstructive sleep apnea syndrome in a Japanese clinical setting

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Objectives: The aim of this study was to evaluate the efficacy and complication of mandibular advance oral appliance (OA) to treat obstructive sleep apnea (OSA).

Methods: Sevety-nine patients (age: 51.8 ± 12.4 years; 74.7% male; Body mass index: 24.7 ± 3.95 kg/m^2) visited Sleep out-patient unit to treat OSA with OA between 2007 and 2013. The diagnosis was established by a polysomnography or a type 3 portable monitor prior to treatment (Apnea-Hypopnea Index: 19.8 ± 11.6). Subjective sleepiness before treatment was evaluated by Epworth Sleepiness Scale (9.93 ± 4.90). Subjective sleep symptoms were evaluated by Athens Insomnia Scale (AIS) prior to and after OA treatment. Pulse oximetry (Pulse Watch PMP-200, Pacific Medico, Tokyo, Japan) with and without OA was evaluated at the follow-up at home. Changes in outcomes were analyzed by paired t-test using MedCalc version 13.1.2 (MedCalc Software, Mariakerke, Belgium). Informed consent was obtained from all the participants, and the study protocol was approved by the local ethical committee.

Results: OSA data presented by 2%, 3% and 4% oxygen desaturation index (ODI) were significantly improved ($P < 0.0001$, < 0.0001 and < 0.0001, respectively). Subjective sleep assessed by AIS was also improved ($P = 0.0045$). Subjects evaluated their snoring were decreased (from 100% to 28%±30%, $n = 35$).

Conclusions: The findings validate the efficacy of OA for treatment of OSA in a Japanese clinical setting. Home monitoring with pulse oximetry may be useful to evaluate effects of OA. Snoring evaluation may be also useful, but nearly half of the subjects (33/68) did not know their changes in snoring.

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Sexual dysfunction in severe OSA

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Background: Obstructive sleep apnea (OSA) is associated with various health-related consequences. Recently, erectile dysfunction (ED) and other sexual dysfunction in men have been shown to associate with snoring and sleep apnea. However, it is still unknown what factors of sleep apnea produce sexual problems.

Methods: Data collected from 90 male patients undergoing in-lab polysomnography for suspected snoring or sleep apnea. Sexual function was assessed by 15-item International index of Erectile Function(IIEF-15) questionnaire. IIEF-15 has five sub domains: erectile function, intercourse satisfaction, orgasmic function, sexual desire, and overall satisfaction. We compared each sub domain and total scores between severe (AHI>30, $n = 30$) and mild-to-moderate (5 < AHI< 30, $n = 32$) OSA groups.

Results: Thirty-eight percentage of all OSA patients had good sexual function (total score 60–75) and 27% had poor function (score 5–43). ED (< 25) was present in 60% of patients with severe group, and 35% of patients with mild-to-moderate group, although these groups are almost same ages (45.5 vs. 44.6). Severe OSA group had more general sexual dysfunction comparing to mild-to-moderate group (45.6 vs. 50). Similar results were obtained for each sub domains. severe OSA group got lower score than mild-to-moderate group.

Conclusions: Erectile dysfunction and sexual dysfunction were prevalent in Korean OSA patients. Severe OSA group got lesser score for sexual function than mild-to-moderate OSA group, suggesting that severe OSA with high AHI is related with sexual dysfunction.

Disclosure: Nothing to disclose.

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Can auto CPAP titration replace CPAP titration of split-night polysomnography?

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Objectives: To find out better evidence supporting home based auto-titration, we performed auto-titrating CPAP at home for patients who were positive for OSA on a sleep laboratory-based diagnostic polysomnography followed by a CPAP titration.

Methods: Ninety three patients were enrolled. They all have undergone in-lab split night polysomnography with CPAP titration, and home auto CPAP titration for more than 7 days. CPAP titration was performed during the latter part of PSG. Then we selected patients with successful titration at both situations. Successful titration criteria was, i) in-lab titration, Apnea-hypopnea index(AHI)< 5 and sleeping time more than 15 min at optimal air pressure, ii) home auto titration, usage date should be more than 7 days. Finally, 35 patients were included. We compared optimal titration pressure and AHI between in-lab titration and auto CPAP titration.

Results: Average age of 35 patients was 52.5. Mean AHI during split night PSG was 57.0 ± 25.64/hr, and optimal pressure was 7.57 ± 2.45mmH2O with decreasing AHI to 1.29 ± 2.24/hr. The patients used home-autotitration for average of 15.24 days, and the rate of usage more than 4 h was 69.8%. Optimal pressure of the home-auto titration was 8.03 ± 2.16 mmH2O, and the mean AHI was 1.65 ± 3.51/hr at optimal pressure. Comparing the optimal pressure and AHI at that pressure, there was no difference between them. p value was 0.09 for the pressure, and 0.16 for AHI respectively.

Conclusion: CPAP titration results did not differ between those in-lab studies vs. home-based autotitration. CPAP titration of split-night PSG is not necessary because autotitration at home offers similar titration results.

Disclosure: Nothing to disclose.

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Effect of gender in prevalence of different comorbidities of obstructive sleep apnea patients

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Objective: Of the study was to examine differences in prevalence of comorbidities between male and female OSA patients.

Methods: Data of consecutive individuals (n = 689; 511 males, 178 females) evaluated with polysomnography, due to suspected OSA, were analyzed. Patients were divided according to OSA severity into three groups and comparisons were made between male and female patients.

Results: Mild OSA was diagnosed in 142 individuals, moderate in 105 and severe OSA in 303 patients. As controls served 139 individuals with AHI < 5/h. An increase in the number of comorbidities in line with OSA severity was observed (1.5 ± 1.3 in mild, 1.7 ± 1.4 in moderate, and 1.8 ± 1.6 in severe OSA; P = 0.048).

In OSA patients, females were older (56.2 ± 10.9 vs. 52.8 ± 13.3 years, P = 0.001) with higher BMI (36 ± 8.7 vs. 32.9 ± 5.9 Kg/m^2, P < 0.001). A higher total number of comorbidities (2.3 ± 1.6 vs. 1.6 ± 1.4; P < 0.001) in women vs. men was also observed. This difference was not observed in controls. Smoking prevalence (current or ex-smokers) was higher in men (75% vs. 46.2%, chi-squared 35.107, P < 0.001). Females with OSA had a higher prevalence of hypothyroidism (21.4% vs. 2.9%, chi-squared 48.145, P < 0.001), depression (13.7% vs. 1.9%, chi-squared 29.239, P < 0.001), arterial hypertension (58.1% vs. 45.7%, chi-squared 5.677, P = 0.021) and heart failure (6% vs. 1.7%, chi-squared 6.490, P = 0.019) compared to males.

Conclusions: Females with OSA apart from being older and more obese, have a higher burden of comorbidities than males. Hypothyroidism, depression, arterial hypertension and heart failure are more prevalent in women with OSA than in men.

Disclosure: Nothing to disclose.

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Slow wave activity during sleep as a marker of impaired vigilance after sleep loss in obstructive sleep apnoea

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Objectives: Slow wave activity (SWA, 0.5–4.5 Hz) during NREM sleep is a marker of homeostatic sleep pressure but has not been related to vigilance impairment in obstructive sleep apnoea (OSA). We investigated the relationship between SWA and vulnerability to vigilance impairment after extended wakefulness in patients with untreated OSA.

Methods: Thirty OSA patients (Age 48.6 ± 9.4 years, BMI 32.4 ± 6.2 kg/m^2, AHI 33.9 ± 24.5events/h), underwent overnight polysomnography (PSG) followed by 28-h awake. Power spectral analysis was applied to all-night EEG data and SWA in NREM and slow wave sleep (SWS) was calculated. Vigilance (4-choice reaction time task) was assessed every 2-h during wake. Reciprocal reaction time (RRT) and accuracy were averaged for 3 daytime (12:00–18:00) and 3 night-time (00:00–06:00) assessments. Change in performance from day-to-night was used to quantify vulnerability to sleep loss. Paired t-tests, bivariate correlations and linear regression were used for analysis.

Results: RRT and accuracy on the vigilance task deteriorated after sleep loss (day vs. night assessments, P < 0.05). Slower reaction speed (RRT) at night-time was related to higher SWA during NREM (r=−0.405, P = 0.032) and SWS (r=−0.509, P = 0.006). Day-to-night change in RRT was also related to SWA during NREM (r = 0.472, P = 0.01) and SWS (r = 0.493, P = 0.008). Linear regression models controlling for age, AHI, BMI and ESS showed that SWA explained 37% and 24% of night-time RRT and change in RRT, respectively.

Conclusion: Greater SWA during baseline sleep in OSA patients was associated with subsequent vigilance impairment following extended wakefulness. Quantifying SWA during PSG may be useful in identifying patients at risk of vigilance failure.

Disclosure: Nothing to disclose.

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Do clinical sleep measures predict vigilance impairment following sleep loss in patients with obstructive sleep apnoea?

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Objectives: Clinical measures of obstructive sleep apnoea (OSA) relate poorly to daytime vigilance performance. Many OSA patients are unimpaired during the day and may only show vigilance decrements following sleep loss. This study determined whether clinical OSA measures explain vigilance impairment vulnerability in OSA patients exposed to sleep loss.

Methods: Thirty OSA patients (Age 48.6 ± 9.4 years, BMI 32.4 ± 6.2 kg/m^2, AHI 33.9 ± 24.5events/hr), underwent polysomnography (PSG) followed by 28 h of extended wakefulness. Vigilance was assessed every 2 h using four choice reaction time task (4CRT) with reaction speed (RS) and accuracy averaged for 3 daytime (1200–1800) and night-time (0000–0600) assessments. Absolute and percentage change from day to night performance was used to quantify individual vulnerability to sleep loss. Bivariate correlations and linear regression were used for analysis.

Results: RS and accuracy deteriorated from day to night ($P < 0.001$ and $P = 0.035$ respectively). No relationship was observed between sleep study measures and daytime 4CRT performance. Study variables (AHI, oxygen desaturation index, % time< 90% SaO2, arousal index) negatively correlated with night-time RS, accuracy and percentage change in accuracy (all $P < 0.05$). Linear regression models controlling for age, BMI and ESS revealed AHI as a significant but not robust predictor of day to night change in 4CRT accuracy explaining 25% of variance.

Conclusion: Sleep study metrics (especially AHI) from baseline PSG relate to subsequent night-time vigilance impairment in OSA. However the clinical significance of this relationship is limited and additional biomarkers need to be examined to better explain individual vulnerability to sleep loss in OSA patients.

Disclosure: Nothing to disclose.

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Modafinil and armodafinil in obstructive sleep apnoea. A systematic review and meta-analysis

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Background: Modafinil and its R-enantiomer armodafinil are wakefulness promoters used to treat excessive daytime sleepiness in narcolepsy, obstructive sleep apnoea (OSA) and shift work sleep disorder. Modafinil's effectiveness in OSA has recently been questioned (European Medicines Agency 2011).

Objectives: This meta-analysis aims to collate all data on modafinil/armodafinil in OSA to assess whether they improve daytime sleepiness.

Methods: We searched Scopus, Pubmed, the Cochrane Register, recent sleep conference abstracts and the US, European and Australian/New Zealand clinical trial registries for every clinical trial conducted testing modafinil/armodafinil in patients with OSA. Identified articles were systematically assessed by two independent researchers until the sample included only randomised, placebo-controlled trials of modafinil/ armodafinil in adult OSA lasting ≥2 weeks where sleepiness was an outcome. Where data was unavailable from published reports, researchers or sponsors were contacted directly for data clarification where required. Data was meta-analysed using RevMan software Version 5.2.

Results: Two hundred and forty-five articles were identified via the systematic search and the independent reviewers agreed that 13 met inclusion criteria. Meta-analysis indicated that modafinil/armodafinil caused a 2.3 point improvement over placebo in the Epworth Sleepiness Score (95%CI 1.7–3.0, $I^2 = 65\%$, 10 trials) and a 3.4 min improvement in the Maintenance of Wakefulness Test (95%CI 2.4–4.4, $I^2 = 27\%$, 6 trials).

Conclusions: Modafinil/Armodafinil improve subjective and objective daytime sleepiness in patients with OSA compared with placebo.

Disclosure: JLC, BJY and NSM have received armodafinil and placebo free of charge from Teva Cephalon for an ongoing clinical trial not included in this meta-analysis and modafinil free of charge from CSL Biotherapies Ltd for two clinical trials, one of which is included in this meta-analysis. We have no other conflicts of interest with relation to this study.

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Do sleep stages affect the occurrence of respiratory events with arousals?

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Objective: In patients with obstructive sleep apnoea (OSA), obstructive respiratory events (OEs) are usually terminated by brief arousals from sleep. However, some OEs terminate without associated arousals. Considering this, we evaluated the association between OEs and arousals in stage N1 and N2 sleep in OSA patients.

Methods: Types (apnoea or hypopnea) and duration of OEs, the degree of desaturation, occurrence and timing of arousals were determined with the diagnostic polysomnography. OE with arousal was defined as the events accompanied with arousals occurring during OE or within 0.5 s after the OE termination.

Results: Fourteen male OSA patients with more than 15 per hour of AHI and without heart diseases and/or psychiatric disorders (Age 53 ± 11 years, BMI 28.2 ± 7.0 kg/m<, AHI 40.0 ± 22.8 /h) were studied. AHI decreased significantly from 58.3 ± 26.1 /h of stage N1 to 28.1 ± 21.2/h of stage N2 ($P < 0.01$). Mean percentages of OEs with arousals over total OEs in stage N1 and N2 were 73.9 ± 12.6% and 61.9 ± 21.0% ($P < 0.01$), respectively. In 11 of 14 patients, OEs with arousals occurred less frequently in stage N2, but not in three patients.

Conclusion: The AHI and the OEs with arousals showed lower values in stage N2 than in stage N1. The deeper sleep, the more OEs without arousals before the event termination might usually occur.

Disclosure: Nothing to disclose.

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Six-months of CPAP treatment enhances slow wave activity and mood in OSA patients

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Objectives: Abnormal brain activity has been reported in patients with untreated obstructive sleep apnea (OSA). Slow wave activity (SWA, 0.5–4.5 Hz), is a physiological correlate of sleep intensity which is lower in NREM sleep and attenuated across the night in OSA. Excessive daytime sleepiness and altered mood states are also associated with OSA, where depression rates of 40% have been reported. This is the first large study to assess changes in SWA across the night in conjunction with mood and sleepiness ratings after 6 months of CPAP treatment.

Methods: Ninety-six OSA patients (69 male, age 50.1 $\pm$ 12.2 years, BMI 32.5 $\pm$ 6.7 kg/m^2, AHI 34.0 $\pm$ 25.2events/hr), attended the sleep laboratory for overnight polysomnography at baseline and after 6 months of CPAP. Participants rated their mood (Depression Anxiety Stress Scale, DASS21) and subjective sleepiness (Epworth Sleepiness Scale). We performed spectral analysis of all-night EEG data (C3/A1) and calculated SWA in NREM and slow wave energy (SWE, sum of absolute delta power) for NREM/REM cycles across the night. Sleep and questionnaire data were compared using paired t-tests.

Results: SWA in NREM sleep significantly increased (Baseline vs. CPAP: 183.4 $\pm$ 166.7 vs. 301.9 $\pm$ 166.8 μV^2,$P < 0.00001$) and SWE was significantly higher in the first 3 NREM/REM cycles after CPAP. Patients were less depressed (10.7 $\pm$ 8.6 vs. 7.1 $\pm$ 8.3, $P = 0.00004$), anxious ($P < 0.00001$), stressed ($P < 0.00001$), and sleepy (11.8 $\pm$ 5.0 vs. 7.7 $\pm$ 4.2,$P < 0.0001$) after treatment.

Conclusion: Six months of CPAP treatment normalised mood and subjective sleepiness in this cohort. Sleep intensity was significantly enhanced. Increased SWA/SWE may be the underlying link to improving mood and sleepiness in OSA patients.

Disclosure: Nothing to disclose.

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Cost-effectiveness of positive airway pressure treatment in patients with obstructive sleep apnea syndrome

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Objectives: Obstructive sleep apnea syndrome (OSAS) is a common disorder that is associated with increased risk of cardio-/cerebrovascular disease and motor vehicle accident. Positive airway pressure (PAP) is the treatment of choice in OSAS but information on the cost-effectiveness of the therapy is limited. We evaluated the cost-effectiveness of PAP treatment in patients with severe OSAS from a healthcare and societal perspective in a Swedish setting.

Methods: Cost-effectiveness was estimated using an adapted Markov model and calibrated to simulate severe OSAS (apnea-hypopnea index $\geq$30 events/h and Epworth sleepiness scale score 11). Primary model outcomes were discounted lifetime costs and quality-adjusted life-years (QALYs), which were used to calculate the incremental cost-effectiveness ratio (ICER) of PAP over a 14-year horizon.

Results: PAP generated a QALY gain of 0.64 compared with no treatment. From a societal perspective the total cost for a treated and untreated patient was €10,356 and €11,475, respectively. The corresponding costs from a healthcare perspective were €8,059 and €7,690. PAP treatment was considered dominant (i.e. more effective than no treatment for less cost) compared with no treatment from the societal perspective and resulted in an ICER of €577 from the healthcare perspective.

Conclusions: Treatment of OSAS with PAP is highly cost-effective in a Swedish setting. From the societal perspective, PAP therapy was considered dominant over the long term. The benefit of the treatment is mainly due to reduction of cost related to cardiovascular disease.

Disclosure: The study was in part supported by ResMed Sweden AB.

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Usefulness of Epworth sleepiness scale for screening patients for severe obstructive sleep apnea among Bulgarian population

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Introduction: Excessive daytime sleepiness (EDS) as a major symptom of Obstructive Sleep Apnea (OSA), assessed by Epworth Sleepiness Scale (ESS), has been extensively used for screening in general practice in Bulgaria. However, recent studies have questioned its credibility for that purpose.

Objectives: The aim of our study was to assess the prevalence of EDS among ambulatory patients recommended for polysomnography (PSG) and its predictive value for severe OSA.

Methods: One-hundred and seventy not previously diagnosed patients, who had visited our sleep lab in the period 2012–2013, were instructed to complete ESS and were subjected to standard physical examination and split-night polysomnography, after signing an informed consent. Severe obstructive sleep apnea was assumed if apneohypopneic index (AHI)>30 and EDS in case of ESS>10. Patients with other sleep disorders were excluded from the study.

Results: One-hundred forty-five of the tested subjects had severe OSA (AHI=86.3 $\pm$ 27.8 vs. 16.6 $\pm$ 7.5 in the rest 25 patients, $P < 0.001$). Only 95 of them had EDS (ESS=14.9 $\pm$ 3.6 vs. 6.6 $\pm$ 1.9 in patients without EDS, $P < 0.001$). The sensitivity of ESS>10 to predict severe sleep apnea was 65.5%, specificity=64% (Pearson Chi-square=0.005), positive likelihood ratio=1.82, and negative likelihood ratio=0.54. Significant but moderate correlation was found between ESS score and AHI (Pearson rho=0.321, $P < 0.001$).

Conclusions: ESS is not a reliable instrument for screening and predicting severe OSA among Bulgarian patients.

Disclosure: Nothing to disclose.

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Increased carbonic anhydrase activity is associated with nocturnal hypoxia in obstructive sleep apnea

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Objectives: The catalytic function of the enzyme carbonic anhydrase (CA) plays a fundamental role in carbon dioxide (CO_2), proton (H^+) and bicarbonate (HCO_3^-) homeostasis. Hypoxia-induced alteration of oxidative metabolism and catecholamine activity have been shown to alter CA activity in various tissues. We hypothesized that CA activity in blood is up-regulated in patients with obstructive sleep apnea (OSA).

Methods: Cross-sectional analysis in a clinical cohort of 70 patients referred to the sleep laboratory with suspected OSA (48 males, age median [IQR] 57 [45–63] years, apnea hypopnea index (AHI) 21 [8–41] events/h). In-lab cardiorespiratory polygraphy was used to assess OSA. CA activity was determined in an in-vitro assay that quantifies the pH change reflecting the conversion of CO_2 and H_2O to HCO_3^- and H^+.

Results: CA activity was associated with AHI, 4% oxygen desaturation index (ODI4) and mean nocturnal oxygen saturation (Spearman correlation r = 0.44, 0.47 and −0.33, $P < 0.001$, < 0.001 and 0.005, respectively). In a generalized linear model controlling for age, sex, body mass index, mean oxygen saturation and use of diuretic medication, there was a positive association between AHI/ODI4 and CA activity ($P = 0.011$ and 0.018, respectively). Office diastolic blood pressure was associated with CA activity after adjustment of sex, age, body mass index, mean oxygen saturation and AHI ($P = 0.046$).

Conclusions: CA activity increased with AHI and measures of nocturnal hypoxemia in OSA patients. Altered CA activity may constitute a component that modulates respiratory control and hemodynamic regulation in OSA patients

Disclosure: Nothing to disclose.

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Prevalence of obstructive sleep apnea syndrome in a population of non severely obese patients with nonalcoholic fatty liver disease

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Background: A high prevalence of obstructive sleep apnea syndrome (OSAS) has been described in severely obese patients with nonalcoholic fatty liver disease (NAFLD), a liver disease associated with obesity and metabolic syndrome. We recently reported that high risk of OSAS with sleepiness, as detected by Berlin Questionnaire and Epworth Sleepiness Scale positivity, is associated with the severity of liver damage in patients with NAFLD without severe obesity.

Aim: To assess the prevalence of OSAS in patients with NAFLD without severe obesity.

Methods: Twenty-four patients with histologically proven NAFLD without severe obesity were consecutively enrolled. A complete polysomnographic (PSG) study was performed in all patients and analyzed by a sleep expert according to the AASM criteria.

Results: Our NAFLD population had the following general characteristics: seventeen males (70%), mean age 57 ± 13 year, mean BMI 28 ± 3 kg/m^2, mean neck circumference 40.5 ± 3.5 cm, waist-to-hip ratio 0.94. PSG analysis revealed that six patients had a normal sleep study (25%), while eighteen (75%) had a sleep study positive for OSAS, as detected by apnea-hypopnea index (AHI) >5. Out of these, eleven (61%) had mild OSAS (AHI < 15), six (34%) moderate OSAS (AHI 15–30), and one severe OSAS (AHI > 30).

Conclusions: In this population of histologically proven NAFLD without severe obesity, we detected a high prevalence of OSAS. Whether OSAS severity is associated with liver damage progression warrants further investigations.

Disclosure: Nothing to disclose.

P650

Acromegaly screening in patients with sleep apnea symptoms

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Acromegaly is rare disease with insidious presentation that usually takes years before the diagnosis. Prevalence is 40–125 cases per million, some screening studies have found a much higher prevalence, suggesting that acromegaly could be underestimated. Acromegaly symptoms are non-specific but acral enlargement is almost universally present at diagnosis.

Aim: Sleep apnea is present in about 40–80% of acromegaly patients. In this study we aims to investigate the presence of acromegaly in a selected population of patients suffering from snoring or suspected sleep apnea.

Methods: Multicenter Spanish study involving 14 Hospital sleep referral units and Endocrinology departments. Patients who were seen in first visit for sleep apnea symptoms and/or hoarseness were offered to participate. A questioner was designed to investigate the presence of symptoms consistent with a diagnosis of acromegaly including: increase in ring size or shoe size, enlargement of the tongue, lips or jaw, paresthesiae in hands or carpal tunnel syndrome and widening of tooth spaces, in addition to a list of other typical symptoms.

A serum IGF-1 was measured in case of positive signs of acromegaly and an OGTT was performed to confirm acromegaly. The project is still ongoing, we present preliminary data.

Results: Two acromegaly were diagnosed form 965 patients screened.

Conclusions: In a selected population of patient suffering from snoring or suspected sleep apnea we found an acromegaly prevalence of 2.1 cases per 10^3 patients screened. It is important that sleep specialists beware of the disease and recognize its symptoms in order to perform an early diagnosis.

Disclosure: Funding support: this investigator study has received a support from Ipsen

P651

Obstructive sleep apnea with insomnia in hypertensive primary care patients - association with sleep complaints, depressive symptoms and self-rated health

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Objectives: To describe the occurrence and characteristics of OSA with insomnia, and explore its contribution to self-rated health in hypertensive outpatients.

Methods: Cross-sectional design including 394 hypertensive patients (52.5% women, mean age 57.8 years, SD 6.7 years). Data were gathered with clinical examinations, polygraphs and scales for OSA symptoms (BSAQ), daytime sleepiness (ESS) and insomnia (MISS). Polygraphy recordings were scored according to AASM criteria. OSA and insomnia was defined as AHI ≥ 5 together with at least moderate insomnia (MISS ≥ 7).

Results: Mild, moderate and severe OSA occurred among 29%, 16% and 14% of the patients. The frequency of OSA with insomnia was 32% in the sample. 39%, 29% and 20% of those with mild, moderate and severe OSA had OSA with insomnia. AHI, saturation time < 90%, HDL cholesterol and total sleep time was higher ($P < 0.001$) among those with OSA and insomnia. However, sleep sufficiency index, depressive symptoms and excessive daytime sleepiness did not differ. Medication with angiotensin converting enzyme inhibitors ($P < 0.05$) and hypnotics ($P < 0.01$) was more common among patients with OSA and insomnia. Linear regression showed that OSA with insomnia ($P < 0.05$), depressive symptoms ($P < 0.001$) and obesity ($P < 0.001$) were significantly associated with self-rated health. Adding gender, diabetes and ischemic heart disease to the model did not change the results.

Conclusion: The occurrence of insomnia was high among hypertensive primary care patients with OSA of different severity levels and does together with depressive symptoms and obesity have a negative impact on perceived health.

Disclosure: Nothing to disclose.

P652

STOPBang as a predictor of severity of obstructive sleep apnea

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Objective: The STOPBang is a validated screening questionnaire for obstructive sleep apnea (OSA). A cut-off score of ≥ 3 is recommended, since it has a high sensitivity for OSA. It is unknown whether the STOPBang can predict the severity of OSA and which cut-off score should be applied. Also unknown is whether a different cut-off point for neck circumference, which is one of the STOPBang-items, will increase diagnostic value.

Method: The STOPBang-scores of 278 Dutch sleep clinic patients were compared with the apnea/hypopnea-index obtainded from their polysomnografy (PSG), the gold standard. The diagnostic value of the different STOPBang-scores and scores with alternative cut-off points for neck circumference of 42 cm in men (STOPBang42) and additionally 37 cm in women (STOPBang37/42) were determined and compared.

Results: The prevalence of OSA was 70.9% and 37.7% for moderate/severe OSA. A cutoff score of 5 showed the best combination of sensitivity (75%) and specificity (63%) to discriminate none/mild OSA from moderate/severe. The STOPBang42 improved specificity (70%, $P < 0.001$)) and showed less false positives, however sensitivity (71%, $P = 0.031$) decreased. The STOPBang37/42 showed no further improvement (sensitivity 70%; specificity 68%).

Conclusion: The diagnostic value of the STOPBang was moderate to good. A cutoff score of 5 showed the highest prediction value for moderate/severe OSA. Since the STOPBang42 resulted in less false positives, this version is preferred. The prevalence of OSA was comparable to other sleep clinics.

Implications: The STOPBang can be usefull as a triage tool. In case of insufficient capacity for sleep registrations moderate/severe OSAS patients can receive priority.

Disclosure: Nothing to disclose.

P653

Vigilance and attention deficits are associated with motor vehicle accidents in sleep apnea patients

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Objectives: Obstructive sleep apnea (OSA) is associated with impaired cognitive function. There is a 2.5 fold overrepresentation of motor vehicle accidents (MVAs) in patients with OSA but the risk is poorly predicted by conventional measures of OSA severity. We attempted to identify useful markers of cognitive dysfunction for identification of patients with elevated MVA risk.

Methods: Patients with suspected OSA ($n = 114$, 75% male, age 51 (12) years, BMI 30 (4) kg/m^2, median Apnea-Hypopnea Index 25 [6 - 49] n/h, mean Epworth Sleepiness Scale (ESS) score 11 (5)) underwent the attention network test (ANT) and the simple reaction time test (GOSLING). Ten-year MVA data were cross-analyzed from the Swedish Traffic Accident Data Acquisition (STRADA) registry.

Results: A history of MVA ($n = 11$) among patients was associated with more frequent lapses (42 [5 - 121] vs. 5 [1 - 25], $P = 0.02$) and fewer responses (238 [158 - 272] vs. 271 [256 - 277], $P = 0.03$) in the ANT compared with no MVA history. In the GOSLING test, reaction time was longer (462 [393 - 551] vs. 407 [361 - 449] ms, $P = 0.05$) in the MVA group and the number of lapses was higher (10 [2 - 45] vs. 7 [2 - 19], $P < 0.01$). OSA severity and the ESS score were poor predictors of MVA ($P > 0.2$, respectively).

Conclusions: Markers of impairment of performance and sustained attention were independently associated with MVA in OSA patients. Our study identifies candidate parameters for objective testing of MVA risk in patients with a common sleep disorder.

Disclosure: Nothing to disclose.

P654

Prone positioning for treatment of obstructive sleep apnoea

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Objectives: The aim of the present study was to evaluate the effect of prone positioning in patients with obstructive sleep apnoea (OSA).
Methods: Fourteen patients, 11 men and three women with a mean age of 51 years, mean BMI of 26, mean AHI and ODI of 26 (min:6; max:53) and 21 (min:6;max:51) respectively, were evaluated in the study. Two ambulatory polysomnographic (PSG) studies were performed. The first night was without any treatment and the second night after four weeks of adaptation to a mattress and pillow for prone positioning (MPP).
Results: Mean AHI and ODI decreased from 26 and 21 to 8 and 7 respectively ($P < 0.001$) with treatment. The mean time spent in the supine position was reduced from 128 to 10 min ($P = 0.02$) and the mean prone time increased from 42 to 174 min ($P = 0.02$). The mean total sleep time was 390 min without treatment and 370 min with the MPP ($P = 0.7$). Ten patients (71%) reduced their AHI by at least 50% and reached a value < 10 with treatment. All patients managed to sleep on the MPP > 4 h per night during the 4-week study.
Conclusions: Prone positioning seems to be efficient in reducing AHI and ODI in most patients with OSA. Further studies are needed to evaluate the long-term efficiency and compliance with the MPP.
Disclosure: Nothing to disclose.

P655

Combination of sleep apnea syndrome and haemangioma of the head and neck region: case study

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Combination of obstructive sleep apnea syndrome with haemangioma of the head and neck region is rare condition, only a few cases are known in the literature. Propagation of this vascular tumor to the pharyngeal space can cause breathing abnormality.
We present the case of 64 years old woman with the complaints of excessive daytime sleepiness, sleep fragmentation, snoring and haemangioma which affects the right part of the face, the labial region, tongue and soft palate. To determine the appropriate therapy of the sleep related breathing abnormality we performed sleep examination, MR scan of the head and neck region, otorhinolaryngological and neurosurgical examination.
Polygraphic examination detected severe obstructive sleep apnea syndrome. The MR examination of the neck showed extensive haemangioma narrowing the pharyngeal region and causing temporal bone destruction on the right side with intracranial propagation. Fiberoscopic examination of the pharyngeal region showed stricture without ventil mechanism of the haemangioma. CPAP titration showed the minimalization of the apnea-hypopnea index and normalization of the oxygen level at 11 water centimeter pressure level. Regular CPAP usage resulted in the improvement of the patient's complains.
Our examination showed that rare case of extreme severe head and neck haemangioma based obstructive sleep apnea syndrome can be treated safely with CPAP device if surgical therapy is not possible. Regular multidisciplinary control examination is necessary to determine the propagation of the vascular tumor and safety of the CPAP treatment.
Disclosure: Nothing to disclose.

P656

Relationship between apnea-hyponea index, Body-Mass-Index and the Epworth sleepiness scale in patient with OSAS

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Objective: Obstructive sleep apnea syndrome (OSAS) has attracted a great attention in recent years, mainly due to the increased number of diagnosed cases and OSAS's, because it appears to be a cause of many acute and chronic diseases. The objective of this paper was to investigate the relationship between the apnea-hypopnea index (AHI), body mass index (BMI), Epworth Sleepeness Scale (ESS) and Snoring index (SI) in patients with OSAS.
Methods: Retrospective analysis was performed on 65 untreated patients, who were subjected to polysomnographic research, according to which AHI, SI and BMI were determined. The Epworth Sleepeness Scale (ESS) was filled in.
Results: In 9.2% (six patients) mild AHI (5–15) was observed. BMI of these patients were characterized by: 50% normal, 50% Overweigcht. ESS (2–11).
In 16.9% (11patients) was noted a moderate AHI (15–30), BMI Overweight, ESS (2–11). 73.9% (48 patients) had Severe AHI (>30). Among them in 83.4% (40 patients) BMI >30 (Obese) was seen, and in 16.6% (eight patients) BMI 25–29.9 (Overweight). In the cohort of these patients ESS >12.
It should be noted that despite the degree of sleep obstructive apnea in all the patients a high rate of snoring index was observed.
Conclusion: As a result of the performed analysis it was revealed that there is a certain relationship between AHI, BMI and ESS, particularly, the patients, having a a severe AHI, show an expressed tendency to the obesity and sleepiness, while the index of snoring is not reliably depended on AHI degree.
Disclosure: Nothing to disclose.

P657

First-night effect and night-to-night variability in patients with suspected OSAS

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Objectives: A recent validation study of the sleep classification system Somnolyzer 24x7 in 97 patients with suspected obstructive sleep apnea syndrome (OSAS) revealed substantial equivalence between Somnolyzer auto scoring and four independent manual expert scorings for all clinically relevant sleep parameters. Thus Somnolyzer offers a 100% reliable and valid tool for exploring night-to-night variability in polysomnographic recordings (PSGs).

Methods: Standard PSGs were recorded in 51 patients with suspected OSAS at two consecutive nights. Both nights (PSG1 and PSG2) were analysed by the Somnolyzer expert system using the recommended AASM 2007 rules for defining hypopneas.
Results: Sleep efficiency increased from 79 ± 13% in PSG1 to 85 ± 8% in PSG2 ($P < 0.001$). Sleep latency shortened from 26 ± 30 min to 17 ± 10 min ($P < 0.05$), REM latency from 102 ± 55 min to 81 ± 50 min ($P < 0.01$). Minutes in stage REM increased from 78 ± 34 min to 92 ± 34 min. Arousals, respiratory events and periodic leg movements in sleep (PLMS) showed no significant group differences between PSG1 and PGS2 (arousal index: 39 ± 22 and 38 ± 21; apnea+hypopnea index (AHI): 40 ± 27 and 39 ± 23; PLMS index: 9 ± 13 and 8 ± 11). Nevertheless, 50% of patients with an AHI< 15 in the first night showed an AHI>15 in the second night.
Conclusions: The study supports previous findings by Newell et al. (Psychiatry Res., 2012) that due to the first-night effect on sleep parameters and the potential impact of night-to-night variability of the AHI it is worth performing a second night in patients admitted for apnea detection, specifically when the result of the first night was negative.
Disclosure: All authors are employees of Philips Austria GmbH

P658

The effectiveness of mandibular reposition appliances (MRA) in treatment of obstructive sleep apnea

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Objectives: Obstructive Sleep Apnea Syndrome (OSAS) has different treatment modalities. OSAS can be treated with Mandibular Repositioning Appliance (MRA). Successful treatment with MRA aims to reduce the Apnea-Hypopnea Index (AHI) with more than 50%. In the range of the MRA therapy, there are several disciplines which make their opinion of these patients. Those are the sleep medicine specialists, the ENT specialist, and Oral & Maxillofacial surgeon. This study aims to identify a correlation of diagnostic clinical significance between all those specialists findings and the reduction of de AHI in OSAS patients.
Methods: Patients had been diagnosed with OSAS in a sleep-wake clinic by two consecutive nights of ambulatory polysomnography. Then they were further investigated by the ENT specialist and Oral & Maxillofacial surgeon. If het MRA therapy was indicated the MRA was constructed. The sleep specialist looked at the amount of AHI, and hypnogram. Then the ENT specialist investigated the upper-airway and nose passage, size of the tongue, and the Mallampatti/ Friedman score. With sleep endoscopy the possible effect of the chin-lift is was estimated. The Oral & Maxillofacial surgeon uses cephalometric measurements which describes the orthoposition on the lateral cephalograms.
Results: The preliminary results of fourteen patients (55 (34–64) years) indicated that the AHI reduced significantly during the MRA therapy ($AHI_{diagnosis}$:18.1 (4.3–41.1); $AHI_{with\ MRA}$:10.3 (4.0–29.7), $P = 0.04$). All the sleep variables were in pursuance of each other.
Conclusions: It is mandatory to evaluate the effect of oral appliances in OSAS treatment in individual patients. More data and further analysis will follow.
Disclosure: Nothing to disclose.

P659

An adjustable mandibular advancement device for the treatment of obstructive sleep apnea syndrome and its implications on glucose metabolism: a prospective 1-year follow-up study

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Objectives: Obstructive sleep apnea syndrome (OSAS) is recognized as an independent risk factor for insulin resistance, glucose intolerance and type 2 diabetes.
The aim of this study was to determine the efficacy of the custom-made adjustable mandibular advancement device (MAD) after 1 year of treatment and its implications on the glucose metabolism.
Methods: A total of 15 patients with mild to moderate OSAS were treated with custom-made adjustable MAD and they were followed-up after 1 year of treatment. Sleep studies in the sleep clinic were performed with and without the MAD and fasting blood samples were obtained at baseline and at the time of follow-up.
Results: The mean apnea-hypopnea index (AHI) decreased significantly from 22.9 ± 5.9 at baseline to 9.75 ± 4.63 after 1 year of treatment ($P < 0.001$), measured with the same polysomnography device. Fasting plasma glucose values (5.26 ± 0.52 to 4.89 ± 0.51 mmol/L, $P < 0.001$) and fasting plasma insulin values (98.12 ± 62.97 to 65.17 ± 58.38 μU/mL, $P = 0.022$) decreased significantly after 1 year of MAD treatment. There were no significant changes in the plasma glucose and insulin values after 120 min of oral glucose tolerance test ($P > 0.05$).
Conclusions: Our results indicate that the tested MAD was effective in reducing symptoms in mild to moderate OSAS patients by decreasing AHI and significantly decreasing fasting plasma glucose and insulin values.
Disclosure: Nothing to disclose.

P660

Factors for successful pharyngoplasty, Two-P4 (Two-piece Palatopharyngoplasty) in patients with obstructive sleep apnea syndrome

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Introduction: Two-piece palatopharyngoplasty (Two-P4) is a modified uvulopalatopharyngoplasty. Two separated scars on both sides of soft palate pull the intact middle soft palate to each side and make pharyngeal space wide. We investigated retrospectively factors about improvements of sleep apnea by Two-P4.

Materials and methods: Sixty patients with OSAS received Two-P4 during 2002 and 2011. We examined 40 patients (AHI ≥ 20) who underwent polysomnography before and three months after the surgery. The age ranged from 17 to 74, average 39.5 ± 11.5 y. o., including 39 men and 1 woman. Their average body mass index (BMI) is 28.1 ± 4.5 kg/m^2.
Results: The average AHI decreased from 55.8 ± 23.9 to 16.9 ± 20.1 after the surgery. The total success rate is 80% (32/40) evaluated by 50% AHI decrement and AHI less than 20. The success rate of Two-P4 was 92.3% among the younger patients (age< 50 y.o.) with BMI< 35 kg/m^2 and Friedman's tonsillar size>1. There are correlations between reduction rate of AHI (AHI-rate) and tonsillar weight (P = 0.001), and between AHI-rate and MP-H (distance from mandibular plane to hyoid bone) after surgery (P = 0.024). There is no correlation between the AHI-rate and AHI, lowest SpO_2 or MP-H before surgery. There are negative correlations between AHI-rate and BMI (P = 0.03) or age (P = 0.015).
Discussion: Important factors for better results of Two-P4 were tonsillar size, age and BMI. The most important factor was the tonsillar weight. MP-H after surgery is another factor for success. Two failed cases received successful MMA. We should also consider about the influence of retrognathia.
Disclosure: Nothing to disclose.

P661

Morbid obesity and woman age are related to the obstructive sleep apnoea syndrome

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Background: The obstructive sleep apnoea syndrome (OSAS) is characterized by a history of snoring and upper airway recurrent obstruction, leading to sleep fragmentation and excessive day time somnolence. Its prevalence is higher in men (2:1), and it has been reported that older women have a higher risk for its appearance. The main objective our work was to relate BMI, age with OSAS in obese women.
Methods: In this study, we included 39 women with morbid obesity, with a BMI higher than 30. All of them underwent an overnight polysomnography. We performed lineal regression and correlation tests for the statistical analysis.
Results: The mean age for these women was 40.6 + 1.77, the mean BMI 45.10 + 1.53 and the mean of AHI was 45.21 + 7.5. Pearson correlation IAH- BMI showed 0.727*, AHI-age 0.435*, BMI-age 0.17. IAH-BMI R2 = 0.52*. Lineal regression AHI-BMI-age, R = 0.79*, R2 = 0.63*, (*P < 0.01). Risk factor for OSAS with BMI Odds ratio 3.3* with a confidence interval CI (2.3–4.3) and age odds ratio 1.3* CI (0.4–2.2) *P < 0.01
Conclusions: These data suggest a strong correlation between OSAS, BMI and age in women. There is a significant correlation between AHI and BMI. This relation increases when age is included. We did not find any relation between BMI and age. It is necessary to include more groups of women, with normal weight and overweight.
Disclosure: Nothing to disclose.

P663

Relationship between anthropometric measures and obstructive sleep apnoea in Mexican population

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Background: Obstructive sleep apnoea syndrome (OSAS) is a consequence of a diminished cross-section area at the upper airway, leading to obstruction and oxygen desaturation, as well as sleep fragmentation. Obesity has shown to be related in 60–70% of the OSAS patients.
Methods: Eighty-nine OSAS patients were included in this longitudinal, prospective, observational and analytic trial. We analyzed: Neck circumference (NC), waist circumference (WC), Hip circumference (HP), waist-hip index (WHI), body mass index BMI), size-wrist index (SWI) and waist-size index (WSI).
Results: We found that the increase in the AHI was associated to an increase in the anthropometric measures were evident only in male patients: BMI (r = 0.61, P = 0.000), NC (r = 0.73, P = 0.000), WC (r = 0.61, P = 0.000) and WHI (r = 0.62, P = 0.000). AHI showed a negative association to SWI (r= −0.43, P = 0.001).
Conclusion: Our results showed a different behaviour, when compared to other Countries population. Anthropometric measures were only significant in the male population, and the most correlated measures were NC, BMI and SWI. In male patients, the anthropometric measures directly correlate to the AHI severity. The rest of the measures are not well studied, and in our study, they showed significant correlations with the severity of sleep disordered breathing.
Disclosure: Nothing to disclose.

P664

HRV does not reflect severity of OSA in elderly

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Objectives: Characteristics of OSA in elderly patients might be different with OSA in middle aged patietns including the clinical impact of OSA severity on cardiovascular disease. Authors tried to figure out the characteristics of elderly OSA by the comparison of demographic, sleep architectural, OSA severity related, and heart rate variability (HRV) data.
Methods: Polysomnographically proved 345 OSA patients over 40 years old were included. They filled out the Hörne and Ostberg Questionnaire (HOQ), Pittsburgh Sleep Quality Index-Korean (PSQI-K), and Epworth Sleepiness Scale (ESS). We compared mean values of ESS, HOQ, PSQI-K, sleep related variables, OSA severity related variables, and HRV variables between 252 middle aged (40–59 years) group and 93 elderly (>= 60 years) group. ANCOVA was performed between two groups after adjustment with height and weight.
Results: Elderly group showed significantly higher PSQI-K and HOQ scores. In sleep architecture elderly group showed significantly longer sleep latency and REM sleep latency; lower sleep efficiency, total sleep time, and slow wave sleep%; higher wake time after sleep onset (WASO), limb movement index than middle aged group. There were no differences in AHI, mean O2 saturation, and total arousal index between two groups. In HRV analysis, NN50 count, percent of NN50, average total power, average low frequency power, average

high frequency power, and HRV triangular index were significantly lower in elderly group.

Conclusions: We could describe Korean elderly OSA patients as having more tendency of morningness, and poor sleep quality in subjective and objective measures. Elderly OSA patients have lower ANS activity and lower cardiac reactivity.

Disclosure: Nothing to disclose.

P665

Comparison of manual and automatic evaluation of polygraphy in patients after acute myocardial infarction

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Objectives: The diagnostic accuracy of ApneaLink™ for detection of sleep apnea (SA) in comparison with polysomnography was evaluated in several studies. Using an automatic evaluation as a screening tool for SA detection has not been evaluated on large sample size. The purpose of this study is to compare manual and automatic evaluation of polygraphy in myocardial infarction (MI) patients.

Methods: We prospectively studied 607 consecutive patients admitted to the hospital with the diagnosis of acute MI. All subjects underwent sleep evaluations using ApneaLink™ after at least 48 h post-admission, provided they were in stable condition. The sleep studies were independently evaluated by medical staff well trained in sleep medicine and by software as well. A Bland-Altman analysis of Apnea Index (AI), Hypopnea Index (HI), Apnea-Hypopnea Index (AHI) and Oxygen Desaturation Index (ODI) was used to assess the level of agreement between these two methods of evaluation.

Results: Bland-Altman analysis indicated that the mean differences are −0.12 (±2.36) for AI, −1.72 (±5.27) for HI, −1.83 (±6.00) for AHI and 4.39 (±5.70) for ODI. The results are supported by quite high inter-correlation coefficients: 0.974 for AI, 0.706 for HI, 0.907 for AHI and 0.871 for ODI.

Conclusion: We found that the manual and automatic evaluation of polygraphy provided the similar results. Based on these results an automatic evaluation could be used as a screening tool and therefore the screening and diagnostics could be move from a sleep laboratory to wider medical community.

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P666

Correlation between blood pressure overreaction during exercise test and severity of obstructive sleep apnea

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Objectives: Obstructive sleep apnea (OSA) is the most important sleep breathing disorder. Arterial hypertension is a common comorbidity in patients with OSA. Blood pressure reaction during exercise test together with prevalence of blood pressure overreaction is not known in these patients.

Methods: Forty patients (31 men) with moderate and severe OSA (mean apnea-hypopnea index (AHI) 50.54) were included into this study. All patients underwent anthropometric measurements, sleep study and exercise testing using bicycle spiroergometry, where functional parameters and blood pressure were measured. Data were statistically analyzed using SPSS version 15 software.

Results: Following mean parameters of OSA were present (AHI 50.54, oxygen desaturation index- 58.67, average night saturation- 90.78%, % of sleep time < 90% SpO2- 23.82). Overreaction of blood pressure during exercise test was found in 21 (52.5%) patients and also there was not found any statistical significant correlation between parameters of OSA and blood pressure overreaction (p-values- AHI- 0.409, ODI- 0.133, average night SpO2- 0.701, % of sleep time < 90% SpO2- 0.828).

Conclusions: Blood pressure overreaction during exercise test was prevalent in patients with OSA, but significant correlation between this pathology and parameters of OSA were not found. It is evident that relationship between blood pressure level during exercise and OSA is more complex.

Disclosure: Nothing to disclose.

P667

Correlation between exercise test results and body composition measured by bioimpedance method in patients with obstructive sleep apnea

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Objectives: Obstructive sleep apnea (OSA) is the most important sleep breathing disorder and obesity plays an important role in it's development. Results of exercise testing in patients with OSA are usually below physiological limits. The precise effect of OSA on patient's performance is not completely understood because body composition plays an important role.

Methods: Forty patients (31 men) with moderate and severe OSA (mean apnea- hypopnea index (AHI) 50.54) were included into this study. All patients underwent anthropometric measurements, sleep study and exercise testing using bicycle spiroergometry and measurement of body composition using bioimpedance method (Bodystat TM). Data were statistically analyzed using SPSS version 15 software.

Results: Classical parameters of physical performance (VO2max/kg, VE max, workload, etc.) and also adjusted parameters according to body composition (such as VO2max/kg of active body mass (ABM)) were measured during exercise test. Using Spearman's correlation analysis we have not found any statistically significant correlation between AHI and results of exercise testing (p-values- VO2max/kg- 0.564, VO2max/kg ABM- 0.762, VE max- 0.682).

Conclusions: In this group of patients with moderate to severe OSA apnea- hypopnoa index did not correlated with exercise test results and also to adjusted values according to body composition measured by bioimpedance method.

Disclosure: Nothing to disclose.

P668

The consolidation of declarative and non-declarative memory in children with sleep disorder breathing

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Objectives: A large amount of studies investigated the role of sleep in different memory processes, but less is known about the effect of sleep disorder on declarative (explicit) and non-declarative (implicit) memory for children. In the present study we examined the effect of disrupted sleep on different memory functions by testing children with sleep-disordered breathing (SDB).

Methods: Twelve children with SDB and 12 healthy control subjects participated in the study. We used a story recall test to measure declarative memory and Alternating Serial Reaction Time (ASRT) task to assess non-declarative memory. This task enables us to separate two aspects of non-declarative memory, namely general skill and sequence-specific learning. There were two session in the experiment for both the SDB and control group separated by a 12-h offline period with sleep.

Results: The SDB group demonstrated impaired declarative memory performance after sleep compared to control subjects. In case of non-declarative memory our data showed differences between the offline changes of general skill learning between the SDB and control group. The control group showed offline improvement, while the SDB group did not. We did not observe differences between the groups in offline changes in sequence-specific learning, however the SDB group showed decreased performance from evening to morning compared to the control group.

Conclusion: Our finding suggests that disrupted sleep in SDB have more influence on cortical structure-guided explicit processes than implicit processes mediated by subcortical structures. Moreover, sleep might have less influence on sequence-specific learning than general skill learning.

Disclosure: Nothing to disclose.

P669

The incidence of atrial fibrillation in hypertensive patients: the role of obstructive sleep apnea

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Objective: The data evidences the higher prevalence of atrial fibrillation (AF) in patients with obstructive sleep apnea (OSA). However, the results of prospective studies are not highly convincing. The objective of our study was to assess in a prospective manner the role of OSA for the AF development in hypertensive obese patients.

Methods: Since 2002 till 2006 out of 493 screened patients we selected 279 obese subjects [190(68%) males; body mass index-34.2 $\pm$ 6.5 kg/m^2] with controlled hypertension and without other known cardiovascular diseases or diabetes mellitus. Based on the sleep study results (Embletta, Iceland) they were divided into 2 age- and sex-matched groups: with OSA - 204 patients, and without OSA - 75 subjects. Every 6 months patients were contacted by phone and once a year came for an office visit. The newly onset AF served as an end point. Cox regression model included apnea-hypopnea and desaturation indices, mean saturation level, hypertension duration, standard risk factors, left ventricular hypertrophy, cardiovascular therapy.

Results: The median follow-up was 108 (67.5;120.0) months. AF has been registered in twelve (5.9%) OSA subjects and three (4.0%) controls [χ^2=0.36; P = 0.77; OR=1.48 (95%CI 0.41–5.40)]. AF onset was not associated with the development of coronary artery disease [χ^2=0.09; P = 1.00; OR=0.74 (95%CI 0.09–5.84)]. None of the variables but hypertension duration was associated with the AF development [OR=1.10 (95%CI 1.04–1.16); P = 0.001].

Conclusions: Our data suggest that hypertension duration is the only predictor of AF development in obese patients with controlled hypertension, and OSA has no additional impact in this cohort.

Disclosure: Nothing to disclose.

P670

Comparison of metabolic and endocrine parameters in patients with moderate and severe obstructive sleep apnea

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Objectives: The pathophysiology of obstructive sleep apnea syndrome (OSAS) has been associated with dysregulation of the hypothalamic pituitary adrenal axis and has been linked to abnormal glucose metabolism and increased diabetes risk. The aim of the current study was to compare parameters of glucose metabolism and hormonal status between moderate OSA (apnea-hypopnea index (AHI): 15–30) and severe OSA (AHI > 30) patients.

Methods: A total of 56 OSA patients (24 moderate and 32 severe) underwent a full-night polysomnography, oral glucose tolerance test (OGTT) and blood sampling for various metabolic and endocrine parameters. Insulin resistance was assessed by the homeostatic model assessment index of insulin resistance (HOMA-IR index).

Results: Fasting plasma glucose level (5.05 $\pm$ 0.54 vs. 5.41 $\pm$ 0.67 mmol/L; P = 0.037), HbA_{1c} (5.4 $\pm$ 0.2 vs. 5.7 $\pm$ 0.3%; P = 0.001) and HOMA-IR index (2.68 $\pm$ 2.08 vs. 4.61 $\pm$ 3.71; P = 0.026) were significantly lower in moderate OSA patients in comparison with severe OSA patients. There were no statistically significant difference in insulin and postprandial glucose levels between groups. Levels of morning plasma cortisol were statistically higher in moderate OSA group (424 $\pm$ 145 nmol/L) comparing to severe OSA patients (303 $\pm$ 93 nmol/L; P < 0.001).

Conclusions: In conclusion we can state that the glucose metabolism was altered in both groups, but more pronounced in severe OSA patients while cortisol levels were higher in moderate OSA patients.

Disclosure: Nothing to disclose.

P671

Nocturia and morbid obesity as predictors for severe apnoea-hypopnoea index and SaO2 decrease

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Background: Nocturia is defined as ;The complain associated to get up from bed to urinate more than twice per night'. It's a common

condition in patients with obstructive sleep apnoea syndrome (OSAS). Despite the relationship between nocturia and OSAS has been established, the risk factors associated to these 2 conditions are not clear yet. The aim of this study is to describe this risk of nocturia and SaO2 in patients with OSAS.

Methods: Three hundred and forty-nine patients were included in this study, all of them without other conditions that may cause nocturia. They were divided into two groups: A) 191 subjects with no nocturia and B) 158 with nocturia. All of them underwent an all night polysomnography. All data were analyzed using a Student-t test for unrelated samples.

Results: No Nocturia vs. Nocturia; AHI* (37.8 + 2.4 vs. 61.79 + 3.01), mean Sa02* (90.8 + 0.25 vs. 86.4 + 0.58), minimum SaO2* (77.2 + 0.87 vs. 70.1 + 1.32), Epworth scale* (9.4 + 0.45 vs. 11.8 + 0.55) *P < 0.01. Morbid obesity: 3.5* (2.1–6.0). Somnolence. 2.03*(1.2–3.3). Odds ratio controlled by age and gender for mean Sa02. Nocturia 4.49* (2.7–7.4), morbid obesity 3.09* (1.8–5.1). Somnolence 1.7* (1.02–2.85). *P < 0.05.

Conclusion: This data suggest that patients with nocturia, who urinate twice or more per night, show an increased AHI, a lower mean SaO2. The significant risk factors for AHI greater than 30 and SaO2 lower than 89% were nychthemeron, morbid obesity and somnolence. We think that more studies are required in order to understand the real roll of nocturia as a predictive clinical key for OSAS.

Disclosure: Nothing to disclose.

P672

Efficacy of the combined approach uvulopalatopharyngoplasty-base of tonghe somnoplasty as a treatment of the obstructive sleep apnoea syndrome

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Background: The Obstructive Sleep Apnoea Syndrome (OSAS) has emerged as a frequent and important health condition in the general population, while its proper management remains controversial. Multilevel surgical approach has shown to be a reliable alternative for the treatment of this condition.

Methods: We performed an auto controlled, prospective, experimental and analytic trial. 30 patients with OSAS were included, and all of them underwent a combined surgical approach of uvulopalatopharyngoplasty and base of tongue somnoplasty. All of them had a preoperatory polysomnographic report, and a postoperative one, 6 months after the procedure. A Student-t test was performed.

Results: We found a decrease in the mean apnoea-hypopnoea index (AHI): preoperative mean = 40.76, postoperative mean = 5.9, P < 0.01. Only one minor and transient complication was found.

Discussion: Multilevel surgical approach seems to be a safe and efficient method for the treatment of selected OSAS patients. The severity degree of OSAS seems to be not important in the results, but only when the patient has a very accurate and systematic selection.

Disclosure: Nothing to disclose.

P673

efficacy of submucosal sodium tetradecyl sulfate inhe soft palate as a treatment of the mild obstructive sleep apnoea syndrome. A pilot study

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Background: As described by Mair et al in 2001, snoreplasty; the application of sclerosant agents in the palate is a promising and cheap alternative to treat snoring. We decided to try this kind of therapy for the management of mild sleep apnoea.

Study design: Experimental, longitudinal, prospective, nonrandomized, self-controlled pilot study.

Methods: Eleven patients were included, all of them with a polysomnographic study showing an Apnoea-Hypopnoea Index (AHI) from 5–20, and with a Müller maneuver showing only retropalatal collapse.

Results: We found significant decrease in the number of apneas-hypopneas and oxygen desaturation as well as in the snoring index (P < 0.05); although no differences were found in the number of arousals.

Conclusion: Sclerosant agents might become a relevant part in the treatment of sleep apnea, in very well selected patients.

Disclosure: Nothing to disclose.

P674

Association of excessive daytime sleepiness with smoking, inflammatory markers and cardiovascular risk

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Objectives: The aims of our study were to determine whether excessive daytime sleepiness (EDS) assessed by using the Epworth Sleepiness Scale (ESS) are associated with sleep variables and biomarkers of inflammation, in obstructive sleep apnea (OSA) patients, comparing to a control group.

Methods: Two Romanian groups, consisting of forty patients diagnosed with OSA and twenty-six healthy controls, were recruited. All subjects underwent cardiorespiratory poligraphy. Plasma endothelin-1 (ET1), lipid profile, C-Reactive Protein (CRP), fibrinogen, uric acid, glycemia and γ-Glutamyl-Transferase (γ-GGT) levels were assessed. Statistical analysis was performed using Spearman correlations tests, two tailed t-test and one-way ANOVA test.

Results: The EDS was statistically significant higher in smokers (n = 41) than in nonsmokers (n = 25) (P = 0.0001). In total smokers patients (study and control groups) correlations were found as follows between EDS and the lowest oxygen saturation (SpO_2) >2sec (%), the % of sleep time spent with SpO_2 < 90% (minutes), the longest duration (minutes) SpO_2 < 88%, snoring (P = 0.0002; P = 0.001; P = 0.0009; P = 0.0003); in OSA group between EDS and Triglycerides/High Density Lipoprotein cholesterol (TG/HDLc) and γ-GGT (P = 0.006; P = 0.01), while in the control group between EDS and CRP, fibrinogen, uric acid (P = 0.004; P = 0.01; P = 0.04).

Conclusions: In smokers patients, the conventional indices of oxygen desaturation during sleep are involved in the pathogenesis of EDS. In OSA patients, EDS may be a predictor for atherosclerosis and a linking pathogenic mechanism with metabolic abnormalities and cardiovascular disease. In healthy patients, the association with established biomarkers of inflammation suggest the potential mechanisms linking OSA to cardiovascular risk.

Disclosure: Nothing to disclose.

Sleep disorders – Insomnia 2

P675

Spindles and slow waves predict treatment responses to cognitive-behavioural therapy for chronic primary insomnia

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Objectives: Chronic insomnia affects up to 15% of the general population, with adverse impacts on physical and mental well-being. Cognitive-behavioural therapy for insomnia (CBT-I) is clinically effective in 60% of patients, while the other 40% are less responsive for reasons that remain unclear. Brain oscillations during sleep (i.e. spindles and slow waves) appear to modulate sleep stability, and may thus contribute to the pathophysiology and treatment response to insomnia. This study examined spindles and slow waves as predictors of treatment response to CBT-I in chronic primary insomnia.

Methods: Eleven primary insomniacs (8F, mean age 37) underwent polysomnography, followed by 6 weeks of CBT-I. Baseline spindle (12–16 Hz) and slow wave activity (0.7–4 Hz) were automatically computed on the C4-O2 EEG derivation and correlated with sleep quality change, as assessed by pre- and post-CBT-I questionnaires (sleep diary and Pittsburgh Sleep Quality Index, PSQI).

Results: During stage N2, higher spindle density at baseline correlated with improvement in sleep quality from PSQI following CBT-I (r = -0.67, P = 0.025), and greater spindle power at baseline correlated with improvement in sleep efficiency from sleep diaries after CBT-I (r = 0.68, P = 0.021). Greater slow wave activity during stages N2 and N3 at baseline correlated with decrease in sleep latency (r = -0.63, P = 0.039) and increase in sleep efficiency (r = 0.75, P = 0.008) from sleep diaries following CBT-I.

Conclusions: These data suggest distinct phenotypes within chronic primary insomnia, whereby patients with altered microarchitecture present a neurophysiological vulnerability to insomnia and are less responsive to CBT-I.

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P676

The effect of mindfulness-based stress reduction on insomnia complaint in naturalistic sample of adult outpatients

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The objective of this study was to determine whether Mindfulness-Based Stress Reduction (MBSR) group therapy can improve insomnia complaint in a heterogeneous sample of adult outpatients.

Thirty-one outpatients participating in an 8-session MBSR group and complaining insomnia were included in the study. The control group consisted in 33 subjects with insomnia complaint recruited in community sample. There were no significant differences between the groups in terms of age, gender, psychopathology and demographic parameters. Assessments were conducted for both groups at baseline; after 8 weeks of treatment (MBSR group); or after the 8-weeks period without therapeutic intervention (control group). Pre-post measurements included two weeks of actigraphy, Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS) and Fatigue Severity Scale (FSS).

Eighteen MBSR participants (mean age 48.7 $\pm$ 13.6; 78% female) and 17 controls (mean age 54.2 $\pm$ 9.9; 64.7% female) completed the study. Only the MBSR participants showed significant pre-post improvements in the PSQI global score (P < 0.01), and in the PSQI subjective sleep quality score (P < 0.01). Despite these improvements, the PSQI global score remained high after the treatment in MBSR group (mean 6.7 $\pm$ 3.8). Surprisingly, a significant increase in the ESS score was observed in control group (pre-post increase P < 0.02). No significant changes were found in actigraphy parameters.

Although MBSR produced a statistically significant change in subjective sleep outcomes, no change was observed in objective actigraphy parameters. The persistence of high PSQI global score indicates that MBSR alone is not a sufficient therapeutic tool for the treatment of clinically significant insomnia complaint.

Disclosure: Nothing to disclose.

P677

Prevalence of insomnia and its impact on anxiety, depression and quality of life in Korean fire fighters

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Objective: The aim of this study is to evaluate prevalence of insomnia and its impact on anxiety, depression and quality of life in Korean fire fighters.

Methods: Using simple sampling method in a cross-section study in Jeonbuk province of Korea, sleep problems, anxiety, depression and quality of life of 1669 professional fire fighters were measured with Patients Health Questionnaire-9(PHQ-9), Generalized Anxiety Disorder 7 item(GAD-7) and brief version of World Health Organization Quality of Life assessment scale(WHOQoL-Brief). Insomnia was measured with 3rd item of PHQ-9, the definition of group with insomnia was people who were not able to initiate or maintain sleep. We measured cross-sectional Odds ratios for the group with insomnia on depression and anxiety by logistic regression analysis.

Results: The prevalence of insomnia of Korean fire fighters was 51.2%. Korean fire fighters with insomnia showed not only more anxiety(P < 0.001) and depression(P < 0.001) but also lower quality of life(P < 0.001). The group that had insomnia were more likely to suffer from depression(OR= 47.537, 95%, CI:33.669–64.323) and anxiety(OR=9.822, 95%, CI:7.529–12.813). The severity of insomnia in Korean fire fighters was positive correlated with depression and anxiety.

Conclusion: These results show that higher prevalence of insomnia in Korean fire fighters have more depression and anxiety, and less quality of life than fire fighters without insomnia. Insomnia are critical risk factor on the depression and anxiety in Korean fire fighters. Early detect of insomnia of fire fighters will be needed, in order to prevent their future depression and anxiety.

Disclosure: Nothing to disclose.

P678

Role of insomnia in perceived stress and coping strategies in subjects with arterial hypertension

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Objective: Aim of the study is to evaluate perceived stress and coping strategies (CS) in subjects (S) with hypertension (H), according to the presence of insomnia

Methods: Three hundred and seventy-one H S at their first visit at the Hypertension Outpatient Unit were enrolled. Perceived Stress Scale (PSS), Brief-COPE, Insomnia Severity Index (ISI), Beck Depression Inventory (BDI), and State-Trait Anxiety Inventory (STAI) were administered. S with other sleep disorders or with incomplete data (n = 41) were excluded.

Results: Data from 330 S were analyzed (males 51%, mean age 57 $\pm$ 13 years). Insomniacs (n = 70, 21%) were older (60 $\pm$ 11 vs. 56 $\pm$ 13 years, P = 0.02), females (62 vs. 46%, P = 0.01) and presented higher SSP (18 $\pm$ 9 vs. 13 $\pm$ 8, P < 0.001), STAI (68 vs. 34%, P < 0.0001) and BDI scores (30 vs. 6%, P < 0.0001) than non insomniacs. In a multiple logistic regression anxiety (OR 8.7, CL 4.8–15.7), but not insomnia (OR 1.6, CL 0.8–3.6), was independent predictor of high PSS. Insomniacs had a lower score of CS such as positive reframing (3.9 $\pm$ 2.1 vs. 4.5 $\pm$ 2.1, P = 0.03), behavioral disengagement (BD) (2.4 $\pm$ 1.2 vs. 2.6 $\pm$ 1.2, P = 0.03) and use of emotional support (ES) (4.2 $\pm$ 2.0 vs. 4.8 $\pm$ 2.1, P = 0.06). After controlling for age, gender, SSP, BDI, STAI, only BD (P = 0.02) and use of ES (P = 0.0005) were significant.

Conclusions: Hypertensive insomniacs show higher perceived stress than non insomniacs; they also present higher comorbities related to insomnia which may affect perceived stress. Insomniacs report less effective coping strategies: reduced use of behavioral disengagement may be related to the 'behavioral engagement' in dealing with insomnia according with the attention-intention-*effort* model.

Disclosure: Nothing to disclose.

P679

Association between insomnia and use of blood pression-lowering drugs in hypertensive patients: a cross-sectional cohort study

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Objective: Insomnia has been associated with increased prevalence, incidence and severity of hypertension. Aim of this study is to evaluate the role of different antihypertensive drug classes in this association.

Methods: Three hundred and seventy-one hypertensive subjects at their first visit at the Hypertension Outpatient Unit were enrolled. Insomnia Severity Index (ISI), Beck Depression Inventory (BDI), and State-Trait Anxiety Inventory (STAI) were administered. Insomnia was defined as ISI>8, depressive symptoms as BDI>10, trait anxiety as STAI >40. Patients with self-reported sleep apneas (n = 29) or with incomplete data (n = 12) were excluded.

Results: Data from 330 patients were analyzed (males 51%, mean age 57 $\pm$ 13 years, antihypertensive treatment 84%, previous cardiac events 9%, diabetes 7%, obesity 24%, smoking 13%, hypercholesterolemia 67%). Insomniacs (n = 70, 21%) were older than non-insomniacs (60 $\pm$ 11 vs. 56 $\pm$ 13 years, P = 0.02); female gender (62 vs. 46%, P = 0.01), anxiety (68 vs. 34%, P < 0.0001) and depressive symptoms (30 vs. 6%, P < 0.0001) were more prevalent in insomniacs. Insomniacs were treated with higher number of antihypertensive drugs (1.8 $\pm$ 1.0 vs. 1.5 $\pm$ 1.0, P = 0.04) and more frequently with angiotensin-receptor-blockers (ARBs, 49 vs. 31%, P = 0.009) and diuretics (50 vs. 28%, P = 0.0007), whereas the use of other drug classes was similar.

In a multiple logistic regression analysis, adjusted for cardiovascular and psychiatric variables, ARBs use (OR 2.4, CL95% 1.1–5.2), depressive symptoms (OR 3.2, CL95%1.2–8.7) and anxiety (OR 2.9, CL95%1.4–6.1) were associated with a higher probability of insomnia.

Conclusions: This cross-sectional analysis suggests that ARBs use may be associated with insomnia in a cohort of hypertensive patients.

Disclosure: Nothing to disclose.

P680

NREM sleep instability is dramatically reduced in patients with chronic insomnia and dependence on high dosage of benzodiazepines

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Objective: Benzodiazepines (BDZs), remain the most commonly prescribed drugs for primary insomnia. These drugs are safe and effective in the short term treatment, while the long-term use may cause dependence and addiction. The aim of our study was to evaluate sleep architecture and sleep microstructure (in terms of cyclic alternating pattern-CAP-analysis and power spectral analysis of sleep) in a relatively large group of long term users of high dose of BDZs for chronic insomnia, consecutively admitted for drug discontinuation.

Methods: Twenty adults with a diagnosis of primary insomnia were enrolled if they received a diagnosis of dependence on BDZs, according to international criteria, compared with a control group of 13 matched healthy volunteers. All subjects underwent a nocturnal polysomnographic recording, after one adaptation night.

Results: Time in bed, REM sleep latency and sleep stage 1% were significantly increased in patients compared to controls, while CAP rate was decreased (8.9 $\pm$ 10.6% vs. 35.7 $\pm$ 9.32, P < 0.0001), in association with a significant decrease of A1%, A1 and A2 indexes. During NREM sleep, patients showed a clear decrease in the relative power of delta band, accompanied by a relative increase of sigma and beta bands, while a time-dependent general decrease of the delta power was observed only for control subjects, during sleep stage 2 and slow wave sleep.

Conclusions: Our study demonstrates a complete disorganization of sleep, especially during NREM sleep, and of sleep homeostatic process, in adults with chronic insomnia and dependence on high dosage of BDZs.

Disclosure: Nothing to disclose.

P681

Perceptions of insomnia and daytime symptoms as a function of objective sleep duration

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Objectives: Two insomnia phenotypes have been proposed based on sleep duration. More biologically rooted, insomnia combined with short sleep duration is linked with higher indices of physiological hyperarousal and increased risk of morbidity. Conversely, insomnia combined with near normal sleep duration appears to be more psychologically rooted. However, little data exists on whether the patient's perspective on sleep and daytime symptoms differ across phenotypes.

Methods: Participants were 345 adults (M_{age}=48.7, *SD*=11.6; 38.5% male) who met diagnostic criteria for persistent insomnia ($M_{duration}$=15.3, *SD*=13.2). Objective sleep duration was based on total sleep time averaged across two consecutive nights of polysomnographic evaluation. Two groups were formed based on a sleep duration shorter (n = 180) or longer (n = 165) than 6.5 h. Participants completed the Insomnia Severity Index, Dysfunctional Beliefs and Attitudes about Sleep Scale, the Beck Depression and Anxiety Inventories, and the Multidimensional Fatigue Inventory.

Results: Unadjusted ANOVAs revealed that individuals with insomnia and adequate sleep duration reported more problems initiating sleep, greater distress and interference of sleep difficulties with daytime functioning, and less sleep satisfaction (all *ps*< 0.01) than those with short sleep duration; trends were also present for more fatigue (P = *0*.073) and greater dysfunctional beliefs about sleep (P = *0*.053) among those with normal sleep duration. Conversely, those with short sleep duration reported more problems with early morning awakenings (P = *0*.031). No differences were observed for depressive or anxiety symptoms between phenotypes.

Conclusions: Differences in patient's perceptions of sleep and daytime functioning warrant further investigation on how each phenotype impacts treatment response and health outcomes.

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P683

Clinical significance of nocturnal 6-Sulfatoxymelatonin excretion in insomnia

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Objectives: Melatonin is an endogenous sleep regulator. We assessed excretion of the major metabolite of melatonin 6-Sulfatoxymelatonin (6-SMT) and its relationships with subjective and objective measures of sleep.

Methods: We studied 39 insomniacs and 40 healthy volunteers, aged 40–70 years. Urine was collected at night (during sleeping and first morning portion) and day portion. Urinary 6-SMT was determined by enzyme-linked immunosorbent assay ELISA (Buhlmann Laboratories AG, Switzerland). The subjects underwent one night of polysomnografy (PSG) monitoring and self-completed sleep questionnaire. Sleep was visually scored using standard scoring criteria.

Results: There were significant differences in nocturnal 6-SMT excretion between controls and insomniacs (Mean±SD 21,1 ± 13,4 vs. 11,0 ± 8,63 μg per night respectively, P < 0,05). Linear correlation analyses revealed significant relationships between excretion of 6-SMT and percentage of delta and rapid eyes movement sleep without any correlation with subjective characteristics of sleep.

Conclusions: Our results support relationship between nocturnal melatonin production and objective characteristics of sleep and lack of correlation with self-reported sleep quality.

Disclosure: Nothing to disclose.

P684

Patients' perceptions of insomnia and its treatments options: a focus group approach

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Insomnia is a widespread condition, but often trivialized/under-treated in practice. This qualitative study explores the perceptions of insomnia and its treatment in adults with chronic insomnia. Four focus groups comprising a total of 17 patients (25–75 years) were conducted before their assignment to a psychological (cognitive-behavioral therapy) or a pharmacological (zolpidem) therapy. Participants were asked to describe their experiences/perceptions of insomnia, help-seeking and treatment preferences. Qualitative data were digitally recorded, transcribed verbatim, and analyzed using the Interpretative Phenomenological Analysis. Three key themes emerged from this analysis: *insomnia, a daily enigma*; *help, please!* and *what is true about treatments?* Participants reported a sort of everyday enigma about sleeplessness ('Why can't I sleep?'). A variety of self-help strategies were used as first intervention for insomnia, followed by consultation with a family physician and, as a last resort, help-seeking from a psychological/specialized sleep resource. Seeking information about insomnia from different social networks brought some confusion among participants ('What information is accurate?'), and generated a skeptical feeling about insomnia treatments. Treatment preferences were based on one's past treatment experiences and on the hope of finding an appropriate/effective intervention for one's particular case. Results highlight a high degree of dissatisfaction with current treatment options and helplessness among individuals with insomnia. There is a strong desire for more tailored therapies, with the need for more guidance/coaching in implementing treatment recommendations. Matching treatment to each patient's needs could improve insomnia treatment adherence, and deserves further attention in other studies. Research supported by NIMH Grant #MH091053.

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P685

Sleep quality and knowledge of sleep hygiene in working population

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Objectives: To evaluate sleep quality and knowledge of sleep hygiene in working population.

Methods: Cross-sectional study was performed in 2012–2013. Participants filled online questionnaire which included Pittsburgh Sleep Quality Index (PSQI), Hospital Anxiety and Depression (HAD) scale, Sleep Beliefs Scale, demographic data and questions about work type, duration.

Results: Three hundred and three currently working people from 25 to 65 years of age took part in the survey. Most of the participants

(80%) showed good or perfect knowledge of sleep hygiene meanwhile sleep quality in 70% of participants was evaluated as poor (PSQI $\geq$ 5) regardless of age. Women's sleep quality was significantly worse than that of men.

Stress at work influenced sleep quality significantly while physical activity at work had lowest impact when relation between type of work and sleep quality was evaluated. Sleep quality correlated significantly with symptoms of anxiety and depression. Regression analysis showed that increase of anxiety value (in HAD scale) by 1 point resulted in PSQI increase by 0,14; and respectively increase of depression value by 1 point resulted in PSQI increase by 0,23.

Conclusions: Study did not show any corellation between sleep quality and knowledge of sleep hygiene. The quality of sleep correlated only with subjectively perceived stress at work and symptoms of anxiety and depression.

Disclosure: Nothing to disclose.

P686

Effect of diaphragmatic breathing, progressive muscle relaxation and guided imagery on perceived stress, and cortisol salivary levels in primary insomnia sufferers: a randomized controlled trial

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Objectives: Insomnia is conceived as the subjective complaint of reduced sleep quantity and/or quality and this complaint must be present quite frequently (at least three times per week) for a considerable period of time (at least for one month). Psychophysiological factors such as stress play a major role in the onset and maintenance of primary insomnia. The aim of this study is to evaluate the short-term effects of diaphragmatic breathing, progressive muscle relaxation and guided imagery on primary insomnia sufferers.

Methods: This is a two-armed parallel group, randomized controlled trial. Primary insomniacs were randomly assigned to undergo either an 8-week CD-based stress management program (n = 27) or a control condition (n = 26). We took salivary cortisol measurements and we use self-reported validated measures to evaluate insomnia, quality of sleep and symptoms of depression and anxiety at baseline, at the 4th week and at the end of 8 weeks. Also, we measured perceived stress and health locus of control at baseline and at the end of the 8 weeks.

Results: At the end of relaxation program, in the intervention group, we noticed decrease in insomnia, improvement on sleep quality, on perceived stress, salivary cortisol and the symptoms of depression and anxiety.

Conclusions: Diaphragmatic breathing, progressive muscle relaxation and guided imagery were reported to benefit patients with primary insomnia as far as the subjective and physiological indices of stress and the symptoms of primary insomnia are concerned. We chose simple techniques which are easily applicable and can be incorporated into routine clinical practice.

Disclosure: Nothing to disclose.

P687

Polysomnographic features in insomniacs with anxiety with or benzodiazepines use

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Background: Insomnia is a prevalent condition worldwide. High levels of anxiety is frequently evident in patients with insomnia and one of the more common classes of prescribed drugs for treatment anxiety and sleep difficulties are the benzodiazepines.

Methods: The study included 150 insomniacs and 50 GS. Subjects underwent a PSG study night. Our main objective was to explore the different sleep parameters in insomniac patients with anxiety (AI) or insomniacs with benzodiazepines use (BZI), compared to a group of primary insomnia (PI) as well as to a group of good sleepers (GS).

Results: TST*: GS (8.0 $\pm$ 0.002) vs. PI (7.89 $\pm$ 0.1), PQI (8.0 $\pm$ 0.02) and BZI (7.9 $\pm$ 0.05). SEI%*: GS (91.5 $\pm$ 0.3) vs. PI (78.9 $\pm$ 1.4), PQI (76.8 $\pm$ 1.09) and BZI (79.5 $\pm$ 1.39). SOL*: GS (9.5 $\pm$ 0.7) vs. PI (38.4 $\pm$ 4.1), BZI (20.2 $\pm$ 2.4) and PQI (45.8 $\pm$ 4.5); BZI (20.2 $\pm$ 2.4) vs. PI (38.4 $\pm$ 4.1) and PQI (45.8 $\pm$ 4.5). SOREM*: GS (98.1 $\pm$ 1.7) vs. PI (112.8 $\pm$ 6.4), PQI (52.8 $\pm$ 2.8) and BZI (119.05 $\pm$ 7.6); PQI (52 $\pm$ 2.8) vs. PI (112.8 $\pm$ 6.4) and BZI (119.05 $\pm$ 7.6). F1%*: GS (10.3 + 0.2) vs. PQI (14.3 + 0.5) and BZI (15.2 + 0.6); PI (12.2 + 0.7) vs. BZI (15.21 + 0.6). F2%*: GS (51.2 + 0.4) vs. PQI (59.2 + 0.5) and IBZ (63.8 + 1.2). PQI (59.2 + 0.6) vs. PI (50.4 + 1.2) and BZI (63 + 1.2); PI vs. IBZ. F4%*: BZI (5.9 + 0.7) vs. PQI (9.5 + 0.6), PI (19 + 1.2) and GS (18.3 + 0.2); PQI (9.5 + 0.6) vs. GS and PI. REM%*: GS (20.1 + 0.3) vs. PQI (17.04 + 0.6) and BZI (15.02 + 0.7); PI (18.03 + 0.7) vs. BZI.

Conclusion: Our data indicate that there are several significant changes in PSG parameters in patients with GS, PI and insomnia secondary to anxiety and in patients with use of benzodiazepines.

Disclosure: Nothing to disclose.

P688

Polysomnographic features in insomniacs with obstructive sleep apnoea

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Background: OSA has been found in almost 50% of insomniac patients. In spite of this relationship, the ICSD-2 does not include this association. PSG is not usually necessary in the assessment of an insomnia complaint, unless there exist symptoms of respiratory or movement disorders associated to insomnia. Our main objective was to explore the different sleep parameters in insomniac patients with OSA compared to a group of psychophysiological insomnia (PI) as well as to a group of good sleepers (GS).

Methods: The study included 192 insomniacs and 50 GS. Subjects underwent a PSG study night. They were grouped according to severity of sleep apnoea index: 50 with mild OSA (OSA-M), 50 with moderate OSA (OSA-Mo), 42 with severe OSA (OSA-S), 50 subjects with PI and 50 GS.

Results: All insomniac groups showed significant changes compared with *GS in the following parameters: TST, SEI, TWT, LS (Light sleep) SWS, REM and number arousals. *TST: IOSA-S (5.9 h $\pm$ 0.06) vs. IOSA-Mo (6.5 $\pm$ 0.14). PI had an increased in

SWS compared to all groups.*LS: PI (63.2 m ± 1.3) vs. OSA-M (74.6 m ± 1.7) OSA-Mo (75.5 m + 1.1) OSA-S (81.3 m + 1.3); *OSA-S vs. IOSA-M and IOSA-Mo.*SOREM: OSA-S (131.29 ± 11.35) vs. OSA-M (93.84 ± 7.9) and GS (98.1 ± 1.7). SWS%: PI (18.5%±1.2) vs. OSA-M (9.4%±1.2), OSA-Mo (8.1%±0.8) and OSA-S (5.6%±1.0).*REM%: OSA-S (12.8%+0.9) vs. PI (18.4%+0.7), IOSA-M (16.8%+0.9) and IOSA-Mo (16.4%+0.7).*Arousals OSA-S (207.5 + 14.5) vs. PI (62.3 ± 3.9) OSA-M (87.7 + 6.1), OSA-Mo (115.1 ± 9.8) *$P \leq 0.05$.

Conclusion: Our data indicate that there are several significant changes in PSG parameters in patients with PI, GS and insomnia secondary to OSA.

Disclosure: Nothing to disclose.

P689

Preliminary study: dreams of insomnia sufferers and their personality

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Introduction: Dream contents are often influenced by the dreamer's personality. While not commonly studied, personality traits can be reflected in dreams and might influence sleep quality. Literature shows that individuals with insomnia (INS) usually score higher on introversion and neuroticism scales than good sleepers (GS). The present study evaluates the possible relationship between dreams and personality in both GS and INS.

Methods: Participants were 16 GS (M*Age*= 32.3 y, SD =5.5) and 16 INS (M*Age*= 35.4 y, SD = 4.8). Dreams were evaluated in relation to content and recall frequency, while personality was evaluated with the NEO-FFI. Scores on the different personality traits were correlated to the content of dreams (analyzed with the Hall & Van de Castle scale) and dream recall frequency. Dreams were collected through diaries.

Results: Bilateral Pearson's correlations showed that aggressions expressed by the dreamer in INS dreams were negatively correlated with the neuroticism score ($r = -0.54$, $P = 0.03$). Results also showed that the higher the score on the neuroticism scale, the lower the number of aggressions expressed by the dreamer. No significant correlations were found for any other personality trait or recall frequency between groups.

Discussion: The exploratory nature of this study prevents from drawing firm conclusions. Still, surprisingly, dream content was seldom linked to personality and status of the dreamer. Although results might partly be explained through the compensation theory, it is possible that INS type (psychophysiological or paradoxical) is linked to personality traits, which in turn are expressed in dream content.

Disclosure: Nothing to disclose.

P690

Coping strategies mediate the effects of insomnia symptoms on maternal depression during pregnancy and following childbirth

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Objectives: During pregnancy and as a new mother sleep deprivation is known to impair mood. We investigated the factors that may mediate this relationship to give mothers with poor sleep more options to help improve their mood.

Method: One hundred and eighty-four women expecting their first babies were recruited into the study. Participants (18 +) had no history of major depression. Outcome variables included depression (Edinburgh Postnatal Depression Scale: EPDS), sleep (Insomnia Severity Index: ISI and Multidimensional Assessment of Fatigue: MAF), coping strategies (Brief COPE) and self-efficacy (Self-efficacy Scale: SES). These were examined using online questionnaires during the third trimester of pregnancy and 6 weeks postnatally.

Results: During pregnancy, insomnia and fatigue explained 32% of the variance in depression ($P < 0.05$). Certain coping strategies including distraction, denial, behavioural disengagement, venting and self-blame collectively mediated the relationship between insomnia and depression ($z = 4.316$, $P < 0.001$) as well as fatigue and depression ($z = 3.88$, $P < 0.001$). At six weeks postpartum, coping strategies including emotional support, instrumental support, venting, positive reframing, planning, acceptance and self-blame mediated the effect of insomnia ($z = 2.09$, $P < 0.05$) but not fatigue on depression. Self-efficacy independently predicted depression both during pregnancy ($P < 0.01$) and the early postpartum ($P < 0.01$).

Conclusions: Although insomnia and fatigue were consistently related to lower mood both during pregnancy and postnatally, coping strategies were important mediators of these relationships. Coping strategies should be considered as a possible approach in preventing poor mood in first time expectant mums.

Disclosure: Nothing to disclose.

P691

Cognitive behavioral therapy in patients with psychophysiological insomnia

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Objectives: Psychophysiological insomnia is the most common form of insomnia and affected up to 10–20% of adult population (Hohagen et al., 1993; Hajak et al., 2001). It has been shown that cognitive behavioural therapy (CBT) is one of the effective treatments in insomnia. Although the efficacy of CBT in treatment of chronic insomnia is well known, there is little comprehensive data on the effects of CBT on subjective and objective sleep parameters.

Methods: The aim of our study was to evaluate the effects of a 6-week CBT program (weekly 90 min sessions) for patients with psychophysiological insomnia using a randomised controlled design. CBT included: sleep hygiene, information about sleep, stimulus control therapy, sleep restriction, relaxing training, cognitive therapy. All participants were randomly assigned to CBT or control wait list. Several questionnaires were filled out before/ after CBT: Pittsburgh Sleep Quality Index (PSQI), Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS-16), Beck Depression Inventory (BDI-II), State-Trait Anxiety Inventory (STAI) and SF-36 questionnaire. During the study period subjects completed a sleep diary.

Subjects underwent ambulatory polysomnography and 24-h heart-rate-variability recording before/ after CBT.

Results: Preliminary analysis showed: five patients with psychophysiological insomnia, aged 25–70 years (mean 45.8 years), 4 female/ 1 male had completed the study so far. Following CBT patients reported decreased sleep latency and increased total sleep time. Changes in heart-rate variability will be presented at the poster presentation.

Conclusions: CBT represents a non-pharmacological therapeutic intervention in psychophysiological insomnia, our preliminary results suggest that it improves subjective sleep quality.
Disclosure: Nothing to disclose.

P692

Melatonin rhythm and sleep timing in community-dwelling insomnia patients

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Objectives: Endogenous circadian pacemaker plays a major role to determine the sleep-wake timing. Changes in the phase relationship between the sleep timing and circadian phase could result in sleep disturbance. We aimed to measure the sleep timing and melatonin rhythm in insomnia patients and normal control (NC) subjects, and to compare their phase relationship between two groups.
Methods: Twenty six insomnia patients (Age:61.7 $\pm$ 9.3 years) and 14 NC subjects (Age:56.1 $\pm$ 11.6 years) were recruited from Public Health Centers in a rural area of Korea in 2013. The actigraphy recording for 7 days was conducted for each subject. Hourly saliva samples were collected five times before individual habitual sleep timing below 15 lux at home. The dim light melatonin onset (DLMO) was defined as the time which the melatonin level was 4 pg/mL.
Results: The mean sleep onset and mean DLMO were not significantly different between two groups. The mean phase angle between the sleep onset and DLMO in insomnia patients was shorter than in NC subjects, but there was no statistical difference.
Conclusions: Insomnia patients did not show any difference in the sleep-wake timing as well as melatonin rhythm compared to NC subjects. Although the phase angles between the circadian rhythm and sleep-wake cycle in insomnia patients were not significantly different than those of NC subjects, it needs to be verified by a bigger sample size.
Support: Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2013R1A1A2009888).
Disclosure: Nothing to disclose.

P693

Stress related sleep reactivity depends on metacognition in primary insomnia

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Objective: Stress-related sleep reactivity is elevated in primary insomniacs (PI). The aim of this study was to evaluate the relationships between insomnia, sleep reactivity to stress and metacognition in PI
Methods: Sixty PI patients (33 females, mean age 52 $\pm$ 15 years) were classified according to DSM-IV-TR criteria at the Psychiatric Units of Pisa University. Insomnia Severity Index (ISI), Pittsburgh Sleep Quality Index (PSQI), Metacognition Questionnaire - Insomnia (MCQ-I), *Self-Efficacy* for Sleep Scale (SES), Ford Insomnia Response to Stress Test (FIRST), Beck Depression Inventory (BDI), Zung Self-Rating Anxiety Scale (SAS), and the State-Trait Anxiety Inventory (STAI) were administered. The relation between each measure and gender (ANOVA on ranks) and age (Spearman correlation) were assessed.
Results: FIRST tended to be higher in women than in men (25.5 vs. 22.9, $P = 0.09$) and was significantly correlated with PSQI (r = 0.29, $P = 0.02$), ISI (r = 0.36, $P = 0.005$), SES (r=,−0.28 $P = 0.03$), MCQ-I (r = 0.33, $P = 0.01$), but not with BDI (r = 0.09, $P = 0.45$), SAS (r = 0.12, $P = 0.34$), STAI (r = 0.03, $P = 0.81$). In a multiple regression model including FIRST as dependent variable and age, gender, ISI, SES, MCQ-I as independent variables, female gender (standardized coefficient 0.26, $r^2 = 0.06$, $P = 0.04$) and MCQ-I (standardized coefficient 0.32, $r^2 = 0.08$, $P = 0.02$) remained independent predictors of FIRST.
Discussion: Cognition traits like metacognition associated with intrusive thoughts may favour subsequent sleep reactivity in response to stressors in insomniacs. If these findings are confirmed, they could help design therapeutic strategies for insomnia, acting selectively on metacognition to reduce stress reactivity.
Disclosure: Nothing to disclose.

P694

The Zurich 3-step concept for the management of behavioural sleep disorders in children: a before and after study

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Objectives: A number of strategies have found to be effective for the treatment of behavioural sleep disorders in children. However, the effectiveness of an intervention that focuses on basic concepts of the two-process model of sleep regulation and also uses behavioural strategies to resolve learned maladaptive sleep habits has not been presented. The object of this study was to describe our intervention which includes such a step-wise approach, to assess changes in sleep-wake variables and behaviour problems, and to compare the level of behaviour problems with healthy references.
Methods: A total of 79 children with behavioral sleep problems (age range 6–47 months, 42% females) were included in the study. Sleep problems were assessed by the Infant Sleep Questionnaire; sleep-wake variables by diary and actigraphy; circadian characteristics of the rest-activity cycle by the non-parametric circadian rhythm analysis; and behaviour problems of children $\geq$ 18 months by the Child Behavior Checklist.
Results: From before to after intervention, a significant decrease of nocturnal wake duration (Cohen's d = -0.34) and a significant increase of the duration of the longest continuous nocturnal sleep period was found (d = 0.19). Furthermore, the variability for sleep onset and sleep end time significantly decreased and circadian rest-activity cycle measures significantly improved. Moreover, parent-reported internalizing and total behaviour problems decreased (d = -0.66) and reached the level of healthy reference after the intervention.
Conclusions: The findings suggest effectiveness of the Zurich 3-step concept using objective and subjective methods. The Zurich 3-step intervention concept may be recommended for use in clinical practice with sleep-disordered children.
Disclosure: Nothing to disclose.

P695

Guided Internet-delivered cognitive behavioral treatment for insomnia: a randomized trial

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Objectives: Insomnia is a prevalent problem with a high burden of disease (e.g. reduced quality of life, reduced work capacity). Cognitive behavioural therapy (CBT) is effective in the treatment of insomnia but is seldom offered. CBT delivered through the Internet might be a more accessible alternative. In this study we examined the effectiveness of a guided Internet CBT for adults with insomnia.

Methods: A total of 118 patients, recruited from the general population, were randomized to the 6-week intervention (n = 59) or to a wait-list control group (n = 59). Patients filled out an online questionnaire and a 7-day sleep diary before (T0) and after (T1) the 6-week period. The intervention group received a follow-up questionnaire 3 months after baseline (T2).

Results: Almost three-quarters (72.9%) of the patients completed the whole intervention. Intention-to-treat (ITT) analysis showed that the treatment had statistically significant medium to large effects (P < 0.05; Cohen's d between 0.40 and 1.06), and resulted more often in clinically relevant changes, on all sleep and secondary outcomes with the exception of sleep onset latency (SOL) and number of awakenings (NA). There was a non-significant difference in the reduction in sleep medication between the intervention (a decrease of 6.8%) and control (an increase of 1.8%) groups (P = 0.20). Data on longer-term effects were inconclusive.

Conclusions: This study adds to the growing body of literature that indicates that guided CBT for insomnia can be delivered through the Internet. Patients accept the format and their sleep improves.

Disclosure: Nothing to disclose.

P696

Empirically deriving distinct insomnia subtypes: The Netherlands Sleep Registry

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Objectives: Because of its heterogeneous presentation, it is hypothesized that insomnia consists of multiple, underlying subgroups outlined by distinct phenotypes. By making use of a wide range of factors, including both sleep-related factors and stable characteristics like traits, we aim to empirically identify these distinct subtypes of insomniacs characterised by either one distinct factor or a combination of factors. Data-driven definition of subtypes will facilitate the understanding of brain mechanisms involved.

Methods: Data of the web-based Netherlands Sleep Registry (www.sleepregistry.org) were used. Included participants had a score of ≥14 on the Insomnia Severity Index (N = 1538). We conducted latent class analyses using Mplus to unravel distinct insomnia subtypes based on 47 constructs measured by questionnaires. These included sleep-questionnaires such as Insomnia Severity Index and Pittsburgh Sleep Quality Index, and constructs suggested to be indirectly related to insomnia.

Results: Latent class analyses revealed four distinct insomnia subtypes. A first subtype (29%) was characterised by low perfectionism- and rumination scores. A second subtype (19%) was characterised by high depression- and anxiety scores, with low scores on the emotional problems-scale of the Quality-of-Life questionnaire. The two remaining subtypes (41% and 11%) were similar on most of the constructs except for the pain-scale of the Quality-of-Life questionnaire. Interestingly, no subtype was distinguished by sleep constructs.

Conclusions: This study provides the first step towards empirically derived insomnia subtypes and is the basis for designing a Sleep Phenotype Survey through which people with insomnia can be subtyped prior to detailed investigation of brain mechanisms involved.

Disclosure: Nothing to disclose.

P697

Sleep coaching - a new approach in the psychological treatment of insomnia

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Objectives: Combining medical (pharmacological) treatment with psychological techniques has proved its usefulness in the treatment of insomnia in various controlled studies. Most of these psychological approaches are based on behavioural therapy. Here we are presenting a new approach called' 'sleep coaching', which combines medical treatment with psychological and psychotherapeutical techniques well-established in Gestalt therapy.

Methods and results: Sleep coaching is based on four concepts: Sleep education, a well-described element of CBT-I, which provides basic knowledge on sleep, sleep disorders and healthy sleep. This technique helps to correct false beliefs about sleep, which keep non-sleepers awake.

CBT-I: The main goal of this technique is to identify maladaptive behaviour and false assumptions about pre-sleep habits and rituals. Hypnosis and relaxation: Insomniacs are often hyperaroused. Techniques of self-hypnosis are helpful to relax, especially in pre-sleep periods. Other techniques such as meditation during the day also release the inner rigidity, which is part of the mechanisms of insomnia.

Gestalt therapy is a psychodynamic, holistic approach based on psychoanalysis. Gestalt therapy involves techniques such as role playing to identify, unfinished business', or so-called „hidden agendas'. Other methods comprise the identification of inner conflicts, which has also proved very helpful. In the light of Gestalt therapy, sleep complaints are only the foreground of a person's background, which is composed by one's biography and personality conditions.

Conclusions: Sleep coaching has been successfully applied in patients with psychophysiological insomnia. Further case studies are necessary to prove this approach also in patients with other sleep disorders.

Disclosure: Nothing to disclose.

P698

Discriminating insomniacs from good sleepers on the basis of regional spectral features of high-density electroencephalography during wakefulness

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Objectives: Insomnia is a widespread disease that severely impacts on daytime functioning of one in three persons (Ancoli-Israel & Roth, 1992). The neurobiological correlates of insomnia remain enigmatic. Here we tested whether good sleepers and insomniacs can be discriminated on the basis of their high-density electroencephalography (HD-EEG) during wakeful rest.

Methods: HD-EEG of 35 subjects, aged 22–69 years, was recorded during 5 min of wakeful rest with eyes open. Spectral features (normalized amplitudes averaged within adjacent frequency bands) of clusters of neighboring electrodes were evaluated as candidate predictors of group membership (Good sleepers, $N = 14$; Insomniacs, $N = 21$), as defined by a cutoff score of 11 on the Insomnia Severity Index (ISI, Morin et al, 2011). Linear Discriminant Analysis (LDA) was run and validated with a reiterated leave-one-out approach. Statistics derived from the confusion matrix were used to assess the classification outcome.

Results: A model with only three predictors (frontal sigma (12–16 Hz), frontal alpha (8–12 Hz), occipital theta (6–8 Hz)) provided an optimal trade-off between the bias and the variance of the classifier, minimizing the prediction error. LDA using these three predictors yielded an accuracy of 0.83, a positive predictive value of 0.90 and a negative predictive value of 0.71, suggesting a good discriminative power. Consistently, ISI scores were significantly correlated to frontal sigma ($r = 0.32$), frontal alpha ($r=-0.43$) and occipital theta ($r = 0.27$).

Conclusions: Spatially segregated spectral features of HD-EEG during wakeful rest characterizes help to tell apart people with insomniacs from good sleepers.

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P699

Effect of erroneous sleep habits upon insomnia and health: data from a national survey

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Sleep hygiene presumes the existence of regular sleep habits, but objective supportive data usually are insufficient.

Objectives: To evaluate the association of poor sleep habits (duration, efficiency and schedules) upon insomnia, health and personal factors.

Methods: Data were obtained from a national survey of 3706 Portuguese inhabitants (18–79 years). Sleep habits included: Sleep efficiency (SE)< >85%, sleep duration< >5 h and < >10 h, time in bed< >10 h, wakeup and bedtime too early and too late. The evaluated health issues were: insomnia (I), obesity (O), diabetes (DIA), hypercholesterolemia (CHO), hypertension (BP), cardiac disorders (HEART), respiratory disorders (RESP), depression (DEP), medication (Med), accidents (A), relationships' impact (REL), humour (H), concentration (CON) and memory(MEM). Analysis used Pearson chi-square, using z transformation and Bonferroni adjustment of p values; Odds ratios and 95% confidence intervals were computed.

Results: Low SE increases the proportion of all health outcomes except CHO; Sleep< 5 h increases the proportion of all health oucomes except CHO, DIA, BP, HEART, MED; Sleep>10 h only increased the prevalence of RESP, A, MEM whereas TIB >10 h increased all the prevalence except tense humour. Too early bedtime is associated with a increased proportion of accidents and sleep related accidents; late bedtime is positively associated with memory, concentration, work problems and sleep related accidents; too early awakening increased the prevalence of HEART, O and I, while wakening too late increased the prevalence of accidents and sleep related accidents.

Conclusions: Sleep related habits and schedules have statistically negative impacts upon daily life, personal features, sleep, health and accidents.

Disclosure: Sanofi-Aventis Grant

P700

Prevalence of subjective sleep disorders in general practice and morbidities associated with it in urban population of the Republic of Moldova

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Objectives: Sleep disturbances as a common health issue in our society has to be managed, therefore the aim of this study was to evaluate the prevalence of sleep disorders in general practice within the urban population of the Republic of Moldova.

Materials and methods: One thousand and sixty-seven questionnaires filled in by general practice physicians, analyzed with SPSS Statistics 17.0.

Results: The prevalence of subjective sleep disorders among patients that consulted a general practitioner are rated to 86.4%. The most common affected age is over 60 years- 29.5%; followed by the range of ages between 50 and 60 years- 29.0%; 40–50 years-14.9%; 30–40 years-7.0%. 68.4% of patients with sleep issues are females and 31.6% are males. The difficulty in falling asleep is noted in 23.9% of cases, intermittent sleep in 19.8%, the same percentage of patients complained an association of the difficulty falling asleep, intermittent sleep and early morning awakening. The most common medical conditions linked with sleep disturbances are cardiovascular diseases- 23.4% followed by neurological disorders- 15.9%, respiratory system diseases- 3.7%, endocrine disorders 3.5% and other diseases −12.4%.

Conclusion: The high prevalence of sleep disorders in our population and the association with several morbidities underscore the importance of sleep problems, as indicators of health status.

Disclosure: Nothing to disclose.

P701

An investigation of dysfunctional beliefs as a mediator of cognitive behavioural therapy for insomnia in a sample with insomnia and depression

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Objectives: Cognitive behavioural therapy for insomnia (CBT-I) affect both insomnia and depression in comorbid samples, but there is a gap in the knowledge about how the treatment works. Cognitive theories of both insomnia and depression, respectively, emphasise how negative inflexible thought content could maintain problems. The aim was to gain a greater understanding of the relationship between sleep-specific dysfunctional beliefs, insomnia, depressive symptoms and CBT-I in sample with insomnia comorbid with elevated depressive symptoms.

Methods: Sixty-four participants were recruited through advertisements and randomised to receive either CBT-I or an active control (relaxation training: RT) in groups during four sessions over seven weeks. Insomnia, depressive severity, and dysfunctional beliefs about sleep were measured pre-, mid- and post-treatment.

Results: Dysfunctional beliefs lowered over the course of treatment. CBT-I was associated with greater reductions of dysfunctional beliefs about sleep compared to RT. Mid-treatment dysfunctional beliefs about sleep mediated between CBT-I and outcomes on insomnia and depression severity. The relationships between dysfunctional beliefs and insomnia, and dysfunctional beliefs and depression were reciprocal.

Conclusion: The results support the perpetuating role of negative inflexible thought content in insomnia and depression. This may have implications for other patient groups with comorbid insomnia and warrants further investigations into treatment mediators. Studies investigating mediators of CBT-I are rare and this study is the first to investigate it for a comorbid sample.

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Disclosure: Nothing to disclose.

P702

The role of positive and negative placebo in the objective nap characteristics of good sleepers

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Objectives: While the role of conscious intention in sleep changes (Morin, 1993, Espie et al., 2006) is well recognized just few studies focused on the contribution of suggestion-based beliefs about future sleep in it quality.

Methods: Twenty-five good sleepers (14 females, 18–29 years old) visited laboratory three times at the afternoon weekend with a 1-week interval. Each time they participated in a 1-h polysomnographic recording randomly assigned to the three different instructions sequence: neutral, positive and negative placebo. Each visit participants have read a brief description of the "Cerebrophone' as an effective insomnia treatment and were told that this experiment aims to prove the effectiveness of this method in changing good sleepers' naps. Under positive placebo condition they were told that an inaudible music based on sleeping human brain waves is presented; under negative placebo conditions - active human brain waves. There was no real sound during the experiment.

Results: Comparing to the neutral instruction positive placebo paradoxically led to sleep fragmentation (WASO, number of awakes) while negative placebo was related only to the shorter longest sleep episode. Participants' belief in the placebo affects sleep quality: confident participants had lower delta sleep latency and longer delta sleep under neutral and positive conditions; lower WASO and number of awakenings in neutral and negative conditions.

Conclusions: Negative and positive placebo have different impact on the nap structure depending on the belief in the placebo effectiveness.

Acknowlegements: Study is supported by Russian Scientific Foundation project 14–15–00671

P703

Decreased plasma orexin levels in subjects with impaired sleep quality

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Objectives: The orexin system has been identified to play an important role in controlling arousal and regulation of sleep and wakefulness. An orexin deficit has been identified as the most important part of the pathophysiology of sleepiness in narcolepsy. Furthermore, sleepiness in sleep apnea also appears to be associated with reduced orexin plasma levels. Although orexin receptor blockade has been identified as a successful new treatment approach to insomnia, a disorder of hyper-arousal, no study has investigated whether orexin plasma levels are elevated in this disorder.

Methods: In this investigation we analyzed the association between the orexin plasma levels and Pittsburgh Sleep Quality Index (PSQI) scores in a sample of 259 subjects (18–55 [M = 33.4] years) from the general population and hypothesized poor sleepers to show higher orexin levels.

Results: Opposite to the hypothesis the global PSQI score correlates negatively with orexin levels (r = -0.199, P = 0.002). Nearly one quarter (24.1%) of the sample was classified as poor sleepers (global PSQI score > 5). In poor sleepers a significantly lower plasma orexin level was found compared to good sleepers (P = 0.014). Further analysis revealed significant negative relationships between the plasma orexin levels and the PSQI component scores "subjective sleep-quality' (r = -0.140, P = 0.03) and 'daytime-dysfunction' (r = -0.194, P = 0.002).

Conclusions: Although a high percentage of the poor sleepers was most likely suffering from insomnia their probable hyperarousal did not appear to be associated with an increase in plasma orexin levels.

Disclosure: Nothing to disclose.

P704

Visual processing in primary insomnia

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Objectives: Although several studies have demonstrated that sleep disorders selectively impair cognitive functions, little is known about the effect of insomnia on visual processing. In our study, visual efficiency was tested by means of a visual search paradigm.

Methods: We evaluated 19 drug-free patients with Primary Insomnia (mean age = 48 ± 14 years) and 20 age-matched control subjects (mean age = 45 ± 14 years).

Participants had to detect the presence/absence of a target (letter T) embedded into a set of characters (respectively, letters Os, Xs or Ls). The test-stimuli were presented without time constraints and subjects were instructed to perform the two-alternative forced-choice task as soon as possible. The saliency of the target with respect to the contextual letters (T vs. Os, Xs, or Ls, respectively) and the distractors' number (15, 30, 60) were manipulated. As dependent variables, accuracy and reaction times were recorded.

Results: While accuracies of both groups were comparable, higher reaction times were generally observed in the insomnia group for all conditions. However, the difference in reaction times between the two groups became larger with the increment of the distractors' number and with the similarity between target and distractors (i.e., the impairment increased with the task's difficulty).

Conclusions: Results show that in insomnia patients visual analysis consistently takes more time and their performance impairs dramatically when the extraction of visual information is more difficult. Those findings demonstrate that sleep disorders, in addition to determine an overall increment of response latency, can critically affect visual processing.

Disclosure: Nothing to disclose.

P705

Insomnia and non-restorative sleep

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Objectives: The Diagnostic and Statistical Manual for Mental Disorders (DSM-5) and the International Classification of Sleep Disorders (ICSD-3) has removed 'non-restorative sleep' as inclusion criterion for insomnia. We investigate how this impacts the prevalence of insomnia, and comorbid insomnia with depression/anxiety.

Methods: 49722 adults, self-diagnosed with sleep problems, completed an online survey. Symptoms of anxiety and depression were assessed with the Hospital Anxiety and Depression Scale. Insomnia was assessed with the Bergen Insomnia Scale (BIS), based on the DSM-IV insomnia inclusion criteria A: >30 min sleep onset latency (SOL), >30 min wake after sleep onset (WASO), >30 min early morning awakening (EMA) and non-restorative sleep; criteria B: tiredness/sleepiness and dissatisfaction with sleep. Insomnia diagnosis is fulfilled when reporting at least one symptom of each criterion A and B for 3 + days per week the last month. We calculated prevalences for insomnia, revised insomnia criteria, insomnia subgroups, and comorbid anxiety/depression.

Results: The insomnia prevalence was reduced from 90.6% (n = 36891) to 78.4% (n = 31920) with the revised criteria. As many as 82.1% had non-restorative sleep insomnia, 64.8% SOL insomnia, 42.0% WASO insomnia, and 42.6% EMA insomnia. The prevalence of comorbid insomnia and depression was reduced from 17.5% to 15.6% ($P < 0.001$), and comorbid insomnia and anxiety was reduced from 29.3% to 26.1% ($P < 0.001$) as calculated with the revised insomnia criteria.

Conclusions: Non-restorative sleep insomnia was the most prevalent subtype, followed by the SOL insomnia. The prevalence of the comorbid conditions insomnia and depression/anxiety was significantly reduced with the revised criteria.

Disclosure: Nothing to disclose.

P706

Work and sleep - a prospective study of stress, work demands, physical work environment and work scheduling

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Objective: There is limited knowledge about the prospective relation between work characteristics (stress, physical work environment, work hours) and disturbed sleep. The present study sought to provide such knowledge.

Method: The study was based on self-rated questionnaire data from two waves of the SLOSH cohort, The Swedish Longitudinal Occupational Survey of Health, an approximately representative sample of the working population in Sweden. In total, 5741 persons (54% women, age 24–72, gainfully employed at both waves) were included in the analyses.

Results: Work-related factors at T1 (e.g. work demands, control, social support, physical work environment, work hours and stress) were analyzed with logistic regression with sleep disturbances at T2 as the outcome. Work demands (OR 95% CI, 1.57; 1.28–1.93) and stress (1.51; 1.27–1.85) at T1 predicted sleep disturbances at T2. When the work related predictors from T1 and T2 were combined, persistent high work demands and stress levels related to disturbed sleep at T2, as did an increase in stress and decrease in social support. A reverse relation between disturbed sleep at T1 and stress and high work demands at T2 was also found, suggesting a bidirectional relationship. Neither shift work, long hours, heavy physical work, noise at work, nor poor lighting conditions predicted disturbed sleep.

Conclusions: Psychosocial risk factors at work related to subsequent self-reported disturbed sleep, but long hours, shift work and physical work environment variables did not. The results are important for understanding the role of work factors in sleep disturbances.

Disclosure: Nothing to disclose.

P707

The efficacy of cognitive behavioral therapy for insomnia by email follow-up after introductory sessions in person

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Introduction: The aim of this study was to review the efficacy of email-conveyed cognitive behavioral therapy for insomnia (CBT-I) after a few sessions in person.

Methods: This was a retrospective study reviewing the data of the patients who underwent combined CBT sessions in person and

follow-up session by emails for primary insomnia. The detailed medical history and evaluation including sleep diaries, Pittsburgh sleep quality index (PSQI), Epworth sleepiness scale (ESS), insomnia severity index (ISI) and Beck depression inventory (BDI) were performed before CBT-I. CBT was done by a neurologist who was trained for CBT-I. Email follow-up of sleep diaries and feedback by email or phone call were done.

Results: Data of four patients (1 female, mean age, 39 $\pm$ 7.53 years) were analyzed. All four took the hypnotics at the time of CBT-I, which were tapered off. All of them had 20 years of education and had professional jobs. Mean PSQI and ISI showed significant improvements after the completion of CBT-I (14 $\pm$ 3.3; 21 $\pm$ 2.2 vs. 5.3 $\pm$ 1.5; 5.6 $\pm$ 3.5) as well as significant improvement of sleep latency and total sleep time. The number of email session was varied from one to 12 sessions. The patient who did not get the CBT session in person got the longest email sessions.

Conclusion: Our study showed email follow-up session is effective for patients with chronic insomnia to complete CBT-I although the number of subjects is small. Combined CBT in person with email follow-up session can increase the feasibility of CBT-I in clinical practice.

Disclosure: Nothing to disclose.

Sleep disorders - Movement disorders

P708

Restless legs syndrome among patients with chronic renal failure on regular hemodialysis

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Objectives: To study the prevalence of RLS in Saudi patients with ESRD and its association with dialysis adequacy, and existing comorbidities.

Methods: This was a cross-sectional multicenter study which was carried out in three dialysis centers in Jeddah, Saudi Arabia, from June 2012 to September 2013. All patients were individually interviewed. Information was collected on demographic, medical and laboratory data, Epworth Sleepiness Scale (ESS), and from the International Restless Legs Syndrome Study Group (IRLSSG) questionnaire.

Results: Three hundred and fifty five patients were recruited. The prevalence of RLS in ESRD patients was found to be 20.2%, majority experienced RLS of moderate to severe level. RLS was significantly associated with OSA ($P < 0.0001$) and ESS ($P = 0.009$); and 78.6% of patients reported daytime sleepiness. Iron deficiency anemia (IDA) was found in 48% of patients. There was a borderline negative correlation between dialysis adequacy and severity of RLS symptoms ($r = - 0.23$, $P = 0.053$). None of comorbid diseases including diabetes mellitus, which was reported in 35% of patients, revealed any association with RLS. The odds of developing RLS increased significantly with increasing BMI ($P = 0.001$). Anti-platelet and anticoagulants were also found to be associated with increased risk of RLS ($P = 0.037$ and 0.035 respectively).

Conclusions: RLS is common in ESRD patients on hemodialysis and it is an important source of sleep disruption. In addition to IDA, medications and BMI may be important risk factors.

Disclosure: Nothing to disclose.

P709

Meta-analysis of sleep and cognition in Parkinson's disease: lessons for research design

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Objectives: It is well-established that sleep disorders have neuropsychological consequences. Studies of night-time sleep problems and cognition in Parkinson's disease (PD), however, paint a mixed picture, with many reporting no relationship between sleep problems and neuropsychological performance. This analysis addresses two questions

1) are particular sleep problems associated with neuropsychological deficits in PD and

2) whether the selection of tests impacts on outcomes.

Method: A literature search was conducted of published and unpublished studies, resulting in 16 papers that met inclusion criteria. Meta-analysis was used to synthesise data and calculate overall effect sizes.

Results: Significant effects were found for global cognitive function, long term verbal recall, long term verbal recognition, shifting, updating, generativity and fluid reasoning.

Conclusions: The effects associated with poor sleep in PD were driven by the few studies that used highly sensitive neuropsychological tests. Most studies used the Mini-Mental State Examination and the Frontal Assessment Battery as their main neuropsychological assessments, concluding that sleep problems had no effect on cognition in PD. More sensitive measures may have produced different results. While REM Sleep Behaviour Disorder undoubtedly impacts on cognition in PD, the effects of other sleep disorders such as sleep apnoea syndromes, insomnia and specific reduction of slow wave sleep remain unstudied.

Research designed for special populations, such as PD, must be guided by both the neuropsychological and the sleep literatures, as neuropsychological deficits can be detected by the careful selection of tests sensitive to subtle cognitive deficits.

Disclosure: Nothing to disclose.

P710

Actigraphy as a diagnostic aid for REM sleep behavior disorder in Parkinson's disease

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Objectives: Rapid eye movement (REM) sleep behavior disorder (RBD) is a common parasomnia in Parkinson's disease (PD) patients. The current International Classification of Sleep Disorders (ICSD-II) requires a clinical interview combined with video polysomnography (video-PSG). The latter is time consuming, expensive and not always feasible in clinical practice. We studied the use of actigraphy as a diagnostic tool for RBD in PD patients.

Methods: We studied 45 consecutive PD patients (66.7% men) with and without complaints of RBD. All patients underwent one night of video-PSG and eight consecutive nights of actigraphy. Based on previous studies, the main outcome measure was the total number of bouts classified as 'wake', compared between patients with (PD+RBD) and without RBD (PD- RBD).

Results: Twenty-three (51.1%) patients had RBD according to the ICSD-II criteria. The total number of wake bouts was significantly higher in RBD patients (PD+RBD 73.2 ± 40.2 vs. PD-RBD 48.4 ± 23.3, $P = 0.016$). A cut off of 95 wake bouts per night resulted in a specificity of 95.5%, a sensitivity of 20.1% and a positive predictive value of 85.7. Seven patients were suspected of RBD based on the interview alone, but not confirmed on PSG; six of whom scored below 95 wake bouts per night on actigraphy.

Conclusions: Actigraphy has additional value besides the clinical interview in the diagnostic trajectory of RBD in PD. The combination of actigraphy and previously reported -sensitive- RBD questionnaires may be a promising diagnostic method.

Disclosure: Nothing to disclose.

P711

Restless legs syndrome and post polio syndrome: a case-control study

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Objectives: To investigate the prevalence of restless legs syndrome (RLS),fatigue and daytime sleepiness in a large cohort of patients affected by post polio syndrome (PPS) and their impact on patient health-related quality of life (HRQoL) compared with healthy subjects.

Methods: PPS patients were evaluated by means of Stanford Sleepiness Scale (SSS) and Fatigue Severity Scale (FSS). SF36 questionnaire was utilised to assess HRQoL in PPS. RLS was diagnosed when standard criteria were met. Age and sex matched healthy controls were recruited among spouses or friends of PPS subjects.

Results: A total of 66 PPS patients and 80 healthy controls were enrolled in the study. A significant higher prevalence of RLS ($P < 0.0005$; O.R. 21.5; C.I. 8.17–57) was found in PPS patients (PPS/RLS+ 63.6%) than in healthy controls (7.5%). FSS score resulted higher in PPS/RLS+ than in PPS/RLS- patients ($P = 0.03$). A significant decrease of SF-36 scores, including *Physical Function* ($P = 0.001$), *Physical Role* ($P = 0.0001$) and *Bodily Pain* ($P = 0.03$) domains, was found in PPS/RLS+ vs. PPS/RLS- patients. Finally, we found that PPS/RLS+ showed a significant correlation between IRLS score and FSS ($P < 0.0001$), as well as between IRLS and most of SF36 items (Physical Role $P = 0.0018$, General Health $P = 0.0009$, Vitality $P = 0.0022$, Social Functioning $P = 0.002$, Role Emotional $P = 0.0019$ and Mental Health $P = 0.0003$).

Conclusion: Our findings demonstrated a high prevalence of RLS in PPS, and that RLS occurrence may significantly influence the HRQoL and fatigue of PPS patients. Moreover this association may suggest that both PPS and RLS may share common neuroanatomical and inflammatory mechanisms.

Disclosure: Nothing to disclose.

P712

Blink reflex and brainstem auditory evoked response in patients with restless legs syndrome after pramipexole

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Objectives: The pathophysiology of Restless Legs Syndrome (RLS) and the related Periodic Limb Movements (PLM) are still unknown. Different hypothesis favour alternative locations as the thalamus, brainstem, spinal cord or the peripheral nerve. The dopaminergic system seems to be involved since dopamine receptor agonists treat RLS and PLM successfully.

Brainstem Auditory Evoked Responses (BAER) and blink reflexes (BR) were performed before and after pramipexole (PPX), investigating possible brainstem involvements in the regulation of RLS.

Methods: Seven men and eight women diagnosed with RLS, all dopamine agonist naive, underwent BAER and BR before and after single dose of pramipexole. An average BAER potential from 2000–4000 monoaurical click stimulus were recorded in 12 subjects. Amplitudes and latencies for BAER waves before and after PPX were calculated. Blink reflexes from 13 subjects were obtained using single electrical supraorbital nerve stimulation compared to paired stimulation. The degree of amplitude and duration changes of the habituated late blink reflex component (R2) before PPX were compared to the degree of habituation after PPX.

Results: No significant differences in BAER wave amplitudes or latencies were found after pramipexole compared to baseline. The habituated R2 blink reflex response showed significantly lower amplitudes and shorter durations after PPX.

Conclusion: Increased excitability in blink reflexes has previously been shown in patients with PLM compared to normal controls. In this study the excitability of the R2 blink reflex response decreased after PPX. This might indicate a response in dopaminergic projections in the brainstem leading to enhanced habituation in patients with RLS.

Disclosure: Nothing to disclose.

P713

Brain iron accumulation with restless legs syndrome in a donor blood Spanish family

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Background and objective: The pathophysiology of restless legs syndrome (RLS) is complex. A genetic component exists but the genes involved have yet to be identified. How these aetiological factors: dopaminergic dysfunction, impaired iron homeostasis and genetic disposition, are inter-related in the genesis of RLS remains unclear. Secondary RLS with iron deficiency -which suggests a disturbed iron homeostasis- remains to be elucidated.Our aim was to report the findings from a unique blood donor Spanish family of three generations with RLS.

Patients and methods: Six family members were diagnosed with RLS defined by the International RLS study group and without familial history of neurologic diseases. Furthermore, the family consists of blood donors for 10–40 years. Neurological examination, ESS, polysomnography, laboratory evaluation (serum iron, ferritin, transferrin, transferrin saturation and soluble receptor, haemoglobin, C-reactive proteine); and a genetic study for haemochromatosis mutations were performed.

Results: Neurological examinations were normal with subtle extrapiramidal features in the grand-father affected with ferropenic anemia and B12 deficiency. PSG showed disturbed nocturnal sleep with a reduction in sleep efficiency and an increased PLMS index. The cranial MRI showed brain iron deposits in basal ganglia. Phenotypic and genotypic studies rule out genetic haemochromatosis or iron overload.

Conclusion: The abnormal iron accumulation in the basal ganglia, in a blood donor family, indicated a complex iron metabolism disorder of the CNS. Further studies are necessary to confirm our findings - overload of central iron even in long term blood donors - and its role in the pathophysiology of RLS with PLMS.

Disclosure: Nothing to disclose.

P714

A cross sectional study of restless leg syndrome in Iranian hemodialysis patients

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Objectives: Despite being frequently described in patients with end-stage renal disease, prevalence of Restless Leg Syndrome in patients under hemodialysis varied considerably and is not well documented in Iran. The aim of this study was to investigate prevalence of RLS in ESRD patients and sleep disorders in Iranian hemodialysis patients.

Methods: Three hundred and ninety-seven consecutive hemodialysis patients were evaluated by means of a face-to-face interview. RLS was diagnosed using the International RLS Study Group (IRLS) criteria. Also, three validated sleep disorder questionnaires (Insomnia Severity Index, Epworth sleepiness scale and Pittsburgh sleep quality index) were completed by the patients.

Results: One hundred and twenty-six patients presented RLS (31.7%; mean age 57.59 + /−15.36y), being more frequent in females ($P < 0.00$). RLS cases showed poorer quality of sleep (Pittsburgh Sleep Quality Index >5, $P = 0.00$), higher scores on the Epworth Sleepiness Scale ($P < 0.00$) and greater scores on the insomnia severity index ($P = 0.00$). There were no significant differences between age, duration of dialysis, etiology of renal insufficiency, intake of nicotine, alcohol or caffeine and associated comorbidities (anemia, hypertension and neuropathy) between patients with and without RLS. ($P > 0.05$)

Conclusion: In this study, prevalence of RLS is near to weighted-mean prevalence of other studies. (Mean: 30%, Range: 8–52%).
This variability can be attributed the narrowness or breadth of the definition plus variations in the time period over which prevalence is recorded.
Use of more rigorous criteria developed by IRLSSG for identifying prevalence and face to face interview can reduce this variability.

Disclosure: Nothing to disclose.

P715

Comparison of restless legs syndrome patients and healthy controls: differences in biomarkers and comorbid conditions

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Objectives: As the pathogenesis of Restless legs syndrome (RLS) is not completely understood and long term consequences of RLS are underestimated, in this study we wanted to specify which biomarkers and risk factors are associated with RLS.

Methods: Using advertisements we asked 30 people with complaints of RLS and 30 healthy controls (matched by gender and age) from age 18–75 to participate. Each participant was carefully examined and questioned by medical professional to prove or rule out the diagnosis of RLS. All the participants filled RLS symptoms severity scale (IRLS), Munich chronotype questionnaire (MCTQ), emotional state questionnaire and M.I.N.I. psychiatric interview. We asked about all comorbid conditions, medications, aggravating and alleviating factors, family history of RLS and subjective sleep quality. We collected blood samples of 40 different biomarkers and confirmed the diagnosis with polysomnography.

Results: In RLS group mean age was 31.7, the start of RLS complaints was at age 24.6 for women and 21.7 for men. Mean IRLS score was 19. Biomarkers showed RLS associations with ferritin, which was low only in RLS women (mean 45.85 vs. 105.96 in RLS men). Symptoms of RLS were significantly associated with asthenia, insomnia, anxiety and depression.

Conclusions: It is important to ask about RLS symptoms in younger and middle-aged groups to get the correct diagnosis and treatment earlier. Ferritin is relevant biomarker associated with RLS. Mood disorders are frequent comorbid conditions to be noticed in RLS patients.

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P716

Predictors for the persistence of symptoms of restless legs syndrome after iron replacement

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Objectives: A substantial portion of restless legs syndrome (RLS) patients with iron deficiency showed incomplete remission after iron treatment. This study was conducted to identify risk factors associated with the persistence or relapse of RLS symptoms after iron treatment.

Methods: In this study, we included RLS patients with serum ferritin below 50 μg/L of an university hospital between 2007 and 2013. A total of 33 subjects with serum ferritin normalized after iron replacement were analyzed, and subjects were classified into 'remission' and 'persistence' group. The two groups were compared on demographic and clinical characteristics and the logistic regression analysis was performed.

Results: RLS symptoms persisted in 18 patients (54.5%) and there were significant differences between the two groups in age at initial diagnosis and pre-treatment IRLS score (remission vs. persistence group; 46.7 $\pm$ 11.8 vs. 57.8 $\pm$ 2.4 years, $P = 0.013$; 20.7 $\pm$ 5.5 vs. 26.1 $\pm$ 6.3, $P = 0.016$). In the logistic regression analysis, older age at initial diagnosis ($\geq$ 55 years) was significantly associated with persistence of RLS symptoms after iron treatment (OR, 6.79; 95% CI, 1.11 - 41.65; $P = 0.038$). Higher per-treatment IRLS score ($\geq$ 21) also increased the odds of symptom persistence (OR, 9.86; 95% CI, 1.35 - 72.08; $P = 0.024$).

Conclusions: More than half of RLS patients with low serum ferritin showed persistence of RLS symptoms after oral iron supplementation, consequently requiring additional treatment. Older age at initial diagnosis and more severe symptom at baseline may predict incomplete response to iron supply in RLS patients with iron deficiency.

Disclosure: Nothing to disclose.

P717

EEG high frequencies and hyperarousal during the sleep onset period in patients with restless legs syndrome

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Objectives: In order to test the hypothesis that a state of hyperarousal might be present during the sleep onset period (SOP) in restless legs syndrome (RLS) during), the electroencephalographic (EEG) spectral content was quantified in untreated patients during SOP and the quiet wakefulness preceding sleep.

Methods: Twenty-seven untreated consecutive patients with RLS, 11 untreated consecutive patients with primary insomnia, and 14 normal controls were included. SOP was defined as the 10-min period centered with the occurrence of the first sleep spindle in the EEG, and then subdivided into SOP-1 (period of 5 min before the first spindle) and SOP-2 (period of 5 min following). Leg movements occurring during SOP were counted and used as a covariate in the statistical analysis. Also, one period of 1 min of artifact-free quiet wakefulness after lights off was identified. EEG spectral analysis was run during these periods using the C3/A2 or C4/A1 channel.

Results: Increased alpha and beta bands and/or beta/delta ratio in RLS vs. normal controls, during both wakefulness preceding sleep and SOP (both parts SOP-1 and SOP-2) were found, which were, however, smaller than the increases found in patients with insomnia.

Conclusions: The results allow us to confirm the original hypothesis of the presence of a state of hyperarousal in RLS during the SOP. A comprehensive treatment for RLS might need to take these findings into consideration.

Disclosure: Nothing to disclose.

P718

Restless legs syndrome in the general population - how often is there an association with distress and disturbed sleep?

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Objectives: We have previously reported that 18% of the adult Icelandic population reports symptoms of restless legs syndrome (RLS) (Benediktsdottir B, 2010). It is not known if this high RLS prevalence is associated with distress or disturbed sleep.

Methods: In an epidemiological study on asthma and allergy (www.ecrhs.org) a random population sample 40–65 years was invited for a type 3 home sleep study (T3, NoxMedical, Reykjavik, Iceland). Those who reported classical RLS symptoms were also asked on a 5-point scale how distressing these symptoms were and if the symptoms disturbed their sleep.

Results: Out of 456 subjects who participated in the study, 433 answered the questionnaire on RLS (95.0%). RLS was reported by 15.9% (n = 69, 11.3% of males and 20.0% of females, P = 0.01). RLS was reported to be moderately or severely distressing by 44.9% and associated with disturbed sleep at least once a week by 42.0% (no gender differences). The majority of those who found RLS distressing, also reported disturbed sleep related to RLS (65.5%, P = 0.003). No significant difference was found in obstructive sleep apnea severity or daytime sleepiness (Epworth sleepiness scale) in those reporting RLS compared to other subjects nor between those with RLS and disturbed sleep and those with RLS only.

Conclusions: In a large general population sample, 15.9% report RLS but only about half of those are distressed by their symptoms and associate it with disturbed sleep. This group more likely needs treatment for their symptoms as the others are likely little affected by their symptoms.

Disclosure: Nothing to disclose.

P719

Late soleus response in restless legs syndrome

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Purpose: This study was to investigate the late soleus response after transcranial magnetic stimulation (TMS) in patients with restless legs syndrome (RLS). We aimed to determine an objective diagnostic tool and prognosis indicator.

Method: In this study, 40 patients with RLS and 40 controls were included. For all patients and controls routine laboratory investigations, electroneurography (ENG) and TMS were performed. Finally the late soleus response latency of 40 RLS patients and 40 age and gender matched controls were compared. All patients were diagnosed with the 4 criteria defined by the American Sleep Academy and the severity was classified according to the international restless legs syndrome scaling group (IRLSSG) classification.

Results: The soleus late response latency in RLS patients and controls was 96 ms (SD: ±12,5) and 81,8 ms (SD:±3,4), respectively. The difference between both groups was statistically significant (P < 0,001). According to the severity of RLS, the late response latency was significantly longer in the severe group (104,5 ms; SD:±8,3 ms n = 24) than in mild-moderate RLS patients (83,2 ms; SD:±3,4; n = 16).

Conclusion: In restless legs syndrome it is known that the corticospinal tract is not directly affected but subcortical inhibition is influenced due to functional spinal neuron impairment. As a result of this study we determined a direct functional impairment of spinal afferent and efferent long reflexes and we recognized that corticospinal late responses are affected in RLS. According to the results of our study we think that TMS can be a new diagnostic modality and a prognostic indicator for RLS patients.

Disclosure: Nothing to disclose.

P720

Is autonomic nervous system involved in restless legs syndrome during wakefulness?

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To investigate cardiovascular autonomic function in patients with restless leg syndrome (RLS) by means of cardiovascular reflexes and heart rate variability (HRV) during wakefulness.

Twelve RLS patients and 14 controls underwent cardiovascular function tests including head-up tilt test (HUTT), Valsalva maneuver, deep breathing, hand grip and cold face. HRV analysis was

performed in the frequency domain both using autoregressive (AR) and fast Fourier transform (FFT) algorithms in rest supine condition and during HUTT.

We observed a significant increase of systolic blood pressure values in supine rest condition and a lower Valsalva ratio in RLS patients respect to controls. Furthermore the significant and physiological changes of HRV at HUTT detected in healthy subjects were not found in RLS patients.

RLS patients exhibit a tendency to hypertension, a reduced amplitude of both sympathetic and parasympathetic responses at HUTT as well a blunted parasympathetic drive to blood pressure changes. These findings support the hypothesis of an autonomic nervous system involvement during wakefulness and consequently the enhanced cardiovascular risk in RLS.

Disclosure: Nothing to disclose.

P721

Respiratory-related leg movements: what is the evidence behind the rules

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Objectives: Current scoring rules exclude leg movements that occur near respiratory events from being scored as periodic leg movements during sleep (PLMS) but differ in whether they exclude leg movements occurring at the end (WASM/IRLSSG) or during a respiratory event (AASM). The aim of the study was to describe the distribution of leg movements in relation to respiratory events and to contribute to an evidence-based rule for the identification and scoring of respiratory-related leg movements (RRLMs).

Methods: Retrospective chart review and analysis of polysomnographic recordings of 64 patients (18–75 years), with AHI > 20, ODI > 10, > 15 leg movements/h of sleep.

Results: Back-averaging of leg movement activity (LMA) with respect to respiratory events revealed that LMA increased shortly before the end of the respiratory events, with peak onset of LMA 2.5 s after the end of the respiratory event. Change-point analysis indicated that LMA was increased over an interval of −2.0 s to +10.25 s around the end of respiratory events. The number of patients with obstructive sleep apnea (OSA) with PLMS index > 15 was 80% when considering the WASM/IRLSSG definition, 67% for the AASM criteria, and 41% when based on the interval identified by change-point analysis.

Conclusions: Leg movements are not augmented at the beginning or middle of respiratory events but are increased around the end of respiratory events over a period significantly longer than specified in current rules which underestimate the number of RRLMs and overestimate the number of PLMS in patients with OSA.

Disclosure: Nothing to disclose.

P722

Predominant PLMs (periodic leg movemtents) in the first cycle of sleep in restless legs syndrom (RLS)

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Objectives: To study polysomnography (PSG) parameters of PLM in RLS.

Methods: Thirty-two patients (18 females −14 males, mean age 63.5 years old) who fullfilled the criteria of the International RLS Study Group (IRLSSG) underwent PSG. All patients had not received medications for RLS for at least 2 weeks prior to PSG.

Results: Twenty seven of the patients (84%) had PLM indices (PLMI) higher than 15/h. In 19 of the 27 PLMS patients (70%), more than 70% of PLMs occurred during the first sleep cycle. Among the above group, early PLM predominance was associated with lower total PLMI ($P = 0.001$) and higher Sleep Efficiency (SE) ($P < 0.001$). Older age was associated with significantly lower probability of early PLM predominance ($P = 0.004$), higher PLMI ($P = 0.003$) and lower SE ($P < 0.001$). Female gender was weakly associated with the early PLM predominance subgroup ($P = 0.099$), and significantly associated with lower PLMI ($P = 0.027$) and higher SE ($P = 0.004$).

Conclusions: Predominance of PLMs in the first cycle of sleep is a frequent polysomnography finding in RLS and correlates with better quality of sleep (lower PLMI, higher SE).

Disclosure: Nothing to disclose.

P723

Periodic limb movements and sleep architecture in RLS patients

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Objectives: Periodic limb movements in sleep (PLMS) are considered to be one of the clinical supportive features of restless legs syndrome (RLS). It is supposed that they are a factor disturbing nocturnal sleep in RLS patients. Aim of this study was to analyze to what extent the number of PLMS measured with PLMS-Index (PLMS-I) disturbs the architecture of sleep of RLS patients.

Methods: We have analyzed polysomnographic recordings of 38 RLS patients. The patients were divided into two groups: Group I with PLMS-I lower than median for the whole group and Group II with PLMS-I equal or higher than the median. Sleep latency (SL), Sleep Efficiency (SE), Sleep stages latencies, Awakenings index (AW-I), Arousals index (AR-I), wake after sleep onset (WASO) were compared between the groups.

Results: There were 19 subjects in Groups I and II. The groups did not differ significantly in terms of mean age and sex distribution (51.6 vs. 48.3 years; M/F: 4/15 vs. 10/9) The mean PLMS-I was 7.3 in Group I and 42.9 in Group II ($P < 0.0005$). Subjects in Group II had longer REM latency (1.8 h vs. 2.7 h, $P < 0.005$), higher AW-I (4.9 vs. 6.4; $P < 0.05$) and higher AR-I (14.4 vs. 20.9; $P < 0.05$). No differences in SL, SE or WASO were found.

Conclusion: Despite large difference in values of PLMS-I only moderate differences in sleep architecture were found. A conclusion that PLMS are not the major factor disturbing nocturnal sleep in RLS patients may be drawn.

Disclosure: Nothing to disclose.

P724

Presence of restless leg syndrome and iron deficiency among third trimester of pregnant women in a Japanese urban clinic

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Objectives: Third-trimester pregnancy is a risk factor for Restless Legs Syndrome (RLS), which has been associated with iron deficiency. Approximately 10–20% of pregnant women experience RLS. The aim of this study is to detect the presence of RLS among third-trimester women and to describe related hematological factors.

Methods: We recruited 51 women during July-October, 2013 from an antenatal clinic in urban Japan. 50 third-trimester trimester women agreed to participate. We used the specific, sensitive and reliable, The Johns Hopkins telephone diagnostic interview (TDI), to assess symptoms for RLS following the International RLS Study Group criteria. Questionnaires used were: International RLS Study Group Rating Scale (IRLS), and Johns Hopkins Restless Legs Syndrome Quality of Life questionnaire (RLS-QOL). Hematological tests used were: ferritin, iron, and hemoglobin. Actigraph assessed leg movement activity.

Results: Women's mean age was 30.3 year-old with 46% being primiparas. Nine (18%) were RLS positive. Pregnant women with and without RLS were not significantly different in ferritin, iron, and hemoglobin. Severity of RLS among the nine women was: mild - 5, moderate - 2, and severe - 2.

Conclusions: In this study of third trimester pregnant Japanese women there was high rate of RLS with no difference in hematologic levels from the women without RLS.

It was approved by the institutional IRB. There is no conflict of interest.

Disclosure: Nothing to disclose.

P725

Association between impulsive-compulsive behaviors and REM sleep behavior disorder in Parkinson's disease: a video-polysomnographic study

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Objectives: we previously showed that patients with Parkinson's Disease (PD) and clinical probable REM sleep behaviour disorder (PD-pRBD) have an increased risk to develop Impulsive-Compulsive Behaviors (ICBs) symptoms assessed by questionnaire[1]. The aims of this study was to compare the frequency of PSG-confirmed diagnosis of RBD in PD patients with and without ICBs assessed by standard criteria[2].

Methods: Seventeen consecutive non-demented PD patients [12M; mean age:62.9 $\pm$ 8.0 years., Hohen &Yahr (H&Y):2.2 $\pm$ 0.6] with one or more current ICBs (PD-ICBs) assessed by clinical interview were identified during their routine evaluation at a movement disorder center. They were matched by sex and age with 17 consecutive PD patients without ICBs history (PD-noICBs, mean age:63.1 $\pm$ 9.3 years, H&Y: 2.2 $\pm$ 0.7). All subjects underwent to a full-night video-polysomnographic recording (vPSG). Sleep scoring was performed blindly to ICBs condition and RBD was diagnosed according to ICDS-3 criteria,[3] including a quantified measure of REM sleep without Atonia (RSWA).

Results: RBD was found in 15/17 (88.2%) PD-ICBs patients vs. 8/17 (47.1%) PD-no ICBs patients (Fisher-exact test: $P = 0.025$). Mean RSWA in PD-ICBs and PD-noICBs was 47.4 $\pm$ 22.8% and 28.4 $\pm$ 26.0% respectively ($P = 0.046$). In one of the two PD-ICBs patients failing to fulfil the RBD diagnostic criteria, video-monitoring showed two very short motor episodes during REM sleep, possibly suggesting a minor RBD.

Conclusion: in the present study, vPSG-confirmed RBD was found in nearly 90% of PD patients with ICBs. RBD might represent a predisposing factor for ICBs in PD.

[1]Fantini et al.,JNNP 2014 in press

[2]Voon et al.,Lancet Neurol 2009

[2]ICDS 3rd ed. Darien, IL:AASM 2014.

Disclosure: Nothing to disclose.

P726

Restless legs syndrome in Czech pregnant women: an epidemiological and genetic study

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Objective: Idiopathic restless legs syndrome (RLS) is associated with common genetic variants in five chromosomal regions. The aim of our study was to evaluate the prevalence of RLS among Czech pregnant women and to further analyze the impact of known genetic determinants for RLS in this population.

Methods: We surveyed 776 pregnant women (18–49 years old) in the 36th–38th week of pregnancy. We used the minimal set of 3 epidemiological questions [DH1] to assign RLS status, disease course and frequency of symptoms. Further, we asked for previous pregnancies and comorbidities. In total 752 pregnant women were genotyped using 12 single nucleotide polymorphisms within the five genomic regions.

Results: The prevalence of RLS during pregnancy was 28.0% (95% confidence interval from 24.9% to 31.2%) in our sample. Of these cases, 71.0% of women had symptoms more than once per week and 49.3% reported symptoms in the third trimester. Leg cramps were marginally more frequent in the RLS group (23% vs. 16%, $P = 0.022$), as was hypothyreosis (13% vs. 8%, $P = 0.033$). We found only a nominally significant one-sided association for SNP rs6710341 in the *MEIS1* gene, ($P = 0.018$), rs3923809 in the *BTBD9* gene ($P = 0.029$) and also rs6747972 in the region of 2p14 ($P = 0.049$).

Conclusions: We demonstrate that RLS is significantly associated with pregnancy in Czech women. The genetic part of the study shows a likely association with *MEIS1* and *BTBD9*, the major risk factors for idiopathic RLS and secondary RLS in pregnancy.

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Disclosure: Nothing to disclose.

P727

Comparison between automatic and visual scoring methods of muscle tone during rapid eye movement sleep in Parkinson's disease

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Objective: To compare three different quantitative methods, two visual (Montréal[1] and SINBAR[2]) and one automatic (Atonia Index[2]) in evaluating REM without atonia in Parkinson disease (PD) patients with and without REM sleep behavior disorder (RBD).

Methods: Thirty-two PD patients were recruited (mean age 63.4 years) and their videoPSG scored. Two parameters were extracted following the Montréal method (%30-s epochs and %2-s mini-epochs containing phasic chin EMG activity); the SINBAR method included: %3-s mini-epochs containing phasic chin EMG activity, %3-s mini-epochs containing any chin EMG activity, %3-s mini-epochs containing any chin or flexor superficialis digitorum (FSD) EMG activity, %30-s epochs containing any chin or FSD EMG activity; finally, the automatic Atonia Index was computed. RBD was diagnosed in 19 patients following the ICSD-3 criteria.

Results: The Montréal %tonic chin 30-s epochs and the SINBAR % 3-s mini-epochs containing any chin activity and %30-s epochs containing any chin/FSD activity performed equally with 100% sensitivity, 76.9% specificity and ROC 0.93. Atonia Index scored slightly lower with sensitivity 94.7%, specificity 69.2% and ROC 0.84, similarly to the SINBAR percentage of 3-s mini-epochs containing any chin/FSD activity. The other parameters performed significantly worse.

Conclusions: All methods tested provided reliable performance in our patients. The inclusion of the FSD did not increase the performance obtained with the chin EMG alone. The automatic approach might be the first choice method for the diagnosis of RSWA that can be followed by a visual quantification in doubtful cases.

[1]Ferri et al.,Sleep Med in press

[2]Frauscher et al.,Sleep 2012

Disclosure: Nothing to disclose.

P728

Prevalence and characteristics of periodic leg movements during sleep in the general population: the Hypnolaus study

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Objective: The aim of this study was to describe the prevalence and characteristics of periodic legs movements of sleep (PLMS) in the adult general population.

Methods: Data from 2162 subjects (51.2% women, mean ±SD age: 58 ± 11 years, range: 40.5–84.4 years) participating in a population-based cohort study (HypnoLaus, Lausanne, Switzerland) was collected. They completed a series of sleep related questionnaires and underwent polysomnographic recordings at home. PLMS index (PLMSI) was determined according to AASM 2007 criteria. A PLMSI>15/h was considered to be of potential clinical significance.

Results: For the whole population the PLMSI was (median [P05 - P95]) 14 [1–75]/hour of sleep and 618 subjects (28.6%) had a PLMSI>15/h (34 [17–97]). Compared to subjects with a PLMSI ≤ 15/h, subjects with a PLMSI >15/h were older (63.7 ± 10.7 vs. 56.4 ± 10.5 years, < 0.001), the percentage of men was higher (53.4% vs. 47%, $P = 0.007$), and they had higher BMI (26.1 ± 4.3 vs. 25.5 ± 4.2, $P < 0.001$). A higher percentage of them had RLS (25.3% vs. 15%, $P < 0.001$), diabetes (14.2% vs. 8.2%, $P < 0.001$), hypertension (54.5% vs. 36.3%, $P < 0.001$) and more of them were taking neuroleptics (2.8% vs. 1.6%, $P = 0.069$), hypnotics (10.8% vs. 8%, $P = 0.037$) and antidepressants (11.5% vs. 8.9, $P = 0.070$). In a multivariate analysis, age, gender (male) and having RLS were independently associated with a PLMSI>15/h.

Conclusions: PLMS are highly prevalent in the general population. Age, male gender and RLS are independent predictors of a PLMSI higher than 15/h. Further studies are needed to evaluate the clinical impact of PLMS.

Disclosure: Nothing to disclose.

P729

Reversible restless legs syndrome in a patient treated with successful kidney transplantation

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Restless legs syndrome (RLS) is a common cause of sleep disturbance and impaired quality of life in patients with end-stage renal failure (ESRD). The pathophysiology of ESRD-related RLS remains unclear but the disappearance of symptoms after kidney transplantation suggests that uremia might play a critical role. Moreover, RLS is a significant risk factor for mortality in kidney transplant recipients.

A 64 year-old man referred to our Sleep Medicine Center complaining of insomnia and uncomfortable sensations with an irresistible urge to move the legs, mostly occurring at the night. Symptoms started one year before associated with haemodialysis, due to ESRD. Neurological and electrophysiological examinations were unremarkable. Video-polysomnography (v-PSG) showed a very high periodic limb movements index (PLMI 124/h) with severe sleep disruption. Epworth sleepiness scale and International Restless Legs Severity Scale (IRLS) scores were 15 and 30, respectively. He received a diagnosis of secondary RLS and was treated with several standard medications, with mild benefit. After seven years of hemodialysis, he underwent a bilateral kidney transplantation and RLS symptoms completely disappeared within five days. At 2-years follow-up, patient was still free of RLS symptoms with IRLS score 0 and a v-PSG showed a clear improvement of sleep parameters including PLMI (0.6/h).

Our case highlights the possibility of a good outcome despite a marked RLS severity and the long dialysis vintage. Since renal failure may impact on sleep parameters, we provide data supporting the use of objective tests such as v-PSG in these vulnerable patients.

Disclosure: Nothing to disclose.

P730

Rhythmic masticatory muscle activity frequency in children

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Tooth-grinding or sleep bruxism (SB) prevalence is often reported in the literature to be highest during childhood and decreasing with age. However, this body of literature is based on parental- and self-reports in the absence of quantitative data. Moreover, classical signs and symptoms associated to SB have been established in the adult SB population, but have not been assessed in the pediatric SB population.

Objectives: This study aims to assess the rhythmic masticatory muscle activity (RMMA) frequency in children with and without self-reports of SB.

Methods: Thirty-two participants were recruited at the orthodontic clinic of the Université de Montréal. Each child received a dental assessment to screen for usual signs and symptoms of SB, and underwent an overnight sleep study at home. Sleep, respiratory and RMMA variables were scored according validated criteria. Two-step clusters analysis to discriminate activity frequency groups was followed by one-way ANOVA to compare groups. Fisher's Exact Test investigated data from the screening questionnaire.

Results: Participants were divided into 3 activity frequency groups: low (n = 12, 1–2 episodes/hr), moderate-severe (n = 13, $\geq$2 episodes/hr) and control (n = 7, $\leq$1 episodes/hr). Group effects for episodes/hr and bursts/hr were significant ($P < 0.001$). Comparisons between groups for both variables were significant. There were no relationships between self-reports of tooth-clenching, tooth-grinding, or craniofacial complaints and the presence/absence of RMMA. Furthermore, dental assessments showed no association between tooth wear and RMMA.

Conclusions: No association was observed between SB parental reports and measured RMMA frequency, suggesting the need to improve parental knowledge regarding their children's SB.

Disclosure: Nothing to disclose.

P731

Polysomnographic study in symptomatic Huntington Disease

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Objectives: To evaluate the sleep pattern and, in particular, the motor activity during sleep in a cohort of patients affected by Huntington Disease (HD).

Methods: Inclusion criteria were: genetically confirmed diagnosis of symptomatic HD, age > 18 years, absence of concomitant medical or neurological diseases. Sleep evaluation included: Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Berlin's Questionnaire (Berlin Q), Bologna questionnaire for daytime sleepiness (BQS), a structured interview for the detection of the diagnostic criteria for Restless Legs Syndrome (RLS), a questionnaire for REM Behaviour Disorder (RBD) and a specific questionnaire for sleep quality in HD. Psychometric measures included: Beck Depression Inventory (BDI), Zung scale for Anxiety and the Maudsley Obsessive Compulsive Inventory (MOCI). Sleep study consisted in a overnight, laboratory based video-polysomnography; montage included 19 EEG, EOG, EMG of submental muscles, anterior tibialis, extensor carpi and a full cardio-respiratory array.

Results: Fifteen patients were enrolled, four men and 11 women, age: 56 $\pm$ 13. HD patients, compared to controls, showed frequent awakenings, increased sleep latency, wake after sleep onset, and reduced amount of slow wave sleep. One patient had apnea-hypopnea (AHI) index >5, consistent with OSA. 12 patients presented periodic limb movements during sleep, involving both lower and upper limbs. No patient presented Restless Legs syndrome, REM without atonia or REM Behaviour Disorder.

Conclusions: HD patients showed a severe sleep disruption. The sleep-related motor pattern was characterized by a peculiar combination of periodic movements during sleep. In contrast with previous reports, no patients presented RLS and RBD.

Disclosure: Nothing to disclose.

P732

Sleep disturbances in essential tremor and Parkinson′s disease: a polysomnographic study

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Objective: Sleep problems are a common non-motor complication of Parkinson's disease (PD). Patients with essential tremor (ET) share a number of motor and non-motor features of PD. To clarify any potential relationships between these disorders, we evaluated and compared the sleep problems in patients with ET and PD using assessment scales and polysomnography (PSG) testing.

Method: Twenty-one consecutive patients with PD, 16 with ET and 14 healthy subjects participated in this study and were compared in terms of sleep related complains, polysomnographic features and final diagnosis of sleep disorder.

Results: Patients with PD were more likely to have a history of REM sleep behavior disorders (RBD) (P = 0,001) and excessive daytime sleepiness ($P \leq 0.05$) than patients with ET. Additionally, PSG data revealed that ET patients had lower mean SpO2 values ($P \leq 0.05$) and REM without atonia (RWA) (P = 0.032) than patients with PD.

Conclusion: This is the first study to use PSG to compare ET and PD, and the results may assist with the differential diagnosis of these diseases.

Disclosure: Nothing to disclose.

P733

Symptom severity of primary restless legs syndroms is not determined by serum ferritin level

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Objectives: The purpose of our study was to investigate the clinical characteristics in RLS patients with low ferritin level compared with RLS patients with normal serum ferritin level.

Methods: Total 242 idiopathic RLS patient were recruited by a neurologist according to 4 clinical criteria defined by the International RLS Study Group. Peripheral blood test was taken to assess serum ferritin, serum iron, hemoglobin, hematocrit and TIBC (total iron binding capacity). The severity of disease in patients diagnosed as RLS was evaluated by RLS severity rating scale.

Results: Patients were classified as RLS with low ferritin group (< 50 ng/mL, $n = 120$) and RLS with normal ferritin group (>50 mg/mL, $n = 130$). Women were more prevalent in patient with low ferritin group (90%) than patient with normal ferritin group (62.3%). Onset age was younger in patient with low ferritin group; low ferritin group: 37.22 ± 13.09, normal ferritin group: 40.67 ± 12.65. The serum iron level was lower in patient with low ferritin group; low ferritin group: 76.43 ± 41.05, normal ferritin group: 102.15 ± 39.08. In RLS severity scale group patient, there are no statistical differences.

Conclusions: Our study suggested that clinical RLS severity could not be correlated by serum ferritin level in primary RLS patient with normal hemoglobin level.

Disclosure: Nothing to disclose.

P734

Assessment of severity and therapeutical response in 70 patients with idiopathic and symptomatic form of restless leg syndrome

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Purpose and object of the study: To evaluate the clinical presentation, form and severity of the disease, the degree of sleep disorders, the effects of the therapy, electroneurographic finding in patients with restless legs syndrome (RLS).

Methods: Somatic and neurological status, laboratory tests, and electroneurography, evaluation of complaints and sleep disorders by Pittsburgh scale of sleep quality (PSQI) and the restless leg syndrome rating scale (RLSRS) before treatment and three months after therapy.

There are 13 patients with idiopathic RLS that are missing electroneurographic evidence of impaired peripheral nerves and muscles. The average age was 55. Before initiation of therapy with dopamine agonists and magnesium, patients were on average with very severe RLS symptoms and an expressed sleep disorder. After three months of treatment, patients were evaluated an average of 5 points in RLSRS and 3 PSQI scale.

The second group of patients is those with symptomatic RLS- 48 women and 7 men with first and second type diabetes mellitus, iron and vitamin B12 deficiency anemia, with chronic renal insufficiency, degenerative changes of the spine, and a woman in labor. 20 patients did not represent electroneurographic changes. The third month of the therapy with dopamine agonists and magnesium are presented a mean improvement in complaints assessed with RLSRS and PSQI, with a larger improvement in the group with iron deficiency anemia.

Conclusion: Patients with RLS in its two forms, have a significant improvement during treatment with dopamine-agonists, and magnesium and those with idiopathic form have a better response to it.

Disclosure: Nothing to disclose.

P735

Predictors of multiple sleep latency test findings in Parkinson's disease

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Objectives: To explore polysomnography predictors of Multiple Sleep Latency Test (MSLT) characteristics in patients with idiopathic Parkinson's disease (PD).

Methods: Retrospective analysis of polysomnography and MSLT data in 35 PD patients. Demographic and clinical variables included age, sex, body mass index, disease duration, part III of the Unified Parkinson′s Disease Rating Scale (UPDRS) and dopaminergic treatment expressed as dosages of equivalent efficacy. These variables were included in a multiple linear regression model, together with polysomnography variables that appeared significantly correlated with the MSLT findings in an univariate comparison.

Results: Mean age of the patients was 64 ± 10 years, 28 were male (80%). Mean disease duration was 8.4 ± 6.1 years, and mean UPDRS III 28.2 ± 13.5. Mean sleep latency on MSLT was significantly correlated with latencies to NREM1 ($r = 0.57$, $P < 0.001$) and NREM2 ($r = 0.55$, $P < 0.001$) on polysomnography, but not with total nocturnal sleep time ($r=-0.06$, $P = 0.75$) or nocturnal sleep efficiency ($r=-0.22$, $P = 0.20$). Similarly, mean sleep efficiency on MSLT was – inversely – associated with polysomnography latencies to NREM1 ($r=-0.50$, $P = 0.002$) and NREM2 ($r=-0.47$, $P = 0.004$), but also with nocturnal sleep efficiency ($r = 0.35$, $P = 0.04$). Multiple linear regression analysis confirmed that sleep latency during polysomnography appeared to be both an independent associate of the mean sleep latency on MSLT (Beta=0.39, $t = 2.55$, $P = 0.016$) and of the sleep efficiency on MSLT (Beta=−0.49, $t=-3.04$, $P = 0.005$).

Conclusions: We identified short sleep latency at polysomnography as independent predictor of MSLT characteristics in PD, thereby confirming previous reports about a paradoxical correlation between the quality of nighttime sleep and daytime vigilance.

Disclosure: Nothing to disclose.

P736

REM sleep behavior disorder in Parkinson's disease as a predictor of cognitive decline

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Objectives: This study aimed to estimate cognitive functions of PD patients with RBD vs. those without RBD.

Background: REM sleep behavior disorder (RBD) is a parasomnia due to the loss of the normal muscle atonia of REM sleep. RBD is often associated with Parkinson′s disease (PD) and sometimes preceding its development for more than 10 years. This could be related to the definite type of PD with more complex and aggressive neurodegenerative process.

Methods: Thirty patients with PD were evaluated with detailed clinical history and examination. PD patients underwent polysomnography (PSG) to confirm the presence of RBD according AASM 2007 criteria. Clinical exam included RBD screening questionnaire (RBDSQ), UPDRS, H&Y, Schwab and England (S&E) scale, Parkinson′s disease Sleep Scale (PDSS), Epworth Sleep Scale (ESS) *and* Montreal Cognitive Assessment (MoCA). Patients were divided into two groups according to the presence of RBD (15

patients in each group). Groups were compared with the use of Mann Whitney U test.

Results: PD patients with RBD were older and with higher frequency of falls ($P < 0.05$). Patients with RBD were worse in MoCA test ($P < 0.05$). The most prominent differences were observed in visual-spatial functions. Patients with RBD had significantly higher score in ESS ($P < 0.05$).

Conclusions: Our results support previous findings that the occurrence of REM sleep behavior disorder in PD patients could be the marker of cognitive decline. We suppose that RBD could be a predictor of a definite type of PD with more complex and aggressive neurodegenerative process.

Disclosure: Nothing to disclose.

Psychiatric and behavioural disorders and sleep

P737

Sleep patterns in adults with a diagnosis of high-functioning autism spectrum disorder: a preliminary analysis

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Objectives: To examine sleep patterns and problems and their relationship with daytime functioning in adults with a diagnosis of high functioning autism spectrum disorder (HFASD) compared to neurotypical (NT) adults.

Methods: Fifteen adults with HFASD (M_{age} = 34.10, *SD* = 5.36) and 15 age, IQ, and gender matched NT adults (M_{age} = 32.26 years, SD = 4.67) completed an online questionnaire battery, 14-day sleep/wake diary, and 14-day actigraphy assessment.

Results: Preliminary analyses showed that adults with HFASD had shorter sleep duration (diary; $P = 0.02$ and actigraphy; $P = 0.01$), later bedtimes (diary; $P = 0.02$), and longer sleep onset latencies (actigraphy; $P = 0.03$). HFASD adults also had larger difference scores between their desired and actual bedtimes ($P = 0.02$) and reported lower refreshment scores upon waking in the morning ($P = 0.02$). All effect sizes for group differences were large. Sleep refreshment scores were correlated with sleep onset latency measures (diary; r = -0.57, $P = 0.03$ and actigraphy; $r = -0.53$, $P = 0.04$), and diary sleep efficiency ($r = 0.54$, $P = 0.04$) in the HFASD group.

Conclusions: These preliminary findings show that sleep problems continue into adulthood in individuals with ASD and that poor sleep has a negative impact on daytime functioning. Consequently, issues regarding sleep should be routinely assessed in adults with HFASD. Data collection for this study is ongoing and it is expected that data from a further 5–10 participants (in each group) will be available at the time of the conference.

Disclosure: Nothing to disclose.

P738

Sleep complaints in adolescent depression: one year naturalistic follow-up study

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Objectives: Sleep complaints are highly prevalent in adolescents suffering from major depressive disorder (MDD). The aims of this study were to describe the longitudinal course of sleep complaints, and to assess the association between sleep complaints and clinical outcome in a sample of adolescents with MDD during naturalistic follow-up.

Methods: A sample of adolescent outpatients (n = 166; age 13–19 years, 17.5% boys) diagnosed with MDD was followed-up during one year in naturalistic settings. Sleep symptoms and psychiatric symptoms were assessed with interviews and self-report questionnaires.

Results: All sleep complaints were less frequent at one-year follow-up compared to baseline. Baseline sleep complaints did not adversely affect clinical outcome at one-year follow-up: although having a less favourable baseline status, depressed adolescents with sleep disturbances at baseline had a significantly steeper improvement of depressive and anxiety symptoms and overall psychosocial functioning over time as compared to adolescents with no/minor sleep complaints.

Conclusions: Our results suggest that sleep disturbances at baseline do not necessarily lead to poorer clinical outcome during follow-up. Larger longitudinal studies combining both subjective and objective measures of sleep in depressed adolescents are needed to clarify the link between sleep and depression further.

Disclosure: Nothing to disclose.

P739

The subjective effect of quetiapine monotherapy on sleep and daytime sleepiness in acute manic patients

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Objectives: This study was aimed to investigate the effect of 6-week quetiapine monotherapy on subjective aspects of sleep in patients with acute bipolar disorder.

Methods: In a Korean multi-center, open-label, 6-week study, patients with bipolar I disorder (manic or mixed episodes) were included. The dose of quetiapine initially started at 200 mg/day and rapid titrated up to 800 mg/day within day 7 according to the clinical judgements. Clinical improvement was evaluated using Young Mania Rating Scale (YMRS) and Clinical Global Impression-Bipolar version (CGI-BP). Extrapyramidal side effects were measured by Simpson-Angus Rating Scale (SARS) and Barnes Akathisia Rating Scale (BARS). Subjective sleep questionnaire modified from Leeds Sleep Evaluation Questionnaire (LSEQ) was used to assess the subjective measures of sleep.

Results: Total 78 (male=30, female=48) patients were included and most of them were inpatients (N = 59, 74.7%). Fifty-nine (75.9%) patients completed the study. Mean changes of YMRS from baseline were significant at days 7, 14, 21 and 42. There were no significant differences from baseline in SARS and BARS at any assessment points. While mean changes of 5 items measuring nighttime sleep from baseline were significantly improved at days 7, 14, 21 and 42, those of hangover behavior next day were not differed between baseline and post-treatment assessments.

Conclusions: Data showed that quetiapine monotherapy had favorable effect on acute manic symptoms and well tolerated. Also this result suggests that quetiapine monotherapy may improve the

self-perceived quality of sleep without any daytime impairment following sleep in acute manic patients.
Disclosure: Nothing to disclose.

P740

Obstructive sleep apnea severity, heart rate variability and depression symptoms

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Objective: This study has been undertaken to focus on the relationship between Heart rate variability (HRV) variation indices and severity of obstructive sleep apnea syndrome (OSAS) based on depression.
Methods: One hundred and ninety-eight persons, suffering from sleep apnea and meeting the inclusion criteria, were chosen for this study. Sleep apnea severity was categorized into two groups. Demographic datas check list and three self-reporting questionnaires including Epworth Sleepiness Scale (ESS), Beck Depression Inventory (BDI) and stop-bang questionnaire were completed, and the two domain HRV (frequency and time domain) automatic calculation by polysomnographic test was used.
Results: Most of these patients suffered from severe sleep apnea (135; 44.6%). High score of BDI was seen in patients suffering from severe OSAS ($P = 0.09$). There was no significant difference between STOP and ESS scores in different groups of OSAS severity ($P > 0.05$). The mean NN50 count was significantly different among different OSAS severity groups ($P = 0.02$). We found a weak inverse association between some frequency domain indices such as average total power and age ($P = 0.002$, $r = -0.22$) and RDI ($P = 0.03$, $r = 0.16$), HF power and age ($P = 0.005$, $r = -0.20$), and LF power. After adjustment for age and BDI score we found a significant relationship between some HRV parameters (such as SDNN, SDNN index, NN50 count, NN50 percent, Ave total power, LF power) and OSAS severity.
Conclusions: We could show difference between sleep apnea severity in OSAS patients and some HRV parameters even after adjustment for age and BDI score.
Disclosure: Nothing to disclose.

P741

Sleep duration and serotonin transporter promoter gene polymorphism in the Palanga community cohort

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Objective: This study was to investigate the relationship between subjective sleep duration and the serotonin transporter promoter genotype (5-HTTLPR) in a population-representative sample of inhabitants of Palanga city in the Western part of Lithuania.
Methods: Sleep duration questionnaire and Hospital Anxiety and Depression Scale were used in 45–84 year old subjects ($n = 829$, 292 males and 537 females). Genotyping was carried out as previously described (Tomson et al. PNPBP 2011, 35:1857–62) and triallelic data classified into three groups, l/l homozygotes ($n = 367$), l/s heterozygotes ($n = 373$) and s/s-homozygotes ($n = 89$), not significantly different regarding age and gender.
Results: Mean sleep duration was significantly decreased in subjects with the s/s genotype (417 ± 72 min), as compared with the l/s genotype (435 ± 86) and l/l genotype (444 ± 69). Anxiety and depression scores (7.28 and 5.63, respectively) were significantly higher in the s/s genotype (l/s: 6.00 and 4.41; l/l: 6.08 and 4.83, respectively). Significant Spearman's negative correlation between sleep duration and depression was found only in the l/l, anxiety was negatively associated with sleep in l/l and l/s but not in s/s subjects.
Conclusions: Shortest sleep duration and most expressed anxiety and depression were observed with the s/s genotype, known to be the vulnerability genotype for negative emotion. In these subjects longer sleep duration is not associated with lower depression and anxiety, suggestive of loss of protective value of sleep.
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P742

Sleep structure and emotional memory processing in police officers and combat veterans with PTSD

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Introduction: Disturbed sleep is a key symptom of posttraumatic stress disorder (PTSD). In a previous study in healthy subjects we found adaptive changes in sleep architecture after emotional experiences, benefitting emotional housekeeping and the attenuation of emotional responses. Little is known, however, about the relation between sleep and emotional memory processing in PTSD. The current study assesses the impact of an emotional stressor on sleep parameters in PTSD patients.
Methods: Traumatized police officers and combat veterans with and without PTSD are compared. The experimental setup involves the presentation of neutral or distressing film fragments in the evening, followed by full polysomnography of undisturbed, whole night sleep, and cued recall of film content on the next evening. The order of the film conditions is counterbalanced across subjects. Emotional state before and after film viewing and during recall is assessed with psychological and physiological measures.
Results: Contrary to many previous studies that found only mildly disrupted (macro)sleep architecture in PTSD, our preliminary results on 13 patients show significantly more N1 sleep ($P < 0.001$), less N3 sleep ($P < 0.001$) and, in addition, significant lower subjective sleep quality ($P < 0.01$). There was a trend towards a higher REM sleep percentage ($P = 0.07$) and a longer duration of rapid eye movement bursts ($P = 0.051$) after the emotional stressor.
Conclusion: Contrary to the literature, sleep architecture appears to be altered in PTSD patients towards a more superficial sleep, with lower subjective sleep quality. Patients tend to respond to an acute non-trauma-related emotional stressor with more 'intense' REM sleep.
Disclosure: Nothing to disclose.

P743

A meta-analysis and model of the relationship between sleep and depression in adolescents

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Objectives: The purpose of this review was to quantify the strength of evidence for a directional relationship between sleep disturbance and depression in adolescents.

Methods: A literature search identified 23 studies investigating the relationship between sleep disturbance and depression in adolescent samples (12–20 years). Thirteen studies explored associations between depression and sleep disturbance; 7 examined the prospective role of sleep disturbance in the development of depression; and 3 investigated the role of adolescent depression in the development of subsequent sleep disturbance. Average weighted mean differences in sleep/depression-related outcome variables were calculated between adolescents with depression, and non-clinical adolescents, or those in remission.

Results: Effect sizes from longitudinal and treatment studies suggest wakefulness in bed acts as a precursor to the development of depression. At follow-up, depressed adolescents had significantly longer sleep-onset (d_+ =0.43, $P < 0.05$), more wake after sleep onset (d_+=0.58, $P < 0.05$), and lower sleep efficiency (d_+=-0.51, $P < 0.05$), compared to adolescents who were non-clinical, or had undergone remission. Little support was found for a predictive role of depressive symptoms (d_+=-0.06, $P > 0.05$) in the development of sleep disturbance.

Conclusions: Based on our findings we present a model for conceptualizing the relationship between sleep disturbance and depression. We propose that increased wakefulness in bed may serve to reinforce ruminative thinking styles and hence perpetuate further sleep disturbance. Our data indicate that over time, it is likely these processes could develop into depression.

Disclosure: Nothing to disclose.

P744

The effects of acupuncture treatment on sleep quality and on emotional measures among individuals living with schizophrenia

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Objectives: Insomnia is a sleep disorder frequently observed among individuals living with schizophrenia. Its causes are varied, and it has serious consequences on daytime functioning and quality of life. Moreover, studies have confirmed that individuals living with schizophrenia are resistant to insomnia medications. Since previous studies have demonstrated the positive influence of acupuncture on several diseases and disorders, the aim of the present study was to examine the effects of acupuncture on sleep quality and on emotional measures among patients with schizophrenia.

Methods: Twenty patients with schizophrenia participated in the study (mean age=43.15, SD=9.42; 10 males and 10 females). The study comprised a seven-day running-in no-treatment period, followed by an eight-week experimental period. During the experimental period, participants were treated with acupuncture twice a week. During the first week (no-treatment period) and the last week of the experimental period, participants filled out a broad spectrum of questionnaires and their sleep was continuously monitored by wrist actigraph.

Results: A paired-sample t-test was conducted, comparing psychopathology score, level of anxiety and objective sleep parameters manifested by patients before and after acupuncture treatment. The results indicated that acupuncture improved total psychopathology score (PANNS) ($t(19)=8.261$, $P < 0.0001$), level of anxiety ($t(19)=5.959$, $P < 0.001$), and objective sleep efficiency ($t(18)=2.857$, $P < 0.01$).

Conclusion: The present study implies that acupuncture can have beneficial effects in improving emotional measures and in treating insomnia in schizophrenic patients.

Disclosure: Nothing to disclose.

P745

Chronic sleep reduction and psychopathology symptoms in adults with high-functioning autism spectrum disorder

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Objectives: To investigate the relationships between sleep, chronic sleep reduction and psychopathology symptoms in adults with a diagnosis of high functioning autism spectrum disorder (HFASD).

Methods: Participants included 15 adults with HFASD and 15 neurotypical (NT) adults matched on age, gender, and IQ. Participants completed a questionnaire battery including the Chronic Sleep Reduction Questionnaire (CSRQ), Patient Health Questionnaire, the State Trait Anxiety Inventory, and the Sleep Anticipatory Anxiety Questionnaire. Participants also completed a 14 day sleep/wake diary and actigraphy.

Results: Adults with HFASD had significantly higher scores on all questionnaire measures. CSRQ scores were significantly and strongly correlated with all psychopathology variables in the HFASD group; however correlations in the NT group were either moderate or strong, except depression which was not significantly correlated with CSRQ scores in this group. Several non-significant moderate correlations between diary and actigraphy variables and psychopathology variables were observed in each group; sleep variables were primarily correlated with sleep anxiety measures in the HFASD group and depression in the NT group. These correlations may have been reduced due to the small sample size.

Conclusions: The CSRQ measures symptoms of chronic sleep reduction and thus the impact of sleep debt. Our preliminary results suggest that the impact of chronic sleep reduction is greater in adults with a diagnosis of HFASD and is highly associated with symptoms of psychopathology. Data collection is ongoing and it is expected that data from a further 5–10 participants (in each group) will be available at the time of the conference.

Disclosure: Nothing to disclose.

P746

Attention deficit hyperactivity symptoms, sleepiness and near-misses driving accidents among a population of French highway drivers

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Objective: To investigate in French drivers the accidental risk of subjects exhibiting Attention Deficit Hyperactivity Disorder (ADHD) symptoms and to explore the factors associated with near-miss driving accidents.

Methods: One thousand and one drivers responded to a specific internet questionnaire included socio-demographics, driving, sleep disorders and attention deficit hyperactivity items (Adult ADHD Self report scale (ASRS)) and the Epworth sleepiness scale.

Results: This sample was divided in two groups (according to the score on the ASRS): drivers without ADHD symptoms and drivers with ADHD symptoms (n = 125). More than 60% drivers with ADHD symptoms complained of excessive daytime sleepiness. Drivers with ADHD symptoms reported significantly more near-misses driving accident ($P < 0.001$) and twice more near-miss sleepy accidents than drivers without ADHD symptoms ($P < 0.05$). Furthermore, nearly 25% of near-misses driving accidents were 'inattention related' for the drivers with ADHD symptoms while 10% of drivers without ADHD symptoms had reported these type of near-miss ($P < 0.005$).

Conclusions: Sleepiness and ADHD symptoms were frequently observed amoung a population of French drivers.These two kinds of symptoms negatively affects driving performances and play a significant role in near-miss accident drivings. Sleepiness at the wheel, particularly in patients presenting ADHD symptoms should be explored and taken into account in the management of these subjects.

Disclosure: Nothing to disclose.

P747

Sleep spindles as biomarkers of memory dysfunction in schizophrenia

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Objectives: Schizophrenia is a devastating brain disorder with diverse dimensions of symptoms like delusions, hallucinations, affective symptoms and alterations in cognition. Deficits in declarative memory are among the most consistent and severe neuropsychological impairments in this disorder and contribute to poor clinical outcomes. The importance of sleep for brain plasticity and memory consolidation is widely accepted and sleep spindles seem to play an important role in these processes. The aim of this study was to test associations of sleep spindles and memory consolidation in patients with schizophrenia and healthy controls.

Methods: We studied 16 patients with schizophrenia (mean age 29 $\pm$ 6 years) on stable antipsychotic medication and 16 healthy controls (28 $\pm$ 6 years). We performed a picture recognition paradigm and used neutral and emotional pictures and compared recognition performance in a sleep and wake condition.

Results: The memory promoting effect of sleep was significantly lower in patients with schizophrenia. Patients showed a marked decrease of sleep spindles.

Significant correlations between sleep spindles density and sleep-dependent facilitation of memory performance were found in patients and healthy controls.

Conclusions: Our hypothesis of sleep spindles as biomarkers of sleep dependent memory impairment in patients with schizophrenia was therefore supported by our results.

Disclosure: Nothing to disclose.

P748

Slow wave sleep, memory and long-term outcome in patients with schizophrenia

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Objecitives: Schizophrenia is a severe brain disorder with positive symptoms like delusions and hallucinations, negative symptoms like affective flattening and cognitive symptoms. Memory impairment is considered to be a strong clinical predictor of poor long-term outcome in these patients. In recent studies significant associations of sleep parameters such as slow wave sleep and memory performance in schizophrenia patients were described.

Methods: We therefore analyzed associations of sleep parameters and parameters of social outcome like occupational functioning and independent living in 15 patients with schizophrenia (mean age 38 $\pm$ 6 years). Polysomnography was performed at t0 and parameters of social outcome were determined at t0 and t1 (= about six years later).

Results: There were no significant associations between sleep parameters and social outcome at t0, but we found a significant association between duration of slow wave sleep at t0 with occupational functioning six years later. Four patients with full employment had a significant longer duration of slow wave sleep as 11 other patients with supported employment, employment disability pension or unemployment. Age between both groups was not different.

Conclusion: These findings suggest that slow wave sleep is an important aspect of long-term psychosocial functioning in patients with schizophrenia.

Disclosure: Nothing to disclose.

P749

Poor sleep is a potential risk factor for aggressive/violent behaviour

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Objectives: Poor sleep is known to exert a negative influence on the course of various psychiatric disorders. Furthermore, there are some indications that sleep loss may diminish emotional control and regulation of aggression, possibly by negatively affecting prefrontal top-down inhibition. If so, this would have important therapeutic implications for aggressive psychiatric patients. The aim of this study is to investigate the prevalence of sleep disorders and the contribution of sleep disturbances to aggressiveness in a forensic psychiatric population.

Methods: Participants were recruited in two forensic hospitals in the Netherlands. Sleep quality, sleep disorders and sleep hygiene

behaviour were examined with the Pittsburgh Sleep Quality Index (PSQI), the Sleep Diagnosis List (SDL) and a semi-structured interview, respectively. Aggression and impulsivity measures were investigated with self-report questionnaires, registered aggressive incidents in the facility and scores on a professional instrument to assess the risk for future aggression.

Results: Half of the 110 participants experienced poor sleep quality (PSQI>5). Almost a third suffered from one or more sleep disorders, especially insomnia (SDL insomnia score ≥ 3). Mental disorders, psychiatric drugs, suboptimal sleep hygiene, stress and/or ruminating and negative sleep conditioning were often mentioned to underlie the sleep difficulties. A worse sleep quality and higher insomnia scores were significantly associated with higher self-reported aggression and impulsivity, involvement in aggressive incidents and clinician-rated hostility.

Conclusions: Poor sleep may constitute an important risk factor for aggressive/violent behaviour. It is therefore highly worthwhile to examine the protective effect of treatment of sleep disorders on aggressive reactivity in (forensic) psychiatric populations.

Disclosure: Nothing to disclose.

P750

Sleep, depression and physical illness in Korean elderly

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Objectives: This study was conducted to collect basic data for the elderly mental health by identifying the impact of the presence of depression and physical illness on sleep.

Methods: Among 1535 Medicaid people at least 60 years of age, 1262 were examined. We investigated the general characteristics and the history of the disease and evluated depression (Short form of Geriatric Depression Scale-Korean version: SGDS-K) and sleep (Pittsburgh Sleep Quality Scale: PSQI).

Results: Among the entire 1262, 520(41.0%) were positive in SGDS-K, and 718 (57%) positive in PSQI. Otherwise, 141(11%) had been diagnosed as stroke, 710 (56%) had hypertension, and 278 (22%) had diabetes mellitus. PSQI positive was correlated with SGDS-K positive and not with physical illness. Depression positive was correlated with physical illness. In regression analysis SGDS-K positive had the biggest amount (19.2%) and dibetes mellitus positive had very small amount(0.2%).

Conclusions: In elderly with sleep disturbaces, depressive mood was major contributing factor. Contrary to expectations, physical illness was not impact on sleep directly. This represents the need of screening for depression in the elderly with sleep disturbances. This study also suggests the possibility for the future study about how much the quality of sleep would improve by treatment of depression.

Disclosure: Nothing to disclose.

P751

Subjective sleep quality and excessive daytime sleepiness in attention-deficit/ hyperactivity disorder in adults

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Objectives: Adults with a diagnosis of attention-deficit/hyperactivity disorder (ADHD) very often report impaired sleep. Since sleep disturbances may lead to excessive daytime sleepiness (EDS), the prevalence of reduced subjective sleep quality and daytime sleepiness was evaluated in ADHD patients. Possible differences between ADHD subtypes, and the role of psychiatric comorbidity in the prevalence of sleep disturbances and EDS were analysed.

Methods: Prior to any diagnostic procedures, adults, who visited the Center for Adult ADHD, were asked to fill in the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS). The prevalence of disturbed subjective sleep quality (PSQI>5) and of daytime sleepiness (ESS>10) in adult ADHD was evaluated and compared between patient subgroups, and between patients with and without any psychiatric comorbidity.

Results: Subjective sleep quality was reduced in 56.8% of 146 enrolled ADHD patients (mean age ± standard deviation: 33.0 ± 9.7 years, range: 18–59; 58% male). ADHD subtypes did neither differ in the frequency of disturbed sleep (PSQI>5, inattentive type': 55.4% vs.hyperactive/impulsive/combined' 58.3%) nor in PSQI total scores. If psychiatric comorbidity was present PSQI total scores were significantly higher (63.5% vs. 51.8%; $P = 0.032$). Higher levels of daytime sleepiness were found in 25% of ADHD patients, without any difference between subgroups and no effect of comorbidity.

Conclusions: Subjective sleep quality was impaired in 57%, and excessive daytime sleepiness was present in 25% of ADHD patients. These rates are higher than in the general population. Impaired sleep quality was associated with psychiatric comorbidity, whereas subjective daytime sleepiness was not.

Disclosure: Nothing to disclose.

P752

Sleep disturbances and psychotic-like experiences in a student population

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Objective: The aim of this study was to determine the relationship between sleep disturbances and psychotic-like experiences in a student population.

Methods: An online survey was sent out to all students at the University of Oxford. 2055 students accessed the survey, of which 369 respondents were excluded from analysis due to missing data, leaving a final sample of 1686 participants. The survey included questions taken from validated questionnaires assessing sleep quality using the Sleep Condition Indicator (SCI), paranoia and hallucinations using the Specific Psychotic Experiences Questionnaire (SPEQ) and demographics.

Results: Twenty percentage of the population met diagnostic criteria for DMS-5 Insomnia Disorder, and 35.5% and 8.6% reported at least one experience of paranoia or hallucination at least once a week respectively. Two step cluster analysis for paranoia and hallucination experiences produced three clusters:

1) low paranoia/low hallucination,
2) low paranoia/high hallucination and
3) high paranoia/low hallucination.

Clusters 2 and 3 showed a significantly higher proportion of individuals who met diagnostic criteria for Insomnia Disorder compared to Cluster 1 (Cluster 1 = 15.2%, Cluster 2 = 32.1%, Cluster 3 = 38.9%, ANOVA: F = 39.3, $P \leq 0.001$).

Conclusions: This student population shows a higher proportion of individuals meeting criteria for Insomnia Disorder compared to the

general population. Moreover individuals who tend to experience more psychotic-like experiences are more likely to meet criteria for Insomnia Disorders compared to those with a low frequency of psychotic-like experiences.

Disclosure: Nothing to disclose.

P753

PTSD associated effects on obstructive sleep apnea and restless legs in the survivors from the Norwegian terror 22/7 2011 attack on Utøya

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The 2011 terrorist attack at the island Utøya killed 69 people, 33 of whom were under the age of 18, and causing physical and mental injuries in hundreds of survivors and relatives. Sleep related breathing disorder and sleep movement disorders are more common in patients with PTSD than in the general population. The aim was to investigate long-time effects on obstructive sleep apnea (OSA) and movement disorders among the survivors.

Methods: Thirty-three survivors and 39 controls, age-/gender and socio-demographic, were studied 18–30 months after the attack. Symptoms of possible OSA were estimated using self-reported items based on their own or their partner's reports on 'snoring', 'breathing cessation during sleep', and 'being tired or sleepy at work or during spare time'. The participants were questioned about RLS, using the diagnostic criteria found in ICSD-II. Only those affirming all four diagnostic criteria were defined as RLS subjects. Psychiatric symptoms were evaluated in 20 survivors by using MINI.

Results: Prevalence of OSA was 20.0% in survivors vs. 0%controls, $P < 0.01$. All those with OSA in the subgroup were diagnosed with PTSD, half were diagnosed with panic disorder and recurrent depression. RLS was reported in 37.1%survivors vs. 7.7% controls, $P < 0.001$. Here, 60% were diagnosed with recurrent depression, 40% panic disorder and 20% PTSD.

Conclusions: Survivors from the Utøya attack report more sleep related breathing and movement disorders 18–30 months after the trauma compared to controls. OSA was strongly associated with PTSD, whilst both OSA and RLS were associated with depression and panic disorder.

Disclosure: Nothing to disclose.

P754

High rates of psychiatric comorbidity in narcolepsy: findings from the burden of narcolepsy disease (BOND) study of 9,312 patients in the United States

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Objectives: To evaluate psychiatric comorbidity patterns in patients with a narcolepsy diagnosis in the United States.

Methods: Truven Health Analytics MarketScan® Research Databases were accessed to identify individuals ≥18 years of age with ≥1 diagnosis code(s) for narcolepsy ± cataplexy continuously insured between 2006 and 2010, and non-narcolepsy controls matched 5:1 (age, gender, region, payer). Extensive sub-analyses were conducted to confirm the validity of narcolepsy definition. Narcolepsy and control patients were compared for frequency of psychiatric comorbid conditions (based on Clinical Classification System [CCS] categories) and psychiatric medication use.

Results: The final population included 9,312 narcolepsy patients and 46,559 controls (each group, average age 46.1 years; 59% female). All categories of mental illness were significantly more prevalent in database patients with narcolepsy vs. controls, with the highest excess prevalence noted for CCS 5.8 Mood disorders (37.9% vs. 13.8%; OR, 4.0 [95% CI:, 3.8, 4.2]), and CCS 5.2 Anxiety disorders (25.1% vs. 11.9%; OR [95% CI], 2.5 [2.4, 2.7]). Excess prevalence of anxiety and mood disorders (narcolepsy vs. controls) was higher in younger age groups vs. older age groups. Psychiatric medication usage was higher in the narcolepsy group vs. controls in the following categories: SSRIs (36% vs. 17%), anxiolytic benzodiazepines (34% vs. 19%), hypnotics (29% vs. 13%), SNRIs (21% vs. 6%), and TCAs (13% vs. 4%) (all $P < 0.0001$).

Conclusions: Narcolepsy is associated with significant comorbid psychiatric illness burden and higher psychiatric medication usage compared with the non-narcolepsy population.

Disclosure: Dr. Black is a part-time employee of, and holds stock options in Jazz Pharmaceuticals.

P755

Effects of bright light therapy on the hospital employees with depressive symptoms and/or daytime sleepiness

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A number of hospital employees suffer from sleep disturbances and/or major depression due to the psychosocial stress and shift-work. Here we report the effects of bright light therapy on depressive symptoms and/or daytime sleepiness.

The subjects were enrolled from among the hospital employees who claimed sleep disturbances and/or depressive symptoms at the annual check-up. After consulting the industrial physician (SY), they gave written informed consent to have bright light therapy. The head-mounting goggles equipped with light emitting diodes were originally designed by TY and YA. The 10,000-lux white light was administered for 30 min immediately after awakening and just before leaving home for a night shift for 14 days. The CES-D scale and the Epworth sleepiness scale (ESS-J) were performed before and after the therapy. Premenstrual dysphoric disorder (PMDD) was also assessed. The sleep quality of the three consecutive nights after a night shift was assessed subjectively by the OSA-MA scale (Japanese).

Eleven women participated in this study, and nine of them were shift-workers. Five shift-workers showed 16 points or more of the CES-D scale at the beginning, suggesting depressive state. Their CES-D score decreased significantly after bright light therapy. The ESS-J score also decreased significantly after bright light therapy. The subjects with higher CES-D or ESS-J score showed better response. The subjective sleep quality did not change significantly. The symptoms of PMDD were not correlated with any variables above.

In conclusion, bright light therapy may be effective in alleviating depressive symptoms and daytime sleepiness of the hospital employees.

Disclosure: This is a collaboration study between Muroran Institute of Technology and Steel Memorial Muroran Hospital. Steel Memorial

Muroran Hospital contributed 550,000JPY (ca. 4000EUR) to Muroran Institute of Technology.

P756

Adolescents diagnosed with depression and their unaffected siblings show a different topographical distribution of sleep slow wave activity compared to healthy controls

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Objectives: Epidemiological studies show an average onset of depressive episodes between 11 and 14 years.Likewise adolescence represents a vulnerable developmental period of the brain. The topography of electroencephalographic (EEG) sleep slow wave activity (SWA), the major characteristic of deep non-rapid eye movement (NREM) sleep, was shown to mirror this process of cortical maturation and functioning. The goal of this study was to assess characteristics of SWA topography in adolescents with depression, their unaffected siblings and healthy controls.

Methods: All-night high-density EEG (128 electrodes) was recorded in 15 adolescents with depression (15.1 $\pm$ 0.3 years) and 15 controls (15.3 $\pm$ 0.3 years). In addition, we examined 7 healthy siblings (14.9 $\pm$ 1.2 years) without any current psychiatric disorder. Study inclusion for the depressed subjects required a diagnosis of a single or recurrent depression, according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). Sleep stages were visually scored and compared between groups. Power maps were calculated, based on average SWA of the first three hours of NREM sleep.

Results: Depressed adolescents exhibited 34.4 $\pm$ 2.4% ($P < 0.05$) more SWA in a cluster of frontal electrodes compared to healthy controls. A similar increase of frontal SWA was found in healthy siblings 72.3 $\pm$ 5.1% ($P < 0.05$). Sleep architecture did not differ between the groups.

Conclusions: Higher frontal SWA in adolescents with depression and their healthy siblings might reflect a neurobiological correlate of increased familial risk for early onset depression.

Disclosure: Nothing to disclose.

P757

The effect of total sleep time on cognitive conflict adaptation in healthy adolescents

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Objective: To examine the effect of total sleep time (TST) on cognitive conflict adaptation in otherwise healthy adolescents.

Methods: The 84 participants were part of a longitudinal study starting in infancy, 48% were female and mean age 15.3 $\pm$ 0.2 y. Motor activity was recorded continuously for a week with actigraphs (Actiwatch-16/64) worn in the nondominant wrist, yielding estimation of TST by means of an automated method (Actiware®). We categorized TST for weekdays and weekend days according to their median values. Participants also performed the Stroop test: they were told to press the key corresponding to the color of the target (red, blue, or green). The words red, blue and green served as incongruent trials (e.g., the word red displayed in blue color) and a string of Xs were the control trials. The cognitive conflict adaptation effect was assessed measuring the reaction time of incongruent trials that followed 2 successive control trials.

Results: TST median values during weekdays and weekend days were 7.8 $\pm$ 1.5 h and 8.5 $\pm$ 2.2 h, respectively. Compared to adolescents who slept less than 8.5 h/night during the weekend, those with longer TST showed shorter reaction time for conflict adaptation (664.3 vs. 734.0 ms, $P < 0.05$). During weekdays, the reaction time was similar for adolescents sleeping less or more than 8.5 h.

Conclusions: Our results show a relationship between TST and the speed for adapting to a cognitive conflict. The speed was slower in adolescents sleeping less than 8.5 h/night during the weekend.

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P758

Insomnia and personality disorders: a pilot study

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Objectives: Comorbidity between insomnia and personality disorders (PD) has been poorly investigated. Atalay (Isr J Psychiatry Relat Sci. 2011) considered the sleep quality into the PD and identified DSM IV-TR clusters A and C as the most associated with insomnia. The aim of this study was to investigate the presence of PD in consecutive patients with a diagnosis of Primary Insomnia.

Methods: We evaluated 70 insomniacs (59% women; mean-age: 42 $\pm$ 11) with the Structured Clinical Interview for DSM (SCID-II, V.2.0) and with the multidimensional battery for assessment of personality (adaptive/maladaptive)-BMVP(A/D).

Results: PD were present in 58.6% of all patients (41/70). Within this group cluster B was the most diagnosed (68%), with a wide presence of narcissistic-PD (57%), whereas less frequent histrionic- (25%), borderline- (15%) and antisocial- (3%) PD. Temperament and character traits showed in PD insomniacs lower scores in the subscales dependence, responsibility, purposeful, social acceptance and higher scores in perfectionism and attentional impulsivity, in comparison to non-PD insomniacs.

Conclusions: Our data show a heightened occurrence of PD in insomnia patients. In contrast with the study of Atalay (2011), we found cluster B as the most frequent in patients with Primary Insomnia. In contrast with previous studies that highlighted the relationship between insomnia and borderline-PD (Battaglia et al., Biol Psychiatry 1999; Bastien et al., J Clin Sleep Med. 2008; Plante et al., J Pers Disord. 2009) we found a higher prevalence of narcissistic-PD in our sample. Future studies should clarify the relationship between PD and insomnia in order to improve treatment strategies.

Disclosure: Nothing to disclose.

P759

Examining the association between basic psychological need satisfaction and sleep-related outcomes in clinical populations

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Objectives: The Self-determination theory (SDT) identifies three basic psychological needs which are essential for well-being. The present study explored whether the satisfaction of the basic psychological needs for autonomy, competence and relatedness, as defined within SDT, are associated with sleep-related outcomes in clinical populations at risk for poor sleep. Secondly, the association between need satisfaction and global mental and physical health was examined.

Method: HIV, Chronic Fatigue Syndrome (CFS) and Insomnia patients completed the Need Satisfaction Scale, Mindful Attention Awareness Scale (MAAS), Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Fatigue Severity Scale (FSS), four self-developed items assessing psychological reasons for sleep disruption and the Medical Outcomes Study 36-item Short Form Survey (SF36).

Results: Preliminary analyses indicated that psychological need satisfaction related to more adaptive daytime functioning in all three clinical groups (current total $N = 145$, M age = 42.1, SD = 11.29, 66% female). Specifically, need satisfaction was associated with less daytime dysfunction, less daytime sleepiness and lower fatigue severity. With regards to qualitative sleep outcomes, in all samples need satisfaction was associated with less sleep disruption due to worrying or experiencing somber thoughts and further related to lower PSQI sleep quality in the HIV sample. In addition, psychological need satisfaction was positively associated with global mental health in each patient group.

Conclusions: The results suggest that psychological need satisfaction may play an important role in determining daytime functioning, fatigue, sleepiness and global mental health in HIV, CFS and Insomnia patient groups.

Disclosure: Nothing to disclose.

Sleep and aging

P760

Nocturia is associated with poor sleep quality in elderly patients with diabetes mellitus, hypertension and hyperlipidemia

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Introduction and objective: Sleep problems are common in the elderly. This may be related to associated co-morbidities such as diabetes mellitus, hypertension and hyperlipidaemia, and its subsequent effects or associated conditions such as obstructive sleep apnoea. Poor sleep quality is associated with decreased quality of life, increased morbidity and mortality.The objective of this study was to assess determinants of poor sleep quality in this group of patients, as it is an often under diagnosed and under treated problem.

Materials and methods: This cross-sectional study was conducted in a primary healthcare setting (Outram Polyclinic) in Singapore. Individuals aged 65 years and above who had at least one of the three co-morbidities were identified. Responders' sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI) questionnaire and were divided into those with good quality sleep and those with poor quality sleep, based on the PSQI score. Information on demographics, co-morbidities and lifestyle practices were collected. Descriptive and multivariate analyses of determinants of poor sleep were determined.

Results: There were 199 responders (response rate 88.1%). Nocturia (Adjusted prevalence rate ratio 1.54, 95% confidence interval 1.06–2.26) was found to be associated with an increased risk of poor sleep quality in elderly patients with diabetes mellitus, hypertension and hyperlipidaemia.

Conclusion: Nocturia is a prevalent problem in the geriatric population and it has been found to be associated with poor sleep quality in our study. Hence it is imperative to address this issue.

Disclosure: Nothing to disclose.

P761

Association of sleep complaints with cardiovascular and all-cause mortality in the Palanga community cohort in the period of 2003–2013

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Objective: This study was to establish association of sleep complaints with cardiovascular and all-cause mortality in the period of 10 years among inhabitants of Palanga city, located at the Western part of Lithuania.

Methods: Sleep complaints in a 35–74 year old representative sample (N = 1602, 600 males and 1002 females) were assessed in 2003 by Basic Nordic Sleep Questionnaire. Age, gender, marital status, education, alcohol use, smoking and physical activity were assessed by sociodemographic and health behavior questionnaires. Mortality data for the period 2003–13 was obtained from the Regional Mortality Register. Binary logistic regression analysis was used to assess the association between sleep complaints and outcomes, adjusted for sociodemographic and health risk factors. P-values less than 0.05 were interpreted as statistically significant.

Results: Cardiovascular diseases were causes for 47.5% of deaths (158 cases) during 2003–2013. Risk for cardiovascular mortality was significantly increased by sleepiness in the morning in whole sample (Odds ratio (OR) =2.09, 95% CI 1.05–4.16) and in females (OR=3.04, 95% CI 1.08–8.55); and by poor sleep quality in males (OR=3.00, 95% CI 1.11–8.11). Risk for all-cause mortality was significantly increased by poor sleep quality only in males (OR=3.28, 95% CI 1.45–7.41). Short or long sleep duration did not predict mortality after adjustment for sociodemographic and health risk factors.

Conclusions: Self-evaluated poor sleep quality increased the risk of all-cause and cardiovascular mortality among males in Palanga.

Disclosure: This research was funded by a grant (LIG-03/2012) from the Research Council of Lithuania.

P762

Prevalence of sleep complaints in the Palanga community cohort in the period of 2003–2013

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Objective: To establish prevalence of sleep complaints during 2003–2013 among inhabitants of Palanga city, located at the Western part of Lithuania.

Methods: The prevalence of sleep complaints in 35–74 year old representative sample was assessed in 2003 (N = 1602, 62.5% females) and 2013 (N = 931, 65.4% females). Difficulties initiating, maintaining sleep, too early awakenings in morning, snoring and breathing pauses during sleep were assessed by Basic Nordic Sleep Questionnaire. Complaints were confirmed when they occured more often than 3–5 nights per week during last 3 months. The comparison of proportions between two groups was performed using z-test. P-values less than 0.05 were interpreted as statistically significant.

Results: Difficulties falling asleep were more prevalent in 2013 (17.1%, 95% CI 14.6–19.4), as compared to 2003 (11.5%, 95% CI 9.9–13.1), $P < 0.001$. Prevalence of difficulties maintaining sleep increased significantly from 43.2% (95% CI 40.7–45.6) in 2003 to 49.7% (95% CI 46.5–53.0) in 2013. Too early awakenings were more prevalent in 2013 (19.1%, 95% CI 16.6–21.7), as compared to 2003 (12.9%, 95% CI 11.2–14.5), $P < 0.001$. Prevalence of snoring was lower in 2013 (21.6%, 95% CI 18.9–24.2), as compared to 2003 (26.2%, 95% CI 24.0–28.3), $P < 0.05$. Breathing pauses, reflecting possible sleep apnea, occurred more often in 2013 (5.6%, 95% CI 4.1–7.1), as compared to 2003 (2.5%, 95% CI 1.7–3.3).

Conclusions: A prevalence of sleep complaints and breathing disturbances during 10-year period was increased in the community of Palanga, therefore sleep quality improvement programmes are recommended.

Disclosure: The research was funded by grant LIG-03/2012

P764

Hormonal-metabolic parameters in perimenopausal women with sleep disorders

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Objectives: To study the circadian rhythms of melatonin secretion and the state of lipid peroxidation and the antioxidant system in perimenopausal women with sleep disorders.

Methods: We examined 72 perimenopausal women: 33 patients with sleep disorders (49.85 ± 3.03 years old) and 39 women were classified as controls (without sleep disorders, 50.36 ± 3.05 years old). Melatonin concentrations were determined in the saliva that was collected 4 times a day (6 a.m.-7 a.m., 12 p.m. -1 p.m., 6 p.m.-7 p.m., 11 p.m.- 12 a.m.). The measurements of substrates and products of lipid peroxidation (diene conjugates, TBARs) and components of the antioxidant system (α-tocoferol, retinol, reduced glutathione, oxidized glutathione) were determined in the blood serum and red cells. We applied the coefficient of oxidative stress that represented ratio of lipid peroxidation products to general antioxidative blood activity (normally it is 1).

Results: It was shown that sleep disorders in the perimenopausal women were associated with an increase in melatonin levels at 6 a.m.-7 a.m. and with a decrease in its concentration at 12 p.m.-1 p.m. and 6 p.m.-7 p.m. as compared to control. There were no significant differences in lipid peroxidation and antioxidant activity parameters levels between groups. The coefficient of oxidative stress was 2,2 indicating the unbalance between free radicals and antioxidant activity in women with sleep disorders.

Conclusion: The results of our study demonstrated development of oxidative stress and disruption of circadian rhythm of melatonin secretion in perimenopausal women with sleep disorders as evidenced by lag phase peak secretion.

Disclosure: Nothing to disclose.

P765

Retrospective study of sleepiness and vigilance in OSAS older patients

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Objectives: Excessive Daytime Sleepiness (EDS) is an important symptom of Obstructive Sleep Apnea Syndrome (OSAS), especially in older patients, to decide the appropriate treatment. Its objective quantification use EEG recordings, but are time consuming and expensive, making them difficult to use for large studies. This study assesses the ability to discriminate EDS in OSAS older patients, using the Epworth Sleepiness Scale (ESS) and the behavioural Oxford Sleep Resistance test (OSleR).

Methods: This was a retrospective study. Participants were community dwelling older patients (age ≥ 65 years) presenting to the sleep centre with OSAS symptoms for a whole night sleep laboratory polygraphy or a polysomnography. OSAS is defined by a respiratory disturbance index (RDI) superior or equal to 5/h. The record night was preceded by self-fulfilled ESS and followed by a one time OSleR at 9 a.m.

Results: There were 42 subjects: 32M,10F, mean age +/- SD:72,1 + /-5,0; BMI:31,6 + /−5,6; RDI:44,1 + /−30,0; ESS:9 + /−4. Only 36 subjects underwent OSleR: 27:pathological response, 9:normal response. 41 subjects had an OSAS (mild:8, moderate:7, severe:26).

Conclusions: Association between OSAS and OSleR was not significant, but tended towards concordance (P = 0,07). Association between OSAS and ESS became significant when the threshold to discriminate pathological EDS was higher: ESS ≥ 12 then P = 0,071, ESS ≥ 14 then P = 0,016. In contrast, there was no correlation between ESS and OSleR.

A higher ESS threshold than in adults should be more effective to assess EDS in OSAS elderly. Given its portability and minimal technical requirements, OSleR may be useful for large-scale assessment of daytime vigilance in older patients.

Disclosure: Nothing to disclose.

P766

Sleep complaints and metabolic syndrome in an elderly population: the three-city study

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Objectives: To examine the association of insomnia complaints, excessive daytime sleepiness (EDS) with metabolic syndrome (MetS) and each of its components in a community-based sample of subjects aged 65 years and over.

Methods: Analyses were carried out on 6354 non-demented subjects recruited from the French Three City Study. MetS was assessed using National Cholesterol Education program Adult Treatment Panel III criteria. Insomnia complaints (difficulty in initiating sleep, difficulty in maintaining sleep, and early morning awakening) and EDS were self-rated and detailed information on medication use was also gathered. Logistic regression models were adjusted for sociodemographic, behavioural, physical and mental health variables.

Results: A total of 977 participants had MetS. Difficulty in maintaining sleep was associated with MetS (OR=1.23, 95% CI: 1.06–1.43) whereas the two others complaints of insomnia were not significantly associated with MetS. EDS independently increased the risk of MetS (OR=1.46, 95%CI: 1.18–1.81 for frequently, OR=1.99, 95%CI: 1.49–2.67 for often, p-trend< 0.0001). EDS-MetS association was independent of

1) past-history of cardiovascular diseases,
2) insomnia complaints and
3) obesity and loud snoring.

EDS was particularly associated with central obesity, high triglycerides, low HDL cholesterol and elevated fasting blood glucose components of MetS.

Conclusion: Our results reported significant independent associations between frequent sleep complaints (EDS and to a lesser extent difficulty in maintaining sleep) and MetS in the elderly with potential implications in term of management and cardiovascular prevention in general geriatric practice. However prospective studies are required

to assess the clear temporal relationships between sleep complaints and MetS.

Disclosure: Nothing to disclose.

P767

Effect of age on the macro- and microstructure of sleep in women

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Objectives: The effect of age on sleep stages, the spectral composition of NREM sleep and sleep microstructure was investigated in a large sample of women.

Methods: Ambulant PSG recordings were obtained on one occasion in 400 non-pregnant women that were randomly selected from a representative sample (oversampling of snorers). Subjects with incomplete data, severe somatic disease or being on drugs that might interfere with sleep architecture were excluded. Thus, 245 women (age: 49 ± 11.1, range 22- 72 years) were included in the present analyses. Sleep scoring, spectral analysis and microstructure analysis (C3-A2) were conducted using automatic analysis and verified manually by a sleep scoring expert. AHI was based upon visual scoring. Linear regressions analyses (adjusted for AHI) with age (continuous) as predictor were conducted.

Results: Age was associated with decreases of Total Sleep Time (η^2 0.09), time in N2 (η^2 0.02), N3 (η^2 0.03), REM sleep (η^2 0.08), and delta power (log transformed) during NREM sleep (η^2 0.04). No significant effect on beta power during NREM sleep and REM density was observed. Spindle density (η^2 0.12) and K-complexes (log transformed) (η^2 0.11) showed a linear decrease by age. Similar results were obtained when only subjects with non-severe AHI were included.

Conclusions: Increasing age was as expected associated with decreased sleep time, which was mostly due to decreased REM duration whereas REM density was not altered. The decrease in sleep spindles and K-complexes during N2 sleep presumably indicates a decrement of sleep protective mechanisms with increasing age.

Disclosure: Georg Gruber is an employee of the Siesta Group

P768

What does good sleep mean in terms of macro and microstructure of sleep in women and how does age affect this relation?

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Objectives: Women complain more of sleep than do men, but little is known about the relation to the macro- and microstructure of sleep and how age affect this relation. This was the topic of the present study.

Methods: Ambulatory polysomnographical (PSG) recordings were obtained in a representative sample of 400 non-pregnant women (oversampling of snorers) and analysed through automatic analysis and manually verified. Subjective sleep quality ratings (poor, rather poor, average, good, very good sleep) at awakening after recording and age (cutoff 50? years) were related to PSG-derived data using a two-factor ANOVA (300 participants after exclusions).

Results: Good subjective sleep and lower age were associated with higher sleep efficiency (91 ± 2 vs. 83 ± 2% for young participants and 85 ± 2 vs. 72 ± 2% for older participants) and less: WASO, changes from sleep to Stage wake, and Stage changes/h). Stage 1% increased with poor sleep (no age effect). Number of sleep spindles increased with poor sleep in young subjects only, while K-complexes and spectral data (delta, theta, beta power in NREM or REM) were not related to sleep quality. Also total sleep time was significantly lower with poor sleep and higher age (418 vs. 373 min for young participants and 386 vs. 328 min for older participants.

Conclusions: Good sleep quality is related to more sleep continuity in a large, representative group of women, although the criteria decrease with age; older women need less continuity for sleep being labeled as 'good' (or poor).

Disclosure: Nothing to disclose.

P769

Polysomnographic data in patients with isolated memory complaints or mild cognitive impairment

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Objectives: Recent studies suggest that sleep disorders precede over the years the onset of clinical signs of Alzheimer's disease (AD).The objective is to study sleep disorders (changes in sleep architecture and/or appearance of sleep disorders) that occur early in mild cognitive impairment.

Methods: Patients with isolated memory complaints or mild cognitive impairment (MEMENTO cohort) were recorded with 2-night polysomnography (PSG) monitoring. Sleep duration parameters (TST), Apnea/Hypopnea index (AHI), Periodic Legs Movements Syndrome (PLMS) index, Sleep structure parameters (% stage 1, 2, 3 and REM), Sleep consolidation parameters (WASO, Sleep efficiency) and Sleep propensity parameters (Sleep Onset Latency) were measured.

Results: Nineteen patients were evaluated (14 females, Age=69 years±6 (range=58–78), BMI=24 kg/m^2 ± 4, Epworth sleepiness scale score=9 ± 4. Mean TST is 389 min ± 63 (range=217–454) with a sleep efficiency of 82%±14. Mean AHI is 21 events/h ± 18 (range=5–68), four patients having an AHI greater than 20. Mean Index of arousal is 27 events/h ± 16 (range=12–73). Mean PLMS index is 15 events/h ± 18 (range=0–53), 8 patients having a PLMS index greater than 15. Sleep structure consists of 6%±3 of stage 1, 51%±10 of stage 2, 20%±6 of stage 3 and 23%±6 of REM. Mean sleep latency is 6 min±6 (range=1–24) and mean Wake time after sleep onset (WASO) is 68 min±62.

Conclusions: Sleep is significantly impaired in patients with isolated memory complaints or mild cognitive impairment. In the future, it will be interesting to compare these data with those of control subjects and to determine the association between sleep disorders and/or PSG patterns and severity of cognitive impairment.

Disclosure: Nothing to disclose.

P770

The feasibility of trialling non-pharmacological interventions for improving the sleep of community dwelling people with dementia

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Objectives: To trial a package of timed bright light therapy, exercise and sleep education for improving the sleep of community-dwelling people with dementia (PWD) and their family carers.

Methods: Pairs of PWD and their family carer were issued with a sleep education booklet and a bright light therapy device and exercise programme for the PWD to use as prescribed on as many days as possible during a 5-week trial. Sleep was monitored using actigraphy for 7 days at the beginning and end of the trial, a daily diary, and standardised questionnaires. Questionnaires also measured cognitive functioning, quality of life, and dementia-related disruption, as well as carers' mental health and coping.

Results: Fifteen pairs participated and nine completed the trial. Six PWD had improvement in their percentage of sleep at night. Those with the most improved sleep also showed some improvement in subjective sleep ratings and carer-rated quality of life. These changes did not always translate into improved sleep or self-reported mental health of carers. Results are presented as case studies which illustrate the variability between pairs and highlight themes associated with success or failure with the intervention, as well as issues with recruitment and compliance.

Conclusions: Non-pharmacological interventions can be used successfully by some PWD living in the community. Given the limited options for treating dementia, it is recommended that these low-risk interventions are considered by clinicians and support workers. Reaching those who might benefit at the right time for them clinically and psychologically is an important consideration.

Disclosure: Nothing to disclose.

P771

Relationship between age and duration event number respiratory syndrome in patients with sleep apnea-hypopnea

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Introduction: Age may have influence in the response of the respiratory center and the dynamic systems that control breathing, so that younger patients presented respiratory events of shorter duration, compared with older patients, warning mechanisms which were more disturbed, they would present longer events.

Methods: Data were collected prospectively from 81 patients polygraph SAHS during the months of September to November 2008. We evaluated the correlation between age and the duration and number of apneas. We used Spearman′s rho correlation. SPSS vs. 15.0 was used for statistical analysis, a value considered significant at $P < 0.05$.

Results: We found a significant correlation between age of patients with SAHS and the duration and number of respiratory events, with a correlation coefficient of 0.447 and 0.21 respectively.

Conclusions: In SAHS patients was evidenced a longer duration of respiratory events in older patients. The cause is not clear and it could be in relation with respiratory control mechanisms or also with the natural history of the disease.

Disclosure: Nothing to disclose.

P772

Fatigue/sleepiness and important aspects of sleep restoration improve across aging

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Objectives: The present study tested the common assumption that sleep and fatigue worsen during aging. Very little longitudinal data are available.

Methods: The WOLF cohort, with 6500 individuals and three measurements was used for analysis of change between the first (T1) and last (T3) measurment (12 years in between) and for three age groups (at baseline): 19–34, 35–50 and 51–70 years – all working at T1. Sleep/fatigue was measured through the Karolinska Sleep Questionnaire (KSQ 15 items with problems occurring never-almost every day of the week, scored 1–6). The data was subjected to a repeated measures ANOVA with age groups as between-groups factors.

Results: Repeated awakenings increased across years ($P < 0.001$) and with increased age ($P < 0.001$). Early awakening increased across the 12 years but not for the oldest age group. Difficulties falling asleep did not increase across years, nor differ between age groups. Across retirement insomnia ($P < 0.05$) and repeated awakenings increased marginally ($P < 0.05$), while difficulties falling asleep did not change. Ratings of difficulties awakening *decreased* across the 12 years ($P < 0.001$), differed between age groups ($P < 0.001$) and fell with retirement ($P < 0.05$). Ratings of being well rested showed similar results. Fatigue *decreased* strongly across the 12 years ($P < 0.001$), but most in the oldest group and least in the youngest group. Fatigue also fell significantly ($P < 0.01$) with retirement. The results for sleepiness were very similar.

Conclusion: Aging has positive effects on fatigue and sleepiness and on restorative aspects of sleep.

Disclosure: Nothing to disclose.

P773

Self-reported sleep satisfaction in elderly predicts self-reported sleep satisfaction over 18 but not over 48-months

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Objectives: To examine to what extent self-reported sleep satisfaction, measured by the sleep sufficiency index (SSI, e.g., the self-

reported average sleep duration divided by the self-reported sleep need), is consistent over time in home-dwelling elderly.

Methods: Self-reported SSI was collected in participants of the CoroKind cohort, which is a cohort consisting of 675 home-dwelling elderly (i.e., age ≥ 65 years) subjects in the municipality of Kinda in Southern Sweden. SSI data was collected at baseline and after 18 and 48 months. Multivariate regression, adjusted for age and gender, was used to assess to which degree baseline SSI could predict SSI after 18 and 48 months, respectively.

Results: Complete data, i.e., for all three time-points, have been collected for 150 of the subjects (mean age 75.5 years, SD 2.75 years, 51.9% women). Baseline SSI was a significant predictor of SSI after 18 months ($P < 0.05$, adjusted R-squared 0.26), but not after 48 months.

Conclusions: SSI, which is a simple measure of self-reported sleep taking individual differences in sleep need into account, is moderately stable over 18 months, but not over 48 months. It is possible that emerging diseases affect the SSI over time by affecting sleep, especially in older subjects.

Disclosure: Nothing to disclose.

P774

Correlates of self-reported short sleep, long sleep and sleep sufficiency index in home-dwelling elderly subjects

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Objectives: Both short and long sleep has been associated to increased morbidity and mortality. The exact mechanisms linking sleep duration to poor health are, however, incompletely understood. The objective was therefore to explore correlates of self-reported short and long sleep and sleep sufficiency index (SSI, i.e., self-reported sleep duration divided by self-reported sleep need) among home-dwelling elderly subjects.

Methods: Six hundred and seventy-five home-dwelling elderly subjects (i.e., age ≥ 65 years) in Sweden. Self-reported data on sleep duration, sleep need, sleepiness (ESS; Epworth Sleepiness Scale), anxiety and depressive symptoms (HAD; Hospital Anxiety and Depression Scale) and perceived health (SF36) were collected. Data on co-morbidities and medication use were collected from medical records. C-reactive protein (CRP), Peak Expiratory Flow (PEF), creatinine and Low Density Lipoprotein (LDL) were also measured. Based on the distribution of the data, short sleep was defined as sleeping 5 h or less, and long sleep was defined as sleeping 9 h or more.

Results: Mean age was 77.7 years (SD 3.8 years), and 52% were females. Gender, age, using sleeping medications and perceived health were associated to SSI. None of the variables were associated to long sleep. Perceived health and hypertension were associated to short sleep.

Conclusions: Fairly few variables were related to sleep duration and sufficiency in this elderly sample.

Disclosure: Nothing to disclose.

P775

Fall accidents and actigraphy in nursing home

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Objectives: How fall accidents or risk to fall are present in long-term actigraphy recordings in nursing home.

Methods: Telemetric actigraphy recordings, institute's health records, and fall accident annotations for 24 nursing home residents were analysed. The longest individual dataset were two and a half years (between Aug 2006 and Jan 2009). Short and long-term indications of fall accident in the actigraphy and functional capacity measures were studied. In addition actigraphic variables' and the functioning score's ability to predict falls during next six month were analysed.

Results: Disturbances in the diurnal activity rhythm were observed close to the fall accidents but these signs were not systematic between the subjects. Only phase (cosinor acrophase) of the activity rhythm differed between the fallers (later phase) and the non-fallers for non-demented subjects. Functioning score or health changes did not explain the fall accidents in the material either.

Conclusions: No strong associations of the actigraphy or the functioning scores with the fall accidents were found in the analysed data set. The fall risk and the events causing the fall accidents can vary a lot and makes the automated fall risk assessment with technology and multivariate data analysis very complex in the nursing home settings. The structured follow-up of fall-accidents since year 2005 in the nursing home studied here, has shown, that at least one third of falls were due the external reasons, like stumbling or slipping. Objective activity behaviour monitoring could help nursing home personnel when solving potential causes of fall accidents a posteriori.

Disclosure: Nothing to disclose.

P776

Sleep microstructure in frontotemporal dementia is equally or even more disturbed compared to that in Alzheimer's disease: a sleep spindle study

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Backround and objectives: Sleep spindles (SS) are cardinal sleep microstructure features and are considered to have a sleep-protecting role. In neurodegenerative processes (e.g., Altzheimer's disease —AD), SS are subject to alterations (e.g., decrease in number). In a previous study, the sleep macrostructure in AD was compared to that in frontotemporal dementia (FTD); sleep macrostructure in FTD was found to be equally or even more disturbed compared to that in AD, in a shorter disease duration, regardless of primary sleep disorders. The present work investigates SS characteristics in the above populations.

Methods: Twelve behavioral-variant FTD (bvFTD) patients (seven men / five women, 62.5 ± 8.6 years) and 16 AD patients (eight men / eight women, 69.6 ± 10.7 years) were studied. Both groups had similar cognitive decline status (mild-to-moderate) while the FTD

patients had a shorter disease duration. All patients underwent full video-polysomnography. SS were detected automatically from the frontal and central EEG leads throughout N2 and N3, and SS density (SSd) was calculated as SS/min.

Results: The SSD values for the AD patients tended to be greater than those for the FTD patients. Both groups tended to have diminished SSd values in the frontal derivations vs. the central derivations. The reduction was much more pronounced in the FTD patients.

Discussion: Similarly to what was observed for the sleep macrostructure, sleep microstructure in FTD, as far as SSd is concerned, seems to be equally or even more disturbed compared to that in AD, in a shorter disease duration.

Disclosure: Nothing to disclose.

Healthcare services, research and education

P777

Characteristics and trends in hypnotics consumption in the largest health care in Israel

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Objectives: To quantify and characterize hypnotics consumption habits among patients insured by Clalit Health Services (CHS) in Israel, and comparison of these during the years 2000 vs. 2010. In addition, to evaluate potential hypnotics tolerance during long-term usage (over 6 months).

Methods: A retrospective query of CHS well managed database. Data was collected for all patients over the age of 18 years who were prescribed with hypnotics in 2000 and in 2010.

Results: Of about 4 million people insured, 6.2% in 2000, and 6.8% in 2010 consumed sleep medications, with about one quarter of these treated for over 6 months. In 2000, 78% of patients were prescribed with a single drug compared to only 54.8% in 2010. While in 2000 Benzodiazepines accounted for 84% of hypnotics, in 2010 this was reduced to 73%. Of all patients treated for longer than 6 months only 11% in 2000 and 9% in 2010 required a dose increase suggesting most patients did not develop tolerance.

Conclusions: Although the prevalence of insomnia is estimated to be around 30%, only 6.2–6.8% of the population consume hypnotics, in 2000 and 2010 respectively. There is a strong increase in prescription of combination of medications from 2000 to 2010, with a tendency of increment in Z-class medication and reduction in benzodiazepines. Patients treated for longer than 6 months did not escalate dosage, suggesting the absence of tolerance. Given the adverse consequences of insomnia, medical provider apprehension regarding long term hypnotic usage needs to be re-thought.

Disclosure: Nothing to disclose.

P778

No law for sleep. Preliminary results from a national survey about sleep patterns in portuguese lawyers

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Objectives: To evaluate sleep patterns, sleep complaints and sleepiness in a sample of portuguese lawyers.

Methods: Twenty-one lawyers (15 Females) were invited to participate in this first step of a national study comprising either subjective and objective assessment of sleep-wake cycle and sleep related complaints. Subjective assessment required the use of Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Berlin Questionnaire (BQ) and Sleep diary (SD) whereas objective evaluation comprised the use of actigraph devices.

Results: Mean age of the sample was 32 ± 5,4 years old with average body mass index of 22,8 ± 2,9 (24,5 ± 3,2 for males and 22,6 ± 2,5 for females). Excessive Sleepiness (ESS ≥ 10) was present in 40% of the females and 50% of the males and 53,3% of the females vs. 50% of the males scored ≥ 5 on PSQI. Total Sleep Time was 7:09 h ± 1:07 h on weekdays and 7:40 h ± 1:15 h in weekends in average. Actigraph based average bedtime is 23:40 h ± 01:26 h on weekdays vs. 01:29 h ± 1:24 h. Wake-up time is 7:55 h ± 0:53 h on weekdays and 9:51 h ± 1:38 h on weekends. Parameters from SD and actigraphy did not differ statistically ($P > 0.05$).

Conclusions: The high prevalence of excessive sleepiness and sleep complaints in this population as well as their average sleep duration which stands on the inferior limit of the accepted normal range suggest that those professionals are at particular risk of sleep deprivation with all its negative consequences for health and professional performance.

Disclosure: Nothing to disclose.

P779

Self perceived sleepiness and risk of obstructive sleep apnea syndrome among cuban health related professionals

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Objectives: To study the prevalence of self perceived sleepiness and risk of obstructive sleep apnea syndrome in a sample of health related professionals.

Methods: A survey comprising two validated questionnaires about sleepiness (Epworth Sleepiness Scale – ESS) and the risk of Obstructive Sleep Apnea Syndrome – OSAHS (Berlin Questionnaire – BQ) was delivered during a major health congress in Havana – Cuba joining a relevant group of cuban health professionals.

Results: One hundred and eleven health related professionals (85 females) with mean age of 43,5 years old (sd: 13,7) completed the questionnaires. Habitual excessive sleepiness (ESS >=10) was perceived by 26,1% of the global sample (69% of females), whereas a high risk of OSAH (BQ) was assumed for 12,6%. For those with habitual excessive sleepiness, a high risk of having OSAH were more likely (20,7%). Excessive sleepiness was negatively associated with age ($r = –0.193$; $P = 0.05$). Motor symptoms associated with tooth grinding or clenching during sleep were assumed by 19,8% of inquirers.

Conclusions: The results of this study showed an important prevalence of sleepiness and increased risk of OSAH among cuban health related professionals. These should be a red flag for the need of directed educational intervention regarding the potential dangers of sleepiness and OSAH. Furthermore, this can help to explain why sleep in only poorly evaluated during general clinical setting and should deserve some reflections.

Disclosure: Nothing to disclose.

P780

An educational intervention to mitigate sleepiness in road transport

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Objectives: Driver sleepiness is a significant concern in transport. We investigated whether driver education on alertness management would mitigate the problem.

Methods: Fifty-two truck drivers (mean age 37.6 years) were randomly assigned to intervention (n = 32) and a control (n = 20) groups. Data was collected during a 2-week period five months before and after a training day that included a lecture and a workshop on alertness management strategies. Sleepiness during trips was measured by the Karolinska Sleepiness Scale, use of sleepiness countermeasures by a diary, and sleep by a diary and actigraphs. Trips were divided into first night (fN), successive night (sN), morning (M), and day/evening (D/E) trips. A trip was defined as 'sleepy' if at least one of the hourly given KSS ratings was ≥ 7.

Results: The intervention group showed no significant changes in the proportion of sleepy trips between the pre- and post-intervention measurements (fN: 39% vs. 32%, sN: 18% vs. 23%, M: 9% vs. 8%, D/E: 5% vs. 6%). This also held true for the use of effective sleepiness countermeasures (caffeine, napping) during a trip (fN: 54% vs. 59%, sN: 44% vs. 48%, M: 21% vs. 33%, D/E: 29% vs. 15%) and the amount of prior sleep (fN: 9.7 h vs. 10.0 h, sN: 7.3 h vs. 6.9 h, M: 8.1 h vs. 7.9 h, D/E: 8.2 h vs. 8.0 h). The results did not differ from those of the controls.

Conclusions: Our results propose that a short alertness management training is not sufficient to reduce driver sleepiness.

Disclosure: Nothing to disclose.

P781

Difficulties in treating sleep problems reported by counsellors working with survivors of sexual assault

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Objectives: This study sought to determine common sleep problems encountered by counsellors working with survivors of sexual assault, and which problems were the most difficult to treat.

Methods: Four focus groups (total n = 29) were conducted with counsellors working with survivors of sexual assault. The focus groups were conducted to gather information about the counsellors' understanding, experiences, knowledge and problems encountered with regard to helping survivors of sexual assault with sleep difficulties. The counsellors also completed a short rating scale designed to examine their confidence in treating sleep disorders. Focus group transcript data was analysed using thematic analysis, and rating scale data was subjected to frequency analysis.

Results: Counsellors consistently agreed that sleep difficulties were a prominent issue for survivors of sexual assault. Common problems impacting sleep included nightmares, hyper-vigilance, safety concerns, restless limbs and medication-related difficulties with falling asleep and frequent waking. Counsellors described experiencing the most difficulty with treating problematic jerking of limbs, sleepwalking, delayed sleep phase issues, and snorting, snoring or gasping for air. Many of the treatment difficulties encountered by counsellors were attributed to resistance and reluctance on the client's behalf to persist with suggested treatments due to an increase in anxiety, or re-experience of their prior trauma.

Conclusions: Counsellors consistently reported a lack of confidence in, and knowledge of, treating sleep breathing related disorders, restless limbs, and any of the more complex sleep difficulties not readily treated with sleep hygiene, psycho-education or relaxation techniques.

Disclosure: Nothing to disclose.

P782

How is tatarstan sleeping?

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Objectives: This clinical epidemiological research analyzed the prevalence of sleeping disorders and its characteristic features, based on inquiry of 1117 patients.

Methods: There were used specially elaborated questionnaire, Epworth Sleepiness Scale (ESS), Hospital Anxiety and Depression Scale (HADS).

Results: The final analysis included 715 forms with male rate 157 (21,9%), female – 558 (78,1%), among them 422 (59%) were citizens, 293 (41%) – villagers. 71% of respondents complained of insomnia. But only 5,15% of them had a visit to doctor about this problem. And only 7,3% were asked about quality of their sleeping during consulting process about different health disorders by doctors. 37,7% of interviewed individuals couldn't term a specialist, that they would be referred to, if they have problems with sleeping. After separating respondents on 3 group according to Visual Analog Scale, it was noted that 44% have 5–6 sleeping hours, 18% less than 4, thuswise 62% of sample representatives sleep under 6 h. Treating sleep disorders 57% use benzodiazepines, 54% prefer herbal therapy.

Conclusions: Dissociation between subjective estimation of sleeping process quality and value of complaints were revealed. It gave us an information about low awareness of population about sleeping disorders problem. There is significant undervalue of relevance of insomnia, and inattention in its adequate correction. Tendency to autotherapy of insomnia was found. Medical society underestimate the importance of this sociomedical problem.

Disclosure: Nothing to disclose.

P783

Reduction of intensive care unit (ICU) simulated noise's effect on the nap by earplugs

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Objectives: It is important that the patients sleep sufficiently for physical and mental recovery after surgery. In our previous study, we showed that the ICU noise increased the sleep latency and modified the sleep structures for even healthy young subjects. We investigate in this study the attenuation of this ICU noise's effect by earplugs and consequently the improvement of subjective/objective sleep qualities.

Methods: Six healthy male subjects (21.7 $\pm$ 1.1 years old) were polygraphically recorded (EEG, EOG and ECG with R&K's criteria) during their nap (30mn) for 1 adaptation day (AD), 2 baseline days (BL-1 and BL-2) and experimental day (EX). The order of BL-2 and EX is counterbalanced. For BL-1, BL-2 and EX, the Ss were exposed in the reproduced ICU noise (48.9 $\pm$ 2.1 dB) recorded from a real ICU. In EX, they were required to use earplugs (NRR=29 dB) in order to attenuate the ICU noise. They were asked before and after their nap for each day to give a sample of saliva for measuring of amylase (stress marker) and to fill in POMS that explores subjective mood states.

Results: We observed a significant difference ($P < 0.05$) between BL (15.6 $\pm$ 5.9mn, the average BL-1 and BL-2) and EX (9.6 $\pm$ 3.54mn) for the sleep latency based on the first spindle appearance. However the other sleep characteristics, amylase content and POMS showed no significant modification.

Conclusion: It is obvious that earplugs are useful for ICU's noise reduction and facilitate the sleep onset. The earplugs will be considered as low-cost, easy-to-use tools for the ICU patient's comfort.

Disclosure: Nothing to disclose.

P784

Sleep disturbances, daytime sleepiness and symptoms of sleep apnea syndrome in first year medical students

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To determine the occurrence, reasons and features of sleep disturbances, intensity daytime sleepiness and sleep apnea syndrome (SAS) in first year medical students.

One thousand and fifty-seven first year medical students (475 boys, 1282 girls) mean age 18.0 $\pm$ 1.6 underwent a semi-structured interview (in 2009–2011 years): questionnaire value subjective characteristics of sleep, Russian version of the Epworth Sleepiness Scale (ESS), screening test of SAS, circadian preference.

Sleep disturbances had 427 (24.3%) students, including a long time to fall asleep (26.0%); short duration of sleep (21.5%); frequent awakenings (30.1%); multiple and disturbing dreams (26.5%). Excessive daytime sleepiness was observed in 43.1% of students with sleep disturbance, the night chronotype had 67.9% of them. Identified gender differences in the severity of daytime sleepiness, so the average value of the total score for ESS was higher in girls $-$8.1 points [95% CI 7.8–8.3], vs. in boys – 7.0 points [95% CI 6.6–7.3], $P < 0.001$. SAS can be suspected in 298 (17.0%) students of all respondents. Among the respondents identified: snoring (7.1%), sleep apnea (2.0%), daytime sleepiness in a relaxed state (10.2%) and in the active state (3.2%), increased blood pressure to a level 140 and 90 mm Hg and more (20.0%), morning headaches (35.7%). The results of our study suggest a high prevalence of sleep disturbances and associated conditions among first year medical students.

Disclosure: Nothing to disclose.

P785

Sleep and health related quality of life in Georgian population

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Objectives: The present study aimed at investigating the association of sleep problems, sleep quality and health status in the population of two cities of Georgia - Tbilisi and Kutaisi.

Methods: Three hundred and four subjects from Tbilisi (mean age 37.07 $\pm$ 10.73) and 91 subjects from Kutaisi (39.4 $\pm$ 10.8) were surveyed. Participants completed Insomnia Severity index (ISI), STOP BANG questionnaire, Pittsburgh Sleep Quality Index (PSQI), Beck depression inventory (BDI-SF), and Short-Form Health Survey (SF-12), consisting assesses of Physical (PCS) and Mental (MCS) Component Summaries. Socio-demographic data (age, gender, marital status, socio-economic status) were also obtained. t-test, correlation, and hierarchical multiple regression analysis were conducted.

Results: Poor sleep quality was observed in 46.1% of Tbilisi, and 33% of Kutaisi sample. High prevalence of insomnia and OSA risk in Georgian population has been detected. Regression analyses in Tbilisi population showed that after adjustments for demographics, health variables (PCS, MCS, BMI, BDI) increases models predictive capacity by 30.4% for PSQI global score ($F_{(8,295)}$=21.185, $P = 0.000$); by 28.3% for ISI ($F_{(8,295)}$=18.353, $P = 0.000$), and by 11.5% for OSA severity ($F_{(8,295)}$=56.026, $P = 0.000$). In Kutaisi sample predictive power increased by 21.9% for PSQI ($F_{(8,82)}$=3.860, $P = 0.001$), by 26.9% for ISI ($F_{(8,82)}$=4.505, $P = 0.000$), and by 4.3% for OSA ($F_{(8,82)}$=14.258, $P = 0.000$).

Conclusions: This study provides evidence of (1) poor sleep quality and prevalent sleep problems in Georgian population; (2) a complex relationship between sleep and health. Increasing the awareness and improving the sleep disorders diagnosis and treatment should be a high priority for the healthcare system in Georgia.

Disclosure: Study supported by SNSF, SCOPES grant IZ74Z0_137415

P786

Alertness, chronic fatigue, and actigraphic sleep between working and off days among nurses under fixed shifts

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Objectives: Fixed rotation shift has been suggested as a better way for nurses' health and performance. This study investigated sleep patterns for consecutive 6 days in nurses under fixed shifts.

Methods: Sixty female nurses (day shift DS=18, evening shift ES=21, night shift NS=21) with a mean age of 31.0 $\pm$ 5.2 years completed sleep diary and actigraphy for 6 days. Mean acitgraphic sleep was calculated for working and off days, respectively. Alertness (Visuo-Analogue Alertness Scale), chronic fatigue (Standard shift-work index chronic fatigue scale), and sleep quality (Pittsburg Sleep Quality Index, PSQI) were assessed during shifts.

Results: 76.7% of nurses complained poor sleep (PSQI >=5) with the worse sleep was in NS nurses (PSQI score=7.9 vs. 6.6 in DS and 5.7 in ES; F = 3.256, $P = 0.046$). No differences were found in alertness and chronic fatigue among nurses under three shifts. Compare their actigraphic sleep between working and off days, NS nurses spent less time in bed during working days (6.4 h vs. 7.0 h in DS and 7.6 h in ES; F = 4.38 $P = 0.017$) but slept more during off days (7.4 h vs. 5.7 h in working days; paired t = 2.79, $P = 0.012$). A high percentage of NS nurses did segment sleep (60.0% vs. 47.6% of ES and 5.6% of DS). There were no differences in sleep efficiency (85.4%~ 89.3%) between working and off days among nurses with different shifts.

Conclusion: Nurses under night shift sleep more during off days to compensate their less sleep during working days and to maintain their alertness and energy.

Disclosure: Nothing to disclose.

P787

Diagnostic models for obstructive sleep apnea in the Australian community: observations from pharmacy-based CPAP providers

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Objectives: 1.) To describe current diagnostic models for obstructive sleep apnea (OSA) in Australia as reported by CPAP practitioners in community pharmacies.
2.) To obtain feedback on models and identify potential areas for practice improvement.

Methods: Semi-structured telephone interviews were conducted with pharmacy-based CPAP practitioners. Participants reflected on their current practices and described diagnostic pathways used in their setting. Subsequently, a joint stakeholder focus group provided feedback on the identified diagnostic models.

Results: Twenty-two telephone interviews were conducted, and six key diagnostic models were identified. These models varied in terms of the diagnostic test used, the practitioner that initiated or interpreted the test, and who discussed results with the patient and made treatment recommendations. While some models were seen to facilitate patient access to OSA services, a nine-member stakeholder group raised medical and ethical concerns over certain models. Medical concerns involved diagnostic tests being initiated or interpreted in the absence of an appropriately trained medical practitioner. Ethical concerns involved potential conflicts of interest for CPAP providers that offered both diagnostic and treatment services. It was acknowledged that no single model would adequately meet community needs and evolving models were needed. Professional practice guidelines to provide a practice framework and delineate roles were proposed.

Conclusions: The unregulated nature of the Australian CPAP industry has seen diagnostic models evolve that may raise medical and ethical concerns. It is important to address these concerns while facilitating patient access to services. Development of professional practice guidelines may promote medically and ethically appropriate, patient-centred care.

Disclosure: Nothing to disclose.

P788

Short sleep is associated with increased hospitalization episodes: results from the 2005–2006 US National Health and Nutrition Examination Survey (NHANES)

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Objectives: Sleep loss is increasingly prevalent in modern society and has been documented to negatively impact health. Growing evidence indicates that insufficient sleep promotes cardiovascular, metabolic and immune dysregulation, thus enhancing the risk of adverse events. Whether short sleep is associated with increased demands on healthcare resources is currently unknown.

Methods: We examined 6128 participants aged 44.5 $\pm$ 0.77 years from the 2005–2006 US National Health and Nutrition Examination Survey. The primary exposure was self-reported sleep duration, categorized as $\leq$5 (short sleep), 6–8 and $\geq$9 h of sleep per night (long sleep). Outcomes of interest were numbers of overnight hospital stays and frequency of healthcare utilization. Multivariate logistic regression models were performed.

Results: Eight hundred and fifty-six (14.0%) participants reported sleeping $\leq$5 h/night, while 589 (9.6%) were identified as long sleepers. Frequency of healthcare utilization was not significantly different across sleep duration categories. Compared with those sleeping 6–8 h/night, short sleepers had two-times higher odds of being hospitalized after controlling for age and gender (OR=2.39; 95% CI=1.80–3.17). No association was observed for long sleepers. Further adjustments for variables related to clinical outcomes as income, smoking and comorbidities (hypertension, diabetes, cardiovascular disease, chronic obstructive pulmonary disease, asthma) only marginally attenuated the relationship (OR=2.10; 95% CI=1.51–2.92).

Conclusions: Short sleep is related to increased hospitalization in a nationally representative sample of US adults, even after adjustment for multiple covariates. Our findings have enormous public health implications, suggesting that chronic short sleep may contribute independently to exacerbating the illness burden on patients and financial demands on the healthcare system.

Disclosure: Nothing to disclose.

P789

The somnonet portal - an open source online tool for assessing quality of structure and process in sleep laboratories

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Objectives: The German Sleep Society (DGSM) established the 'Check List of Process Quality' in 1999. In 2009, participation in this quality program has become mandatory for DGSM accredited sleep labs. Three consecutive case reports from each lab were peer-reviewed by highly experienced specialists by using a standardized check list including details on anamnesis, diagnostic and therapeutical procedures, comorbitities, physicians report, night protocol, and polyomnographic parameters.

Methods: Comments of the reviewers are forwarded to the labs. While the first two rounds were done by paper and pencel, the somnonet online platform has been established in 2012. Sleep labs provide information on structure quality by themselves and reviewers give their rating also online.

Results: Compared to the first rounds, the use of the somnonetz portal decreased the time of conduction, measured from the beginning of the one-month patient sampling period until the end of the review process, from 8 to 5 months. The most crucial point was a high acceptance resp. an easy usability in accordance to the protection of data privacy and different levels of allocations.

Conclusions: The somnonetz online portal is an effective and well accepted tool to accelerate the assessment of structure and process quality even by considerung data protection. Also the cross validation of structure information - e.g. conducted nights vs. personal hours and equipement, becomes easier. In addition a patient register platform with different areas and focuses is implemented within the somnonetz project.

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P790

What do UK junior doctors' know about sleep disorders? A systematic literature review

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Objectives: Sleep disorders are common and have serious consequences on health. It is important that sleep disorders are recognised and managed correctly. In my experience core medical trainees (UK junior doctors, 2–3 years post-graduation) lack this knowledge. The present study is a systematic review of the literature on what is known about knowledge and education of sleep disorders in post-graduate trainees in the UK.

Methods: A literature review of PubMed and EMBASE was performed using: '(((sleep education) OR (sleep knowledge) OR (sleep training))) AND ((residents OR students OR (allied health professionals) OR clinicians OR doctors))'. Final search date 23.04.14.

Results: This search revealed 1991 articles of these 89 were related to sleep education and knowledge. 4 further articles were identified by a reference search. This search identified one questionnaire study based in the UK, performed in 1998. In this study questionnaires were sent to the organisers of preclinical and clinical courses in all UK medical schools. They received a 71% response rate. The median time spent in undergraduate teaching was five minutes (15 min for preclinical teaching and zero in clinical teaching). An international study of 12 countries (409 medical schools, not in the UK) revealed about 2.5 h was spent on sleep disorders education. The literature search did not reveal studies evaluating sleep knowledge in junior doctors or medical students in the UK.

Conclusions: The current literature suggests UK medical schools spend little time on sleep disorders, knowledge gained in foundation and core medical training has not been studied.

Disclosure: Nothing to disclose.

P791

Is the quality of portable sleep monitoring the same using hook-up video instructions as for in-clinic hook-up instructions?

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Introduction: The aim of this study is to compare the quality of portable sleep apnea monitoring (type 3 sleep study) after routine in-clinic hook-up vs. hook-up video instructions in a randomized double-blinded study.

Methods: Subjects on the waiting list for a sleep study were randomized to either in-clinic or video instructions. All were measured with the T3 portable sleep monitor (Nox Medical). The Nox T3 online video was translated from English to Icelandic. The overall quality and length of the measurements was assessed as well as the quality of the chest and abdominal respiratory inductance plethysmography (RIP) belts, the nasal cannula and pulse oximetry.

Results: In this ongoing study, out of the first 15 subjects, 7 were randomized to in-clinic instructions (6 males and 2 females, mean $\pm$ SD age 48.7 $\pm$ 7.5 years, BMI 25.9 $\pm$ 4.7 kg/m^2) and 8 to video instructions (5 males and 2 females, mean age 50.8 $\pm$ 11.1 years, BMI 29.4 $\pm$ 3.6 kg/m^2). The mean overall quality of the sleep studies was 87 $\pm$ 18% and 92 $\pm$ 13%, respectively for in-clinic and video instructions (P = 0.54). The mean length was 450 $\pm$ 58 min and 449 $\pm$ 81 min, respectively (P = 0,98). The quality of the RIP belts was 100% in all the recordings. No significant difference was found in the quality of the nasal cannula and oximeter signals between in-clinic and video instructions.

Conclusion: These preliminary findings suggest that video instructions provide the same quality of type 3 sleep studies as in-clinic instructions. This allows for minimized in-clinic interview time and telemedicine access to sleep studies in distant rural areas.

Disclosure: Nothing to disclose.

P792

Sleep quality in Sweden: are there diffferences from north to south and between native and foreign born residents?

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To examine sleep quality differences in Sweden between North vs. South residence and between native and foreign born residents.

In March-June, 2001 a postal survey was sent to a random sample of Swedish residents aged 19 -75. The response rate was 70.9% (n = 1209). The participants were categorized as northern (6) or southern (15) based upon county of residence split at the 61.0 latitude. Sleep quality measures included: subjective sleep dissatisfaction (SSD), difficulty in initiating sleep (DIS), difficulty staying asleep (DSS), non-restorative sleep (NRS), and use of sleep medication (USM).

One thousand and six subjects (83.2%) lived in southern region and 203 (16.8%) in northern. 557 men (46.1%) and 652 women (53.9%) responded to questions regarding sleep quality. No significant differences were found between the southern and northern regions of Sweden. However, significant differences are found between native and foreign born residents and by gender. Foreign born residents reported higher SSD 15.7% vs. 23.7%, $P < 0.05$; DIS 5.7% vs. 12.2%, $P < 0.01$ and USM 7.1% vs. 14.8%, $P < 0.01$. Females reported significantly poorer quality sleep than males.

Southern and northern Sweden has large variations in weather conditions and sunlight duration yet the reported sleep quality did not differ between the two regions. This may perhaps be due to being a highly developed country with access to similar facilities; such as the ability to darken the bedroom in light months and use artificial light in the dark months. A greater proportion of foreign born Swedish residents reported poor sleep quality which warrants further investigation.

Disclosure: Nothing to disclose.

P793

Large scale sleep evaluation made possible by mobile technology and fitness heart rate monitors

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Objective: Evaluate sleep duration, quality and efficiency in the general population.

Methods: we used a mobile application, a validated proprietary sleep measurement software based on Heart Rate Variability, sound recording using mobile phones and a cloud based data analysis and integration. The application was offered to users interested in

evaluating their sleep and and getting personalized advice on how to improve it, if needed. Data has been collected between January 23rd and April 10th 2014 and included a few simple questions regarding sleep complaints, continuous Heart Rate at night for those who owned a Bluetooth enabled fitness belt, snore recording using the iPhone microphone and an automated sleep diary. Users got next day reports regarding their sleep.
Results are based on 2466 nights with belts from 264 users and 4311 nights from 1400 users without belts.
(1) Users with belts: average night recording time 449 min (SD 87), average night sleep time 381 min (SD 81), sleep efficiency 85% (SD 5.5), mean number of awakenings 14.4 (SD 7.9), mean arousal index 12.1 (SD 5.7), mean night Heart Rate 61.8 (SD 9.4), mean night time with snoring detected 13.4% (SD 17.6).
(2) Users without belts: recording time 419 min (SD 138), sleep efficiency 89% (SD 23), number of awakenings 1.7 (SD 2.2), percentage time snoring 14% (SD 19).
Conclusions: Mean nightly sleep in the population is less than 7 h indicating chronic sleep deprivation. Arousal index may represent a simple and available screening tool for Obstructive Sleep Apnea.
Disclosure: Employees of HypnoCore, a hight tech company that develops sleep assessment and improvement methods

P794

How bad is the sleep-wake cycle on first year medical students?

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Objectives: This study aims to analyse sleep-wake cycle and the effects of social jet lag on first year medical students.
Methods: A quantitative and transversal study, conducted at the Laboratory of Neurobiology and Biological Rhythms of the Federal University of Rio Grande do Norte, Natal, Brazil. Instruments for data collection: Munich Chronotype Questionnaire, Morningness Eveningness Questionnaire of Horne and Östberg, Pittsburgh Sleep Quality Index, Epworth Sleepiness Scale, Beck's Anxiety and Depression Inventories, Actimeter, Anthropometric measures and Academic Performance. Statistical significance was considered for $P < 0,05$.
Results: Forty-one students were evaluated, 22 (54%) male and 19 (46%) female. Mean sleep duration was 5:51 (± 0:55), sleep onset was 12:04 am (± 0:47) and 93% (38) of the students reported to use alarm clock. Social jet lag had an average of 1:57 (± 1:10), 40% had 2 h or more and there was a statistical difference between evening and morning chronotypes. 82,5% (33) have poor sleep quality and 57,5% (23) excessive daytime sleepiness. Sleep quality was correlated with social jet lag, sleep duration, sleep onset, chronotype, Interdaily Stability (IS60) and anxiety. In addition, academic performance was correlated with sleep onset, sleep quality and IS60.
Conclusions: Students with excessive academic demand present a few sleep impairments such as shorter sleep duration, sleep deprivation, poor sleep quality and daytime sleepiness. Evening types are more sleep deprived. These aspects reflect on academic performance.
Disclosure: Nothing to disclose.

Cell and molecular biology and genetics

P795

The participation of chaperone Hsp70 in sleep modulation in rats

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Objectives: The biosynthesis of proteins and other macromolecules is supposed to be the key function of sleep. Heat shock proteins (HSP) assist in protein folding and take part in sleep modulation. It was determined that exogenous Hsp70 injected into a liquor brain system or into the ventrolateral preoptic area (VLPO) of the hypothalamus in rats and pigeons induced an increase in non -rapid eye movement (NREM) sleep time [Pastukhov et al., 2004–2010; Ekimova, 2013]. The present research aims to investigate an influence of decreased Hsp70 content in the VLPO on sleep in rats.

Methods: Experiments were carried out in male Wistar rats housed under controlled conditions in an isolated chamber. To decrease the level of Hsp70 lentiviral vector pLKO.1-shRNA-Hsp70 was injected into the VLPO. Electrophysiological data and body temperature were recorded using telemetry system.

Results: Hsp70 content in the VLPO is reduced by 60% after pLKO.1-shRNA-Hsp70 microinjections. A decrease in Hsp70 level leads to reduction of both NREM sleep and REM sleep time due to a decrease of episodes number that indicates the suppression of sleep initiation mechanisms. This effect is observed in a dark (active) phase of day since the 6th day after transfection. Since the third week significant increase of NREM sleep time in a light phase of day appears. It is likely to be associated with compensatory influence of other brain structures related to NREM sleep regulation.

Conclusion: Results of our investigation suggest the involvement of Hsp70 in the VLPO into molecular mechanisms of sleep modulation.

Disclosure: Nothing to disclose.

P796

Sleep and wakefulness duration and distribution are regulated by MAPK2 and MAPK3 phosphorylation

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Introduction: Sleep is a complex behaviour and its functions and molecular pathways remain elusive. Evidence suggests that sleep occurs at a cellular level with predictive changes in gene expression. Nevertheless, how wakefulness and sleep trigger molecular changes is largely unknown.

Methods: To study and understand the molecular pathways of sleep, we used a model of sleep in vitro. In this study we investigated the effect of MAPK2 and MAPK3 phosphorylation on the transcriptional markers of sleep. For this purpose, we used an inhibitor of MAPK phosphorylation (U0126) in our primary cortical cultures and assessed gene expression. Additionally, the same inhibitor was directly perfused in the lateral ventricle of mice during 7 days and vigilance states were assessed.

Results: In vitro: when cultures were pre-treated with U0126, transcriptional correlates of sleep were largely inhibited.

In vivo*:* results suggested that MAPK1 and MAPK2 are quickly phosphorylated during wakefulness (less than twenty minutes) (n = 4; p-value=0.03). Inhibitor of MAPK phosphorylation reduced NREM sleep duration over 24 h (P = 0.036) moreover sleep during the dark period was reduced by half (P = 0.036). Sleep was also more consolidated as short episodes of wakefulness (>15sec) were reduced in U0126 treated mice (P = 0.023) (n = 9 and 7, respectively for inhibited and control).

Conclusion: MAPK pathway could be the missing link between the vigilance states and the underlying changes in gene transcription.

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Disclosure: Nothing to disclose.

P797

Changes in potassium channel genes expression during spontaneous sleep-wake cycle and sleep deprivation

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Objectives: Cholinergic neuron-specific potassium channels that react directly to the concentration of sleep regulators like adenosine and nitric oxide (NO) might be involved in sleep homeostasis by hyperpolarizing of the cholinergic cells.

The aim was to investigate the expression level of genes coding cholinergic neuron-specific ATP sensitive (Kir 6.2/Sur1) and NO sensitive leak (TASK1/3) potassium channels during normal sleep and after sleep deprivation (SD) in basal forebrain (BF) and cortex (CX).

Methods: Standard deviation was performed by gentle handling during 3, 6 and 12 h. The amount of Kir6.2/Sur1 and TASK1/3 transcripts was measured by real-time qPCR.

Results: We found a diurnal variation in Kir6.2/Sur1 expression in the BF and CX. Kir6.2 expression was lowest at 11AM in the BF while there was no diurnal pattern in the CX. SD led to the levelling up of the diurnal pattern in BF. Sur1 had a highest expression level at 2PM in the BF and 8PM in the CX, but after SD this pattern disappeared. TASK1/3 expression showed diurnal variation only in the CX with highest level at 11AM, this pattern was preserved after SD.

Standard deviation led to the robust but transient increase of Kir6.2 expression in the BF, but not in the CX. Sur1 transcripts level was increased after 6 h SD in the BF and after 12 h in the CX.

Conclusions: The expression level of Kir 6.2/Sur1 and TASK1/3 potassium channels in the BF and the CX has a diurnal pattern and SD lead to the up-regulation of Kir6.2/Sur1 transcripts.

Disclosure: Nothing to disclose.

P798

The effect of maternal sleep on epigenome of newborn

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Objectives: DNA methylation is one of the key epigenetic mechanisms that mediate the effect of environment on gene expression.

The aim of this study was to find out if impaired quality of maternal sleep during pregnancy leads to changes in methylation of the fetal genome and, eventually, to characterize the consequences of these changes for the child's development.

Methods: Our sample comprised 32 full-term newborn from the CHILD-SLEEP cohort. The DNA was extracted from umbilical cord blood collected at delivery and epigenotyped by the Illumina450K chip. We searched for changes in methylation of genome-wide distributed CpG sites in relation to subjective quality of maternal sleep during pregnancy ('How well have you been sleeping during the past month'), that was used as a continuous variable in analysis with R- Packages MINFI, IlluminaHumanMethylation450kmanifest and Limma. Pathway analyses were performed with the Ingenuity Systems.

Results: The methylation level of eight sites in the fetal genome associated to mother's quality of sleep at $P < 1x10^{-4}$ (unadjusted), comprising genes involved in DNA synthesis and micro-RNA targeting. Pathway analysis for the sites with $P < 1x10^{-3}$ showed enrichment of genes involved in Cell Death and Cellular Development ($P < 5x10^{-5}$), Cellular Growth and Proliferation, and Cellular Development.

Conclusions: This is to our knowledge the first study that relates mother's sleep during pregnancy to the neonate's genome-wide methylation. It seems plausible that poor maternal sleep quality during the fetal life could have an effect on developmental processes at cellular level during the very early development.

Disclosure: Nothing to disclose.

P799

Circadian clock genes, insomnia, sleepiness and shift work disorder

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Objectives: To investigate whether circadian clock gene markers predict insomnia, sleepiness, and shift work disorder (SWD) in Norwegian nurses employed in various work schedules.

Methods: Saliva samples were provided by 691 nurses participating in 'the SUrvey on Shift work, Sleep and Health among nurses' ('SUSSH'). A total of 663 Single Nucleotide Polymorphisms (SNPs) located in genes related to the circadian clock were analysed to test the correlation between genetic variants and the following phenotypes: insomnia (assessed with the Bergen Insomnia Scale), daytime sleepiness (assessed with the Epworth Sleepiness Scale), and items providing the basis of identifying SWD.

Results: Nominal associations were found between *a.* insomnia and marker(s) in *ARNTL*, *NPAS3*, *RORA* and *NR1D1*, *b.* sleepiness and marker(s) in *CAMTA1*, *RORC*, *NPAS3* and *RORA*, and *c.* shift work disorder and marker(s) in *CLOCK*, *CRY1*, *NPAS3*, *RORA* and *POLR3H*. However, none of the associations remained significant after correcting for multiple testing.

Conclusion: The results indicate that specific variants in circadian clock genes are not strongly associated with insomnia, sleepiness, or SWD. Studies with larger statistical power are needed to investigate whether specific genetic variants exert real effects on these phenotypes. From the present study, we conclude that *NPAS3* and *RORA* are the clock genes which merit most attention in future research on insomnia, sleepiness, and SWD.

Disclosure: Nothing to disclose.

P800

Epigenetic fingerprint of stress in a Finnish shift-working occupational cohort

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Objectives: In this study, we investigated the effects of psychosocial stress on genome-wide DNA methylation in a shift-working nurse cohort. A population-based sample was used to examine the correlates of our findings at level of gene expression.

Methods: Using Illumina's 450k platform, we measured peripheral blood leucocyte DNA methylation profiles of over 450 000 CpG sites genome-wide in 20 individuals from the shift-working nurse cohort (10 from a high and 10 from a low stress environment) and examined gene expression on 518 individuals from a population-based sample. Methdological validation of the methylation levels was performed with EpiTYPER. Methylation data was analyzed in the R-environment using bioconductor's MassArray and MINFI packages and SWAN algorithm. Pathway analysis was performed with the Ingenuity Pathway Analysis tool.

Results: Among 20 nurses, we observed differential methylation between high- and low stress groups in 2749 CpG sites ($P < 0.005$), corresponding to 1677 unique genes. These genes were involved in metabolic disorder-, autoimmune disease- and cancer pathways. Using the best 100 gene hits $P < 10e{-}5$) from the nurse cohort, we found strong correlation between subjective experience of exhaustion and gene expression in the population data ($n = 13$ with $P < 0.0005$ and $n = 35$ with $P < 0.05$). A number of these genes were related to metabolic functions, cancer and catalysis of DNA methylation.

Conclusions: These preliminary results suggest that psychosocial stress correlates with methylation in genes related to metabolic and autoimmune diseases and cancer. This merits further investigation of stress outcomes and shift-work in demanding work environments.

Disclosure: Nothing to disclose.

P801

Genetic influences on total sleep duration in babies at 8-months: preliminary findings

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Objectives: There are strong genetic influences for consolidation of sleep duration infancy, but only a few studies have so far researched the genetic factors underlying the process. In this study, we aim to

search for genetic factors influencing total sleep time of babies at 8 months′ of age.

Methods: The genome wide association study was performed on DNA from 363 newborn infants from the CHILD-SLEEP birth cohort, genotyped using the Illumina Infinium humanomniexpress_24v1_0_a beadchip. Quantitative genetics models were used to examine the genetic influence to total sleep time in eight months infants by using PLINK software (http://pngu.mgh.harvard.edu/~purcell/plink/).

Results: None of the SNPs reached genome-wide significant association ($P < 5x10-8$) to total sleep time as was expected with the moderate sample size. However, nine variants from five different chromosomal loci reached suggestive significance of $P < 1x10-5$. While most of these variants were on non-coding regions, the association peak on chromosome 8 covered a gene involved in ATP metabolism.

Conclusions: We observed suggestive evidence for involvement of a variant from a gene contributing to ATP metabolism in sleep length of infants at 8 months of age. Interestingly, in recent GWAS, another gene (ABCC9) involved in ATP metabolism was associated in sleep length in adults (Allebrandt et al. 2013). The results of the present study need a replication in a larger sample and we are currently performing additional genotyping in larger number of infants ($n = 1400$) from the CHILD-SLEEP cohort.

Disclosure: Nothing to disclose.

P802

In vitro generation of dynorphin, NARP and MCH expressing neurons from mouse fibroblasts

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Introduction: The sleep disorder narcolepsy is characterized by excessive daytime sleepiness, sleep attacks, cataplexy, hypnagogic hallucinations, and sleep paralysis. Loss of orexin, dynorphin and NARP peptides within the lateral hypothalamus is well established in the brain of narcolepsy patients. In the present project taking advantage of induced pluripotent stem cell techniques we are aiming at producing neurons expressing lateral hypothalamic markers including NARP, Dynorphin and orexin to test their physiological properties *in-vitro*.

Methods: Neuronal differentiation was done using embryonic body formation method from mouse fibroblast derived induced pluripotent stem cells (iPSCS).

Results: The iPS cells were established and were characterized. Using modified version of an established protocol (1), in preliminary studies, we coaxed iPSC lines toward hypothalamic progenitors and it resulted in expression of hypothalamic genes Rax, Six3, and Vax1. We observed the expression of Ihx9 in all SHH treatments and Ihx6 gene in 10, 30, 50 ng/mL treatments. The expression of these markers indicates that we have generated cells of the region lateral to PVN and VMH nuclei. Treatment of the EBs with FGF8 and FGF12 resulted in the expression of dynorphin and BMP7 caused the expression of MCH and NARP. Experiments are ongoing to achieve the expression of other markers like orexin and evaluate the transcriptional and physiological properties of these neuronal cells and also to obtain similar hypothalamic cells from human fibroblasts.

Conclusion: FGF and BMP signaling are involved in the expression of lateral hypothalamic marker genes.

References: 1- Wataya et al, PNAS, 2008.

Disclosure: Nothing to disclose.

Neurobiology

P803

Uncorrelated sleep-related activity in the avian hippocampus and nidopallium

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Objectives: By synchronizing neuronal activity between the hippocampus and neocortex during slow-wave sleep (SWS), slow-waves are thought to coordinate the transfer of information temporarily stored in the hippocampus to the neocortex for long-term storage and integration with pre-existing memories. Although birds exhibit SWS, the apparent lack of connections between the hippocampus and many brain regions thought to be homologous to the neocortex, such as the nidopallium, questions whether slow-waves perform a similar function in birds. The aim of the current study was to explore whether slow-waves in the nidopallium are correlated with activity in the hippocampus.

Methods: We used a 64-channel silicon probe to make acute, simultaneous recordings of both regions in anaesthetized female zebra finches (*Taeniopygia guttata*).

Results: Recordings revealed slow-waves in the nidopallium and, to a much lesser extent, in the hippocampus. Slow-waves in the nidopallium propagated as waves of neuronal activity (i.e. local field potentials and related multi-unit activity), similar to our earlier findings on slow-waves in the avian hyperpallium (Beckers et al. 2014). However, slow-waves do not appear to propagate between the nidopallium and hippocampus. Additionally, we found evidence of a slow-gamma rhythm ($\pm$40 Hz) in part of the hippocampus.

Conclusions: These results are consistent with avian neuroanatomical data and suggest that the nidopallium and hippocampus do not work as a coordinated system during sleep. However, additional sub-regions of the nidopallium and other brain regions need to be evaluated before concluding that a fundamental difference exists between how mammals and birds process hippocampal memories during sleep.

Disclosure: Nothing to disclose.

P804

Peripubertal diet-induced obesity impairs sleep quality through changes in the dopaminergic system during aging in mice

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Obesity coincides with sleep disturbances including excessive daytime sleepiness and decreased sleep quality. Despite the fact that obesity is a major health threat, its incidence is rapidly rising, especially in adolescents. Since puberty is a period during which brain functions undergo dynamic remodelling, it was of interest to examine the impact of pubertal overweight on sleep-wake behaviour during adulthood.

To this end, we generated a peripubertal diet-induced obesity (ppDIO) model by exposing male C57BL6N mice to a high-fat/high-carbohydrate diet (HFD) for six weeks from the time of weaning, while control mice were maintained on standard diet. To monitor sleep-wake behaviour, mice were implanted with EEG and EMG electrodes at different ages (three, six and twelve months).

Cessation of HFD exposure resulted in increased wakefulness and concomitant increase in dopamine contents in the lateral hypothalamus of ppDIO mice at the age of three months. Similar changes were also observed in control mice that had been fasted for 24 h, suggesting that HFD withdrawal and fasting lead to similar states. In contrast, ppDIO mice aged six and 12 months exhibited an increase in sleep time and a decrease in sleep quality. Interestingly, sleep profiles observed in these mice were reminiscent of those in overweight humans. Dopamine contents in the lateral hypothalamus of ppDIO mice were decreasing with age.

These findings suggest that ppDIO promotes sleep disturbances during aging. Alterations in the dopaminergic system could be causally related to these sustained ppDIO-induced changes in vigilance.

Disclosure: Supported by the European Union (FP7-SWITCHBOX Project).

P805

The Gln460arg polymorphism of the P2RX7 gene affects human sleep

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Objectives: The P2RX7 gene was identified as a susceptibility locus for affective disorders. A non-synonymous coding single nucleotide polymorphism (SNP) in this gene (rs2230912), the Gln460Arg variant is associated with major depression. In depressed patients characteristic sleep-EEG changes are well documented. Also healthy controls at high risk for depression show sleep-EEG aberrancies. We investigated whether carriers of the risk variant of the P2RX7 gene show sleep-EEG changes.

Methods: Sleep-EEG was recorded in 53 young healthy volunteers. Psychiatric disorders were excluded in their own and family history. Conventional and quantitative sleep-EEG analyses were performed. We compared homozygous (A/A) (n = 39) subjects with heterozygous (A/G) (n = 14) carriers of the risk variant.

Results: Sleep EEG differed significantly between groups. In the A/G genotype sleep period time was shortened (A/G mean $\pm$ S.E.M. 449.8 $\pm$ 8.6 min vs. A/A 464.9 $\pm$ 2.6 min, $P < 0.05$); the number of entries from stage 2 into shallow stage 1 and wakefulness was elevated during first sleep cycle (A/G 5.14 $\pm$ 1.26 vs. A/A 2.05 $\pm$ 0.34, $P < 0.01$); peak frequencies of all sleep spindles were lower particularly in parietal derivations (A/G 12.7 $\pm$ 0.13 Hz vs. A/A 13.4 $\pm$ 0.06 Hz, $P < 0.001$). Beta frequencies were enhanced during stage 2.

Conclusions: Healthy volunteers with a potential risk for depression related to their P2RX7 genotype differ in the sleep EEG from the non-carriers. In the genotype instability of stage 2 and changes of sleep spindles and of beta frequencies were observed.

Disclosure: Nothing to disclose.

P806

Artefact correction of sleep electroencephalographic recordings during arterial spin labelling-magnetic resonance imaging based on independent component analysis

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Objectives: Simultaneous EEG-fMRI recently has been used to localize sleep-associated brain activity. Correction of gradient artefacts in the EEG has been approached with different techniques; however, these were mostly tailored to reduce echo planar imaging gradient artefacts. We aimed at developing an artefact-correction algorithm for EEG/arterial spin labelling (ASL)-MRI measurements. Few attempts have been made to devise such algorithms and no study employed EEG and ASL-MRI during sleep.

Methods and results: Healthy males (4 h sleep restriction the night before) were instructed to sleep while 64 channel-EEG and ASL-MRI were simultaneously recorded at 3T.

EEG data pre-processing included scanner artefact removal (template correction), cardioballistogram detection and removal, downsampling and filtering.

To clean the sleep EEG of ASL gradient artefacts, scanner data were combined with EEG data from outside the scanner (sleep lab).

The requisite high sampling rates and long recordings create computationally demanding datasets.

Therefore, we created a subset - several minutes of 'outside'/'inside' data each - to yield balanced sample data. We performed an independent component analysis (ICA) and created an artefact-specific filter based on the data subset.

The combination of 'outside'/'inside' data enhanced scanner-related artefact identification on the basis of ICA components' power spectra and map topographies. Application of an artefact-specific component filter to the simultaneous EEG data yielded artefact-cleaned data.

Conclusions: We removed ASL gradient artefacts and showed that corrected sleep EEG power spectra resembled 'normal' sleep EEG power spectra.

Disclosure: Supported by SNSF-Sinergia Grant CRSII3-136249.

P807

The associations between adolescent sleep, diurnal cortisol patterns and cortisol reactivity to dexamethasone suppression test

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Objective: Information on the associations between objectively measured sleep and hypothalamic-pituitary-adrenal axis function in early adolescence is scarce.

Methods: We examined associations between average sleep duration and quality (sleep efficiency and wake after sleep onset (WASO)) and (1) diurnal cortisol patterns and (2) cortisol reactivity to a low-dose (3 μg/kg) overnight dexamethasone suppression test (DST) in a birth cohort born in 1998 (N = 265 participants, mean age 12.3 years, SD = 0.5). We also explored (3) if sleep duration and quality were affected the nights after the DST exposure. Sleep was measured with actigraphs for 8.4 days on average. Cortisol was measured diurnally during two days. Participants were exposed to dexamethasone in the evening of first day.

Results: In boys, short sleep duration was associated with higher cortisol upon awakening and lower cortisol awakening response (CAR; $P < 0.05$ and $P < 0.01$). Long sleep duration in boys associated with higher CAR ($P < 0.02$). Lower sleep quality in boys associated with lower CAR ($P < 0.06$). In girls, no significant associations were detected. Sleep quantity and quality were unassociated with responses to the DST. There were no effect of DST on sleep ($P > 0.15$ in between subject analyses).

Conclusions: The average sleep patterns showed associations with diurnal cortisol patterns only in boys during early adolescence. Sleep was not associated with cortisol reactivity to DST and the exogenous corticosteroid exposure did not affect sleep significantly.

Disclosure: Nothing to disclose.

P808

Modulation of hypothalamic MCH-expressing neurons by pharmacogenetic tools strongly alters the sleep-waking cycle in mice

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Objectives: Evidence supports a role of hypothalamic neurons secreting melanin-concentrating hormone (MCH) in sleep induction and maintenance. These neurons are indeed maximally active during paradoxical sleep (PS) based on Fos staining during PS rebound and juxtacellular unit recordings across the natural sleep-waking cycle in rats. Intracerebroventricular MCH infusion induces an increase in both PS and Slow-Wave Sleep (SWS) in rats, whereas acute optogenetic activation of MCH-secreting neurons at PS onset extends the duration of PS, but not SWS episodes. Our aim is to decipher the precise contribution of MCH neurons to SWS and/or PS regulation with a pharmacogenetic approach using DREADD tools in mice.

Methods: Male transgenic MCH-cre mice (12 weeks old) were bilaterally injected within tuberal hypothalamus with either inhibitory (AAV-hSyn-hM4di-mCherry) or excitatory (AAV-hSyn-hM3dq-mCherry) DREADDs and prepared for chronic polysomnographic recordings. Four weeks later, effects on vigilance states were analyzed in response to ip CNO treatments.

Results: Inhibition of MCH neurons at light onset dose-dependently increased SWS quantities compared to saline, due to a dramatic increase in bout duration whereas PS amounts and bout numbers are only slightly reduced. Pharmacogenetic inhibition of MCH neurons after a PS-specific deprivation did not affect PS homeostasis. Ongoing experiments indicate that excitation of MCH neurons may facilitate PS promotion and inhibit SWS.

Conclusion: The present results suggest that MCH-expressing neurons may play a key role in the fine-tuning of the sleep-waking cycle by a modulation of SWS to PS transition. Indeed MCH neurons appear to inhibit SWS to facilitate PS promotion.

Disclosure: Nothing to disclose.

P809

Effects of rocking movements on sleep onset and memory performance

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Objectives: Rocking movements appear to affect human sleep: Commuters doze off in a rattling train and babies fall asleep when being rocked in a cradle. Recent research suggested a facilitated transition from wake to sleep due to lateral rocking movements during nap sleep. However, the relationship between rocking movements and sleep is poorly understood to date.

Methods: Polysomnographic recordings were performed in 12 male subjects (age: 21–28 years) during three nights (two motion nights (MN), one baseline (B) without motion). Rocking movement axes and frequencies were preselected by the subjects and applied using a robotic bed-platform. Sleep dependent changes in memory performance were assessed with a word-pair learning task. Subjects completed a questionnaire, rating how pleasant the different nights were. Sleep stages were scored visually according to standard criteria.

Results: Rotational movements were rated more pleasant than translational movements, with best ratings for the roll-axis (hammock like motion). Overall, nights with motion were rated 'more pleasant'. However, preliminary analysis revealed that sleep onset latency was not affected by rocking movements (MN1: 11.50 $\pm$ 3.76 min, (mean $\pm$ standard deviation); MN2: 10.98 $\pm$ 6.04 min; B: 9.66 $\pm$ 5.52 min). Memory performance increased over night but showed no differences among conditions.

Conclusion: Motion nights were preferred by the subjects. However, sleep onset was not facilitated. Whether rocking movements alter sleep EEG patterns need further investigation.

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Disclosure: Nothing to disclose.

P810

Corticotropin-releasing hormone receptors-2 mutation in the dorsal raphe neurons increases sleep and stress-coping behaviour in mice

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Objectives: The relationship between sleep-wake and stress responses is complex. The *dorsal raphe nucleus,* located in the *brainstem*, plays a pivotal role in both sleep-wake and stress responses. One of the potent mediators in the stress system and a major regulator of wakefulness is corticotropin-releasing hormone (CRH) that has receptors (Crhr1 and Crhr2), especially Crhr2 is densely distributed in the dorsal raphe nucleus. However, the involvement of Crhr2 in sleep has received less attention than Crhr1. Thus, we studied sleep-wake and anxiety-like behaviour in conditional Crhr2 mutant mice which are devoid of Crhr2 in the dorsal raphe neurons.

Methods: 24-h sleep-wake activity and cortical brain temperature were monitored in adult male Crhr2 mutant mice and their wild-type littermates. Their anxiety-like behaviours were evaluated by open field, light-dark box and forced swim test.

Results: Crhr2 mutant mice spent in NREM sleep more than wild-type mice during the first half of the dark period. Relatively low brain temperature was associated with increased sleeping episodes during that period. In the light period, NREM sleep amount was comparable in both genotypes while mutant mice showed fragmented NREM sleep architecture. A decreased level of anxiety-related behaviour but increased stress coping behaviour was observed in mutant mice.

Conclusions: Mutation of Crhr2 in the dorsal raphe neurons yielded increases in NREM sleep and stress-coping behaviour. This suggests that mutant mice are less sensitive to activate dorsal raphe neurons via CRH, making them soporific and less vulnerable to stress conditions.

Disclosure: Nothing to disclose.

P811

Comparison of trancranial magnetic stimulation evoked electroencephalography potentials between waking and non-rapid eye movement sleep states

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Objectives: We experience the sleep-wake cycle on a daily basis, but what related underlying processes change in the brain?

Methods: Using electroencephalography (EEG), the spread of the evoked potentials of non-sensory task-independent transcranial magnetic stimulation (TMS) to the occipital areas V1 or lateral occipital cortex in waking and non-rapid eye movement (NREM) sleep was compared in the study. We hypothesized that a) right-hemisphere slow negative potentials evoked by V1 TMS are reduced in NREM sleep, and b) stimulating different target sites leads to different activation patterns.

Results: Results showed significant interactions between different regions and states of consciousness in influencing the evoked EEG activity, suggesting different activation patterns in response to TMS when sleeping or awake.

Conclusions: The data confirms and extends previous results.

Disclosure: Nothing to disclose.

P812

Defining the role of specific neuronal populations of the basal forebrain in sleep-wake behaviour using opto-dialysis: a novel method combining optogenetics and in vivo microdialysis

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Objectives: The complexity of the neuronal composition in the basal forebrain (BF) has long prevented a clear understanding of the causal role of each neuronal subtype on modulating cortical activity. Cortically-projecting cholinergic and parvalbumin expressing GABAergic neurons are suggested to modulate cortical activation. To define their specific roles, we have developed a novel opto-dialysis method combining EEG/EMG recording, in vivo microdialysis, and optogenetics.

Methods: ChAT-ChR2-EYFP-BAC (ChAT-ChR2) mice, and AAV-ChR2 transduced Parv-cre (PV) mice (for selective cholinergic and GABAergic stimulation respectively) were outfitted with EEG/EMG electrodes, and an opto-dialysis probe, aimed at the BF area.

The experiment consisted of a baseline day and an experimental day, when a 10s stimulation paradigm was repeated every min for 2 h, using 10 ms laser pulses (473 nm) at selected frequencies (8 Hz for ChAT-ChR2, 40 Hz for PV). To antagonize the muscarinic receptor-mediated input on BF GABAergic neurons in ChAT-ChR2 mice, atropine was administered by reverse-microdialysis during cholinergic stimulation.

Results: The 8 Hz stimulation in ChAT-ChR2 mice (n = 5) resulted in a 39% reduction in EEG delta power (0.5–4 Hz) when compared to the pre-stimulation period; decreased NREM to wake latency by ~15s (117 trials); and increased the total amount of wakefulness by 84% (n = 5). This increased wakefulness was attenuated to 28% when atropine was simultaneously perfused (n = 3). 40 Hz stimulation in PV mice (n = 2), to excite PV expressing GABAergic neurons, increased wakefulness by 24%.

Conclusions: These results indicate that stimulating BF cholinergic neurons may promote cortical activation both directly and indirectly mediated by activation of neighbouring cortically-projecting GABAergic and/or glutamatergic neurons.

Disclosure: Nothing to disclose.

P813

Repetitive activations of lateral and perifornical hypothalamic regions elevate CSF OrexinA conten and fasten sleep-wakefulness recovery from experimentally induced comatose state

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Objectives: Study evaluates hypothalamic Orexinergic system as the neuronal substrate for speed up regulation of disturbed sleep homeostasis and sleep-wakefulness recovery from experimental comatose state. Pre-clinical evidences in this regard are very sparse and we are studding this question for the first time.

Methods: In cats (n = 3) modeling of experimental comatose state was made by large doses of anesthetics (Sodium ethaminal). Immediate EEG registration lasted continuously for 72 h. 30 min after comatose state serial electrical stimulations (8–12v, 200c/sec, 0.1 msec) of lateral and/or perifornical hypothalamus were started, lasted for 1 h with the 5 min intervals between subsequent ones, applied by turn to the left and right side hypothalamic regions. CSF OrexinA content was measured by ELISA. Statistical processing was made by Students' t-test.

Results: Large doses of anesthetics lead to whole disruption of sleep-wakefulness alternations. Forebrain falls into comatose state and pathological pattern of electrical activity (exaggerated spindle activity with strongly desynchronized inter-spindle periods) takes the dominant position. Spontaneous recovery starts with restoration of light slow wave sleep EEG, taking approximately 25 h. Repetitive activations of lateral and/or perifornical hypothalamus significantly speed up light- and deep slow wave sleep recovery by 8–10 h. Acceleration was also noted in forced restoration of passive and active wakefulness EEG. Significant elevation was noted in CSF OrexinA Content.

Conclusion: Repetitive activations of Lateral and Perifornical hypothalamus significantly elevate CSF OrexinA content and speed up recovery from comatose state.

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P814

Characterisation of the role of extrasynaptic $GABA_A$ receptors in sleep and mood regulation in a rodent model

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Objectives: Extrasynaptic γ-aminobutyric acid $(GABA)_A$ receptors containing the δ subunit mediate tonic $GABA_A$ transmission and have been implicated in sleep and mood regulation. Our aim was to characterise their role in the regulation of local, activity-dependent regulation of sleep slow waves and the manifestation of anxiety and mood disorder phenotypes.

Methods: Electroencephalogram/electromyogram (EEG/EMG) recordings combined with an established model of local sleep regulation (i.e. whisker stimulation in enriched environment) were performed in control wild-type (WT) and transgenic mice lacking the δ-$GABA_A$ subunit ($\delta^{-/-}$). Mice also underwent a battery of behavioural paradigms (elevated plus maze task (EPM), novelty suppressed feeding task (NSFT), forced swim task (FS), grooming test (GT), resident intruder task (RIT), object location task (OLT)) to characterise differences in anxiety- and depressive-like behaviours between genotypes (n = 8–10/sex).

Results: While no significant effects of genotype or sex were observed in the EPM, FS and grooming tests, $\delta^{-/-}$ mice, irrespective of sex, displayed significantly lower stress-induced anxiety levels compared to controls in the NSFT ($P < 0.01$). Male $\delta^{-/-}$ mice also exhibited heightened aggressive-like behaviour in the RIT ($P < 0.05$). In addition, hippocampal-dependent spatial recognition memory was impaired in $\delta^{-/-}$ mice compared to control animals ($P < 0.05$), while no effect of sex was observed on performance.

Conclusion: This study identified a role for extrasynaptic δ-$GABA_A$ receptors in the regulation of selective mood behaviours and memory in mice. Analysis of EEG/EMG recordings to investigate the role of δ-$GABA_A$ receptors in the regulation of local activity-dependent generation of slow waves is ongoing.

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P815

Repetitive activation of lateral and perifornical hypothalamus regions elevate CSF OrexinA content and fasten recovery of normal sleep cycles from deep anesthesia induced sleep

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Objectives: Study evaluates hypothalamic Orexinergic system as the neuronal substrate for speed up regulation of disturbed sleep homeostasis and recovery of sleep-wakefulness cycle behavioral states from deep anesthesia induced sleep. Pre-clinical evidences in this relation are very sparse and their investigation is highly topical.

Methods: In wild rats (n = 12), after Surgical implantation and postoperative recovery, deep anesthesia was induced by chloralhidrate and/or sodium ethaminal. EEG registration, started immediately, lasted continuously for 48 hs. 10 min after anesthetic drugs electrical stimulations (8–12v, 200c/sec, 0.1 msec) of lateral and perifornical hypothalamus were started. Stimulations lasted for 1 h with 5 min intervals between subsequent ones applied by turn to left

and right side hypothalamic parts. CSF OrexinA content was measured by ELISA. Statistical processing was made by Students' t-test.

Results: Repetitive activations of lateral and perifornical hypothalamic orexin-containing neuronal regions significantly speed up wakefulness recovery from both type of narcotic sleep. The first fragments of wakefulness were soon followed by normal deep slow wave sleep episodes. Especially strong influence of serial electrical stimulations of hypothalamic orexin-containing neurons was manifested in the recovery of REM sleep taking 23–24 hs during spontaneous recovery and becoming more than two times shorter under the impact of serial activations of orexin-containing neurons. Significant elevation of CSF OrexinA content was noted in stimulated animals.

Conclusions: Repetitive activations of lateral and perifornical hypothalamus significantly elevate CSF OrexinA content and speed up normal sleep-wakefulness cycle recovery from deep anesthesia-induced sleep.

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P816

State-dependencies of auditory evoked potentials during NREM sleep disclose their neurophysiological origins

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Objectives: Neurophysiological origins of the earlier components of auditory brainstem response (ABR) are known to be located in the auditory nerve and neurons in the brainstem. On the other hand, those of the later components are not clearly known. For distinguishing from the earlier ABR components originated in the brainstem, the later components are tentatively called AEP (auditory evoked potential) here. Since the cortically evoked response was expected to depend on the activity state, up and down, of cortical neurons, in order to clarify the neurophysiological origins of AEP we investigated the state dependency of AEP on a slow EEG oscillation during NREM sleep in rats.

Methods: In sixteen adult Sprague-Dawley rats, ABRs were recorded under restricted conditions in addition to the polygraphic recordings, where across sleep-wakefulness states acoustic stimuli (about 78 dB, 0.1 ms duration) with 110 ms interval were presented to the left ear. EEG data were digitized with 16-bit resolution at a sampling rate of 30,000 Hz for extracting the ABR, and 1,000 Hz for determining neuronal activity states.

Results: Putative up-state was determined in terms of the phase of slow EEG oscillation (1–4.5 Hz) where the amplitude of high frequency EEG activity (55–65 Hz) above the average level, otherwise putatively down-state. We found that the amplitudes of AEP (waves VIII or later) showed the state-dependency in contrast with no significant state-dependency shown for the earlier ABR components (waves I to VII).

Conclusions: The later ABR components were suggested to be originated in the thalamocortical system because of their state-dependency.

Disclosure: Nothing to disclose.

P817

Indications that the EphA4 receptor regulates sleep in mice

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Introduction: The distribution of sleep and wakefulness varies according to time-of-day, and the recovery aspect of sleep has been linked to mechanisms controlling synaptic strength. EphA4 is an adhesion molecule which controls synaptic function. The aim of this study is to determine the role of EphA4 in sleep regulation.

Methodology: 1) Using electrocorticography [ECoG] in mice lacking EphA4 (provided by K. Murai and bred on site), we measured vigilance states (wake, non-rapid eye movement [NREM] and REM sleep) in male mice (ten-week-old) from the 3 genotypes (n = 15 wild-type [WT], 16 heterozygous [HET] and 13 homozygous mutants [KO]) during a baseline [BL] day.

2) The expression of EphA4 and its partners was measured by quantitative PCR [qPCR] in the cerebral cortex [CX], the hippocampus [HP], and a thalamic/hypothalamic [TH/H] region at 4 times of the day [ZT0, ZT6, ZT12 and ZT18].

Results: 1) REM sleep duration was lower in KO than in WT mice during 24 h BL especially in the rest period. KO mice also showed longer wake and NREM sleep bout duration in the rest period compared to WT.

2) Time-of-day affects the expression of EphrinB3, the principal ligand of EphA4, but not that of EphA4. EphrinB3 was significantly increased at ZT12 in comparison with other times in the CX and the TH/H region.

Discussion: These results suggest that EphA4 may act to favor REM sleep duration and sleep consolidation via an interaction with its binding partner EphrinB3.

Disclosure: Nothing to disclose.

Comparative and evolutionary studies

P818

Bird-like propagating sleep-related brain activity in Nile crocodiles

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Objectives: In mammals and birds, slow-waves are the defining feature of slow-wave sleep (SWS). In contrast, most studies on reptiles reported intermittent high-voltage spikes (HVS) during sleep, suggesting that SWS evolved independently in mammals and birds. To gain a better understanding of the potential relationship between HVS and slow-waves, we mapped their spatiotemporal distribution across brain regions in anesthetized Nile crocodiles (*Crocodylus niloticus*).

Methods: Local field potentials (LFP) were recorded simultaneously from the dorsal cortex and dorsal ventricular ridge (DVR) using 8x8 Multi-Electrode Arrays (Neuronexus) in four juvenile crocodiles under isoflurane (0.7–1.5%) anesthesia.

Results: HVS similar to those reported in naturally sleeping crocodilians (Flanigan et al. 1973) were observed across all LFP sites. The occurrence of HVS was inversely related to the level of anesthesia. Cross-correlation coefficients indicated that HVS typically occurred first in the ventrolateral sites and propagated in a dorsomedial direction. However, individual HVS propagated in complex, traveling patterns across the DVR and dorsal cortex, in a manner similar to that recently described for avian slow-waves (Beckers et al. 2014).

Conclusions: The relationship between HVS and anesthetic depth and the propagation of HVS are similar to that described for avian slow-waves using similar methods. However, HVS occurred less frequently. HVS may reflect short depolarizations of neuronal membrane potentials comparable to the longer 'up-states' of slow-oscillations described in mammals and birds. If correct, then an increase in the frequency and duration of up-states evolved independently in birds and mammals, perhaps in association with the evolution of large complex brains.

Disclosure: Nothing to disclose.

P819

Sleep disorders in population in Novosibirsk (Russia)

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Objectives: The aim of the study was to elucidate the epidemiological characteristics of the sleep disturbances in population of Novosibirsk (Siberia, Russia).

Methods: A randomized representative sample of 45–69-year-old residents of both genders (n = 4171) was studied in a framework of the HAPIEE study in Novosibirsk from 2003 to 2005. The sleep disturbances were studied by using the Jenkins Sleep Questionnaire (JSQ). The test was validated for the Russian population in the course of a large-scale epidemiological study performed in a framework of the WHO MONICA Program from 1984 to 1994.

Results: The incidence rate of the extreme and pronounced sleep disturbances was 21% of the population with female predominance (24% in women vs. 18% in men). The patterns of the sleep disturbances lasting 15 and more nights per month were as follows: frequent spontaneous sleep interruptions (20%); anxious thoughts while falling asleep (10%); unsatisfying sleep (10%); and disturbing dreams (7%). The rate of the disorders with the insufficient or excessive sleep duration was 7%. Sleep duration of less than 5 hs per night was found in 5% of population; sleep duration of more than 10 hs per night was detected in less than 2% of population.

Extreme and pronounced abnormalities in the sleep duration were found in 61% of population.

Conclusions: Data showed high prevalence of the sleep disturbances associated with a high level of psychosocial factors in the study population. The study demonstrated a great demand in prevention of the sleep disturbances in 45–69-year old population.

Disclosure: Nothing to disclose.

P820

Insomnia symptoms and all-cause and cardiovascular mortality: a prospective register-based study among Finnish and Lithuanian adults

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Objectives: Evidence on the association between insomnia symptoms and mortality is limited and inconsistent. We examined the association between insomnia symptoms and all-cause and cardiovascular disease (CVD) mortality in two cohorts to improve generalizability.

Methods: The Finnish data comprised 6605 employees of the City of Helsinki, aged 40–60-years at baseline in 2000–2002. Mortality data were derived from the Statistics Finland until 2012 (n = 213). The Lithuanian data comprised 1602 citizens of Palanga, aged 35–74 years at baseline in 2003. Mortality data were derived from the Regional mortality register until 2013 (n = 141). In both cohorts, insomnia symptoms comprised three items on frequency of difficulties initiating and maintaining sleep. Covariates were age, marital status, education, drinking, inactivity and obesity. Logistic regression analysis was used.

Results: In the Finnish cohort, only difficulties initiating sleep were associated with all-cause mortality among men after full adjustment (OR 3.44, 95% CI 1.44–8.18). In the Lithuanian cohort, difficulties initiating sleep and early morning awakenings were associated with CVD mortality but among women only. These associations also remained for both difficulties initiating sleep (OR 2.60, 95% CI 1.05–6.44) and for early morning awakenings (OR 3.39, 95% CI 1.31–8.79) after full adjustment including employment status.

Conclusions: Insomnia symptoms were mainly unassociated with mortality, except difficulties initiating sleep were strongly associated with all-cause mortality among Finnish men, and with CVD mortality among Lithuanian women. Contrasting effects of insomnia symptoms might explain inconsistencies in previous studies that have not

distinguished different symptoms or examined women and men separately.

Disclosure: The Lithuanian research was funded by a grant (LIG-03/2012) from the Research Council of Lithuania

P821

Investigation about the cultural context in preferred bed position: an ethological approach

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Objectives: The aim of this study was to extend the results of the Spörrle & Stich (2010), that investigated sleep behavior in evolutionary perspective in German population. Our study used the same experimental approach in another cultural context.

Methods: Participants were asked to arrange a bed and other pieces of furniture on floor plans that were experimentally manipulated with respect to the direction in which the door opened and the presence of a window. Also, participants they were asked to draw their own bedroom. The perception of these two bedrooms, the sleep quality and the anxiety level of participants were assessed using questionnaires.

Results: Contrary to Germans, ours results showed that Brazilian people did not choose a safe bed position as described in the previous study. In German study, the safe bed position was characterized by

(a) a direction was allowed to see the door,

(b) a maximal distance between door and bed and

(c) a location on the same side where the door opened.

While in our study the position of the bed was consistent in terms of direction and distance, the location was not influenced by the side where the door opened. Further, questionnaires revealed that the need of comfort prevailed over the need of safety.

Conclusions: This transcultural study highlighted that ethnicity could be a sufficient factor to vary the causes of a same behavior. We also agree that this kind of studies could challenge beliefs about what should be an environment that promotes sleep hygiene.

Disclosure: Nothing to disclose.

Behaviour

P822

The timing of daytime sleep episodes between 12-h night shifts does not affect neurobehavioural performance

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Objectives: Performance declines during the night are associated with a misalignment of the sleep-wake cycle and the circadian pacemaker. The timing of daytime sleep episodes may influence performance on the night shift by affecting the accumulation of homeostatic sleep pressure and the circadian contribution to sleep quality. The aim of this study was to compare night-time performance following daytime sleep opportunities scheduled at different times.

Methods: Twelve healthy young males (M±SD; aged 22.9 ± 5.2 years) were recruited to participate in a repeated-measures laboratory study with three counterbalanced conditions. Conditions differed only in the timing of 7-h sleep opportunities scheduled in 12-h breaks between two consecutive 1800-to-0600 h night shifts. Depending on the condition, sleep opportunities

(i) began immediately after the first shift, 0700 h-1400 h;

(ii) finished before the second shift, 1000 h-1700 h; or

(iii) were split between these times, 0700 h-1030 h and 1330 h-1700 h. Psychomotor vigilance tasks (PVT) were conducted on shift to assess reciprocal response times (RRT; 1/ms x1000).

Results: Based on data from the first six participants, mean RRT on the second night shift was 4.33 ± 0.29. A repeated measures ANOVA revealed that the timing of daytime sleep opportunities had no significant effect on performance [$F(2,10)=0.21$, $P = 0.81$].

Conclusions: Preliminary findings suggest that the positioning of sleep opportunities immediately before or after consecutive 12-h night shifts may not affect night-time performance. Splitting daytime sleeps also does not appear to be detrimental. The arrangement of daytime sleeps may be more important for 8-h night shifts where there is greater opportunity between shifts to accumulate sleep pressure.

Disclosure: Nothing to disclose.

P823

Noninvasive detection of sleep/wake changes in orexin/ataxin-3 transgenic narcoleptic mice across the disease onset

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Introduction: The orexin/ataxin-3 transgenic (TG) mice exhibit a phenotype similar to human narcolepsy. Hypocretin-containing neurons in TG mice were selectively ablated postnatally and over 99% were lost by 84 days old. In this study, we evaluated the sleep/wake changes of narcoleptic mice from 2 weeks to 98 days old using a noninvasive piezoelectric sensor.

Method: The PZT sensor can detect movements, the heart rate, and respiratory variations. Mice were simply placed on the PZT-sensor for 3 hs during the light period, and the recordings were repeated on 14, 28, 56, 84, and 98 days old.

Result: We that sleep bout length in TG mice, but not in WT mice significantly decreased with age, with significant differences between the genotypes over 56 days old. We found a unique PZT signaling pattern during sleep, by absence of movement accompanied with distinct heart beat signals, termed as 'Immobile with Heart Beats (IMHB)'. IMHB is divided into gradual onset type (IMHBg) and sudden onset type (IMHBs, wake preceding 40 sec). IMHBs were observed specifically in TG mice, while IMHBg were observed in both WT and narcoleptic mice with similar frequency. An age dependent increase in IMHBs was seen in TG mice.

Conclusion: The PZT is useful as a noninvasive sleep and behavior monitoring system, as we successfully detect the progresses in sleep fragmentation in narcoleptic mice. Since IMHB appeared during resting and when the body muscle was flaccid, IMHBs may reflect occurrences of cataplexy, while, IMHBg may reflect the occurrences of REM sleep.

Disclosure: Nothing to disclose.

P824

NREM sleep is increased in high-aggressive, but not in non-aggressive rats by an immune challenge

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Sleep is altered in response to an immune challenge: NREM sleep is increased and fragmented, REM sleep is inhibited. Different levels of trait aggressiveness are associated with specific patterns of neuroendocrine and autonomic stress responsiveness. Sleep and immune response are affected by stress. Aim of the present study was to test the hypothesis that sleep patterns are differentially affected by an immune challenge in animals that differ widely for aggression.

High-aggressive (HA, $n = 7$) and non-aggressive (NA, $n = 8$) rats were selected on the basis of their latency time to attack a male intruder in the resident-intruder test. Afterwards, they were instrumented for chronic polygraphic recording of sleep-wake patterns and kept at constant temperature (24 °C), on a 12:12 h light:dark cycle. At dark onset, on different days, each rats was intraperitoneally injected with pyrogen free saline (vehicle, VEH) and 250 μg/kg lipopolysaccharide. Administrations were randomly scheduled. Recordings began immediately after administration.

In HA rats, lipopolysaccharide administration induced a significant and long lasting (from hour 3 to hour 8 post-injection) increase (in comparison to VEH administration) in NREM sleep. No changes in NREM sleep were induced by lipopolysaccharide administration in NA rats. REM sleep was inhibited in both HA and NA rats, but with a different time course.

Fever helps in fighting infection. It has been proposed that sleep changes induced by immune activation help in mounting a febrile response. Results suggest that HA rats present a better sleep response to an immune challenge than NA rats.

Disclosure: Nothing to disclose.

P825

Evoked K-complexes as a dynamic interplay between cortical wake-like excitation, large-scale resetting hyperpolarization, and thalamic patterning: a high-density EEG study of human NREM sleep

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Objectives: We are unconscious of sensory stimuli during sleep. Are we insensitive or some complex process happens? Subjectively, we have all experienced perception while sleeping, like stimuli awareness after post-earthquake awakenings. Recently, we administered to healthy subjects simple acoustic, tactile and visual stimuli for inducing evoked K-Complexes (eKCs): we showed that for 200 milliseconds sleeping brains start processing stimuli in sensory-specific cortical areas (P200 wave), but this wake-like activities induce diffuse half-a-second's electrical silence in higher-level cortical areas (N550 wave), erasing consciousness and protecting sleep.

Methods: Here we investigate whether P200 is a real wake-like activity, being the later positive P900 wave (up state) a consequence of a cortico-thalamo-cortical entanglement following the N550 (down state) reset. We thus measured EEG power spectra of P200 and P900 eKC components.

Results: (i) P200s are wake-like cortical excitation mainly constituted by beta/gamma activity significantly higher than in baselines (EEG epochs preceding sensory triggers) and P900s; (ii) P200-like excitations when KCs are not evoked are detected over primary sensory areas as beta/gamma increases;
(iii) P900s are mainly constituted by sigma/low-beta activity (significantly higher than in baseline and P200s), the thalamic-spindle spectral expression.

Conclusions: Results describe the emergence of wake-like sensory activities (P200s), capable of opening activity-dependent K+ channels, thus inducing down states (N550s) mainly in fronto-central regions, followed by cortical-neurons rebounds, which, via cortico-thalamic volleys, trigger matrix thalamic nuclei and reticular thalamic nucleus to generate spindles. This is mirrored by significant increase of sigma/low-beta activity on up states (P900s).

Disclosure: Nothing to disclose.

P826

Stop and revive? The effectiveness of nap and active rest breaks for reducing drivers sleepiness

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Objectives: The purpose for this study was to determine the relative benefit of nap and active rest breaks for reducing driver sleepiness.

Methods: Participants were 20 healthy young adults (20–25 years), including 8 males and 12 females. A counterbalanced within-subjects design was used such that each participant completed both conditions on separate occasions, a week apart. The effects of the countermeasures were evaluated by established physiological (EEG theta and alpha absolute power), subjective (Karolinska Sleepiness Scale), and driving performance measures (Hazard Perception Task). Participants woke at 5am, and undertook a simulated driving task for two hours; each participant then had either a 15-minute nap opportunity or a 15-minute active rest break that included 10 min of brisk walking, followed by another hour of simulated driving.

Results: The nap break reduced EEG theta and alpha absolute power and eventually reduced subjective sleepiness levels. In contrast, the active rest break did not reduce EEG theta and alpha absolute power levels with the power levels eventually increasing. An immediate reduction of subjective sleepiness was observed, with subjective sleepiness increasing during the final hour of simulated driving. No difference was found between the two breaks for hazard perception performance.

Conclusions: Only the nap break produced a significant reduction in physiological sleepiness. The immediate reductions of subjective sleepiness following the active rest break could leave drivers with erroneous perceptions of their sleepiness, particularly as physiological sleepiness continued to increase after the break.

Disclosure: Nothing to disclose.

P827

On-road driver sleepiness: what are Australian drivers experiences and awareness of sleepiness while driving?

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Objectives: Driver sleepiness contributes substantially to road crash incidents. Simulator and on-road studies clearly reveal an impairing effect from sleepiness for driving ability. However, drivers might not appreciate the dangerousness of driving while sleepy and this could translate to their on-road driving behaviours. This study sought to determine drivers' on-road experiences of sleepiness, their sleep habits, and personal awareness of the signs of sleepiness.

Methods: Participants were a random selection of 92 drivers travelling on a major highway in the state of Queensland, Australia, who were stopped by Police as part of routine drink driving operations. Participants completed a brief questionnaire that included: demographic details, awareness and on-road experiences of sleepy driving, and sleep habits. A modified version of the Karolinska Sleepiness Scale (KSS) was used to assess subjective sleepiness during the last 15 min of driving.

Results: Participants rating of subjective sleepiness was quite low with 90% reporting at or below 3 on the KSS. Participants were reasonably aware of the signs of sleepiness; with a number of these correlated with on-road experiences. The participants sleep debt correlated with their alertness ($r = -0.30$) and the hours spent driving ($r = 0.38$).

Conclusions: These results suggest that drivers had moderate or substantial experience of driving when sleepy and many were aware of the signs of sleepiness. As many of the participants reported driving long distances after suboptimal sleep durations, it is possible that their risk perception of the dangerousness of sleepy driving maybe erroneous.

Disclosure: Nothing to disclose.

P828

Academic performances in adolescents with behaviorally-induced insufficient sleep syndrome

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Objectives: The aims of the current study were to compare the academic performance between adolescent with and without Behaviorally-induced Insufficient Sleep Syndrome (BISS). In addition, the

current study also aimed to investigate the independent predictors of academic performances among BISS-related factors.
Methods: Based on the sleep duration, the Epworth Sleepiness Scale (ESS) for measuring daytime sleepiness and the weekend oversleep representing sleep debt, 51 students with BISS and 50 without BISS (11th or 12th grade) were recruited from 18 high schools. They reported their academic performance in the form of class ranking quartile. The Korean version of Composite Scale (KtCS) for morningness-eveningness, Beck Depression Inventory (BDI) for depression, and Barratt Impulsiveness Scale (BIS) for impulsivity were also administered.
Results: Adolescents with BISS reported poorer academic performances compared to those without BISS ($t = 2.39$, $P = 0.02$). Adolescents with BISS also showed more eveningness ($t = 18.79$, $P < 0.001$, higher BDI score ($t = 4.23$, $P < 0.001$) and higher impulsiveness ($t = 2.70$, $P < 0.01$). Longer weekend oversleep predicted poorer academic performance in adolescents with BISS even after controlling for ESS score, KtCS score, BDI score and BIS score ($\beta = 0.42$, $P < 0.01$).
Conclusions: BISS among adolescents was associated with poor academic performances. In addition, sleep debt, as represented by weekend oversleep, was found to predict poor academic performance independently from depression, impulsiveness, weekday sleep duration, daytime sleepiness and morningness-eveningness.
Disclosure: Nothing to disclose.

P829

Daytime nap: restores performance parameters and is not affected by mental fatigue

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Objectives: The study was aimed to reveal the effects of a nap on performance and visuomotor coordination parameters of a mentally fatigued subject. Additionally we compared sleep quality in fatigued and control subjects.
Methods: Fourteen subjects of a main group (eight male, six female, aged 18–28) took part in two experiments each. They solved arithmetic problems as quickly as possible for 90 min. Then subjects had a lunch and a nap time (60 min in bed at 3 pm) or stayed awake in a no nap experiment. After that to check the performance changes they performed the same task for 40 min. The matched control group just had a nap in the same conditions.
Results: Mental fatigue manifested in destabilization of working speed and eye movement parameters during work. In the no nap conditions instability persisted after a rest period. If a subject had a nap, performance parameters stabilized. Main and control groups had no significant difference in sleep structure and demonstrated big individual differences. Average sleep latencies and sleep times were 13 and 41 min in main and 11 and 46 min in control group. Average times in all sleep stages were also similar.
Conclusions: Daytime nap aids in recuperation from mental fatigue caused by moderate cognitive workload and stabilizes of performance parameters. In the same time, sleep structure is not significantly affected by fatigue or the changes are masked by typical big individual differences in the nap structure.
The work is supported by RFH grants 12-36-01296 and 12-36-01390.
Disclosure: Nothing to disclose.

P830

The morningness-eveningness preference and the temperament and character in Koreans without any Axis I psychiatric disorder

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Objectives: The morningness-eveningness preference is refers to preference for time of day for doing various activities. There were some study that it was closely related to personality style. The purpose of this study is to investigate the relationship between morningness-eveningness preference and the biogenetic temperament and character in Koreans without any Axis I psychiatric disorder.
Method: Subjects without current or past Axis I psychiatric disorder ($n = 59$, 21 male, 38 female, 36.5 ± 13.6 age years old) were enrolled.
It was evaluated by the Korean version of Structured Clinical Interview for DSM-IV (K-SCID) or the Korean version of Composite International Diagnostic Interview (K-CIDI),
All subjects completed the Morningness-Eveningness Questionnaire (MEQ) and Temperament and Character Inventory (TCI).
Result: MES score positively correlated with age. Men had lower MES score than women. Novelty Seeking (NS) and Harm Avoidance (HA) negatively correlated with MEQ scores. In addition, Self-Directedness (SD), Cooperativeness (CO) and Self-Transcendence (ST) positively correlated with MEQ score. After controlling age and sex, correlation with MES score remained in NS, HA, SD and CO, while correlation between MES and S.D disappeared. Regarding the interactive effects of variables, multiple regression analysis indicated that MES were related to age, NS and HA.
Conclusion: Older, low NS and low HA had preference to morningness. Our result suggests that the specific pattern of temperament and character are related to morningness-eveningness preference. Further research with a larger sample covering wide range of age might show the change of the morningness-eveningness preference with the development of the personality.
Disclosure: Nothing to disclose.

P831

What is the relationship between natural variations in sleep duration and emotion recognition ability?

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Objectives: Experimental studies suggest that sleep-deprived individuals struggle to recognize emotions of moderate intensity in others. However, these studies use emotional faces morphed with neutral faces and contradict each other regarding which emotions are affected. The objective of the current study was to investigate how natural variations in sleep relate to the ability to recognize emotions in others. For a more ecologically valid stimuli, we used a recently developed test with presentations of dynamic expressions of several different emotions.
Methods: Two hundred and ninety-one participants filled out a sleep diary and performed an emotion recognition test. The test included audio clips, and video clips with and without sound, of actors conveying different emotions. Sleep measures for the previous night were assessed along with accuracy and reaction time for recognizing

the emotions. The emotion displays were 'easy' or 'hard' depending on how difficult they were to categorize.
Results: Participants had slept between 0 h and 11 h (m = 454 min, sd=87 min) with a good average sleep quality. There were no effects of sleep duration, quality, or sufficiency on emotion recognition, regardless of whether the emotion was easy or hard (p's>0.05). In addition, neither of the sleep measures were related to reaction time.
Conclusions: Natural variations in sleep duration and quality were not related to emotion recognition ability. The results might be due to self-selection bias or lack of extreme sleep deprivation, but it is possible that when faced with ecologically valid displays of emotion, sleep duration has no, or very minute, effect on emotion recognition ability.
Disclosure: Nothing to disclose.

P832

An experimental study comparing the effects of reading on an Ipad or in a book on polysomnographic-assessed sleep

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Objectives: To investigate whether reading a story for 30 min on an Ipad or in a book in bed prior to sleep will significantly affect polysomnographic (PSG)-assessed sleep parameters.
Methods: Fourteen students (12 female, two men) with a mean age of 25.1 years (SD = 3.1) underwent ambulatory (sleeping in their own beds at home) PSG recordings for a total of three nights (one adaptation night, two test nights). The reading material comprised two different set of stories, read from an Ipad or from a book. Both the order of the set of stories and reading media (Ipad vs. book) were counterbalanced. Illumination was assessed in both reading conditions with a PCE-172 luxmeter.
Results: The illumination was significantly higher in the Ipad-condition (m = 55.9 lux) compared to the book condition (m = 28.0 lux). Still, no significant differences between the conditions were found for any of the sleep variables (total sleep time, time in bed, latencies and time in N1, N2, N3 and REM sleep, sleep efficiency, sleep fragmentation and arousals).
Conclusion: The results suggest that despite of the illumination being significantly higher in the Ipad-condition, reading on an Ipad or in a book before nocturnal sleep does not affect sleep differently.
Disclosure: Nothing to disclose.

P833

What makes adolescents suicidal? The role of sleep

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Objectives: One of the common complaints during adolescence are sleep difficulties. They can have severe consequences for the affected persons' health. By now there are no clear results in the existing literature examining the link between sleep difficulties, aggression, and suicidality. The present study examines, if there is a link between sleep problems, aggression, and suicidality in a sample of healthy adolescents.
Method: Adolescents sleep behavior (PSQI), aggressive behavior (subscale 'aggressive behavior' FEPAA), and their suicidal tendencies (PAYKEL-Scale) were assessed. To control for the influence of depressive symptoms the Youth Self Report (subscale anxiety/depression) was applied. 93 healthy adolescents aged 14 to 18 years (30% male; M = 15.97 years) participated in our study.
Results: A mediation model was applied. It showed a significant influence of sleep difficulties on suicidality, even after controlling for depressive symptoms. The influence of aggressive behavior on suicidality was also significant, whereas the link between sleep difficulties and aggressive behavior appeared to be not statistically significant.
Discussion: The results showed a heightened risk for suicidalty in adolescents with sleep difficulties and in adolescents with heightened scores in aggression measures. This link between sleep difficulties and suicidality, and aggression and suicidality in adolescents points towards implications for different forms of prevention and intervention. Therefore it is necessary to conduct future studies to explore the link between sleep complaints, aggression, and suicidality in adolescents in more detail.
Disclosure: Nothing to disclose.

P834

Cage exchange does not disturb sleep in the rat on a 24-h basis

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Objectives: Placing a male rat within a cage that was previously occupied by another male rat (cage exchange, CE) is a stressful procedure which has been shown to induce a 2-h sleep disturbance (Cano at al., J. Neurosci., 2008). Since sleep disturbance following cage exchange may represent a model of human insomnia, aim of the present study was to make an assessment of this treatment on a 24-h basis.
Methods: Six Sprague-Dawley rats (300–350 g) kept under normal laboratory conditions (12 h:12 h light-dark cycle, ambient temperature 24°C) were implanted, under general anaesthesia (Diazepam, 5 mg/kg, i.m., Ketamine, 100 mg/kg, i.p.) with electrodes for the EEG, and nuchal and diaphragmatic EMG recording, a thermistor for brain temperature recording, and a catheter for arterial pressure recording. After at least a one-week recovery from surgery, animals underwent a two-day recording for the baseline (BL). The day after, a CE was carried out at light-on and, at light off, an extra amount of bedding used by the previous cage occupant was added as a reinforcer.
Results: No statistically significant changes were observed in: i) the relative 12-h amount of NREM sleep (NREMS) and REM sleep (REMS): Light) NREMS: BL, 50.8 $\pm$ 1.6%; CE 49.6 $\pm$ 1.0%; REMS: BL, 12.4 $\pm$ 0.9%, CE, 13.5 $\pm$ 0.5%); Dark) NREMS: BL, 22.6 $\pm$ 1.2%; CE, 23.6 $\pm$ 2.0%; REMS: BL, 5.7 $\pm$ 1.1%, CE, 5.5 $\pm$ 0.5%; ii) the number of NREMS episodes: Light) BL, 278.2 $\pm$ 14.3; CE, 242.8 $\pm$ 17.6; Dark) BL, 154.0 $\pm$ 9.0; CE, 154.0 $\pm$ 16.8%.
Conclusions: Cage exchange in the rat does not induce sleep disturbances resembling human insomnia on a 24-h basis.
Disclosure: Nothing to disclose.

P835

Sleep and brain activity after early life stress in female rats

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Objectives: Early life stress has been shown to alter sleep and lower brain activity during sleep and wakefulness in male rats. Disadvantageous early life conditions may give rise to gender specific behaviour and stress reactivity in adulthood. The present study aimed to investigate effects of maternal separations in early life on sleep parameters and brain activity during sleep and wakefulness in adult female rats.

Methods: During postnatal day 2–14 female rat pups were exposed to either long (LMS; 180 min) or brief maternal separations (BMS; 10 min) (n = 6, both). A telemetric device was implanted subcutaneously and 24 h EEG and EMG recordings performed at 5 months of age.

Results: Adult LMS and BMS rats showed similar total sleep time, as well as duration of different sleep stages and sleep fragmentation during both the 12 h inactive and the 12 h active phase. However, LMS offspring showed higher EEG power within gamma range (35–60 Hz) during REM sleep compared to BMS offspring ($P < 0.05$). Otherwise, no differences were found for sleep and wakefulness specific EEG frequencies (delta, 0.5–4.5 Hz; theta, 5.5–9.5 Hz; and beta, 19.5–34.5 Hz).

Conclusions: In contrast to male rats, female rats exposed to different early life conditions displayed similar behaviour in terms of sleep parameters in adulthood. Brain activity in the gamma range during REM sleep was however higher in LMS offspring compared to BMS offspring. These findings support the notion of gender specific reactions in adult behaviour and brain activity following early life maternal separation.

Disclosure: Nothing to disclose.

P836

Validating and extending the three process model (TPM) of alertness in airline operations

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Objectives: Sleepiness and fatigue are important risk factors in the transport sector and bio-mathematical sleepiness, sleep and fatigue modelling is increasingly becoming a valuable tool in Fatigue Risk Management Systems (FRMS). The present study sought to validate the inner workings of one such model, Three Process Model (TPM), on aircrews and extend the model with functions to model jetlag as well as individual differences and directly estimate the probability of any sleepiness level in any shift sequence with or without knowledge of sleep timings.

Methods: We collected sleep (n = 1089) and sleepiness (n = 4616) data from 91 aircrews in a real life situation by means of an application running on a handheld touch screen computer device (iPhone, iPod or iPad) and used the TPM to predict sleepiness with varying level of complexity of model equations and data. The data was analyses using multilevel linear and non-linear (ordinal logistic) mixed effect regression models to validate individual components of the model, assess the influence of individual differences and provide direct estimates of risk.

Results: The results validated the TPM, but explorative analyses suggest it could be improved and reduced to include only two-processes (S+C) with adjusted phases of the circadian process based on a single question of circadian type. We also estimated reference limits accounting for 50%, 75% and 90% and the probabilities (risk) of any level of sleepiness.

Conclusion: The TPM was validated on aircrew and extended to support jetlag, individual differences with reference limits, circadian type and direct modelling of sleepiness risks.

Disclosure: Jeppesen AB is marketing scheduling and FRMS services/products

P837

Greek financial crisis: from loss of money to loss of sleep?

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Objectives: A negative effect on public health of the Greek population as a result of the financial crisis is reported. The aim of this study was to examine the effect of the financial crisis on sleep and health outcomes of employees of the National Railway Organisation who had to face mandatory job transfers, significant reductions in salaries and anticipation of job loss.

Methods: Data were analysed retrospectively. A questionnaire of sleep characteristics and habits and the Epworth Sleepiness Scale (ESS) had been answered in 2005 by 226 male employees working at 7 different railway stations in Greece. Comparisons were made with the answers to the same questions given in 2010 by 224 employees working at the same railway stations.

Results: A significant reduction in reported night-time sleep duration was observed ($P < 0.001$), accompanied by an increase in the prevalence of nightmares ($P < 0.001$), sweating at sleep ($P < 0.001$), feeling of suffocation ($P < 0.001$), and daytime sleepiness ($P < 0.001$), accompanied by an increase in ESS score ($P < 0.001$). An increase in consumption of anti-acid medication was also observed, associated with number of years at work (OR =1.152, P = 0.038).

Conclusions: Within the Greek financial crisis, sleep duration decreased, while sleep disturbances increased among public employees, facing job insecurity.

Disclosure: Nothing to disclose.

P838

The interplay between habitual sleep duration and sleep need in risky decision-making

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Objectives: Sleep duration was reported to predict risky decision-making, but it remained unclear whether individual difference in sleep need mattered in such relationship. We aimed to study whether sleep duration interacted with sleep need in predicting risky decision-making.

Methods: Sixty-two young adults (aged 17–25) reported their habitual sleep duration (Pittsburgh Sleep Quality index) and their subjective need of sleep. Thirty-four (54.8%) of them whose habitual

sleep was between 4–6.5 h per night formed the 'short-sleep group', while the rest (45.2%) who slept for >6.5 h formed the 'control group'. All completed the Risky-Gains-Task, and their reaction time (RT) in choosing safe- and risky options was taken as indication of their decision-making time.

Results: Group differences on age, gender and body-mass-index were non-significant ($ps>0.05$). Regression analyses showed that sleep duration significantly moderated the relationship between sleep need and RT in making both safe ($F(8,31)=4.69$, $P = 001$) and risky decisions ($F(8,30)= 2.857$, $P = 017$). For safe options, RT in the short-sleep group increased less with increasing sleep need than control group. For risky decisions, RT in the short-sleep group decreased with increasing sleep need while it increased among the control group.

Conclusions: When sleeping less than 6.5 h, high sleep need individuals spent less time than those with lower sleep need in making risk-related decisions. Our results highlighted the need to consider both sleep duration and sleep need in investigating the role of sleep in risky decision-making.

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P839

Sleep and risk of accidents and injuries of adolescents attending classes in two rotating shifts

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Objectives: Several studies examined relationship between insufficient and irregular sleep and risk behaviours of adolescents whose classes started in the morning. We examined that relationship in adolescents who attended classes in the afternoon every other week, and had more opportunities for sufficient sleep but showed more irregular sleep schedules.

Methods: We analysed data of adolescents 11–18 years of age from primary ($N = 1105$) and secondary schools ($N = 1258$). A Croatian version of School Sleep Habits Survey was used to collect data on sleep characteristics, daytime sleepiness, and risk of injuries and accidents.

Results: Groups of adolescents reporting none, one, and more than one accident or injury in the previous six months differed in sleep duration on week when school was scheduled in the morning ($P < 0.001$), bedtime delay between weekend and school week with morning schedule ($P < 0,05$), and daytime sleepiness ($P < 0.001$). No difference was observed between the three groups in measures of sleep duration irregularities or in bedtime delay between a school week with morning and a week with afternoon schedule.

Conclusions: The results indicate that insufficient sleep in the week when school starts in the morning is predictive for risk of injuries and accidents even in a school system in which adolescents have opportunity to sleep enough every other week when school is scheduled in the afternoon. Irregularities of sleep schedules and duration in such school system do not seem to have negative consequences for risk of injuries, with the exception of the bedtime delay on weekend.

Disclosure: Nothing to disclose.

P840

Sleeping with dogs - results of an internet-based survey

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Introduction: According to surveys conducted annually by the American Pet Products Association, more than 45% of dogs sleep in their owners` beds. This gives rise to the question: Is this trend also seen in other countries? To find answers, we decided to conduct a survey with the focus on sleeping habits of pet owners in Austria.

Methods: Between July and October 2013, pet owners were invited to answer a web-based questionnaire on the frequency of sharing their beds with a dog. The online survey developed by experts of the ISWF and the Clever Dog Lab Vienna consisted of 22 questions addressing various aspects related to sleep habits and sleep quality.

Results: From the 635 completed questionnaires, 631 were analysed. A total of 93% of the participants were females (mean age: 38.5 years) and 43% of the sample owned more than one dog. Results showed that 78% of participants sleep regularly with their pet (s) in the same bed/room. Although 26% described their sleep as mildly, but frequently disrupted by the pet, the overwhelming majority believed their sleep quality to be positively influenced by the presence of the dog (9.1; maximum 10 points). They also rated their sleep as 'sounder' (8.7) and 'deeper' (8.1), fall asleep 'more easily' (8.6), and 'feel safer' (8.2).

Discussion: Our results are in line with the findings of surveys conducted in the US. Thus, we conclude that sleeping with dogs is a common sleeping arrangement. However, the question which remains unanswered is: Is this a healthy habit?

Disclosure: Nothing to disclose.

P841

Absence of rapid eye movements during sleep in zebrafish

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Objectives: Zebrafish (*Danio rerio*) have emerged as an excellent model for sleep research but to our knowledge no attempts have been made to discern if sleep in zebrafish entails REM-NREM cycles. In the current experiment we measure eye movements and changes in respiration during sleep in zebrafish.

Methods: We use custom-written image analysis routines to quantify eye movements and respiration across the sleep-wake cycles. Sleep was defined according to previously established behavioral criteria. Eye movements and respiration was quantified during periods of immobility at day, at night and at night with lights-on.

Results: During periods of immobility with lights-on eye movements are prominent. In contrast, during periods of immobility with lights-off there are no discernable eye movements. Moreover, we found no eye movements during behaviorally defined sleep. During periods of immobility with lights-on eye movements are prominent. In contrast, during periods of immobility with lights-off there are no discernable eye movements. Moreover, we found no eye movements during behaviorally defined sleep. We show significant reduction in respiratory rate following the onset of behaviorally defined sleep.

Conclusions: Eye movements and respiratory rate measurements do not indicate that zebrafish possess REM-NREM cycles. We do not rule out that other phasic REM components such as cardiac arrhythmias or myoclonic twitches are coherently expressed during sleep but we conclusively show that zebrafish do not have sleep related rapid eye movements.

Disclosure: Nothing to disclose.

Sleep deprivation 2

P842

Mechanically controlled REM sleep deprivation yields non-REM sleep fragmentation and selectively reveals REM sleep-related brain structures in mice

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Objectives: Sleep deprivation is applied to challenge homeostatic sleep-wake regulation. Compared with total sleep deprivation, REM sleep deprivation (RSD) is more difficult to perform. So far, inverted flower-pot methods are used to achieve RSD. However, the flower-pot method is principally stressful and eliminates a nonnegligible amount of non-REM sleep. Therefore, we designed a new machinery to conduct stressless RSD and tried it out to determine REM sleep-activated brain structures.

Methods: C57BL/6N mice, implanted with EEG/EMG electrodes, underwent RSD from light onset for 36 h. A few hours before RSD the mice were placed into a rotating wheel connected to a computer-controlled motor system which activated the wheel when the mice fell into REM sleep. Half of them were continuously under recordings after RSD, while the others were sacrificed immediately or 10 h after RSD for c-Fos staining.

Results: RSD eliminated 95.7% of REM sleep on average, while >77% of non-REM sleep was preserved in comparison with baseline. Right after RSD, mice stayed awake for a few hours, then REM sleep predominated during Zeitgeber time 19–24 (206.1% vs. baseline). Although non-REM sleep episodes became fragmented during RSD, the amount of non-REM sleep returned to the baseline level during recovery. C-Fos-positive cells were barely found in the paraventricular nucleus, while in amygdaloid structures more c-Fos activation was presented than in the brainstem when accumulation of REM sleep appeared.

Conclusions: Our theta activity-based RSD method caused least stress-related activation in the brain, suggesting its potential use for studying REM sleep homeostasis and related structures.

Disclosure: Nothing to disclose.

P843

Sleep slow-wave activity predicts changes in human cortical excitability during extended wakefulness

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Objective: Slow-wave activity (SWA: 0.75–4.0 Hz) is a classical hallmark of sleep homeostasis. It is associated to synaptic down-scaling, leading to a gradual decrease of cortical excitability during sleep. Here we investigated whether SWA predicts subsequent human cortical excitability during extended wakefulness.

Methods: After 8 h nocturnal sleep, 19 healthy young men (18–30y) followed a 28 h sleep deprivation protocol under constant routine conditions, during which they underwent 8 EEG recordings of transcranial magnetic stimulation (TMS)-evoked potentials. Sleep was scored using AASM criteria, and power spectra were calculated. Cortical excitability was inferred from the amplitude of the first component of TMS-evoked potentials over prefrontal cortex. A linear regression between frontal SWA (upper asymptote during first NREM sleep cycle) and cortical excitability was computed.

Results: Analyses reveal a significant positive regression between first NREM cycle SWA and cortical excitability assessed after 24 h of continuous wakefulness, during the so-called 'sleep-promoting zone', i.e. when the circadian system maximally promotes sleep ($r = 0.27$; $P = 0.03$). Interestingly, first NREM cycle SWA significantly and positively regresses with the overnight variation of cortical excitability, i.e. the change observed from the evening wake-maintenance to the morning sleep-promoting zones ($r = 0.23$; $P = 0.05$).

Conclusions: Our data show that sleep SWA is tied to the subsequent buildup of cortical excitability during prolonged wakefulness, particularly during critical time windows for the interplay of circadian and sleep homeostasis processes. We speculate that this buildup of cortical excitability during wakefulness increases subsequent SWA during sleep, through a mutual interaction.

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Disclosure: Nothing to disclose.

P844

Modification of sleep architecture, microsleeps, subjective sleepiness and maintenance of wakefulness capacities during a week of sleep restriction

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Objectives: Sleep restriction (SR) is a major concern in modern societies. Only few studies investigated its consequences on diurnal sleepiness and maintenance of wakefulness capacities. In addition, the modification of sleep architecture during these nights in comparison with baseline and recovery ones remains poorly documented, as are the number and duration of microsleeps observed during the days of experiment.

Methods: Eleven healthy male volunteered (20–36 years old, intermediate chronotype) to participate in seven nights of SR (4/24 h) after two nights of baseline. Then, three recovery nights and 8 days after, two other recovery nights were proposed. Subjects completed Karolinska Sleepiness Scale (KSS) and Maintenance of Wakefulness Test (MWT) at baseline (D0), during SR (D1, D4 and D7) and during recovery (D10 and D20), while continuously recorded for EEG analysis.

Results: During SR, total sleep time decreased while sleep efficiency improved. Sleep architecture evolved with an increase in the proportion of N3 and a decrease in N1, N2 and REM. Maintenance of wakefulness capacities decreased progressively, whereas the number and the cumulative duration of microsleeps, and KSS scores increased sharply during SR. Recovery nights allowed all sleep values, maintenance of wakefulness capacities and KSS scores to return to baseline levels with a rebound in N1, N2 and REM and a decrease in N3.

Discussion: Despite a modification of sleep architecture, and while subjects were conscious of the deleterious effects of SR, they were no longer able to stay awake in MWT and they even had more frequent and longer microsleeps.
Disclosure: Nothing to disclose.

P845

Driving while fatigued in slippery road conditions - a neglected issue

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Objectives: Fatigued drivers generally experience problems of keeping the vehicle within the lines and often apply a sudden or hard corrective steering wheel movement. When driving on slippery roads, such movements might increase the risk of ending off road due to the unforgiving nature of slippery roads. The aim of the present study was to test this hypothesis.
Methods: Twelve young men participated in a driving simulator experiment with two counter-balanced conditions; normal vs. slippery road x day (alert) vs. night (fatigued) driving. Time-on-task effects were also tested. The participants drove ca. 52 km on monotonous two-lane highway and rated their sleepiness seven times using Karolinska Sleepiness Scale (KSS). Standard deviation of lateral position (SDLP) was a measure of driving performance while blink durations (BD) were extracted from electrooculogram. Data was analysed with mixed-effect multilevel ordinal logistic and linear regression models.
Results: There was an increase in SDLP ($P = 0.001$) and BD ($P < 0.001$) over driving time but no main effect of night drive or slippery road condition. Subjective sleepiness (KSS) was higher during the night drive ($P < 0.001$) with an interaction indicating lower sleepiness during slippery road conditions at night ($P < 0.05$) and a three way interaction suggesting a small but statistically significant ($P = 0.039$) increased sleepiness with driving time at night with slippery road conditions.
Conclusion: The results indicate that driving in demanding road condition (i.e. slippery road) might further exhaust already sleepy drivers. This is not reflected in driving behaviour probably due to short driving duration in this experiment.
Disclosure: Nothing to disclose.

P846

Sleep deficit and sleep problems, the main concern to shift workers with disruptive schedules. A fatigue issue?

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Objectives: The aim of this work was to understand at what level diurnal sleepiness and sleep disturbances are prevalent in airline pilots, and its influence on perceived fatigue.
Methods: A self-report questionnaire was developed composed of socio-economic, labor questions and psychological assessment scales. Associations with these variables and levels of fatigue were performed in univariated and multiple regression analysis. Short/medium haul (SM-H) and Long haul (L-H) pilot's samples were analyzed separately, due to the different characteristics of these flights.
Results: Subjective prevalence values for sleep disturbances (35.1%) and daytime sleepiness (57.7%) were calculated for the total sample of pilots ($n = 456$). Regarding SM-H the values obtained were respectively 34.4% and 61.8%; for L-H 36.2% and 51.2%. Variables associated with fatigue in SM-H were early starts ($P < 0.05$), night periods ($P < 0.05$), sleep disturbances ($P < 0.01$), diurnal sleepiness ($P < 0.01$). These last two variables presented statistically significant predicting values for fatigue (R = 0.433). For L-H pilots variables associated with fatigue were: night periods ($P < 0.01$), sectors flown ($P < 0.05$), duty hours ($P < 0.05$), hours flown ($P < 0.01$), sleep disturbances ($P < 0.01$) and diurnal sleepiness ($P < 0.05$), the last three presenting statistically significant predictive values for fatigue (R = 0.593).
Conclusion: Daytime sleepiness and hours flown were suggested as predictors for fatigue in both types of flights. However, for L-H flights, sleep disturbances were also suggested as predictors. Time zone crossing and circadian disruptions may be the cause of this difference between types of flights.
Disclosure: Nothing to disclose.

P847

Sleep and fatigue study in flight attendants of a Portuguese commercial airline

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Objectives: Sleepiness and fatigue are major concerns in modern aviation operations due to high risks related to performance and alertness impairments compromising safety. The goals of this investigation were to analyze subjective sleep and fatigue prevalence in a group of portuguese flight attendants and compare subjective sleepiness in two groups with different sleep-wake rhythms according to type of work schedule (shift vs. non-shift work).
Methods: Subjective sleepiness was measured using the Epworth Sleepiness Scale (ESS) previously validated in portuguese (Cronbach α=0,772), and subjective fatigue with the Fatigue Severity Scale (FSS). A sample of 203 Flight Attendants (shift-workers) completed both scales together with a work related questionnaire. A second sample of 500 non-shift portuguese workers completed the ESS.
Results: Non-shift workers had a lower ESS mean score (8,57 $\pm$ 4,06), than the group of shift-workers (flight attendants) (11,79 $\pm$ 4,57) (P = 0,000). Pathological levels of sleepiness (ESE $\geq$ 10) were more prevalent in flight attendants (70,4%) than in controls (43%) (P = 0,000). This sample of flight attendants showed a FSS mean score of 4,89 $\pm$ 1,15 and 92% revealed pathological levels of fatigue.
Conclusions: Inadequate sleep-wake rythms related to shift-work result in higher levels of subjective sleepiness when compared with non-shift workers. There is a high prevalence of pathological sleepiness and fatigue in this group of flight attendants although being influenced by short and long-haul flight operations. Long-haul results in high fatigue due to long periods awake and circadian disruption and short-haul results in high sleepiness and fatigue due to sleep loss, and early awakenings.
Disclosure: Nothing to disclose.

P848

Vascular response to 1-week sleep restriction. A metabolic response?

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Objectives: Sleep loss is suspected to induce endothelial dysfunction, a key factor in cardiovascular risk. We examined whether one week of sleep restriction (SR) involves endothelial dysfunction and is linked to inflammatory and endocrine responses.

Methods: Twelve healthy men volumteers were followed during baseline (B, 8 h sleep), after 1 (SR1) and 6 (SR6) days of SR (4 h sleep: 02:00–06:00) and after 1 (R1) and 12 (R12) recovery sleep nights (8 h sleep). Changes in cutaneous vascular conductance (CVC) induced by local application of methacholine (MCh), cathodal current (CIV) and heat (44°C), finger CVC and skin temperature (Tfi) were studied at 10:00 and 16:00, during local cold exposure (5°C, 20 min) and passive recovery (22°C, 20 min).

Results: Compared with baseline (B), MCh and heat CVC changes were decreased in SR6 (10:00 and 16:00) and R1 (10:00). No effect of SR was observed in Tfi and CVC during immersion whereas values were lower during SR6 (10:00 and 16:00) and R1 (10:00). These changes were associated with an increase of bodyweight (SR6), insulin, IGF-1, free IGF-1 and MCP-1 plasma levels (10:00) and decreased ACTH plasma level. From SR2 to R12, TNF-alpha and IL-1beta blood mRNA levels were higher than B (10:00). Compared to B, cortisol salivary levels were lower at 07:00 from SR2 to R12.

Discussion: These results demonstrate that SR reduces endothelial-dependant vasodilatation and local tolerance to cold. This endothelial dysfunction is independent of blood pressure and sympathetic activity but associated with cortisol, inflammatory response and glucose metabolism.

Disclosure: Nothing to disclose.

P849

Objective sleepiness in young and older adults during 3-weeks of chronic sleep restriction

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Objectives: Sleep restriction increases sleepiness and negatively affects performance. Prior studies have indicated that older adults tolerate acute sleep deprivation better than young adults, but whether this is true for chronic sleep restriction (CSR) is not known. We assessed the effects of age on CSR-induced sleepiness.

Methods: Data from ten healthy young (18–27;6f) and ten older adults (55–70;4f) who participated in a 39-day inpatient study were analyzed. The study consisted of 3 baseline days (time-in-bed (TIB) 10 h/24 h), followed by 3 weeks of CSR-forced-desynchrony (5.6 h TIB/24 h) and 8 recovery days (TIB 10 h/24 h). Sleep was recorded each night, and objective sleepiness was assessed by the number of slow eye movements (SEMs) per day recorded during waking EEG recordings conducted throughout each day. Two-Way RM-ANOVA was used to assess the impact of age group and study segment (baseline, CSR, recovery).

Results: The number of SEMs increased across the CSR segment and were significantly higher during CSR compared to the baseline or recovery segments ($P < 0.001$). After CSR, SEMs rapidly decreased back to baseline levels. There was no significant difference in the number of SEMs between young and older subjects ($P = 0.800$) in any segment, despite the older subjects sleeping significantly less than the young in each study segment ($P < 0.001$).

Conclusions: In both age groups objective sleepiness increased similarly across the 3 weeks of CSR and recovered back to baseline values after the end of CSR, despite the reduced sleep duration in the older subjects.

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P850

Sleep loss negatively affects employability and perceived leadership skills

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Objective: Previous research shows that sleep-deprived people are perceived as less attractive and more tired than their well-rested selves. Attractive people are more often ascribed qualities such as social competence, potency, and intellectual competence. These qualities are especially desirable for leaders, but also for employees. The objective of this study was to find out whether sleep loss and perceived tiredness might affect employability and perceived leadership skills, as well as perceived intelligence and trustworthiness.

Method: Twenty-four people were photographed on two separate occasions, at least one week apart. In one photograph they had slept no more than 4 h/night for two consecutive nights and in the other they had spent at least 8 h/night in bed for two consecutive nights. The photographs were rated by 61 observers on leadership ability, employability, trustworthiness, and intelligence. The observers also rated participants' attractiveness and tiredness.

Results: When participants were sleep deprived, they were rated as less good leaders ($P < 0.001$), less employable ($P = 0.001$), and less trustworthy ($P = 0.01$) compared to when they had slept. Sleep-deprived participants were also rated as less attractive ($P = 0.006$) and more tired ($P = 0.011$). There was no difference in ratings of intelligence ($P = 0.105$). Looking more tired was strongly related to being perceived as a poorer leader, less employable, less trustworthy, and less intelligent (p's< 0.001).

Conclusions: The study confirmed previous findings of sleep deprivation affecting attractiveness and perceived tiredness, and showed that sleep-deprived people are judged as being worse leaders, as well as being less employable and less trustworthy.

Disclosure: Nothing to disclose.

P851

Sleep deprivation reduces the long latency startle response in zebrafish

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Objectives: Insufficient sleep results in low-grade inflammation which, in the long run, may lead to metabolic disturbances such as increased risk of obesity, type II diabetes or cardiometabolic diseases. How the sleep restriction (SR) induces these changes at molecular level is not known.

The aim of the project is to develop methods to study these changes in detail by using zebrafish larvae as an animal model.

Methods: We used 1–2 week old zebrafish larvae which were sleep-deprived in dark with constant water flow for 6 h (11 p.m until 5 a.m.). After the sleep deprivation, the responses to mild electrical stimuli (5 V, 1 mA) were recorded with a high-speed video camera (1000 images/s) and the responses were normalized to the control fish without the water flow.

Results: Compared to controls, the sleep deprived larvae showed less startle responses during the remaining dark phase ('Dark',5–9 a.m.) and the beginning of the light phase ('Light',9 a.m.−1 p.m.). Long latency C-turns (LLC) accounted for most of the decrease in startles, whereas the faster, Mauthner cell-mediated short latency C-turns (SLC), were not statistically significantly changed. The reduced reactivity to the electric impulses was considered as increased arousal threshold, a common consequence of sleep deprivation.

Conclusions: We have developed a new gentle and natural method to sleep deprivate zebrafish larvae. In future, we will continue to explore the effects of SR at gene expression level and also to use live-imaging to visualize the time scheme of both the metabolic and inflammatory changes during SR.

Disclosure: Nothing to disclose.

P852

Acute total sleep deprivation potentiates cocaine-induced hyperlocomotion in mice

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All drugs with abuse potential induce an increase in dopamine release in the mesolimbic dopaminergic system, which leads to hyperlocomotion in rodents. Sleep deprivation also seems to play an important role in the events related to the neurotransmission of the dopaminergic system by potentiating it's behavioral effects. In this scenario, the aim of the present study was to investigate the effects of total sleep deprivation (6 h) on the acute cocaine-induced locomotor stimulation in mice. Animals were sleep deprived or maintained in their home cages and subsequently treated with an acute i.p. injection of 15 mg/kg cocaine or saline and observed in the open field. Total sleep deprivation for 6 h potentiated the hyperlocomotion induced by acute cocaine administration. In addition, the cocaine sleep deprived group showed a decreased ratio central/total locomotion compared to the cocaine control group, which might be related to an increase in the impulsivity of mice. Our data indicate that acute periods of sleep loss should be considered risk factors for cocaine abuse.

Disclosure: Nothing to disclose.

P853

Effects of sleep deprivation on behavioural laterality in mice

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Objectives: Behavioural and cerebral asymmetries are ubiquitous in the animal kingdom, and have been shown to be modulated by sleep and sleep deprivation (SD). We investigated whether preceding sleep-wake history affects the behaviour of mice performing visual discrimination task (VDT), involving left or right turning after trial initiation and making a choice between two images displayed on a touchscreen.

Methods: Eight adult male C57BL6/J mice were trained to visually discriminate a 45° oriented grating pattern (positive) from 0° or 90° oriented patterns (negative) until >85% accuracy. On the experimental day animals were tested during a 60-min session immediately after ~6 h of SD or after undisturbed sleep. The task difficulty varied from 'easy' (45° vs. 0°,10°,80°,90°), 'intermediate' (45° vs. 20° or 70°) to 'difficult' (45° vs. 30° or 60°). The direction of turning after trial-initiation and the choice of either the left or right image was determined for each trial.

Results: Each individual had a left-right preference for turning after trial initiation, which was not affected significantly by SD ($P = 0.76$, Student's paired T-test), and was unrelated to task difficulty. The number of most frequently made choices of an image displayed on the side ipsilateral to the preferred turning side, in those trials when it was correct, was significantly decreased by $34.3 \pm 13.3\%$ ($P = 0.02$) after SD.

Conclusions: The results suggest that SD affects motor strategy in a task where behavioural or cerebral laterality is relevant. We conclude that the decrease in left-right asymmetry may contribute to some cognitive deficits after SD.

Disclosure: Nothing to disclose.

P854

Efficient paradoxical (REM) sleep homeostatic regulation in mice: reports on sleep architecture and neuronal activation

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Objectives: Studying paradoxical sleep (PS) homeostatic regulation requires the use of specific PS deprivation (PSD) and the evaluation of the subsequent recovery period. The inverted flower-pot technique has been extensively used in rats but only a few studies were conducted in mice. Furthermore, sleep data were reported only during rebound. With the emergence of transgenic mice and new technologies such as optogenetics, mice are increasingly used raising the need for a reliable method of PSD in mice.

To fulfil this need, we refined the PSD method and thoroughly analyzed sleep during the whole protocol. We also studied activation of hypocretin/orexin and MCH neurons using Fos and neuropeptides double immunohistochemistry to verify whether mechanisms of sleep regulation would be similar in mice to what has been described in rats.

Results: We showed that 48 h of PSD was highly efficient with residual amount of PS only 2.2%. Slow-wave sleep and waking quantities were similar to baseline, except during the first 4 h of PSD where slow-wave sleep was highly reduced. We obtained a significant PS rebound, with a latency of 113.1 min. We found that 34% of hypocretin/orexin neurons were activated during PSD while 27% of

MCH neurons were activated after rebound. Corticosterone level showed a two-fold increase after PSD but returned to baseline level after rebound.

Conclusion: In agreement to rat data, we were able to obtain, in mice, an efficient PSD and induce a significant PS rebound with a strong activation of the melanin concentrating hormone neurons.

Disclosure: Nothing to disclose.

P855

Does more sleep matter? Differential effects of NREM- and REM-dominant sleep on sleepiness and vigilance

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We investigated effects of NREM and REM predominant sleep periods on sleepiness and psychomotor performances measured with visual analog scales and the psychomotor vigilance task, respectively. After one week of stable sleep-wake rhythms, 18 healthy sleepers slept 3 h of early sleep and 3 h of late sleep, under polysomnographic control, spaced by two hours of sustained wakefulness between sleep periods in a within subjects split-night, sleep interruption protocol. Power spectra analysis was applied for sleep EEG recordings and sleep phase relative power proportions were computed for six different frequency bands (delta, theta, alpha, beta, gamma). Both sleep periods presented with similar sleep duration and efficiency. As expected, phasic NREM and REM predominances were obtained for early and late sleep conditions respectively. Albeit revealing additive effects of total sleep duration, our results showed a systematic discrepancy between psychomotor performances and sleepiness levels. In addition, sleepiness remained stable throughout sustained wakefulness during both conditions, whereas psychomotor performances even decreased after the second sleep period. Disregarding exchanges for frequency bands in NREM or stability in REM, correlations between outcome measures and EEG power proportions further evidenced directional divergence with respect to sleepiness and psychomotor performances respectively. Showing that the functional correlation pattern changed with respect to early and late sleep condition, the relationships between EEG power and subjective or behavioral outcomes might however essentially be related to total sleep duration rather than to the phasic predominance of REM or NREM sleep.

Disclosure: Nothing to disclose.

P856

Changes in anxiety, affect, and emotion regulation among sleep-restricted healthy adolescents: an experimental investigation

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Inadequate sleep is consistently shown to presage the development of affective problems and disorders but little is known about the mechanisms underlying these relationships. Experimental sleep research focused on emotional functioning has primarily been conducted in adults but there is need to understand these relationships when sleep and emotion regulatory systems are developing. The current used an experimental sleep restriction protocol to test relationships between sleep, anxiety, affect, and emotion regulation in a sample of 42 adolescents ages 13 to 17 years (M = 15.05, SD=1.43) without any psychiatric or medical disorders. Teens were randomly assigned to a Restricted (4 h) or Idealized (9.5 h) sleep condition following one week of normal sleep (assessed with wrist actigraphy). At baseline and on the day following the sleep manipulation adolescents' completed a battery of measures including the State Trait Anxiety Index (STAIC) and the Positive and Negative Affect Schedule for Children (PANAS-C). An emotion regulatory task using the International Affective Pictures System (IAPS) also was conducted. Analyses revealed significant within-group and between group differences in anxiety and affectivity. Notably, the Sleep Restricted group evidenced increases in state anxiety and decreases in positive affectivity at the second assessment. The latter group also demonstrated decreased emotion regulatory ability when viewing negatively-valenced images. Findings are consistent with previous research showing inadequate sleep to produce adverse changes in emotional functioning and extent these outcomes to youth. Findings will be discussed in terms of their implications for future studies and early intervention efforts.

Disclosure: Nothing to disclose.

P857

Chronic partial sleep deprivation affects event-related potentials evoked by a saccadic task

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Objectives: Total sleep deprivation is known to attenuate the amplitude of event-related potentials in attention tasks with manual reactions. The effects of chronic sleep deprivation are studied less often, and very few studies address the saccadic reaction. This study aimed to describe the impact of chronic partial sleep restriction on amplitudes of P300 components, P3a and P3b, evoked in saccadic task.

Methods: A dense-array EEG was recorded simultaneously with eye tracking in 24 subjects (12 females; mean age 22.7 $\pm$ 1.6 years). A spatial cueing paradigm was employed to induce leftwards and rightwards saccades to the target. Congruent and incongruent trials were analysed separately. The sessions were scheduled at four times of day, in two conditions: after a week of full recovery sleep and after a week of sleep restriction by 33% of individual sleep need.

Results: An ERP analysis of the congruent trials revealed P3b potential (peak at 330 ms after the target onset), whereas incongruent trials showed strong P3a potential (peak at 280 ms after target onset). The amplitudes of both P3a and P3b decreased in sleep deprivation (P3a: $F(1,23)=14.9$, $P < 0.001$; P3b: $F(1,23)=9.2$, $P = 0.006$). Time-of-day did not affect the amplitudes of these potentials.

Conclusions: Chronic partial sleep deprivation affects neural processing in two ways: it reduces frontal attention engagement during task processing and disturbs temporal-parietal mechanisms involved in stimulus evaluation and memory storage. The results

indicate that the consequences of sleep deprivation can be observed even in simple and, to some extent, automatic reactions such as saccades.

Disclosure: Nothing to disclose.

P858

Sleepiness at the wheel in European truck drivers

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Objective: The present study aims to investigate European truck drivers' sleepiness, accident risk and near miss sleepy accidents (NMSA).

Methods: Prospective cross sectional study performed from November 2011 to October. 2012 conducted in highway rest areas specifically reserved for professional truck drivers. Drivers stopping at the rest areas between 16 h00 and 23 h00 were randomly approached. Trained investigators administered a structured interview.

Results: Three hundred and seventy-five truck drivers accepted to participate with an acceptance rate of 70%. Their mean age was 43.5 $\pm$ 9.5 years and 98% were men. The mean professional driven distance per year was 125.000 $\pm$ 51.037 Km, drivers started their trip 1.3 $\pm$ 1.5 days before. Today's mean distance drive was 443 $\pm$ 130 Km.

Three percent of the truck drivers (N: 11) had a sleepiness episode leading to a NMSA during this trip and 9% had to stop because of an episode of sleepiness.

NMSA drivers have a higher risk, compared to drivers without a NMSA, of sleeping less than 6 h the night prior to the first working day (OR:3.9; [CI: 1.1 - 15.7]), of sleeping less than 6 h between two working days (OR 5 [CI: 1.3 - 18.7]), of having had an accident during the preceding year (OR 6.2 [CI: 1.6 - 41.5]) or an NMSA during the preceding year (OR 5.3 [CI: 1.1 - 19.7]).

Conclusion: Sleep deprivation and the antecedent of an accident or a NMSA constitutes a major risk factor for near miss sleepy accidents.

Disclosure: Nothing to disclose.

P859

Severe sleepiness and insufficient sleep in connection with different shift types: results from a field study in road freight transport

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Objectives: The previous studies on shift work have found sleepiness particularly prevalent on night and morning shifts, and cumulative over successive workdays. The current study examined whether some shift types are more risky in terms of severe sleepiness on duty and insufficient sleep prior to duty hours in road freight transport.

Methods: Fifty-four drivers (mean age 38.1 years) underwent 2-weeks field measurements including recordings of sleep using actigraph and diary, and sleepiness using the Karolinska Sleepiness Scale (KSS). Criteria for *severe sleepiness* was set to KSS $\geq$ 7. Daily sleep < 6 h was defined as *insufficient sleep*. The data comprised of 474 shifts categorized into morning, day/evening, first and successive night shifts.

Results: Sleepiness and sleep loss were both significantly associated with shift type (X^2 = 24.91, P < 0.991 and X^2 = 11.26, P = 0.010, respectively). Compared to day/evening shifts, the risk of sleepiness was greater for night shifts, especially for first night shifts (OR 7.16, P = 0.002). The risk of insufficient sleep was increased only prior to successive night shifts (OR 3.48, P = 0.017). Morning shifts were not significantly associated with increased risk of sleepiness (P = 0.457) or sleep loss (P = 0.333).

Conclusions: The findings propose that in road freight transport *first* night shifts are the most vulnerable shifts in terms of severe sleepiness, and *successive* night shifts in terms of insufficient prior sleep. The former was not explained by sleep loss in the present data. Also, contrary to the earlier studies, morning shifts were not observed to be associated with an increased risk of sleepiness or sleep loss.

Disclosure: Nothing to disclose.

P860

Sleepiness and vigilance during on-the-road driving: a behavioral and physiological investigation of time on task and sleep deprivation effects

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Objectives: Sleep deprivation and Time-On-Task (TOT) have detrimental effects on driving performance and sleepiness due to sleep deprivation exacerbated the TOT effects. This additional effect of sleep deprivation and TOT has not been studied in real driving conditions. Electroencephalography (EEG) is one of the best methods to assess the physiological variations of vigilance and sleepiness during driving. Our aim was to assess the effects of sleep deprivation both alone and associated with TOT on driving performance and on EEG.

Methods: Twenty six healthy participants (25–45 years old) performed a one hour on-the-road monotonous driving task after one night of normal sleep and after one night of sleep deprivation. We measured the Standard Deviation of Lateral Position (SDLP), a measure of road tracking error. Continuous EEG was recorded and spectral power was obtained over three bilateral clusters (frontal, central, parieto-occipital) in the theta (4- 8 Hz), alpha (8–12 Hz) and beta (12- 30 Hz) bands.

Results: SDLP increased after sleep deprivation and varied with TOT only after sleep deprivation. Alpha and theta EEG increased after sleep deprivation and varied with TOT and interaction between sleep deprivation and TOT was found. Beta EEG increased with TOT only in the sleep deprivation condition. Changes in SDLP and EEG did not correlate significantly.

Conclusions: Our results demonstrated driving and EEG decrements associated with sleep deprivation and TOT and confirmed previous simulator studies. Our study revealed for the first time an additional effect of sleep deprivation on TOT on EEG in real driving conditions.
Disclosure: Nothing to disclose.

P861

Sleep insufficiency among Korean adolescent students: from 9th Korea Youth Risk Behavior Web-based Survey (KYRBS) 2013

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Introduction: The present study aimed at investigating the severity and patterns of sleep insufficiency in students. And related mental and behavior health conditions according to the nationwide survey data.
Methods: The analysis is based on data from the Ninth Korea Youth Risk Behavior Web-based Survey (KYRBS), 2013. Total of 72435 students from 7th to 12th grades completed the anonymous self-administered web-based questionnaire. 63307 students (31,616 males, and 31,691 females) were finally enrolled.
Results: Mean total sleep time (mTST) 6.45 ± 1.40 h, mean sleep time 0:18(±76 min), mean awake time 6:44(±44 min). Mean total sleep time became remarked shorted as the students advance to higher grades (7th:7.50 ± 0.01 h, 8th:7.19 ± 0.01 h, 9th:6.88 ± 0.01 h, 10th:5.93 ± 0.01 h, 11th:5.79 ± 0.01 h, 12th:50.52 ± 0.01 h), with moderate correlation($P < 0.01$,rho:−0.541). The mTST also correlated with total time spent in chair related to academic works($P < 0.01$,rho:−0.312), but minimum with total time spent in chair for non-academic works($P < 0.01$,rho: 0.040). Short mTST(< 7 h) were highly related to mental health questionnaire indicating higher stress, depression and despair, and suicide ideation, plan, attempts($P < 0.01$). Further on short mTST is related to use of alcohol, smoking and recreational drugs.
Conclusion: Sleep insufficiency among Korean adolescent increase in their severity according to their advancement in grades. While emphasis in adequate sleep time has long been educated, short sleep duration remains unchanged with even more intensified academic stress. Aside from academic work loads, less attention have been given to mental and behavior conditions related to sleep insufficiency. Although cause and consequence is unclear, they also needs close attention for managing sleep insufficiency in adolescence.
Disclosure: Nothing to disclose.

P862

Inter-individual differences in the tolerance to sleep deprivation: the effects of circadian flexibility

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Objectives: The current study was designed to investigate the influence of individual differences in the flexibility of the circadian rhythm on sleepiness, during 28 h of sleep deprivation.
Methods: Based on the flexibility of the circadian rhythm, as measured with the Circadian Type Inventory (CTI), 17 rigid (mean age 23 years, SD=4.9) and 17 flexible types (mean age 22 years, SD=4.5) were selected. These participants were deprived from sleep for 28 h, in controlled laboratory conditions. Subjective and performance based sleepiness were determined during the sleep deprivation period by using the Karolinska Sleepiness Scale (KSS; hourly measures) and the Psychomotor Vigilance Task (PVT; two-hourly measures), with a focus on reaction speed (RS).
Results: An increase in subjective and performance based sleepiness was observed under conditions of prolonged wakefulness (F_{KSS}(5.476,164.285)=52.643, $P < 0.001$; F_{PVT_RS}(5.134,143.749) =12.995, $P < 0.001$). Flexible types displayed higher levels of subjective sleepiness during the day, at 9 h and 16 h ($P < 0.05$), whereas from 21 h onwards they indicated lower levels of subjective sleepiness in comparison with rigid types ($p_{03\ h} < 0.001$, $p_{21\ h,\ 22\ h,\ 00\ h,\ 01\ h,\ 03\ h,} < 0.01$, $p_{23\ h,04\ h} < 0.01$). Furthermore, higher performance based sleepiness was shown in rigid in comparison with flexible types, from 21 h till 03 h ($p_{21\ h,\ 23\ h,\ 01\ h} < 0.05$).
Conclusions: Different sleepiness profiles were found in flexible vs. rigid participants, whereby flexible types showed less subjective and performance based sleepiness during nighttime. The results suggest that it is important to take into account the flexibility of the circadian rhythm when evaluating the tolerance to sleep deprivation.
Disclosure: Nothing to disclose.

P864

Individual variability of EEG patterns in drowsiness

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Operator activity is wide spread in modern society. There are many cases in which operator's drowsiness could lead to dangerous consequences, though, so the task of non-optimal operator's state detection is undoubtedly essential. The main problems on this way are complexity of operator's state changes and individual differences in physiological parameters.
Our research continues several previous studies that demonstrated good efficiency of Bayesian and CSP methods for the task of drowsiness recognition by EEG. Such algorithms allow us to detect drowsiness using automatically detected individual EEG patterns from training data set.
Current study was performed for estimation of both classifiers stability. Four healthy subjects were participated in four experiments with driving simulator each. All subjects were partially sleep-deprived before experiments. Interval between experiments was no less than one week. 19-electrodes EEG, EOG, electric skin response, eye-tracking data, driving performance and video of subject's face were recorded. Expert rate was made by two independent experts for each experimental video. All data obtained were averaged for 10-seconds long intervals.
Cross-validation of results obtained showed that drowsiness recognition based on training set from other experiment is rather effective (75–90%). We believe that such studies could lead us to much more effective approach to drowsiness recognition using individual variability of EEG parameters.

We believe that such studies could lead us to much more effective approach to drowsiness recognition that could deal with individual variability of EEG parameters.

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Disclosure: Nothing to disclose.

P865

Obstructive sleep apnea syndrome and sleep disturbances among Brazilian airline pilots

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Objectives: To estimate the prevalence of obstructive sleep apnea syndrome and sleep disturbances in airline pilots.

Methods: This epidemiological study was conducted with Brazilian airline pilots. Data collection started in December 2013 and was completed in March 2014. Results of 391 pilots who voluntarily accessed online questionnaire are presented. The questionnaire included sociodemographic characteristics, working conditions and sleep aspects. The prevalence of obstructive sleep apnea syndrome (OSAS) was estimated using the Berlin Questionnaire. Three indices related to sleep were obtained from the Karolinska Sleep Questionnaire: sleep quality, awakening problems and sleepiness. Associations between OSAS and indices related to sleep problems being assessed through chi-squared test.

Results: The average age of respondents was 38.2 years. (SD 8 years.) and seniority at work was an average of 15.7 years (SD 7.9 years.). Most were men (98%), with higher education (59.8% undergraduate or graduate) who lived with a partner (88.5%). Work shifts were irregular and most involving night shifts (97.2%). The prevalence of OSAS in the population was 44.4%. Poor sleep quality index was verified in 10.1%, awakening problems index in 22.4% and sleepiness index in 7%. We found an association between OSAS and poor sleep quality, awakening problems and sleepiness ($P < 0.01$).

Conclusion: There is a high prevalence of OSAS in this population. Our results suggest that sleep problems are associated with OSAS. These data indicate that this population might have difficulties to be alert during work hours.

Acknowledgement: ABRAPAC.

P866

Sleep-related crashes in urban, low speed environments

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Objectives: Sleep-related crashes occur most frequently in rural, high speed driving environments. However, comparatively little is known about urban, low speed sleep-crashes. The current work addresses this knowledge gap.

Methods: Queensland (Australia) police reports for of all crashes occurring in low (≤ 60 km/h) speed zones between 1/1/00 and 31/12/09 were examined. Attending police officers identified all crash attributes, including 'fatigue/fell asleep'. Driver/rider involvement in crashes was classified as 'sleep-related' or 'not sleep-related'. All associated variables were compared using Chi-square tests (Cramer's V = effect size). An alpha level of 0.001 determined statistical significance.

Results: There were 273,733 drivers/riders involved in a crash within a low speed zone; 1,411 (0.5%) were attributed as 'sleep-related'. Those involved in a 'sleep-related' crash were more likely to be male, aged 16–29 years and the sole occupant. Additionally, those involved in a 'sleep-related' crash were more likely to be above the prescribed alcohol limit. Fatality/hospitalisation, hitting a stationary object and having a head-on collision were more common in 'sleep-related' than 'not sleep-related' crashes. 'Sleep-related' crashes were prevalent at weekends. Approximately 80% of 'sleep-related' crashes involved a single vehicle, compared to 20% of 'not sleep-related'. The majority of 'sleep-related' crashes (50.7%) occurred between midnight and 6am.

Conclusions: Sleep-related crashes are not confined to high speed rural environments. Low speed 'sleep-related' crashes commonly involve young males who are the sole vehicle occupant. These crashes are often fatal and frequently involve head-on collision or hitting a stationary object. Driver sleepiness awareness campaigns should include low speed sleep-related risks.

Disclosure: Nothing to disclose.

Sleep disorders - Breathing 3

P867

Decrease of respiratory events in patients with OSAS, using a mandibular advancement device (MAD), assessed with split night polysomnography, in a Mexican population

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Background: Mandibular advancement devices (MAD) represent a feasible choice in the treatment of obstructive sleep apnoea syndrome (OSAS), in well selected patients. The aim of this study is to assess the efficacy of MAD in 30 patients with OSAS, using split night polysomnography (SNP) in a multidisciplinary clinic sleep center in Mexico.

Methods: An auto controlled clinical trial was used in assessing the efficacy of MAD in 30 patients with snoring and OSAS. Clinical evaluation was made every 2 weeks to adjust treatment and observe changes in clinical symptoms. Three months after placement of the MAD a SNP was performed, using the MAD in the second half of the night, in order to compare the respiratory results.

Results: The results found the SNP show significant changes with use of MAD ($P < 0.05$): Decrease in Snore Index (159.95 to 32.46/hr) and in AHI (22.45 to 4.63/hr), increase in SaO2 (89.98 to 91.39%) and changes in the subjective evaluation of the patients, including with the Epworth Sleepness Scale (14.4 pts -4.6pts).

Conclusions: The use of MAD is an alternative in the management of OSAS, in well selected patients, and used in a multidisciplinary fashion. When evaluated using a SNP, expenses can be decreased both, for treatment and evaluation methods.

Disclosure: Nothing to disclose.

P868

Non-intrusive apnoea / hypopnoea detection system via graph-signal analysis of Microsoft Kinect captured depth video

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Quality of sleep greatly affects a person's physiological well-being. Traditional sleep monitoring systems, e.g., full multi-sensing sleep monitoring devices like Philips Alice PDx, are accurate in measuring various vital signs, but are expensive and intrusive with sensors attached to various body parts, disturbing the natural sleep of a patient.

We propose an inexpensive, non-intrusive, sleep monitoring system using only depth video captured by a Microsoft Kinect camera. Not relying on the lighting condition of a dark sleeping room, a Kinect camera projects infrared light patterns to capture depth images of the sleep patient. The 11-bit captured depth video is first encoded using an efficient H.264 implementation. Then temporal denoising is performed using a graph-based motion smoothness filter, so that unwanted temporal flickering can be removed. We analyze the recorded depth data to track the patient's chest and abdomen movements over time. Specifically, we estimate parameters of our proposed dual-ellipse model in each image. Sleep events are detected via a graph-based classifier trained on statistics of estimated ellipse parameters. Experiments show first that our temporal denoising scheme outperforms conventional bilateral filter when removing flicker. Second, comparing against data collected for 6 patients from a full polysomnography with the respiratory events scored according to AASM 2007 guidelines, we show that our classifier can detect normal vs. abnormal breathing (apnoea / hypopnoea) with 100% sensitivity and specificity for 50 test samples. Further, our classifier is more robust to errors in training data than two conventional implementations of support vector machine (SVM).

Disclosure: Nothing to disclose.

P869

Prevalence and risk factors of snoring habitual among the Saudi population

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Introduction: Snoring is often viewed as a social nuisance without health consequences. However, some epidemiologic studies revealed that snoring alone might be related to hypertension, ischemic heart disease, and stroke. Local epidemiological studies are lacking. Hence, such a study was needed to estimate the size of the problem and its predicting factors.

Objective: To determine the prevalence and predictors of habitual snoring among the Saudi adult population.

Methods: This is a cross sectional study, conducted from March 2013 until June 2013 in Jeddah, Saudi Arabia. The targeted study population was school employees aged (30–60) years that were randomly selected and interviewed by trained physicians. Modified Wisconsin Sleep Questionnaire was used. Anthropometric measures and blood pressure were also recorded according to standard methods. Based on frequency of snoring per week, candidates were distributed as habitual, moderate and non-snorers.

Result: A total of 2682 cases were recruited. Females made up 52.1% ($n = 1397$) of the study population. 40% of the study population was snorers. The population was divided into: habitual snorers 23.5% ($n = 630$); moderate snorers 16.6% ($n = 445$), and non-snorers 59.9% ($n = 1607$). Using multivariate analysis, factors that were found to independently predict snoring include aging, gender, daytime sleepiness, hypertension, family history of snoring and OSA, water-pipe smoking and finally consanguinity.

Conclusion: This study reveals snoring is a quite common disorder in the Saudi population. Aging, male gender, daytime sleepiness, hypertension, family history of snoring and OSA, water-pipe smoking and consanguinity were all found to be significant independent risk factors for snoring.

Disclosure: Nothing to disclose.

P870

Obstructive sleep apnea, hypothyroidism and cognition

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Objectives: To assess the impact of obstructive sleep apnea syndrome (OSAS), obesity and hypothyroidism and their potential synergic effect on sleep pattern, vigilance and cognitive functioning.

Methods: Fifty OSAS patients and twenty age, sex and BMI matched healthy controls underwent in lab nocturnal polysomnography, multiple latency sleep test, standardized questionnaires for sleep quality, fatigue, sleepiness, TSH, fT3 and fT4 evaluation and neuropsychological tests. Subjects were divided in four groups: non obese OSAS, obese OSAS, hypothyroid OSAS patients and healthy controls.

Results: Hypothyroid OSAS showed worse scores in subjective sleep quality and fatigue compared with controls and non obese OSAS, with a positive correlation between TSH level and Fatigue Severity Scale and Epworth Sleepiness Scale. Mean daily sleep latency was significantly lower in all three clinical population as compared to control, while single naps latencies were different mainly for hypothyroid OSAS. Neuropsychological testing pointed out no significant differences among the three OSAS groups, but OSAS patients, considered as a whole, showed decreased performances in attentive and executive frontal tasks, compared with healthy controls. Sleep efficiency and Wake After Sleep Onset and microstructural sleep variables showed significant correlations with attentive and executive frontal tasks.

Conclusions: Sleepiness and perceived fatigue occur particularly in hypothyroid OSAS patients. Cognitive deficit was similar among the three OSAS groups and impaired compared with healthy controls. The observed correlation between neuropsychological examination and macro and microstructural variables suggest a role of sleep disruption, more than respiratory disturbance per se, on cognition.

Disclosure: Nothing to disclose.

P871

Persistent sleepiness after CPAP treatment in obstructive sleep apnea patients

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Objectives: To assess the comorbility occurrence or other sleep pathology associated to sleepiness post CPAP treatment.

Methods: Patients with SAOS effectively treated with CPAP and persistent sleepiness during the day (Epworth Scale (ES) >10) were included. They had CPAP compliance > 6 h/night, 90% nights, for more than 6 months. We did another clinical history and we repeated CPAP titration and then they underwent polysomnography (PSG) followed by a multiple sleep latency test (MSLT), both of them with CPAP.

Results: Twenty-two SAOS men (mean age 55 $\pm$ 11 years, mean BMI 28 $\pm$ 5Kg/) were included. Index apnea-hipopnea was 43 $\pm$ 13. Mean ES without CPAP 16 $\pm$ 4, mean ES after 1 month with CPAP 7 $\pm$ 4, mean ES 6 months with CPAP 15 $\pm$ 3.

PSG with CPAP only showed increase stage N3 (p: 0.04). The MSLT was pathologic in 13 patients (mean sleep latency: 6 min).

A clinic diagnostic could be done in eighty-five per cent of the patients (Idiopathic hypersomnia, depression, circadian rhythm disruption, chronic sleep restriction, restless legs syndrome). Fifteen per cent of the patients with hypersomnia could not be diagnosed.

Conclusions: In most cases a structured sleep history was sufficient to establish the diagnosis.

85% of patients had other associated sleep disorders or depression. In 15% of cases, the cause of sleepiness was not identified, so it is not possible to exclude the existence of structural lesions in the central nervous system.

Disclosure: Nothing to disclose.

P872

Intermittent hypoxia induced genioglossal contractile dysfunction can be alleviated by adiponectin

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Objectives: To investigate the effects of chronic intermittent hypoxia (CIH) on genioglossus contractile properties and intensive role of adiponectin(Ad) in rats.

Methods: Wistar rats were randomly divided into 3 groups: normal control (NC) group, CIH group, and CIH+Ad group with 13 rats in each. Rats in NC group were kept breathing normal air, while rats in both CIH and CIH+Ad groups experienced the same CIH environment (CIH 8 h/day for successive 35 days). Rats in CIH+Ad group were given intravenous Ad supplement. After 35 days' CIH exposure, the genioglossus contractile properties were compared among the three groups.

Results: Twitch tension, time to peak tension, half relaxation time and tetanic tension were significantly lower in CIH group than those in NC group(all $P < 0.01$). By contrast, these contractile properties were improved in CIH+Ad group. On average, the tetanic fatigue indexes (TFI) of the three groups were decreased more rapidly in the first 20 s than during the subsequent 100 s. TFI in the NC and CIH+Ad groups were significantly higher compared to the TFI in the CIH group.

Conclusion: CIH could lead to impaired genioglossus contractile properties and decreased fatigue resistance in rats. Such changes could be partially offset by supplementation of adiponectin.

Disclosure: Nothing to disclose.

P873

Adiponectin protects the genioglossus of rats against chronic intermittent hypoxia-induced injury via inhibition of endoplasmic reticulum stress

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Objective: To investigate the effects of chronic intermittent hypoxia (CIH) on endoplasmic reticulum stress (ERS) and associated apoptotic pathways in genioglossus, as well as the possible intervention role of adiponectin (Ad) supplement in rats.

Methods: Wistar rats were randomly divided into three groups: normal control group (group A), CIH group (group B), and CIH+Ad group (group C) with 15 rats in each. Rats in group A were kept breathing room air, while rats in groups B and C experienced the same CIH environment. Rats in group C were given intravenous adiponectin supplement. After 35 days' CIH exposure, western

blotting was applied to detect expressions of ERS signals and associated apoptotic pathways.

Results:

Expressions of proteins involved in ERS were enhanced in group B behaved as:: a) GRP78 expression was significantly higher than that in groups A and C ($P < 0.01$); while no significant difference was shown between groups A and C ($P > 0.05$);

b) Compared to those in groups A and C, all the expressions of ERS signals such as p-PERK, p-eIF2α, p-IRE1α, XPB1s and ATF6 in group B were significantly increased (all $P < 0.01$), with no significant difference between groups A and C (all $P > 0.05$).

ERS-associated apoptotic pathways were remarkably activated in group B. Transvenous supplement of adiponectin improved the above CIH-induced pathological changes in group C.

Conclusion: CIH could enhance ERS and induce activation of ERS-associated apoptotic pathways in genioglossus, which could be significantly improved by adiponectin supplement.

Disclosure: Nothing to disclose.

P874

Treatment decisions among 175 participants of Akershus sleep apnoea project (ASAP) with obstructive sleep apnoea

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Current clinical guidelines for treatment of obstructive sleep apnoea (OSA) are not conclusive. Treatment options are disputed in particular for persons with an apnoea hypopnea index (AHI) of 5–15. Participants of the Akershus Sleep Apnoea Project (ASAP) diagnosed with OSA were after baseline assessment offered treatment. The aim of the current study was to retrospectively assess the first treatment decisions offered.

The source population comprised 289 consecutive participants of the ASAP that underwent additional psychiatric and neurocognitive testing between June 2006 and April 2007. 175 (60.3%) were diagnosed with OSA defined by an AHI $\geq$ 5 and Berlin Questionnaire high risk. Among these, 72 had AHI between 5 and 14.9 and 104 had AHI $\geq$15. 58 participants were examined by an upper airway pressure recording between 1–112 (mean 16) weeks after inclusion. Data has been extracted by manual chart review.

Forty-one (23.4%) of the participants accepted treatment with positive airway pressure (PAP), 30 (17.1%) were offered surgery and 4 (2.3%) were offered a postponed decsion.100 (57%) had no further contacts with the otorhinolaryngology department after participation in the ASAP. Two patients with an AHI < 15 were treated with PAP and 9 received surgery. 18 out of 58 participants (31%) were operated after upper airway pressure recording.

Less than 50% of participants in a community-based study diagnosed with OSA were treated and most treated participants had AHI $\geq$ 15. Accepting upper airway pressure recording increased the probability of being treated with surgery.

Disclosure: Nothing to disclose.

P875

The role of compliance with positive airway pressure use on blood pressure in patients with obstructive sleep apnea

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Background-aim: Scientific data about the effects of positive airway pressure (PAP) treatment on blood pressure (BP) control are continuously increasing; however they are controversial. We aimed to determine the long term effects of compliance with PAP therapy on BP in both hypertensive and normotensive patients with obstructive sleep apnea (OSA).

Methods: One thousand one hundred sixty eight consecutive patients with newly diagnosed OSA, who have been recommended PAP therapy, were followed up for a minimum of 2 years. Patients with previous cardiovascular disease were excluded. BP was measured at baseline and after 2 years of PAP treatment. In addition, the correlation between the changes in BP with different levels of PAP compliance, gender and OSA severity was assessed.

Results: At the end of the 24-month follow-up period, in the hypertensive group of patients ($n = 410$), a significant decrease was shown in systolic (-10.5 mm Hg, $P < 0.001$) and diastolic BP (-3.7 mm Hg, $P < 0.001$). Furthermore, in the patients without hypertension ($n = 578$), a significant decrease was noted both in systolic and diastolic BP (-5.6, $P < 0.001$ and -4.5, $P < 0.001$, respectively). A correlation between the magnitude of change in BP and hours of use of PAP ($r = 0.14$, $P = 0.005$) was observed.

Conclusions: Long-term use of PAP treatment as well as increased hours of PAP use showed significant reductions in BP not only in patients with OSA and hypertension, but also in normotensive patients. Therefore a significant potential reduction in cardiovascular mortality and morbidity should be expected in these patients.

Disclosure: Nothing to disclose.

P876

A non-invasive technique to detect respiratory effort during sleep

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Objectives: A key factor in the diagnosis of obstructive sleep apnea is assessment of respiratory effort during sleep. The gold standard for measuring respiratory effort is esophageal manometry. This technique is rarely used because its invasiveness.

A non-invasive technique is described to detect respiratory effort of the diaphragm and the sternocleidomastoid muscles using surface electromyography (EMG) electrodes.

Methods: Polysomnography was applied in 18 patients with suspected sleep-disordered breathing, including 6 bipolar electrodes spread around the abdomen at the height of the diaphragm and 2 bipolar electrodes placed on the sternocleidomastoid muscles.

The diaphragm and sternocleidomastoid signal were visually scored in periods with known respiratory events.

Results: In total, 1792 respiratory events, of which 1462 hypopnea's and 330 apneas, were detected. Using diaphragm signal an accuracy of 73% is achieved. Using sternocleidomastoid signals an accuracy of 68% is achieved. Using both diaphragm and sternocleidomastoid signals an accuracy of 85% is achieved in all subjects and an accuracy of 91% is achieved in the group of subjects with a body mass index below 30.

Conclusions: These results suggest that respiratory events can be detected from the diaphragm EMG. In addition, the sternocleidomastoid muscles appear to be active during normal breathing, which is in contrast with the former believe that they only have an accessory function.

The detection of respiratory events is increased when both signals are used.

Disclosure: Nothing to disclose.

P877

A case-control study: the influence of smoking intensity on quality of sleep in a population of obstructive sleep apnea syndrome patients vs. habitual snorers

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Objective: Current and former-smoking are major risk factors for snoring, but whether smoking is an independent risk factor for OSA is not entirely clear. Only a few studies analyzed the relationship with smoking intensity (pack-years index-PY).

Methods: We retrospectively analyzed 4 populations: OSA active-smokers, former-smokers, never-smokers and habitual snorers smokers (with comparable comorbidities and dependencies) regarding demographic data, smoking status and its influence on polysomnographic findings.

Results: Seventy-one OSA patients: 13 (18%) women, 58 (82%) men, 25 (35%) never-smokers, 19 (27%) active-smokers (PY=21.5 $\pm$ 10.7, Fagerstrom=3.5 $\pm$ 2.1), 27(38%) former-smokers (PY=25.9 $\pm$ 18.8); mean values: age=54.3 $\pm$ 13 years, Epworth=8.2 $\pm$ 5.4, total sleep time(TST)=5.6 $\pm$ 2 h, arousal index (AI)=29.7 $\pm$ 13.7/h, AHI=38.1 $\pm$ 12.6/h. There were no differences between active-smokers/former-smokers/never-smokers except a higher AI for OSA active-smokers compared to never-smokers (34.6 $\pm$ 8.3/h vs. 20.54 $\pm$ 6.2/h, P = 0.02) at a comparable AHI, but the difference is not maintained for AI without respiratory events (17.8 $\pm$ 5.39/h vs. 13.3 $\pm$ 1.31/h, P = 0.29). OSA active-smokers (19) were compared with ronchopaths active-smokers (11) similar in terms of smoking intensity (PY=23.2 $\pm$ 8.5, age=41.1 $\pm$ 11.7 years, Epworth=4.09 $\pm$ 2.1, Fagerstrom=4.6 $\pm$ 2.3, TST=4.7 $\pm$ 2.3 h) and only an unexpected high AI in ronchopats (15.8 $\pm$ 5.6/h) were noted. AI without respiratory events was similar in ronchopats and OSA active-smokers (12.9 $\pm$ 4.8/h vs. 17.8 $\pm$ 5.3/h, P = 0.34). There was no difference in TST, efficiency, sleep latency, sleep stages. In OSA active-smokers only, AI without respiratory events correlates with PY index (r = 0.53 P = 0.01), not with nicotine dependence.

Conclusions: Our study using a control group of smoker ronchopats (without evaluation of esophageal pressure) found that smoking intensity correlates with higher AI without respiratory events and so with a higher degree of sleep disruptions in OSA active-smokers mainly.

Disclosure: Nothing to disclose.

P878

Electrophysiological evaluation of the relationship between the levels of body mass index and apnea hypopnea index

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Objectives: The purpose of this study is to relieve the electrophysiological properties of the connection between 'body mass index'(BMI) and 'apnea-hypopnea index' (AHI) and to emphasize the importance of this relation for sleep health.

Methods: One hundred and twenty subjects between 20 and 65 years of age, were divided to four groups according to BMI and degree of sleep-disordered breathing (SDB):(1) BMI=18,5–24,9 kg/m^2, healthy (n = 30), (2) BMI=25–29,9 kg/m^2, overweight, SDB (n = 30), (3) BMI=30–39,9 kg/m^2, obese,SDB (n = 30), (4) BMI $\geq$40 kg/m^2, morbidly obese, SDB (n = 30). Polysomnography recordings of the subjects were recieved in 'Erzurum Training and Research Hospital', Turkey. The electrophysiological properties achieved were AHI, sleep efficiency (%) and duration (minutes) of total sleep, and of nREM1,2,3 and REM periods. The effect of BMI values on these electrophysiological values was analyzed with One Way ANOVA test, and the statistical evaluation of the difference between the groups was done by Duncan's multiple comparison procedures. The degree of the relation between the parameters was determined by Pearson Correlation Test.

Results: While there was significant positive correlation between BMI and AHI levels (r = 0,470**), there was significant negative correlation between BMI and sleep efficiency (r= $-$0,235*) or duration of REM period (r=$-$0,281**). AHI levels belonging to group1 and 2 were significantly lower than those of groups3 and 4 (P = 0,000). The level of sleep efficiency was lowest in group4 (P = 0,027). The duration of nREM2 was significantly higher in group2 and group3 (P = 0,092). The durations of nREM3 and REM period were significantly shorter in group4 comparing with group1(respectively P = 0,009; P = 0,000).

Conclusion: This study has revealed the effects of different BMI levels on the sleep electrophysiology. We have shown that the subjects who had higher BMI levels might have higher AHI levels, and hence changes in sleep efficiency and quality could disturb sleep health.

Disclosure: Nothing to disclose.

P879

Relationship between symptoms of sleep disordered breathing and severity of obstructive sleep apnoea in a reference sleep center

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Objectives: To assess how symptoms of sleep disordered breathing (SDB) predict a diagnosis of obstructive sleep apnoea (OSA) and its severity.

Methods: The sample comprised 1095 adults (29.3% women) with suspected OSA referred to Haukeland University Hospital between 2011 and 2013. Mean age 48.4 ± 13.4 years and body mass index 29.5 ± 5.3 kg/m2. All patients underwent polygraphic sleep studies. OSA was diagnosed and classified according to the apnea-hypopnea index (AHI) as normal (< 5), mild (5–14.9), moderate (15–29.9) or severe (≥ 30). Symptoms of SDB included snoring, breathing cessations during sleep and daytime sleepiness, considered as positive if occurring 'sometimes (several times a month)', 'often (several times a week)' or 'always', collected from the Karolinska Sleep Questionnaire.

Results: 40.7% of the subjects had a normal AHI whereas 29.8% had mild, 16.2% moderate, and 13.3% severe OSA. Snoring (reported by 91.5%) yielded a sensitivity/specificity of 96.0%/10.4% and 98.6%/9.6% for moderate and severe OSA, respectively. Similarly, breathing cessation (reported by 66.4%) and daytime sleepiness (reported by 92.7%) yielded sensitivities/ specificities of 76.8, 81.5%/38.0%, 35.9% and 92.9%, 95.2%/7.4%, 7.7%. Positive answers to all three questions (reported by 61.6%) resulted in a sensitivity/specificity for moderate and severe OSA of 72.4%/42.9% and 79.5%/41.1%, and a negative/positive predictive value of 78.8%/34.7% for moderate OSA and 92.9%/17.2% for severe OSA.

Conclusions: Subjects reporting symptoms of SDB should undergo sleep studies as the predictive values of the symptoms are low. However, the probability of severe OSA is low if not all symptoms are present.

Disclosure: Nothing to disclose.

P880

Nasal symptoms and dimensions measured by acoustic rhinometry in relation to PAP use in the Icelandic sleep apnea cohort study

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Objectives: To evaluate the possible role of the nose in the pathogenesis of obstructive sleep apnea (OSA) and its role in adjustment to treatment with positive airway pressure (PAP).

Methods: Untreated patients diagnosed with moderate to severe OSA from 2005–2010 were invited to participate in the Icelandic Sleep Apnea Cohort study (ISAC). On entry, acoustic rhinometry (AR) was performed and nasal symptoms score assessed. PAP compliance and symptom score was assessed after two years.

The primary variable on AR signifying nasal dimension is the minimum cross-sectional area of the narrower nasal cavity without the patient being given nose drops.

Results: A total of 822 OSA patients participated (665 males, 157 females). 741 (90%) OSA patients returned on 2 year follow-up. 475 (64%) were using PAP and 266 were non-users.

There is no significant association between the AR variables and OSA severity (apnea-hypopnea index, oxygen desaturation index and hypoxia time). There is no significant association between the AR variables and PAP compliance. However, greater nasal dimensions are associated with male gender ($P < 0.02$) and increased body mass index ($P < 0.006$).

A significant inverse correlation is found between AR variables and nightly nasal blockage at baseline ($P < 0.008$) and after two years ($P < 0.02$). This relationship remains significant after correcting for body mass index. There is an inverse relationship between nightly nasal blockage as the subjects reported in the first interview and PAP usage ($P < 0.03$).

Conclusions: Subjective nasal patency on start of PAP treatment is associated with better compliance.

Disclosure: Nothing to disclose.

P881

The influence of abdominal fat distribution measured by DEXA on the severity of sleep apnea in postmenopausal women

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Objectives: Body fat distribution may influence the severity of sleep apnea. The authors compared abdominal fat distribution seen in postmenopausal women with parameters recorded by cardiorespiratory polygraphy. The objective of this study was to characterize the relationship between the quantity as well as the distribution of abdominal fat and the severity of sleep apnea, in postmenopausal women.

Methods: Total and regional fat mass was determined by DEXA (dual energy x-ray absorptiometry). Protocols for measuring total and abdominal fat were used. The quantity of abdominal fat was assessed in the region between the second and fourth lumbar vertebrae. The severity of obstructive sleep apnea was evaluated by cardiorespiratory polygraphy.

Results: Sixty-two postmenopausal women suffering from sleep apnea were studied. Mean age of the study population was 57.54 ± 7.48 years. The severity of apnea was categorized as mild-to-moderate, if AHI was in the range of 5 to 30, whereas an AHI above 30 signified severe apnea. Total and abdominal fat content were 44.89 ± 5.86% and 50.15 ± 5.24% in patients with severe OSAS ($n = 38$), whereas these indices were 42.70 ± 7.99% and 46.20 ± 8.42% in the subset with mild-to-moderate sleep apnea. According to Student's two-tailed *t*-test, the difference between group means was significant for percentage body fat in the abdominal region ($P = 0.023$), but not for total body fat ($P = 0.13$).

Conclusion: Excess abdominal fat content aggravates sleep apnea in postmenopausal women.

Disclosure: Nothing to disclose.

P882

HMPAO SPECT with acetazolamid challenge predicts the need of early intervention in OSAHS cases with normoxaemia

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Objectives: Neurocognitive problems and excessive daytime sleepiness are frequently reported by patients with OSAHS. Hemodynamic changes provoked during the night might account for these daytime symptoms. The question of the contribution of desaturation, sleep fragmentation or hypoxia to these changes has not been previously put to test. In our present study rCBF and brain perfusion reserve was evaluated by the acetazolamide test using Tc-99 m- HMPAO SPECT.

Methods: Study population comprised of 47 consecutive male patients with an Epworth score above 10 and complaining of subjective cognitive dysfunction as memory and attention deficit. Considering the oxigen saturation profile patients got ranked into two distinct subgroups.

Group1. (*n*:20, mean age:27.8 years) OSAHS cases with normoxemia - oxigen level higher than 90% both during apnea and interpnea -.

Group2. (*n*:15, mean age: 38.7 years) OSAHS cases with intermittent hypoxia and reoxygenation (IHR) - oxigen level lower than 90% during apnea but higher than 90% during interpnea-.

Both group underwent HMPAO SPECT rCBF and acetazolamide testing.

Results: *Group1.* SPECT disclosed left parieto-temporal (*n*:9) and right parieto-temporal (*n*:6) and extensive left fronto-parieto-temporal convex lateral (*n*:4) hypofixation.

Group2. SPECT unveiled right prefrontal lateral (*n*:6) and left prefrontal lateral (*n*:5) and left parieto-temporal (*n*:2) hypofixation.

Conclusion: Considering the frequency and extension of hypofixation, normoxemia and sleep fragmentation provoked similar rCBF changes as classic IHR OSAHS cases. The different areas involved in different OSAHS subtypes should come into consideration when planning neuropsychological evaluations.

Disclosure: Nothing to disclose.

P883

Long term follow-up reveals increased risk of mortality and morbidity in supine dominant OSA patients

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Objectives: In supine dominant obstructive sleep apnea (OSA) most of the respiratory events occur in supine position [1]. Although the events in supine position can be more severe than events in non-supine position [2], the mortality and morbidity risks of supine compared to non-supine dominant OSA patients is not fully known. Presently, we investigate connection between supine OSA and morbidity and mortality in different OSA severity categories.

Methods: Ambulatory polygraphic recordings of 793 patients were retrospectively (median follow-up: 194.5 months) analyzed. Information on morbidity and causes of death was obtained from patient medical records and Statistics Finland, respectively. Risk ratios of morbidity, all cause mortality, and cardiovascular mortality of supine and non-supine dominant OSA patients were compared.

Results: Morbidity and mortality were higher in supine dominant OSA patients: risk ratios of all cause mortality 1.68, 1.82, 3.54*; cardiovascular mortality 2.37, 2.28, 5.44*; non-fatal cardiovascular events 1.85, 2.17, 3.02* in mild, moderate and severe categories, respectively. Corresponding risk ratios for non-supine dominant OSA patients were: all cause mortality 0.88, 1.43, 1.34; cardiovascular mortality 1.15, 1.49, 1.40; and non-fatal cardiovascular events 1.42, 1.44, 1.37. Statistically significant risk ratios are indicated with *.

Conclusions: Significantly elevated risks of mortality and morbidity were observed in patients with severe supine dominant OSA. To conclude, the current results underline the importance of the supine-AHI when considering the cardiovascular risk of OSA.

Acknowledgements: Financial support from Seinäjoki Central and Kuopio University Hospitals is acknowledged.

Disclosure: Nothing to disclose.

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P884

Is HLA-DRB1*03 a risk factor for obstructive sleep apnoea syndrome?

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Objective: In spite of progress made for sleep disorders such as Restless Leg Syndrome and Narcolepsy, the genetic basis of Obstructive Sleep Apnoea Syndrome (OSAS) remains largely unidentified.

HLA class II genotyping is widely used to support Narcolepsy diagnosis. No such robust association exists between HLA and OSAS. The objective of this study was to explore the genetic association of HLA with OSAS in a northern Portuguese population.

Methods: A cohort of 127 patients with OSAS (110 males and 17 females, mean ages 52/42) were studied. HLA-DRB1 genotyping was performed using sequence-specific primer PCR. A control population of 223 healthy individuals was used. Statistical evaluation relied on Chi-Square and Fisher's exact tests, and an allelic level stepwise logistic regression using forward selection.

Results: HLA DRB1*03 allele frequency was significantly overrepresented in patients (25% vs. 15%, $P = 0.016$). No significant differences were found for other HLA-DBR1 alleles.

Conclusions: Our results shows a positive association of HLA-DRB1*03 with OSAS in Portuguese patients. HLA studies in sleep disorders are useful not only to confirm the diagnosis but also to identify individuals at risk. Although preliminary, these results fit with the findings of Brunetti (2005) that reported, for an Italian population of children with OSAS, that this allele was significantly overrepresented (24.4% vs. 12.8%, $P = 0.03$). Together, these results suggest that HLA genotype may be a useful tool in the evaluation of sleep disorders beyond Narcolepsy.

Disclosure: Nothing to disclose.

P886

Evaluation of hypertension and obesity in the severity of the syndrome of obstructive sleep apnea in 100 patients

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Objectives: To evaluate the influence of arterial hypertension(AH) and overweight on OSA. The indications were apnea/hypopnea index (AHI)/ h, oxygen desaturation (OD) and the size of continuous positive airway pressure (CPAP). 100 patients were studied: 18 women and 82 men in the age of 26 to 79 y.o. All patients were studied in two nights:respiratory polygraphy(RP) and CPAP titration with RP control.

Methods: somatic and neurological status, RP, titration with CPAP.

Results: Of all patients, 58% were with hypertension and 78% were with body mass index(BMI) >30. With AHI > 30/h were 100% of patients with hypertension and 76% of those without hypertension. From all studied with BMI > 30 and AHI > 30/h were 74%. In 62% of patients with hypertension and BMI > 30, 97% had AHI > 30/h. There were seven patients without hypertension and BMI < 29, from which 3 had AHI > 30/h. From patients with hypertension and BMI > 30–76% of them had OD < 75%, and from those with hypertension and BMI < 29 only two had such. Patients after CPAP treatment without hypertension and BMI < 29 have no symptoms and in those with hypertension and BMI > 30, AHI was <10/h in 70% of the examined. From all examined a CPAP pressure of >12mmH_2O was found in 46 mainly in the group of patients with hypertension and BMI > 30.

Conclusions: AH is not an independent risk factor influencing the severity of the OSA. The combination of overweight and AH significantly impact the severity of the OSA and on the OD. Patients with BMI > 30 respond poorly from the applied CPAP treatment.

Disclosure: Nothing to disclose.

P887

Excessive daytime sleepiness and risk of obstructive sleep apnea in patients with chronic kidney disease on hemodialysis

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Objective: To assess excessive daytime sleepiness and risk of obstructive sleep apnea in patients with chronic kidney disease (CKD) on hemodialysis.

Methods: Epworth sleep scale (ESS) and Berlin Questionnaire were applied in the evaluation of patients undergoing hemodialysis in a single nephrology center in the city of Sao Paulo (SP) Brazil were evaluated.

Results: Were involved 170 patients (102 male) with mean age of 56.70 ± 16.12 years, mean weight of 68.89 ± 07.12 Kg, mean BMI of 24.93 ± 3.47 kg/cm^2. The major comorbidities found were Diabetes Mellitus (45.88%) and hypertension (76.47%). Regarding the assessment of excessive daytime sleepiness 63% had a score ≥ 10 on the ESS. According to Berlin questionnaire, thirty-three patients had low risk for obstructive sleep apnoea (OSA), while 137 patients (80%) presented a high risk. The clinical and demographic characteristic of our population is quite similar to that described in the literature, highlighting the prevalence of patients with hypertension as underlying disease.

Conclusion: In patients with CKD undergoing to hemodialysis was observed a high prevalence of excessive daytime sleepiness. When analyzing the risk for OSA by Berlin Questionnaire, a considerable number of patients presented a high risk, especially when we analyzed the association of Diabetes Mellitus and hypertension.

Disclosure: Nothing to disclose.

P888

Obstruction severity in diagnostics of sleep apnea

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Objectives: Obstructive sleep apnea (OSA) is diagnosed based on apnea-hypopnea index (AHI). However, AHI does not contain information on severity of individual respiratory events. We introduce adjusted AHI parameter incorporating obstruction and desaturation event severities with traditional AHI and compare them in estimation of the risk of mortality and morbidity related to OSA. The added value of adjusted AHI in diagnostics and clinical decision-making with individual OSA patients was explored (1–4).

Methods: Adjusted AHI was applied to ambulatory polygraphy in retrospective follow-up (mean ± SD, 198 ± 24.7 months) of 1068 patients studied due to clinical OSA suspicion. Morbidity and mortality related to OSA were investigated. Adjusted AHI was introduced to allow using the AASM guidelines for diagnostics of the severity of OSA.

Results: Patients with moderate to severe OSA had higher mortality rate compared to those without OSA. Adjusted AHI was superior to traditional AHI in detecting patients with the highest risk of cardiovascular mortality or morbidity. Furthermore, it was found easily applicable and potentially suitable for clinical use.

Conclusions: Adjusted AHI should be applied to OSA diagnostics. It improves the recognization of those patients with the highest risk of severe health consequences of OSA. Individual clinical decision-making will benefit from the use of this new diagnostic parameter.

Acknowledgements: Financial support from Kuopio University Hospital is acknowledged.

Disclosure: Nothing to disclose.

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P889

Vigilance decrements and erectile dysfunction in patients with sleep apnea

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Objectives: Obstructive sleep apnea (OSA) is associated with erectile dysfunction (ED) as well as with cognitive impairments in the realm of vigilance and sustained attention. The purpose of this study was to establish whether patients with OSA demonstrate an association between ED and objective performance deficits on a sustained attention task sensitive to daytime sleepiness.

Methods: We used a prospective cross-sectional analysis of 381 male in-patients undertaking diagnostic polysomnography for suspected OSA. Erectile dysfunction was assessed by the 15-item 'International-Index-of-Erectile-Function' (IIEF-15) questionnaire. The Epworth-Sleepiness-Scale (ESS) served as a measure of subjective daytime sleepiness. For performance measures, we used core task-parameters of a 25-min Mackworth-Clock-Test.

Results: OSA (apnea-hypopnoe-index >5/h) was present in 347 patients (91%) and ED was diagnosed in 246 patients (65%). With more pronounced ED severity, patients scored worse in all vigilance-task-parameters ($ps < 0.008$) and demonstrated more manifest impairments in overall vigilance performance (no ED: 30%, mild to moderate ED: 38% and severe ED: 53%; $P = 0.001$). Multivariate stepwise regression analyses including established risk factors for ED, OSA or vigilance impairments revealed a significant independent and robust association between erectile function (EF) and most core vigilance-test-parameters. For the same regression model with the Epworth-Sleepiness-Scale as independent variable, ESS was independently associated with measures of performance instability.

Conclusions: In OSA patients, the severity of erectile dysfunction demonstrates a positive, very robust association with impaired vigilance performance, independent of other known risk factors for ED or OSA. These results suggest a direct relationship between endothelial dysfunction in ED and neurobehavioral cognitive deficits.

Disclosure: Nothing to disclose.

P890

Serum vitamin D levels are reduced in obstructive sleep apnea patients and increase after continuous positive airway pressure therapy

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Introduction: Vitamin D has pleiotropic effects modulating numerous metabolic processes. It is reported a link between obstructive sleep apnea (OSA) syndrome and low vitamin D and high parathormone (PTH) levels. The aim of this study was to evaluate the effect of seven-night continuous positive airway pressure (CPAP) therapy on serum vitamin D, PTH and calcium levels in patients with severe OSA syndrome.

Methods: Venous blood samples were taken at baseline from severe OSA patients (Apnea-Hypopnea Index >30/h) and controls. Moreover, OSA patients underwent a final morning blood sample after seven-night CPAP therapy.

Results: Fifty-nine OSA patients were enrolled into the study and compared to 32 healthy subjects.

At baseline we found lower vitamin D and higher PTH levels in OSA group compared to controls. Notably, male-OSA showed lower PTH and vitamin D levels with respect to female-OSA patients.

We found a significant increase of vitamin D coupled with a decrease of PTH levels in OSA patients after seven-night CPAP therapy. In particular, considering vitamin D levels, the CPAP effect was evident in male, but not in female patients. At contrast, after CPAP therapy PTH levels were significantly reduced in both male and female patients.

Discussion: The present study confirms that OSA patients suffer from low vitamin D and higher PTH levels. However, CPAP therapy promotes the increase of vitamin D and the decrease of PTH concentrations particularly in male-OSA patients, probably because of sexual differences in hormones secretions, which affect bone mineralization, calcium homeostasis and both vitamin D and PTH levels.

Disclosure: Nothing to disclose.

P891

Respiratory and non-respiratory arousals induce changes in intracranial oxygenation in sleep disordered patients measured with near-infrared spectroscopy

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Objectives: Obstructive sleep apnea syndrome, restless legs syndrome, and insomnia are associated with an increased risk of cardio- and cerebrovascular morbidity. Hypoxemia and autonomic activation due to repetitive arousals are examples of possible mechanisms mediating this risk. We have found earlier that disruptions in sleep continuity (cyclic alternating pattern) are associated with transitory cerebral hypoxia in healthy subjects. In this study we measured the effects of respiratory and non-respiratory arousals on cerebral and extracranial oxygenation in patients suspected for a sleep disorder.

Methods: 42 patients were recruited. We combined continuous whole night near-infrared spectroscopy (NIRS) registration with the usual diagnostic polysomnography. Analysable NIRS signal was obtained from 21 patients. Responses of oxyhemoglobin (HbO2), deoxyhemoglobin (HbR) and total haemoglobin (HbT) were averaged during and after hypopneas, obstructive apneas and non-respiratory periodic leg-movements.

Results: During arousals associated to apnea or hypopnea episodes, HbO_2 and HbT decreased temporary while HbR increased. After a non-respiratory related leg movement there was a decrease in HbO_2 and HbT but not a significant change in HbR.

Conclusions: Temporary reductions of HbO_2 and HbT are possibly mediated by the cerebrovascular autoregulatory response during autonomic arousal. Both respiratory and non-respiratory arousals cause temporary dips in intracranial blood oxygenation which can be

one of the mediating factors for unfavourable vascular changes associated with sleep disorders.
Disclosure: Nothing to disclose.

P892

OSAS diagnosis and CPAP treatment in relation to cardiovascular disease (CVD). An assessment based on health economics

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Background and objectives: OSAS is known to be linked with increased morbidity and mortality, especially due to cardiovascular disease (CVD). Both diagnosis, based on polysomnography (PSG), and treatment with CPAP, imply considerable expenses. In this study, the long-term cost-effectiveness of CPAP treatment vs. no treatment in patients with OSA, as it examines the effect of this treatment on the incidence of CVD, is under investigation.
Methods: A Markov model was used to monitor the disease evolution in patients with OSAS based on published evidence. Data on treatment costs were collected from public hospitals in Greece. The Markov model is constructed for adults (age >55 years), suffering form severe type OSAS (AHI $\geq$ 30), and lasts for 45 years. This model comprises several cycles, and within each cycle, each patient may remain free of CVD, may develop CVD, and may decease due to a cause related to CVD or due to other causes.
Results: CPAP was found to be a cost - effective strategy compared to no treatment; the latter was due to the reduction of the cost for the CVD treatment, while it was valid only for the male population. Secondly, CPAP was more effective than no treatment, as it increases the life expectancy in both males and females.
Conclusions: CPAP was found to be clinically more effective than no treatment in relation to CVD, and a cost-effective strategy in male population.
Disclosure: Nothing to disclose.

P893

Reduced brain grey matter density is associated with lower oxygen saturation during sleep and vascular burden

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Objectives: Vascular burden, which is defined by a high number of vascular risk factors, and nocturnal hypoxia often coexists in individuals with obstructive sleep apnea (OSA). Combined together, these conditions could lead to several neuroanatomical alterations including reduction in brain grey matter density (GMD). This study aimed to evaluate the relationship between sleep variables, vascular burden, and GMD in the context of OSA.
Methods: Thirty-eight subjects (8F; age: 63.1 $\pm$ 5.1 years; mean apnea-hypopnea index [AHI]: 15.3 $\pm$ 16.0 varying between 0.2–67.3) underwent a polysomnography recording and a daytime T1-weighted magnetic resonance imaging. Correlations (peaks $P < 0.001$ uncorrected, clusters >50 voxels) with age as covariate were used to assess the relationship between regional GMD, respiratory variables (AHI, oxygen saturation) and vascular burden.
Results: Lower nocturnal mean oxygen saturation was associated with a reduced GMD in the left parietal lobule (BA 40) and the left inferior frontal gyrus (BA 9). Higher vascular burden was associated with a global and diffuse reduction in GMD in several regions of bilateral frontal, parietal and temporal lobes. No correlations were found between AHI and GMD.
Conclusions: Modest reductions of GMD were observed in the left hemisphere in association with nocturnal decreased in oxygen saturation. A more diffuse pattern of reduced GMD across the brain was associated with vascular burden. Although OSA may contribute to neuronal damage, our results suggest that vascular comorbidities have a major role in GMD alterations. Future studies should investigate OSA patients with and without vascular comorbidities in relation to their daytime functioning.
Disclosure: Nothing to disclose.

P894

Excessive daytime sleepiness and risk of obstructive sleep apnoea in patients with bronchiectasis

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Objectives: To evaluate excessive daytime sleepiness and risk of obstructive sleep apnoea in patients with bronchiectasis.
Methods: An observational study was carried out involving 21 patients with bronchiectasis at the Sleep Laboratory of the Nove de Julho University (Sao Paulo), Brazil. Personal and clinical data; abdominal and neck circumference were collected. The Berlin Questionnaire (BQ) and the Epworth Sleepiness Scale (ESS) also were administered.
Results: Mean age was 51.6 $\pm$ 15.1 years; 57.1% of the patients were female and mean BMI was 23.9 $\pm$ 3.7 kg/m^2. The median ESS was 7.5 (0–23). A low risk for the obstructive sleep apnea (OSA) syndrome was found in 61.9% (BQ) of the subjects and there was a predominance of obstructive lung disease. Mean total sleep time was 282.7 $\pm$ 69.5 min, with sleep efficiency of 79.2 $\pm$ 29.2%. Sleep stages 1 and 2 were altered and the mean value of AHI was 3.7 $\pm$ 4.9 events/h. The number of arousals was 5.6 $\pm$ 2.9/h. The oxyhemoglobin desaturation index was 5.9 $\pm$ 8.9/h and minimum oxyhemoglobin saturation was 84.5 $\pm$ 5.8%, during sleep.
Conclusion: In our study, patients with bronchiectasis did not showed excessive daytime sleepiness and had a low risk of OSA.
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Disclosure: Nothing to disclose.

P895

Association between obstructive sleep apnea severity and changes in regional cerebral perfusion in older individuals: a high resolution SPECT study

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Objectives: Obstructive sleep apnea (OSA) is associated with nocturnal hypoxia and sleep fragmentation, which could lead to impairment in daytime brain functioning. A few neuroimaging studies have explored brain functioning in OSA, but most of them included middle-aged adults and did not considered multiple indicators of OSA severity. This study aimed to examine the relationship between OSA severity and regional cerebral blood flow (rCBF) in older OSA individuals.

Methods: Fifty-nine subjects (15F; age: 64.2 ± 6.6 years) with a mean apnea-hypopnea index (AHI) of 16.3 ± 14.3 (varying between 0.2–65.5) underwent a polysomnography recording and a daytime ^{99}Tc-HMPAO SPECT. Correlations (peaks $P < 0.001$ uncorrected, clusters >50) with age and body mass index as covariates were used to assess the relationship between rCBF and three indicators of OSA severity (micro-arousal index, AHI, oxygen saturation).

Results: Higher micro-arousal index was associated with increased rCBF in the left superior frontal gyrus (BA11). Higher AHI was associated with increased rCBF in the left thalamus and the right caudate nucleus, but decreased rCBF in the left middle frontal gyrus (BA9) and the right precuneus (BA7). Lower nocturnal oxygen saturation was associated with decreased rCBF in the middle and superior frontal gyri (BA9-8).

Conclusions: Our results suggest that changes in rCBF are associated with OSA severity in older individuals and are mostly observed in the frontal lobe. These changes in rCBF had different pattern for variables associated with hypoxia and sleep fragmentation. Future studies should investigate whether OSA related changes in rCBF predict cognitive deficits in this patient group.

Disclosure: Nothing to disclose.

P896

Duration and degree of O_2 desaturation in voluntary apnea vs. longest obstructive apnea in patients with obstructive sleep apnea syndrome of severe degree

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Objectives: To establish if there is a correlation between the duration and the degree of O_2 desaturation in voluntary apnea (VA) and longest obstructive apnea (LOA) in patients with severe obstructive sleep apnea syndrome (OSAS).

Methods: The sample included 10 sever [AHI 51 ± 18 (mean ± SD)] OSAS patients [47.2 ± 12 years (mean ± SD), 9M/1F]. AHI was determined by ambulatory nocturnal cardiorespiratory polygraphy, LOA and O_2 desaturation was extracted from respiratory and SO_2 evaluation. VA was determined after a simple inspiration, duration and O_2desaturation was determined using the same cardiorespiratory polygraphy (Porty 6 SleepDoc). The StatsDirect statistical software package was used to analyze the data.

Result: VA duration was 21.1 ± 10.3 s [mean ± SD] vs. 48.1 ± 18.5 s LOA duration, $P < 0.001$; O_2 desaturation during VA was 4.1 ± 2.6% [mean ± SD] vs. 23.2 ± 15.3% in LOA, $P < 0.001$.

Conclusion: There is different tolerability for hypoxia in awake and during sleep in sever OSAS patients. VA duration is 2 times smaller than LOA, degree of O_2desaturation is greater than about 6 times during LOA. During VA patients tolerated only 4% of O_2 desaturation, while during LOA 23%.

Disclosure: Nothing to disclose.

P897

Night eating syndrome and obesity with obstructive sleep apnea, preliminary study

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Objectives: Night eating syndrome (NES) is a disorder characterized by evening hyperphagia and nocturnal ingestions, in addition to sleep and mood disturbances. Obesity is the largest risk factor for obstructive sleep apnea (OSA) and obese individuals the prevalence of this is 30%. The aim of the study was to evaluate between obesity, night eating syndrome and sleepiness in the OSA patients.

Methods: Overnight polysomnography was performed for diagnosis obstructive sleep apnea syndrome. Night eating syndrome diagnosis was made according to the diagnostic criteria for this. Age, sex, body mass index (BMI), Epworth sleepiness scale (ESS) score and apnea-hypopnea index (AHI) were recorded.

Results: One hundred (64,5%) men and 55 (35,5%) women were investigated. Their mean age was 48,8 ± 10 years and their median BMI 32,7 kg/m^2 (min-max, 19,8–65,7). Median of AHI was found 32/h (min-max, 5–145) and also ESS score was found 15 (min-max, 2–24). 13,5% (male: 17 patients, female: four patients) of our patients met criteria for NES diagnosis. The ESS score was significantly correlated with AHI but there were not found relationship between ESS score and BMI. No associations were found between NES and BMI and the severity of the OSA. But, the majority of the patients with NES were male and young.

Conclusions: We found that significant daytime hypersomnolence was associated with AHI, but there was not any relation with obesity. The ratio of NES in OSA patients was 13,5%. NES contributes to obesity in the OSA patients and additional treatment of this may be useful for obesity.

Disclosure: Nothing to disclose.

P898

Markers of endothelial function in men with obstructive sleep apnea with and without metabolic syndrome

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Endothelial dysfunction as well as metabolic syndrome (MS) are linked to cardiovascular complications. MS is highly prevalent in OSA. Mechanisms of endothelial dysfunctions in OSA are not completely understood. The aim of the study was to evaluate markers of endothelial function in men with OSA with and without MS.

Methods: 65 men with OSA and 12 snorers (controls), matched for age were included in the study. Overnight polysomnography was performed. All the components of MS were evaluated. Serum concentrations of sVCAM-1 and E-selectin were measured.
Results: Serum concentrations of sVCAM-1 and E-selectin were higher in OSA patient group compared to the controls. 34 of OSA patients had MS. Serum concentrations of sVCAM-1 and E-selectin did not differ in OSA patients with and without MS. Apnea/hypopnea index (AHI) and oxygen desaturation index (ODI) did not differ in OSA patient groups with and without MS. Both sVCAM-1 and E-selectin concentrations correlated with ODI in OSA patient group.
Conclusions: Markers of endothelial function were more increased in OSA patient group compared to snorers. Severity of OSA but not presence of MS appeard to be more involved in endothelial dysfunction in OSA.
Disclosure: This study was partly supported by the Scientific Foundation of Lithuanian University of Health Sciences.

P899

Long-term CPAP effect on body compositions and cardiometabolic factors in obstructive sleep apnea

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Background: Studies investigating the effect of continuous positive airway pressure (CPAP) on body compositions and cardiometabolic risk factors in obstructive sleep apnea (OSA) have conflicting results which is due to lack of appropriate placebo control, underlying comorbidity of enrolled subjects, and short CPAP treatment.
Aim: This study aimed to investigate six-month CPAP effects on body composition, blood pressure, glucose metabolism, lipid profile, metabolic and cardiovascular risk score, and visceral fat in healthy patients with severe OSA.
Method: Twenty-four non-smoker, healthy man with severe OSA [apnea-hypopnea index (AHI) $\geq$ 30/h] were randomised into six-month therapeutic (n = 12) and sub-therapeutic (n = 12) CPAP (1cmH_2O) groups. The endpoints were changes in blood pressure, fat mass and fat free mass (FFM), fasting insulin, HOMA-IR, levels of triglyceride, cholesterol, high-density lipoprotein (HDL), and low-density lipoprotein (LDL), metabolic score, 10-year cardiovascular risk, and visceral fat. Results were analysed based on intention-to-treat.
Results: Twenty-two completed the trial. The six-month therapeutic CPAP could significantly improve sleep latency in multiple sleep latency test (MSLT) and increase FFM compared to subtherapeutic CPAP. However, CPAP did not modify blood pressure, glucose metabolism, lipid profile, metabolic score, cardiovascular risk score, and visceral fat.
Conclusions: Six-month CPAP therapy could increase FFM but could not modify cardiometabolic factors in patients with severe OSA.
Disclosure: This work was supported by ResMed Respiratory Medicine Institute Clinical Study Fund

P900

Eating patterns and sleepiness among truck drivers

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Objective: The aim of this study was to identify dietary patterns and their association with sleepiness in long and short haul truck drivers.
Methods: Over 70% of the sample consisted of male drivers. A questionnaire on sociodemographic aspects and lifestyles was applied. Sleepiness scales (Karolinska Sleepiness Scale - KSS) were filled out eight times per day, and a 24-h food recall was answered in 2 days of work and 1 day off.
Results: Three (3) dietary patterns, Brazilian traditional (beans, rice, fishes and poultry, sausages, coffee/tea), prudent (roots, dairy products, eggs, olive and vegetal oil) and western (fast foods, soft drinks, sauces), were identified. Statistical analysis revealed significant differences in mean levels of sleepiness between groups (KSS = 3.8 SE = 0,05 for short and KSS = 3.3 SE = 0,06 for long haul; $P < 0.01$). Effects of significant interaction between dietary patterns, work hours and time of day ($P < 0.01$) were found. The drivers who had a prudent pattern of diet had the highest average sleepiness between 03:00 and 5:59 h, independent of their work hours. For those who adopted the other eating patterns the highest average score of sleepiness was around midnight.
Conclusions: Our findings show an association of diet with sleepiness, especially with regard to the prudent pattern. The prudent pattern seems to delay the truck drivers' sleepiness. This result indicates the need to understand better the relationship between sleepiness and eating patterns.
Disclosure: Nothing to disclose.

P901

Sleep apnea and oxidative stress

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Oxidative stress can be the result of exogenous factors like pollution, alcohol and drug consumption, smoking, deficient and oxidant nutrition or endogenous factors like chronic inflammatory processes. The objective of the present review was into determine if sleep apnea would be a risk factor for oxidative stress, and if the apnea treatment reversed the induced changes in oxidative balance.
In this review 80 original articles sought in the Medline database between 1994 and 2014 were included. They has focused on the study of changes in various biological parameters of oxidative stress in sleep apnea as well before and after treatment with continuous positive airway pressure. The parameters considered were lipid peroxidation, superoxide dismutase (SOD′s), glutathione peroxidases (GPx), thioredoxin reductase (TrxR).
The results showed that in subjects with sleep apnea and who do not follow treatment, lipid peroxidation increased while antioxidants such as superoxide dismutase (SOD′s) glutathione peroxidases (GPx) and thioredoxin reductase (TrxR) decreased compared to the healthy patients. After treatment by Continuous Positive Airway Pressure, the reactive derivatives of oxygen and lipid peroxidation decreased and antioxidant capacity increased proportionally to the treatment duration.
This study showed that sleep apnea was a risk factor for oxidative stress and that the treatment with continuous positive airway pressure could protect against oxidative stress caused by nocturnal intermittent hypoxia.
Disclosure: Nothing to disclose.

P902

Tae-eum type as an independent risk factor for obstructive sleep apnea

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Obstructive sleep apnea (OSA) is prevalent and associated with several kinds of chronic diseases. There has been evidence that a specific type of Sasang constitution is a risk factor for metabolic and cardiovascular diseases that can be found in patients with OSA, but there are no studies that address the association between the Sasang constitution type (SCT) and OSA. The purpose of this study was to investigate the association between the SCT and OSA. A total of 652 participants were included. All participants were examined for demographic information, medical history, and completed an interviewer-administered questionnaire on life style and sleep-related variables. Biochemical analyses were performed to determine the glucose and lipid profiles. An objective recording of OSA was done with an unattended home PSG using an Embla portable device. The apnea-hypopnea index (AHI) and oxygen desaturation index (ODI) were significantly higher in the Tae-eum (TE) type as compared to the So-eum (SE) and the So-yang (SY) types. Even after adjusting for confounding variables, the TE type still had a 2.34-fold (95% CI, 1.11–4.94; $P = 0.0262$) increased risk for OSA. This population-based cohort study found that the TE constitutional type is an independent risk factor for the development of OSA.

Disclosure: Nothing to disclose.

P903

Serum levels of microRNA-92a are associated with cardiovascular disease in obstructive sleep apnea

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Objectives: Obstructive sleep apnea(OSA) significantly increases the risk of cardiovascular disease (CVD). Endothelial dysfunction is one of the underlying pathophysiological mechanisms of cardiovascular disease, and may be altered in OSA. MicroRNA-92a is a new marker for endothelial disfunction. The aim of this study was to evaluate the relationship of serum microRNA-92a levels with cardiovascular event, severity of OSA, and polysomnographic parameters in patients with OSA.

Methods: We performed a retrospective study. An OSA-validated sleep questionnaire covering the most important cardiovascular risk factors was applied to all subjects. Furthermore, patients received a complete general physical examination and biochemistry test. Patients were divided according to their apnea-hypopnea index (AHI) scores into non-OSA group(AHI < 5), OSA group (AHI > 5). Coronary angiogram was performed in all patients to define CVD.

Results: A total of 100 patients, with a mean age of 67.22 ± 8.70 years, were included in this study. There were 39 and 61 patients in non-OSA group and OSA group, respectively. Serum miR-92a levels were significantly different between groups (non-OSA group: 4.42 ± 3.12, OSA group: 11.54 ± 9.34, F = 5.609, $P = 0.039$). Besides, serum miR-92a levels were significantly correlated with AHI, oxygen desaturation index ($P < 0.05$). Serum miR-92a levels were significantly higher in patients with CVD compared with those without (13.83 ± 7.32 vs. 5.03 ± 3.26, F = 13.234, $P = 0.001$). Multiple regression analysis demonstrated that independent predictors of CVD were serum miR-92a and diabetes in patients with OSA.

Conclusions: In OSA patients, miR-92a level is up-regulated. Our data suggest that miR-92a might have potential for predictor for CVD in patients with OSA.

Disclosure: Nothing to disclose.

P904

Prevalence of sleep-related accidents among Saudi drivers

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Introduction: The prevalence of sleepy driving and sleep-related accidents (SRA) varies widely, and no data exist regarding the prevalence of sleepy driving in Saudi Arabia. Therefore, this study was designed to determine the prevalence and predictors of sleepy driving, near-misses, and SRA among drivers in Saudi Arabia.

Methods: A questionnaire was developed to assess sleep and driving in detail based on previously published data regarding sleepy driving. The questionnaire included 50 questions addressing socio-demographics, the Epworth Sleepiness Scale (ESS), driving items, and the Berlin Questionnaire. In total, 1219 drivers in public places were interviewed face-to-face.

Results: The included drivers had a mean age of 32.4 ± 11.7 years and displayed a mean ESS score of 7.2 ± 3.8. Among these drivers, 33.1% reported at least one near-miss accident caused by sleepiness. Among those who had actual accidents, 11.6% were attributed to sleepiness. In the past 6 months, drivers reported the following: 25.2% reported falling asleep at least once during driving and 20.8% had to stop driving at least once because of severe sleepiness. Younger age, feeling very sleepy during driving, and having at least one near-miss accident caused by sleepiness in the past 6 months were the only predictors of accidents.

Conclusions: Sleepy driving is prevalent among male drivers in Saudi Arabia. Near-miss accidents caused by sleepiness are an important risk factor for car accidents and should be considered as a strong warning signal of future accidents.

Disclosure: Nothing to disclose.

P905

Bus drivers' working hours and their effects on sleep and fatigue

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Objectives: Bus drivers have very irregular work hours characterized by long shifts, early morning shifts and late evening shifts. The aim of the present study was to examine how bus drivers' working hours affects sleep and fatigue.

Methods: The study included 60 local transport bus drivers (18 females, median age: 52 years, range: 24–64 years) who were monitored with actigraphy during two weeks. The drivers also completed a sleep/wake diary that included ratings of sleep quality (1 good - 5 poor),

fatigue (1 low - 5 high) and sleepiness (Karolinska Sleepiness Scale, KSS).

Results: Early morning shifts (start time before 06 h) showed reduced sleep length (5 h and 40 min, SD: min) compared to days off (6 h and 49 min) and afternoon shifts (start time after 09 h, 6 h and 38 min). Fatigue peaked during early morning shifts (mean: 3.2 ± 1.1) compared with days off (2.6 ± .9) and afternoon shifts (2.7 ± .9). The differences were statistically significant ($P < 0.05$). Days off and afternoon shifts showed higher sleep quality (mean≈2.2) compared with the other shifts (mean≈2.7). There were no statistically significant differences in actigraphy-estimated sleep efficiency and peak KSS between shifts. Severe sleepiness (dozing off) occurred during 19% of the early morning shifts.

Conclusions: The results demonstrated that early morning work causes sleep loss and increased fatigue, and the findings are in agreement with earlier research on train drivers and airline pilots. The sleep disturbance and elevated fatigue observed during early morning shifts may have negative consequences for safety and work performance.

Disclosure: Nothing to disclose.

P906

The Epworth Sleepiness Scale for screening of the drowsy driving: comparison with the maintenance of wakefulness test in an Iranian sample of commercial drivers

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Objectives: Traffic fatalities are a major cause of morbidity and mortality in Iran. Occupational sleep medicine field needs more cost-effective and applicable tests for screening purposes. This study reports on a pilot screening study for drowsy drivers in an urban Iranian sample of commercial drivers. Sleep latency in the Maintenance of Wakefulness Test *(MWT)* is a reasonable predictor of driving simulator performance in drivers. In this study, we evaluate whether the Epworth Sleepiness Scale *(ESS)* and *MWT* are equally useful in drivers with possible Excessive Daytime Sleepiness (EDS).

Methods: 46 consecutive road truck drivers in a transportation terminal entered into this study. Drivers filled in the Iranian version of the *ESS* before undergoing the *MWT*. The *ESS* score more than 8 considered as a clinically significant daytime sleepiness.

Results: The *ESS* score of patients with normal and abnormal MWT was 3.24 ± 2.4 and 4.08 ± 3 respectively which was not significantly differenced (P value = 0.34). No significant correlation was found between the ESS and sleep latency in *MWT* (r = -0.28, 95% CI = -0.58 to 0.02). By using the receiver operating characteristic analysis, the area under the curve was found to be 0.57 (95% confidence interval = 0.37–0.77) which is not statistically acceptable (P value = 0.46).

Conclusions: Our finding showed that the *MWT* and *ESS* do not measure the same parameter.

Disclosure: Nothing to disclose.

P907

Positive impact on readmission rate of adaptive servo-ventilation therapy in heart failure

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Introduction: Though adaptive servo-ventilation (ASV) is effective for the treatment of congestive heart failure (CHF), it is unclear whether starting ASV inhibits readmission in one patient when compared with before starting it. Hence, we analyzed specifically the change in admission rate in patients who started ASV.

Methods and results: Admissions in 36 severe CHF patients who started ASV were retrospectively counted separately during 12 months before and after the commencement points (consecutive 24 months). Patients who died after ASV were excluded. The admission occurred 2.03 ± 1.44 times during period without ASV and 1.028 ± 1.30 times during ASV period ($P = 0.003$). Kaplan-Meier survival analysis showed that the readmission-free rate at 12 months was significantly improved during ASV period ($P < 0.0001$).

Conclusion: Readmission was significantly decreased by ASV even in one year older severe CHF patients.

Disclosure: Nothing to disclose.

Sleep disorders - Hypersomnia

P908

Substructural atrophy in the mesiotemporal lobe in patients with narcolepsy

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Objectives: To investigate the morphological changes of mesiotempporal lobe and its relationship with clinical features in narcolepsy.

Methods: 33 narcolepsy patients with cataplexy and 35 age-/gender-matched controls (mean ± SD: 27 ± 6 years) underwent 3.0 T MRI. The hippocampus (Hp) and the amygdala (Am) were manually traced and then converted to surface meshes with 2004 sampling points (=vertices). The Jacobian determinant was computed to explain local volume at each vertex. We assessed group differences in local volume using vertex-wise two-tailed t-tests. Associations of volume alterations with clinical parameters were examined using correlation coefficient r. Multiple comparisons were corrected using the false discovery rate (FDR) at =0.05. According to histology, we schematically outlined mesitemporal substructures on the template.

Results: Bilateral Hp atrophy (183 vertices) were identified mainly located within the CA1 subfield (FDR < 0.05). Significant Am volume reduction was found in the areas of the centromedial (CM, 102 vertices) and laterobasal nuclear groups (LB, 35 vertices). There was no volume increase in patients relative to controls (FDR > 0.2). After controlling depressive mood, age, and gender, Hp-CA1 atrophy and Am-CM atrophy were associated with longer duration of daytime sleepiness and shorter mean REM sleep latency ($|r| > 0.44$, $P < 0.01$). The Am-CM atrophy was associated with longer duration of cataplexy ($|r| > 0.47$, $P < 0.005$).

Conclusion: Subfields atrophy in narcolepsy that was found relative to controls suggests that CA1 of the Hp and centromedial area of Am are closely related to the severity of narcolepsy and play a crucial role in the circuitry of cataplexy.

Disclosure: Nothing to disclose.

P909

Narcolepsy with cataplexy post A/H1N1 vaccination - the first case reported from Cuba

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Narcolepsy with cataplexy is the most frequent type of central hypersomnia and has been recently linked to H1N1 vaccination either in children and adults. Although cases from Europe, United States and Brasil have been published, its mechanism is relatively unknown. Authors describe a case report of a 15 years old boy who developed narcolepsy with cataplexy after H1N1 vaccination in Havana. As far as it is concerned this is the first case reported from Cuba.

Disclosure: Nothing to disclose.

P910

Excessive daytime sleepiness and metabolic syndrome: a population-based study of women

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Objectives: Excessive daytime sleepiness (EDS) has been associated with specific independent symptoms associated with metabolic syndrome (MS); however it is unclear whether this relationship is sustained among individuals who meet criteria for the syndrome.

Methods: 706 women aged 21–94 year (median = 58 year, IQR 46–70), were included for analysis. Anthropometric measurements, lifestyle, mood, and health factors were obtained. Sleep duration was categorized as short (≤5 h), average (5–8.9 h) and long (≥9 h). Sleepiness was assessed using the Epworth Sleepiness Scale (ESS), and scores of ≥ 10 indicated EDS. The presence of MS was assessed according to criteria outlined by the International Diabetics Federations recommendations (2005). MS was classified if the following criteria were satisfied; waist circumference >88 cm; and any two of; raised blood pressure (systolic ≥130 mm Hg; and/or diastolic ≥85 mm Hg), treatment for previously diagnosed hypertension (use of diuretics, β-adrenergic, antihypertensive and/or hypoglycaemic medication), and/or previous diagnosis of type 2 diabetes (self-report).

Results: Overall, 95 (13.5%) women reported EDS. Those with EDS were heavier ($P \leq 0.002$), had a greater BMI ($P = 0.003$), and were more likely to report MS ($P = 0.004$). The association between EDS and MS was sustained following adjustment for age, BMI, mood disorders, medication use and hours' sleep (adjusted OR = 1.96, 95% CI = 1.09–3.53, $P = 0.03$). These findings were not explained by physical activity, alcohol intake, or socio-economic status.

Conclusion: These data suggest that EDS is associated with the presence of MS among this cross-sectional, population-based sample of women. Additional research is required to assess temporal associations with underlying sleep pathology.

Disclosure: Nothing to disclose.

P911

Health related quality of life in Korean patients with narcolepsy

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Objective: The aim of this study is to evaluate the health-related quality of life (HRQoL) in Korean patients suffering from narcolepsy.

Methods: Subjects included 55 narcoleptic patients diagnosed at the St. Vincent hospital, South Korea, who met the International Classification of Sleep Disorders (ICSD) criteria for narcolepsy. A standardized face to face interview was used to inquire about the disease and its burdens to the patients. HRQoL was recorded using the 36-item short-form Medical Outcomes Study (SF-36). Factors of influence on decreased HRQoL were evaluated by using correlation analyses.
Results: In our study 78.2% of patients showed Pittsburgh Sleep Quality Index (PSQI) over 6, and 74.5% of patients suffered from excessive daytime sleepiness which was measured by Epworth Sleepiness Scale (ESS) over 11. 54.5% of subjects showed Beck Depression Inventory (BDI) score over 14. All domains of SF-36 were statistically correlated with both by BDI and ESS (inverse correlation). Physical Functioning, Role limitations due to physical health, Role limitations due to emotional problems, Mental health, Social functioning, Bodily Pain and General health except Vitality were significantly correlated with PSQI (inverse correlation).
Conclusions: The quality of sleep, daytime sleepiness, depressive symptoms correlate with HRQoL. Daytime sleepiness is more highly correlated with social functioning while overnight sleep disturbance is more highly correlated with mental health. More studies are needed to confirm these results, so we will recruit normal health group and insomnia patients.
Disclosure: Nothing to disclose.

P912

The correlation of dream recall and clinical variables in narcoleptics

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Objectives: The relation between the dream recall and the sleep onset REM period identified during the multiple sleep latency tests (MSLT) on diagnosed the narcolepsy patients, and the characteristics of dream recall, narcolepsy symptoms, and the revelation frequency of HLA-DQB1*0602, have been investigated.
Methods: From Mar. 2004 through Sep., 2004, 35 patients(16 male, 19 female; average age 32.1 $\pm$ 13.2) were chosen. The patients were divided into three groups according to the number of dream recalls after sleep onset REM period in the MSLT; a group which recall all the dreams(n = 19), a group which recall dreams partially (n = 10), and a group which do not recall dream at all (n = 6).
Results: Dream recall during REM sleep was reported 69%, but dream recall during NREM sleep was reported only 18% while MSLT was done. Among the three groups which were classified by the number of dream recalls during MSLT, no significant differences were found regarding the demographic features and the clinical symptoms. In polysomnography tests, the time in bed of the group which did not recall dream at all proved to be longer (P = 0.006) than that of the group which recalled partially. The group which recalled all dreams showed less (P = 0.010) percentage of stage 1 sleep than the other two groups. In MSLT, not any significant difference in the average sleep latency, the frequency of REM period, or in the revelation frequency of HLA-DQB1*0602 was identified.
Conclusion: In this study, the number of dream recalls during REM sleep was greater than those of NREM sleep.
Disclosure: Nothing to disclose.

P913

Safety results from a 12-week open-label, multicenter study of sodium oxybate in patients with narcolepsy

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Objective: To evaluate the safety of sodium oxybate (SXB) in a 12-week, open-label study in patients who participated in SXB trials without being titrated to clinical effect or were SXB-naïve.
Methods: SXB was initiated at 4.5 g/night and titrated in 1.5 g increments to 6, 7.5, or 9 g/night or down to 3 g/night; stable doses of stimulants and antidepressants were allowed. Dose adjustments and safety assessments occurred every 2 weeks. Safety was the primary outcome. Efficacy was evaluated using the Narcolepsy Symptom Assessment Questionnaire (NSAQ), which assessed overall symptoms on a 5-point scale ('much worse' to 'much improved') and changes in specific symptoms; responders were defined as 'much improved' or 'somewhat improved' at week 12.
Results: 171 (85%) of 202 patients completed treatment; 8 patients (4%) discontinued for adverse events (AEs) but none discontinued for lack of efficacy. Mean age was similar across doses (41.9 $\pm$ 14.9 years), but anthropometric data were significantly different (P < 0.05); heavier patients were titrated to higher doses. AEs were reported in 114 patients (56%); 5 were serious AEs (2 were treatment-related: headache; psychosis). The most common AEs were nausea (10%), headache (7%), and dizziness (5%). Final doses were 3 g (n = 5), 4.5 g (n = 29), 6 g (n = 80), 7.5 g (n = 66), and 9 g (n = 22). Overall, 90% of patients were responders; 60% rated their overall narcolepsy symptoms as 'much improved,' which appeared dose-dependent (P = 0.029). Most patients also reported improvements on individual symptoms.
Conclusions: The safety profile of SXB in this study was consistent with parent clinical trials; most patients were responders based on the NSAQ.
Disclosure: This study was funded by Jazz Pharmaceuticals.

P914

HLA dosage effect in narcolepsy with cataplexy: additional evidence for a direct involvement of the HLA-DQ molecule in the development of the disease

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Narcolepsy with cataplexy is a sleep disorder caused by the loss of hypocretin producing neurons in the hypothalamus. It is characterized by a strong association with a specific HLA allele: *HLA-*

*DQB1*06:02*. Therefore, an autoimmune process has been hypothesized. However, the association may also be due to a gene in close linkage with *HLA-DQB1*06:02*. A functional HLA-DQ molecule consists of a DQ*a* and a DQ*b* chain. *HLA-DQB1*06:02* (DQ*b*) has a strong preference for binding with HLA-DQA1*01:02(DQ*a),* and together they form the functional DQ0602 dimer. A dosage effect would be expected if the HLA-DQ0602 dimer itself is directly involved in the aetiology. An increased expression of the HLA-DQ0602 dimer is expected in individuals homozygous for *HLA-DQB1*06:02-DQA1*01:02* but also in individuals heterozygous for *HLA-DQB1*06:02* and homozygous for *HLA-DQA1*01:02*. To study the impact of the expression of the HLA-DQ0602 dimer on narcolepsy susceptibility, 274 Dutch narcolepsy patients and 1272 Dutch control subjects, all of them positive for *DQB1*06:02* (heterozygous and homozygous) were HLA-genotyped with attention not only for *DQB1* but also for *DQA1*01:02*.

*DQB1*06:02-DQA1*01:02* homozygosity was significantly more seen in patients when compared with controls (O.R. 2.42) confirming previous observations. More importantly, a significantly higher prevalence of homozygosity for *DQA1*01:02* was found in HLA-DQB1*06:02 heterozygous patients compared to controls (OR = 2.26, $P < 0.0002$). The latter finding cannot be explained by a gene closely linked to HLA-DQB1*06:02 and clearly supports a direct role of the HLA-DQ molecule in the development of disease.

Disclosure: Dr. Lammers has served as a paid member of the UCB advisory board and received lecture fees and conference travel support from UCB pharma. Dr. Lammers also did consultancy for UCB pharma and provided expert testimony for UCB pharma, Jazz pharmaceuticals, and Bioprojet. A. The other authors report no financial conflict of interest.

P915

Traffic exposure: increased risk of both daytime sleepiness and habitual snoring

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Objectives: The prevalence of snoring and daytime sleepiness is high and a large proportion of these symptoms is not explained by traditional known risk factors. Knowledge about possible association between snoring and daytime sleepiness with traffic air pollution and noise is lacking.

Methods: As part of the Respiratory Health in Northern Europe study (http://www.rhine.nu), 12319 subjects (53% women) aged 38–65 years answered in 2010-12 a questionnaire on exposure to traffic air pollution. We performed logistic regression with bedroom near a road with moderate/much traffic and bedroom with traffic noise as proxies for traffic air pollution exposure. Outcomes were habitual snoring and daytime sleepiness (more than 3 days a week). Analyses were sex-stratified and adjusted for study centre, age, smoking habits, educational level, physical activity and body mass index.

Results: Ten % lived near a busy road and 6% slept in a bedroom with traffic noise. Habitual snoring was reported by 24% and daytime sleepiness by 22%. Both men [OR 1.5 (1.2, 1.9)] and women [OR 1.4 (1.0, 2.0)] had significantly increased risk for daytime sleepiness after adjustment. After adjustment for covariates, women who slept in a bedroom with traffic noise had 1.51 times higher odds (95% CI: 1.2, 1.9) for habitual snoring than unexposed women.

Conclusions: Traffic air pollution and noise exposure measured by living close to a busy road, increase the prevalence of daytime sleepiness in both sexes. Habitual snoring is 50% more common in women sleeping in a bedroom with traffic noise.

Disclosure: Nothing to disclose.

P916

Polysomnographic and actigraphic characteristics of patients with H1N1-vaccine-related and sporadic narcolepsy

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Objectives: Incidence of narcolepsy was increased in many European countries after pandemic H1N1 influenza vaccine, Pandemrix©, was used in late 2009. The risk was increased especially in children and adolescents, but to a lesser degree also in adults. We aimed to compare the characteristics in Multiple Sleep Latency Test (MSLT), polysomnography, and actigraphy among H1N1-vaccine-related and sporadic narcolepsy patients.

Methods: 125 unmedicated narcolepsy patients, aged 4–61 years, with the available data from MSLT and polysomnography and/or actigraphy of 1–2 weeks were included in this case-series study. Of those, 69 (55%) were diagnosed to have an H1N1-vaccine-related narcolepsy and 56 a sporadic narcolepsy.

Results: Patients with H1N1-vaccine-related narcolepsy had shorter diagnostic delay, younger age at diagnosis, lower periodic leg movement index during sleep, and earlier sleep-wake rhythm compared with sporadic cases; all differences were statistically significant. They also had shorter sleep latency and more sleep onset REM periods in MSLT, but these results were strongly age-dependent. Actigraphy showed quantitatively less sleep and more sleep fragmentation than polysomnography.

Conclusions: Regarding polysomnographic and actigraphic characteristics, there were no dramatic deviations between H1N1-vaccine-related and sporadic narcolepsy. Circadian rhythms indicated some interesting new findings with respect to the H1N1-vaccine-related disease. Actigraphy recording of one to two weeks is useful in studying nocturnal aspects of narcolepsy and sleep-wake rhythms of narcoleptic patients.

Acknowledgments: We thank Anne Huutoniemi and Raili Reemets for valuable help with organizing the data.

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P917

Glucose tolerance in patients with narcolepsy and matched healthy controls

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Objectives: Observations of disturbed glucose metabolism in narcolepsy with cataplexy and orexin-A deficiency are controversial. Some evidence for a role of orexin-A in energy metabolism arises

from the location of orexin producing neurons in the hypothalamus, animals with orexindeficiency and intracerebroventricular orexin-A administration. Furthermore, narcoleptics tend to be obese, have a higher prevalence for diabetes type 2 and a metabolic syndrome. Whereas most narcoleptics seems to have metabolic changes, some patients are normal or underweighted. This indicates the existence of two forms of narcolepsy with respect to glucose metabolism.

Methods: We performed an oral glucose tolerance test (OGTT) in 26 participants. The group consists of 13 patients with narcolepsy with cataplexy and 13 BMI and age matched healthy subjects. To exclude influence of sleep disturbance, all subjects slept the night before OGTT under polysomnografic control.

Results: No correlations of sleep and glucose parameters were found. Multivariat analysis of variances with the factors 'time' (minutes after glucose intake), 'group' (narcolepsy and control group) and 'BMI' (normal and overweight) showed a significant interaction effect of the three variables ($P = 0.028$) and a significant main effect of time ($P < 0.001$). Post hoc t-tests showed a significant higher glucose level in obese narcoleptics 120 min after glucose intake ($P = 0.003$).

Conclusions: Whereas fasting glucose shows no differences between groups, postprandial glucose tolerance was disturbed in obese narcoleptics. These findings confirm the assumption of two different types of narcolepsy regarding glucose metabolism and give further evidence for an involvement of orexin in glucose metabolism.

Disclosure: Nothing to disclose.

P918

Improvement of divided attention in narcolepsy by intranasal orexin-A

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Objectives: In narcolepsy with cataplexy, a disease most likely caused by an orexin deficiency, apart from sleep and metabolic dysregulation neuropsychological impairments have been described. Whereas these patients showed no differences in most short-term tests of attention, deficits in divided attention have been described. These deficits also persist under stimulant medication.

Methods: In a double blind, placebo-controlled experiment, we administrated in repeated measures randomized intranasal orexin-A and placebo to 14 patients with narcolepsy and cataplexy in the morning. After administration performance of attention were determined at three times a day (10:40 a.m., 12:15 p.m. and 3:40 p.m.) by the subtest 'Geteilte Aufmerksamkeit' of the Test for Attentional Performance.

Results: After orexin-A patients had fewer false reactions ($P = 0.026$) and a tendency towards a reduced reaction time ($P = 0.079$).

Conclusions: Intranasal orexin-A in the morning enhances impaired attention in patients with narcolepsy and cataplexy. Whether this activation effect is a direct consequence of orexin-A or mediated by more stable wakefulness remains unclear and needs further studies with lager sample sizes and other attention tests.

Disclosure: Nothing to disclose.

P919

Differences in sleep architecture between narcolepsy and idiopathic hypersomnia: an overnight polysomnographic study

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Objectives: To determine differences in sleep architecture between patients with narcolepsy and idiopathic hypersomnia (IH), with potential diagnostic application.

Methods: Retrospective analysis of overnight polysomnography (PSG) data in 58 hypersomnia patients (narcolepsy $n = 27$, IH $n = 31$). Sleep diagnoses were made by experienced clinical somnologists based on the ICSD-2 criteria. Sleep architecture was objectified using several measures. The sleep fragmentation index (SFI) was defined as the total number of transitions from either sleep or wake divided by the total sleep time (TST) in hours. The transition index (TI) per sleep stage was defined as the total number of transitions out of that sleep stage divided by TST in hours. For the most discriminative parameters, formal diagnostic performance was assessed.

Results: Narcoleptic patients showed an increased number of sleep stage shifts (SFI narcolepsy 21.4 $\pm$ 7.7, IH 14.1 $\pm$ 5.0, $P \leq 0.001$). Sleep fragmentation was most pronounced in NREM1 sleep (TI-NREM1 narcolepsy 7 $\pm$ 2.8, IH 3.8 $\pm$ .2.1, $P < 0.001$). With a cut-off at 7, TI-NREM1 had diagnostic value for narcolepsy (sensitivity 55.5%, specificity 90.5%). A percentage of TST spent in NREM1 sleep (NREM1%) of more than 10% yielded a sensitivity of 63% and specificity of 93.5% for narcolepsy. The presence of a sleep-onset REM period (SOREMP, REM latency <15 min) and/or NREM1% >10% had a sensitivity of 70,4% for narcolepsy with a specificity of 93.5%.

Conclusion: Indices of nocturnal sleep fragmentation may have diagnostic value for narcolepsy. The percentage of TST spent in NREM1 besides the presence of a SOREMP was shown to have the best discriminatory properties.

Disclosure: Nothing to disclose.

P920

The utility of sleep onset REM (SOREM) in differential diagnosis of central hypersomnias

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Although upcoming criteria will mandatorily require measurements of cerebrospinal fluid hypocretin-1, in its absence, nocturnal polysomnography and multiple sleep latency test (MSLT) remain important diagnostic tools in diagnosis of central hypersomnias.We investigated the utility of sleep onset REM (SOREM) in differential diagnosis of central hypersomnias.We evaluated a total of 101 patients consecutively within the last three years, who had a normal polysomnographic examination (other than the presence of SOREM and/or REM without atonia) and had a latency of $\leq$8 min in MSLT. We classified patients into three groups as narcolepsy group with at least two SOREM; idiopathic hypersomnia group with no SOREMs

and para-idiopathic hypersomnia group with one SOREM.Gender was similar between two groups.The mean age was lowest in narcolepsy group (32.2 ± 13.6 years) and highest in idiopathic hypersomnia group (51.1 ± 16.0 years, $P < 0.001$), para-idiopathic hypersomnia group (45.9 ± 14.3 years) was in between.In polysomnography, sleep onset ($P = 0.037$) and REM latency(0.005) were shorter in narcolepsy and para-idiopathic hypersomnia group than idiopathic hypersomnia group.REM without atonia was present in 38.3% of narcolepsy group, 23.8% in para-idiopathic hypersomnia group, and in 11.8% of idiopathic hypersomnia group ($P = 0.045$). In MSLT, sleep onset was 2.9 ± 2.3 min in narcolepsy group, 2.9 ± 1.3 min in para-idiopathic hypersomnia group, and 7.2 ± 2.2 min in idiopathic hypersomnia group ($P < 0.001$). Cataplexy was present in 51.1% of narcolepsy group, 4.8% of para-idiopathic hypersomnia group, but none of idiopathic hypersomnia group ($P < 0.001$).These data show the presence of SOREM, regardless of its number, has a value in determination of subtypes of central hypersomnias.

Disclosure: Nothing to disclose.

P921

Patients with narcolepsy in Slovenia

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Objectives: To determine the number of patients with narcolepsy in Slovenia, describe their typical clinical features and the diagnostic criteria they met on polysomnography (PSG), the mean sleep latency test (MSLT) and HLA typing.

Methods: Retrospective study of all narcolepsy patients referred to the National Sleep Disorder Centre at the Institute of Clinical Neurophysiology, University Medical Centre Ljubljana in the period from May 1994 to September 2013.

Results: There are currently only 38 patients with the diagnosis of narcolepsy in Slovenia. The average time lapse from onset to diagnosis is 17 years. The time lapse is much longer for older patients. The prevalence of narcolepsy in Slovenia is 1.85 to 100 000 inhabitants. All patients had excessive daytime sleepiness (EDS), 89% cataplexy, 66% hallucinations and 37% sleep paralysis at the time of diagnosis. Characteristic changes on PSG and MSLT were present in 97% of all tested patients. HLA DQB1*0602 is present in 88% of all tested patients. The most common differential diagnoses found were obstructive sleep apnoea syndrome (OSAS) and hypersomnia. Large majority of patients is on medications and the drug mostly prescribed in recent years is sodium oxybat.

Conclusion: The prevalence of narcolepsy in Slovenia is much lower than expected and the disease is most likely underdiagnosed. Patients' clinical features are consistent with those in literature and the overwhelming majority met the diagnostic criteria on PSG and MSLT.

Disclosure: Nothing to disclose.

P922

Decreased CPT1 function is associated with and a risk factor for narcolepsy and essential hypersomnia

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Background: Narcolepsy is often associated with metabolic abnormality and nocturnal sleep disruption. We identified *CPT1B* gene as a novel narcolepsy-susceptible gene and found that abnormally low serum acylcarnitine was associated with the diagnosis of narcolepsy. To clarify the details of altered fatty acid metabolism and its clinical relevance, we measured individual acylcarnitines and evaluated CPT1 function in narcolepsy and essential hypersomnia (EHS) patients.

Methods and findings: Subjects were hypersomnia patients visiting Japan Somnology Center (94 narcolepsy, 49 EHS) and 68 healthy controls. 26 major individual acylcarnitines were measured in red blood cells by electrospray tandem mass spectroscopy.

Decrease of long chain acylcarnitines were observed in both narcolepsy and EHS. We calculated the ratio of C0/(C16~C18) as a marker for CPT1 function. CPT1 function was lower in narcolepsy ($P < 0.0001$) and in EHS ($P = 0.017$) compared to controls, indicating the decreased CPT1 function was involved in hypersomnia. We also identified the risk SNP was associated with lower CPT1 function in narcolepsy ($P = 0.020$). Logistic analysis revealed that CPT1 function was associated with the hypersomnia diagnosis with odds ratios of 1.62 ($P < 0.001$) for narcolepsy and 1.41 ($P = 0.019$) for EHS. Furthermore, narcolepsy patients with severe nocturnal sleep disruption showed lower CPT1 function

Conclusions: We identified altered concentration of acylcarnitines and decreased CPT1 function in hypersomnia. CPT1 function was a risk factor for hypersomnia. We also revealed the clinical relevance of CPT1 function in narcolepsy symptom. Our results provide further evidences that inappropriate fatty acid metabolism was critically involved in the pathophysiology of hypersomnia.

Disclosure: Nothing to disclose.

P923

Alteration of white matters in narcolepsy with cataplexy; diffusion tensor imaging study

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Objectives: Most of the previous neuroimaging studies demonstrated relevant lesions with hypocretin system. Recently there is increasing interest in the psychiatric phenotype of narcolepsy and the possibility of direct consequence of the pathophysiology of the disease. We applied diffusion-tensor imaging (DTI) for measurements of mean diffusivity (MD) a fractional anisotropy (FA) to investigate brain white matter change and correlation with clinical manifestation of narcolepsy.

Methods: We investigated white matter alterations in 22 narcolepsy with cataplexy patients, comparing to 26 healthy controls using whole head diffusion tensor imaging (DTI). We performed voxel-wise statistical analysis of the FA and MD images using Tract-Based Spatial Statistics method. The FA and MD differences between narcolepsy and controls were examined using permutation-based statistical analysis. We also examined the relationship between the diffusion measures and neuropsychiatric data.

Results: Patients with narcolepsy showed significant FA decreases were localized in the bilateral white matter adjacent to the anterior cingulate, fronto-orbital area, the frontal lobe, anterior limb of internal capsule and corpus callosum. Positive correlation between MD and

Beck depression inventory (BDI) score in the white matter tracts of the bilateral middle, inferior frontal gyrus, bilateral superior temporal gyrus and bilateral anterior cingulate gyrus.

Conclusions: This study showed that White matters in anterior head are extensively affected in patients with narcolepsy relative to controls. Alterations of frontal and cingulate white matter in relation to depression scores in patients may provide another anatomical substrates for depressive mood and emotional instability in patients with narcolepsy.

Disclosure: Nothing to disclose.

P924

Sleepiness and performance is disproportionate in patients with nonorganic hypersomnia compared to idiopathic hypersomnia, narcolepsy and obstructive sleep apnoea syndrome

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Objective: To determine the diagnostic value of sleepiness and performance tests to differentiate between Nonorganic Hypersomnia (NOH), Idiopathic Hypersomnia (IH), Narcolepsy (NAR) and Obstructive Sleep Apnoea Syndrome (OSAS).

Methods: Retrospective comparison of the Multiple Sleep Latency Test (MSLT) and Steer Clear reaction time test (SC) in four patient groups complaining about excessive daytime sleepiness (EDS; Epworth Sleepiness Scale >10): 24 patients with NOH, 18 patients with NAR, 31 patients with IH and 38 patients with mild to moderate OSAS.

Results: The mean sleep latency in MSLT indicated mild objective sleepiness in patients with NOH (8.6 $\pm$ 4.2 min), IH (7 $\pm$ 3 min) and OSAS (6.9 $\pm$ 3.8 min), but more severe sleepiness in patients with NAR (2.6 $\pm$ 1.7 min). In the SC, patients with NOH performed worst (error rate = 8.8% $\pm$ 9.6) and similar to patients with NAR (8.3% $\pm$ 8.3), while patients with OSAS (5.1% $\pm$ 5.2; $P = 0.018$ compared to NOH) and IH performed much better (4.3% $\pm$ 2.8; $P = 0.021$ compared to NOH).

Conclusions: Among sleepy patients, the combination of a high error rate in the SC along with mild sleepiness in an objective vigilance test (MSLT) in a patient with subjective sleepiness is suggestive of NOH and discriminates the three most ambiguous groups (NOH, IH and NAR) of sleepy patients. This disproportionately high error rate in NOH may be caused by factors unrelated to sleep pressure such as anergia, reduced attention and motivation affecting performance but not EEG based sleepiness measurements.

Disclosure: Nothing to disclose.

P925

Norwegian H1N1-vaccinated Kleine-Levin syndrome and idiopathic hypersomnia cases - is narcolepsy the only CNS hypersomnia occurring after pandemrix?

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Objectives: The CNS hypersomnias, narcolepsy, Kleine-Levin syndrome (KLS), and Idiopathic Hypersomnia (IH) have been considered so-called spectrum disorders/a disease continuum. Since the dramatic increase in narcolepsy cases after the 2009/10 H1N1-massvaccinations with Pandemrix in Norway we have centrally registered all reported CNS hypersomnia cases. We here present the Norwegian KLS and IH cases occurring after Pandemrix-vaccination.

Methods and results: 4 KLS and 2 IH cases have occurred after Pandemrix-vaccination in 2009–13. The KLS patients were 14–16 years, ♀:♂ 1:3, disease onset 1, 11, 30 and 32 months after vaccination (case 2 possibly had disease onset already after 1–2 months as school reported huge coffee consumptions and altered behaviour). KLS-symptoms were recurrent hypersomnia periods (4/4), zombie-like behaviour (3/4), cognitive symptoms (4/4), hyperphagia (3/4), hypersexuality (1/4). 2/2 were HLA-DQB1*0602-positive and had normal CSF hypocretin-1 levels (asymptomatic period). EEG was normal in 1/2 (asymptomatic period) and abnormal with slow wave activity in 1/2 (hypersomnia period). The IH cases (2/2 ♀, 51 and 13 years) had onset of monosymptomatic excessive daytime sleepiness 1 and 10 months after vaccination, respectively. PSG showed at total sleep time >10 h, MSLT with a mean sleep latency $\leq$8 min without REM-sleep. CSF hypocretin-1 was normal in 1/1.

Conclusions: In accordance with a single unpublished Irish KLS case, the Norwegian KLS and IH cases point to that narcolepsy may not be the only CNS hypersomnia associated to Pandemrix-vaccination. However, increased incidence and a causal association are not established which needs further investigation in Norway and other Pandemrix-vaccinated populations.

Disclosure: Nothing to disclose.

P926

Educational challenges for children with narcolepsy in Norway

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Objectives: Prompted and funded by the Norwegian Health Directory, we have since 2010 followed up children who developed narcolepsy after 2009 (+/- Pandemrix-vaccination). Our aim was to study the school experience of these children, and to explore how those responsible for teaching coped to the situation to stimulate learning processes.

Methods: School observations and interviews of >20 children with narcolepsy +/- Pandemrix-vaccination. Interviews of parents, teachers and employees in community care services.

Results: The report from all interviewed was that school performance was deteriorated after development of narcolepsy. Teachers and parents were expecting the children to perform normally due to the understanding that despite some attention difficulties, the intelligence and cognitive capacity was maintained. The teachers misunderstood the behavioural consequences (anger, frustration, aggression) of the narcolepsy core symptoms (micro-sleep and sleepiness). Hence, they tried to use the traditional child educational reward-systems to control the children's anger/frustration, which was useless and contributed to further frustration, because the child cannot control the sleepiness causing the behaviour.

The children reported to spend all their energy trying to follow-up in school and a reduced self-image, lack of social life and reduced sport/leisure activities.

Conclusions: We find that narcoleptic children do not have a proper learning environment, mainly explained by insufficient knowledge about narcolepsy core symptoms by the teachers (and parents). We also find indications that this results in reduced social life after school.

We advocate the need for early and specific information about educational approaches in order to optimize learning environment for narcolepsy.

Disclosure: Nothing to disclose.

P927

Diagnostic potential of nocturnal sleep stage transitions to identify narcolepsy type 1

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Introduction: The diagnosis of narcolepsy type 1 (NT1) is based on the presence of cataplexy, on MSLT and nocturnal polysomnography findings and on cerebrospinal hypocretin-1 measurement. Hypocretin-1 is a key neurotransmitter to promote wakefulness and to stabilize wake and sleep states. We aimed at evaluating the diagnostic significance of nocturnal sleep stage transitions and of sleep onset REM periods (SOREMPs) in the context of central disorders of hypersomnolence.

Methods: We evaluated the occurrence of SOREMP and of sleep stage transitions between sleep and wakefulness, and non-REM - REM sleep and wakefulness, and non-REM sleep stage 1 - non-REM and wakefulness (W-N1-NR-R) in the nocturnal sleep of 96 consecutive patients with NT1 (n = 41), narcolepsy type 2 (NT2, n = 7), idiopathic hypersomnia (IH, n = 19), and 'subjective' excessive daytime sleepiness (sEDS, n = 29).

Results: NT1 and NT2 had more frequently SOREMP than IH and sEDS. NT1 patients had more transitions between different combinations of sleep stages and wakefulness, most notably the W-N1-NR-R transition index. ROC curve analysis confirmed that both SOREMP (area under the curve of 0.741 $\pm$ 0.054, $P < 0.0005$) and the W-N1-NR-REM transition index (area under the curve of 0.732 $\pm$ 0.052, $P < 0.0005$) had a comparable sensitivity and specificity profile to identify NT1.

Conclusions: The nocturnal occurrence of SOREMP and of high sleep stage transitions comparably identify NT1 in the differential diagnosis of central disorders of hypersomnolence. In their absence, the MSLT and cerebrospinal hypocretin-1 measurement are mandatory for a correct diagnosis.

Disclosure: Nothing to disclose.

P928

Weight loss persists in narcolepsy patients using sodium oxybate

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Objectives: Two thirds of narcolepsy patients are overweight and half of them obese. Why narcolepsy patients gain weight, is unknown. Recent observations have shown that patients may lose weight when using sodium oxybate (SXB). This study is done to establish if this weight loss persists.

Methods: Sixty-two adult narcolepsy with cataplexy patients were included. Weight and length were measured in order to calculate Body Mass Index (BMI) before and during a prolonged treatment period with SXB and/or modafinil. A mixed effect regression model was performed to compute BMI alterations. Baseline BMI, medication, time, and gender were selected as fixed effects and participants and time as random effects.

Results: Forty-three patients were treated with SXB monotherapy, 19 with modafinil monotherapy, and four started SXB treatment as add on to a stable dose of stimulants for at least 3 months.

There was a trend of a higher baseline BMI in the SXB group (mean $\pm$ SD: 28.6 $\pm$ 4.6 kg/m2 vs. 26.3 $\pm$ 4.5 kg/m2 $P = 0.07$). BMI tended to increase over the mean two year follow up period in the modafinil group (+0.97 kg/m2, SE: 0.52, $P = 0.07$), which differed from the BMI decline in the SXB group (-3.27 kg/m2, SE: 0.75, $P < 0.001$). In the SXB group females lost more weight than males (-2.67 kg/m2, SE: 1.08, $P = 0.01$).

Conclusions: Weight loss in narcolepsy patients using SXB remains over a two-year period, particularly in females. Modafinil treatment does not result in weight loss.

Disclosure: C.E.H.M. Donjacour and G.J. Lammers have in the past received research grants, lecture fees and travel grants from UCB pharma. G.J. Lammers is also a memeber of the Xyrem advisory board. No grants were received for this study.

P929

Oral L-carnitine as treatment for narcolepsy during pregnancy: a case report

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Objectives: The management of narcolepsy during pregnancy is still unclear and puzzling. Oral L-Carnitine was recently demonstrated effective in reducing excessive daytime sleepiness in narcolepsy patients. Moreover, L-Carnitine therapy present no contraindications during pregnancy and could be advantageous. We test oral L-Carnitine treatment in a narcoleptic patient during pregnancy.

Methods: Oral L-carnitine therapy titrated up to 500 mg b.i.d was administered to a narcolepsy patient during pregnancy. Subjective and objective daytime sleepiness were assessed after conception and before L-Carnitine treatment as well as at the end of the second trimester,by means of Epworth Sleepiness Scale (ESS) and Multiple Sleep Latency Test (MSLT).

Results: The patient was diagnosed as affected by narcolepsy without cataplexy when she was 25-year old. She was successfully treated with modafinil. Since she manifested the need to be pregnant modafinil was slowly withdrawn. After conception patient complained severe sleepiness. Her ESS was 19 and MSLT documented a mean sleep latency (MSL) of 4.2 min and three sleep-onset REM periods (SOREMPs). Therefore, patient started oral L-Carnitine treatment titrated up to 500 mg b.i.d. Patient well tolerated therapy and referred a progressive improvement of sleepiness. At the end of the second trimester ESS was 14 and MSLT showed a MSL of 16 min without SOREMPs.

Conclusions: The management of narcolepsy during pregnancy is still debated. We report the first patient successfully treated with oral L-Carnitine during pregnancy. The safe profile of L-Carnitine in pregnancy should induce to evaluate its efficacy in large controlled studies.

Disclosure: Nothing to disclose.

P930

Clinical efficacy of intravenous immunoglobulins (IVIg) in pediatric type-1 narcolepsy: a case-controlled study

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Objectives: Immunotherapy has been reported in children and adults with narcolepsy with cataplexy (NC). The aim of the present study is to evaluate the clinical efficacy of high-dose IVIg in NC pediatric patients.

Methods: A retrospective case-controlled study was conducted. Post-IVIg NC children (n = 24) were matched and compared to non-post-IVIg NC patients (n = 24), using the differences in clinical scale scores obtained during the first and follow-up visits [(Ullanlinna Narcolepsy Scale - UNS, Pediatric Daytime Sleepiness Scale - PDSS, and Child and Adolescent Sleepiness scale – CASS] and the median sleep latency increase (Maintenance of Wakefulness Test-MWT). Statistic tests used were generalized linear models.

Results: 24 NC children (including 71% post (A) H1N1 vaccine cases) received three IVIg infusion sessions (1 gr/kg/day) on a 4-week interval basis (mean age 11.3 yo). Significant differences were found in post-IVIg compared to non-post-IVIg for PDSS and CASS scores ($P < 0.01$ and $P = 0.02$ respectively for modafinil treated patients and $P = 0.01$ and $P = 0.03$ respectively for methylphenidate treated patients). Mean sleep latency scores at MWT improved in the post-IVIg group to 13[11;16] min after IVIg infusions whereas in the control group, mean sleep latency dropped to 5.9[3.3; 10.4] min at the end of the follow-up period.

Conclusion: High-dose IVIg therapy showed clinical efficacy in NC children by increasing mean sleep latency on MSLT measures and by decreasing subjective daytime sleepiness on sleepiness scales. None of the patients experienced significant side effects from IVIg infusions.

Disclosure: Nothing to disclose.

P931

Symptoms of attention-deficit hyperactivity disorder (ADHD) in pediatric narcolepsy

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Background and objective: Retrospective reports in adults with narcolepsy have identified childhood symptoms of attention-deficit hyperactivity disorder (ADHD) as a significant area of difficulty. The aim of the current study was to evaluate the burden of ADHD symptoms in children with narcolepsy.

Methods: This was a cross-sectional, observational, non-randomized study. Children (n = 108, aged <18 years) presenting with narcolepsy with cataplexy (NC) or without cataplexy (NwoC) were seen in four french national reference centers and compared with age matched healthy controls (n = 67). Between-group statistical comparisons were conducted within a generalized linear models framework.

Results: ADHD symptoms were approximately 2-fold greater compared with controls, significant educational problems were evident compared with controls. For total ADHD symptoms, there was a 2-fold increase in the NwoC group vs. controls ($P < 0.001$) and a 1.8-fold increase in the NwC group vs. controls ($P = 0.001$). For inattention symptoms, there was a 2.2-fold increase in the NwoC group vs. controls ($P < 0.001$) and a 1.9-fold increase in the NwC group vs. controls ($P < 0.001$).

Conclusion: We confirm that ADHD symptoms represent a significant burden in children and adolescents with narcolepsy. Although there are some limitations to the study, these findings may have relevant clinical and therapeutic applications in the future.

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P932

Effector and regulatory T-cells in narcolepsy

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Background and objective: Narcolepsy is a rare disease which affects approximately 5 out of 10 000 individuals and is due to the selective loss of neurons secreting hypocretine. Recrudescence of narcolepsy was observed after vaccination against or in people infected with influenza (A) H1N1 virus in 2010. The disease is closely associated with Major Histocompatibility Complex (MHC) type II, with 95% of the patients carrying the HLA-DBQ10602 allele. Recently, CD4 T cells cross-reacting with hypocretine epitope(s) and H1N1 epitope(s) have been identified in vaccinated and infected patients. This strongly suggests that narcolepsy is an autoimmune disease.

Methods: As autoimmune diseases are caused by an imbalance between regulatory T cells (Treg) and effector T cells (Teffs) responses, we analyzed these cell populations in pediatric narcoleptic patients (NC, n = 35) vs. pediatric controls (Controls, n = 32).

Results: We found similar percentages of Treg in both groups, although the proportion of activated Treg was higher in NC patients. In addition, the numbers of memory CD4 T cells ($CD62L^+$ $CD45RA^-$), $CD69^+$ CD4 + and $CD69^+$ CD8 + activated T cells were higher in

NC patients. These results support an autoimmune origin of NC, and should prompt further studies of Tregs in NC.
Disclosure: Nothing to disclose.

P933

Association between sleep duration, unmet sleep need and excessive daytime sleepiness in Korean adults

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Objective: The aim of this study was to examine the separate and combined association of both sleep duration and unmet sleep duration to excessive daytime sleepiness (EDS) in Korean adults.
Methods: The subjects included 2769 Korean adults aged 19 years and older in a multi-stage clustered sampling from 15 administrative districts. They completed questionnaires about sleep habit over the previous 1 month. The question regarding sleep need was 'how many hours do you think is enough?' Habitual sleep duration was defined by [(weekday sleep duration $\times$ 5 days) + (weekend sleep duration $\times$ 2 days)]/7 days. Unmet sleep duration was calculated as sleep need minus habitual sleep duration. The participants with an Epworth Sleepiness Scale >10 were considered as having EDS.
Results: The prevalence of EDS was 330 (11.9%). 31.9% reported not getting at least 7–8 h of habitual sleep. Unmet sleep duration above 0 was evident in 30.2%. In adjusted multivariate logistic regression analysis, unmet sleep duration was related with EDS [(0 to <2 h, OR = 1.75; 95% CI: 1.75–2.41), ($\geq$ 2 h, OR = 2.29; 95% CI: 2.29 (1.64–3.20)]. However, short habitual sleep duration (vs. 7 to <8 h) was not statistically significant [(<6 h, OR = 0.97; 95% CI: 0.64–1.48), (6 to <7 h, OR = 1.06; 95% CI: 0.77–1.460)].
Conclusion: EDS is associated with unmet sleep duration but not habitual sleep duration when evaluated both variables together. We suggest individual unmet sleep duration is more important in terms of EDS.
Disclosure: Nothing to disclose.

P934

Physical fitness in narcolepsy

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Objectives: Physical fitness is modified by genetic factors and by training (the amount of physical exercise performed). Narcolepsy is associated with obesity/overweight and there is no clear evidence of higher energy consumption in narcolepsy. We can thus speculate that the intensity of physical activity in narcolepsy is lower and that the muscles of narcoleptic patients are not able to utilize the energy at a higher rate.
Methods: The measure of physical fitness is maximal oxygen uptake - VO_{2max}, (spiroergometry). We used the following protocol: 3 min 0, 5, 3 min 1 W/kg and the ramp 10W/10 s until a subjective maximum effort. 21 subjects suffering from narcolepsy type 1 and 8 patients suffering from narcolepsy type 2 were included in the study. Their average age was 34.9 $\pm$ 11.5 (SD) years, disease duration 15.8 $\pm$ 10.5 years, and BMI 30.3 $\pm$ 5.8. Age and sex control subjects were taken from the 'International Biological Program' study.
Results: The VO_{2max} was in male patients 33.1 $\pm$ 4.2 mL/kg/min and in male control subjects 40.4 $\pm$ 3.4 mL/kg/min (P = 0.01). Female patients reached the value of 28.3 $\pm$ 5.5 mL/kg/min and female control subjects 32.4 $\pm$ 4.2 mL/kg/min (P = 0.03).
Conclusion: We found poorer physical fitness in narcolepsy. Poorer fitness in narcolepsy may be caused by minor training or by genetic factors.
The study was supported by the grant IGA NT 13238-4/2012
Disclosure: Nothing to disclose.

P935

Amygdalar volume in narcolepsy type 1 and 2 and in controls

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Objectives: Amygdala has a key role in detection and processing of emotional signals. Emotions trigger cataplexy in narcolepsy type 1 (N1). Abnormal amygdalar reactivity on humorous stimuli on fMRI was described in N1. Recently several microstructural changes were noted in amygdala in N1 patients but not in narcolepsy type 2 (N2) subjects. Our preliminary results showed a reduced volume of amygdala in N1 patients, thus we decided to compare amygdalar volume in N1 and N2 patients and healthy subjects using more sophisticated methods.
Methods: Twenty one patients with N1, 45 patients with N2 and 37 healthy controls participated in the study. They were examined in the same MR scanner 1.5 T, the measurement was carried out as T1W 3D image with a slice thickness of 1.0/0 mm.The amygdalar volume was assessed manually in ScanView.cz program and automatically by brain segmentation using Freesurfer (FS).
Results: The average left amygdala volume was in N1 patients 1.44 cm^3 (FS: 1.46 cm^3), in N2 patients 1.45 cm^3 (FS: 1.55 cm^3) and in controls 1.45 cm^3 (FS: 1.53 cm^3). The average right amygdala volume was in N1 patients 1.41 cm^3 (FS: 1.54 cm^3), in N2 patients 1.44 cm^3 (FS: 1.62 cm^3) and in controls 1.4 cm^3 (FS: 1.68 cm^3). No differences were found in amygdalar absolute volumes or in amygdalar volumes related to whole brain volumes.
Conclusion: Automatic nor manual amygdalar volumometry did not found any differences between N1 and N2 patients and controls.
Disclosure: Supported by the grant IGA NT 13238-4/2012

P936

Marked improvement of narcolepsy symptoms during treatment with baclofen - a case report

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Objectives: Sodium oxybate, one of the most effective medications in all symptoms of narcolepsy is known to act via the gamma-aminobutyric acid receptor type B (GABA-B receptor). However, a prototypical GABA-B agonist - baclofen occurred to be ineffective in

narcolepsy, suggesting that GABA-B agonism alone is not sufficient to improve narcolepsy symptoms.

Methods: We present a case of 27-years old female with narcolepsy and cataplexy, who showed good clinical response to baclofen. First symptoms appeared when the patient was 20 years old. Excessive daytime sleepiness (EDS) with attacks of irresistible sleep was followed by disturbed nighttime sleep and REM sleep disorders. Four years later partial cataplexy started with frequency of 1–2 attacks daily. At the age of 25 years the patient was admitted to our Sleep Disorders Center.

Results: Diagnosis of narcolepsy was established on the basis of polysomnography and multiple sleep latency test. The patient was HLA DQB1*0602 positive. The patient was treated with methylfenidate (10–30 mg/day), then with modafinil (200 mg/day), both with insufficient response and adverse events. On the ground of unavailability of sodium oxybate in Poland, the patient tried baclofen at the dose of 50–60 mg before sleep with a very good effect on the night sleep and EDS (improvement in Epworth Sleepiness Scale from 22 to 10 points). The patient reported also reduction of cataplexy to 2–3/week.

Conclusion: Although baclofen is not regarded as effective treatment of narcolepsy, it may be helpful in some patients, when sodium oxybate is not available.

Disclosure: Nothing to disclose.

P937

Swiss Narcolepsy Scale: a valid tool for the identification of hypocretin-1 deficient patients with narcolepsy

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Objectives: In a previous study (J Sleep Res. 2004; 13: 395–406) we reported the high sensitivity (96%) and specificity (98%) of a new scale based on five questions for the diagnosis of narcolepsy with cataplexy (NC). The aims of the present study are: To assess the value of the Swiss Narcolepsy Scale (SNS) in a new series of patients with NC, to compare its sensitivity and specificity with the Ullanlinna Narcolepsy Scale (UNS) and the Epworth Sleepiness Scale (ESS); and to evaluate it in the identification of CSF hypocretin-1 deficient patients with narcolepsy (NC-h1d).

Methods: We prospectively studied by questionnaire (including SNS, UNS and ESS) patients with NC (n = 85, all with assessment of CSF hypocretin-1 levels) and patients with excessive daytime sleepiness of other origin (EDS, n = 122) in our centers (Zurich/Leiden). Causes of EDS included idiopathic hypersomnia (n = 23), behaviorally induced sleep insufficiency syndrome (n = 32), restless legs syndrome (n = 7), sleep disordered breathing (n = 22), and hypersomnia due to medical disorders (n = 9).

Results: For the diagnosis of narcolepsy the following sensitivities/specificities were found: SNS (score <0) 86% and 89%; UNS (score >14) 100% and 62%; ESS (score ≥14) 91% and 54%. For the diagnosis of NC-h1d the sensitivities and specificities were: SNS 92% and 89%, UNS 100% and 62%, ESS 93% and 54%.

Conclusions: In this larger study we confirm (i) the high sensitivity and specificity of the Swiss Narcolepsy Scale, (ii) its superiority compared to the UNS and the ESS for the diagnosis of NC, in particular for the identification of NC-h1d.

Disclosure: Nothing to disclose.

P938

The impact of the ICSD-3 MSLT/PSG criteria on the diagnosis of narcolepsy

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Objectives: The recently published 3rd edition of the International Classification of Sleep Disorders (ICSD-3, American Academy of Sleep Medicine, Darien, IL, 2014) revised the diagnostic criteria for narcolepsy. Among other changes, it states that 'a sleep onset REM period (SOREMP) (within 15 min of sleep onset) on the preceding nocturnal polysomnogram (PSG) may replace one of the SOREMPs on the MSLT'. We investigated whether this additional criterion would have an impact on the diagnostic classification of hypersomnic patients according to MSLT/PSG parameters.

Methods: Database review: records of all unmedicated patients evaluated with a five session MSLT and previous PSG for the differential diagnosis of hypersomnia from 2001 to 2013 with complete data were included.

Results: Out of 545 patients, 92 fulfilled the ICSD-2 criteria for narcolepsy (≥ 2 SOREMP and mean sleep latency (MSL) ≤ 8 min) in the MSLT. Forty patients had 1 SOREMP and an MSL ≤ 8 min, and were thus candidates for diagnostic reclassification. Among them one single patient showed a SOREMP in the preceding nocturnal PSG. In patients fulfilling the ICSD-2 criteria for narcolepsy, the probability of SOREMPs in the PSG increased with the number of SOREMPs in the MSLT [2 MSLT-SOREMPs (n = 32): 9%; 3 MSLT-SOREMPs (n = 21): 24%; 4 MSLT-SOREMPs (n = 22): 32%; 5 MSLT-SOREMPs (n = 17): 82%].

Conclusions: The new provision in the ICSD-3 that a SOREMP in the nocturnal PSG preceding the MSLT may replace one of the SOREMPs in the MSLT will probably have only a minor effect on the diagnosis of narcolepsy.

Disclosure: Nothing to disclose.

P939

Narcolepsy cataplexy atypical associations: lucid dreaming and Diogenes syndrome

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Objectives: To describe narcolepsy cataplexy with uncommon associations.

Clinical history: A 36 year old female, has Narcolepsy since she was 12 years old.

Sleepiness was very severe, sleep attacks and refreshing naps; cataplexy, triggered by emotions, induced life threatening situations; hypnagogic hallucinations: auditory, somesthesic and feeding, and sleep paralysis. Prior to the narcolepsy she was a school-leader, afterwards she gained weight and suffered bullying, with progressive withdrawal from school and social activities and a progressive restriction to her house and her room.

The diagnosis was made 14 years later. The PSG revealed an intermediate insomnia with Periodic Limb Movements of sleep

(index = 21.4/h) and in the MSLT the mean sleep latency was 0.85 min, with 3 SOREM's and a mean REM sleep latency of 2 min. In 2013 she had: Obesity: BMI = 37.65; depression with suicidal ideation together with irritability and aggressive instincts; nightmares; lucid dreaming- allowing a parallel life and used frequently around the day; litter hoarding mainly for domestic bottles, cans, yogurt recipients, objects abandoned in the trash, leaves falling from plants or trees, etc.; no job or social life; menstrual irregularities (possible syndrome of polycystic ovarian syndrome). Hormones were normal, VitaminD was low.

A multidisciplinary approach was started: sleepiness and weight were reduced and she became a little more independent. There was marked resistance to proceed with diet, regular habits, occupation and refusal/denial to approach lucid dreaming and litter hoarding.

Conclusion: The association with excessive lucid dreaming and litter hoarding is rare, but the impacts are severe.

Disclosure: Nothing to disclose.

P940

Psychosis in narcolepsy as a side effect of sodium oxybate

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Hypnagogic and hypnopompic hallucinations are characteristic symptoms of narcolepsy, as are excessive daytime sleepiness, cataplexy and sleep paralysis. Narcolepsy patients may also experience daytime hallucinations unrelated to sleep-wake transitions. The effect of medication on hallucinations is of interest since treatment of narcolepsy may provoke psychotic symptoms. We aim to analyze the relation between sodium oxybate (SXB) treatment and psychotic symptoms in narcolepsy patients. Furthermore, we analyze the characteristics of hallucinations to determine their nature as mainly psychotic or hypnagogic and raise a discussion about whether SXB causes psychosis or if psychosis occurs as an endogenous complication in narcolepsy.

We present altogether four patients with narcolepsy who experienced psychotic symptoms during treatment with SXB. In addition, searched the literature for descriptions of hallucinations in narcolepsy and similarities and differences with psychotic symptoms in schizophrenia.

Three out of four patients had hallucinations typical for psychosis and one had symptoms that resembled aggravated hypnagogic hallucinations. Two patients also had delusional symptoms primarily associated with mental disorders. Tapering down SXB was tried and helped in some cases. Adding antipsychotic treatment (risperidone) alleviated psychotic symptoms in two cases.

Psychotic symptoms in narcolepsy can appear during SXB treatment. Hallucinations resemble those seen in schizophrenia however the insight that symptoms are delusional is usually preserved. In case of SXB-induced psychotic symptoms or hallucinations, reducing SXB dose or adding neuroleptic medication can be tried.

Disclosure: Nothing to disclose.

P941

Multiple sleep latency test may be not sensitive in obstructive sleep apnea with comorbid narcolepsy revealed by cerebrospinal-fluid orexin low levels

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Objectives: We report the case of a patient complaining of marked excessive daytime sleepiness (EDS) affected by obstructive sleep apnea (OSA) with comorbid narcolepsy-cataplexy (NC) revealed by cerebrospinal-fluid (CSF) orexin levels analysis.

Methods: Polysomnography (PSG), multiple sleep latency test (MSLT) and lumbar puncture (LP) where performed.

Results: A 38-year-old man complained of intense EDS and subtle episodes of knee weakness, elicited by laughing. His Epworth Sleepiness Scale (ESS) score was 17. PSG documented severe OSA (Apnea-Hypopnea Index - AHI 57.9/h), MSLT showed a mean sleep latency (MSL) of 8 min without sleep-onset REM periods (SOREMPs). He started continuous airway positive pressure treatment (CPAP), but, at the follow-up, he complained of the worsening of the EDS (ESS 21), despite of good CPAP compliance. PSG under CPAP therapy documented an AHI of 3.2/h. MSLT performed at this time documented a MSL of 2.7 min, without SOREMPs. During each nap of MSLT several obstructive apneas were observed with sudden awakenings and arousals. Since the cataplectic-like attacks endured, we performed a LP to quantify CSF orexin levels, which resulted 45.6 pg/mL (orexin deficiency <110 pg/mL). Furthermore, he carried the HLA-DQB1*06:02 allele.

Conclusions: Our report suggests that in narcolepsy-comordid OSA patients MSLT may be affected by a reduced sensitivity and specificity. In fact, in our case apneic events during the diurnal naps in MSLT probably avoided REM sleep. Hence, in these cases CSF orexin levels assessment may be the diagnostic tool able to achieve the correct diagnosis.

Disclosure: Nothing to disclose.

P942

Complete loss of F-waves during cataplectic attacks in patients with narcolepsy

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Objectives: Cataplexy is a hallmark symptom of narcolepsy with cataplexy (NC). Our current pathophysiological understanding of cataplexy has been based on the assumption that the loss of muscle tone during cataplectic attacks CA is identical to muscle atonia in REM sleep. Recently, F-waves have been shown to be a valuable surrogate marker for spinal inhibition in REM sleep. Here we present F-wave recordings in three patients with NC prior, during and after a CA to test whether the level of spinal excitability in cataplexy equals that in REM sleep.

Methods: We tried to trigger CA in eight patients diagnosed with NC. In three patients a CA attack could be provoked and F-waves assessed using the same methodology detailed elsewhere (Salih et al., 2011).

Results: In all three patients, F-waves were completely inhibited during the CA, totalling a persistence of F-waves of 0% in each individual case. F-waves immediately reappeared at the end of the attack.

Conclusions: The complete unresponsiveness of spinal motoneurons during CAs exceeds the extent of spinal inhibition in REM-sleep. This finding supports earlier assumptions suggesting common spinal pathways in cataplectic attacks and in REM sleep, however that brainstem mechanism in these two states may differ and by consequence the extent of spinal inhibition. The complete loss of F-waves in CA as opposed to partial suppression of F-waves in REM may be considered as an indication that supraspinal circuits involved in the generation of CA differ partly to those leading to mixed motor activity in REM.
Disclosure: Nothing to disclose.

P943

Treatment response of subjective and objective measures of sleepiness in narcolepsy with cataplexy

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Objectives: Excessive daytime sleepiness is a defining symptom in narcolepsy with cataplexy. It can be assessed subjectively with the Epworth Sleepiness Scale (ESS) or objectively measured by means of the Multiple Sleep Latency Test (MSLT) or Maintenance of Wakefulness Test (MWT). Stimulants represent the treatment of choice, but potential differences of its effect on subjective and objective measures of excessive daytime sleepiness have rarely been reported.
Methods: In our data base, we identified ten out of 70 patients with narcolepsy with cataplexy, in whom both MSLT and MWT were performed at treatment-naïve baseline and under treatment with stimulants.
Results: Mean age was 35 $\pm$ 14 years; half of the patients were female. Treatment consisted of sodium oxybate in six patients, modafinil in three patients, and methylphenidate in one patient. Under treatment, ESS scores significantly decreased from 15.2 $\pm$ 4.4 to 10.1 $\pm$ 3.0 (P = 0.003). On MSLT, mean sleep latency remained unchanged under treatment (1.4 $\pm$ 1.3 vs. 1.7 $\pm$ 1.0, P = 0.43), but the number of SOREM periods significantly decreased from 3.7 $\pm$ 0.5 to 2.2 $\pm$ 1.5 (P = 0.01). Conversely, mean sleep latency on MWT improved under treatment from 5.0 $\pm$ 4.4 to 10.2 $\pm$ 6.2 (P = 0.003), while the number of SOREM periods remained stable (1.1 $\pm$ 1.1 vs. 0.8 $\pm$ 1.5, P = 0.39).
Conclusions: In narcolepsy with cataplexy, treatment with stimulants produces differential effects on subjective and objective measures of sleepiness. Subjective amelioration of sleepiness is paralleled by improved MWT yet unaltered MSLT findings, suggesting enhanced resistance to a persistingly overwhelming sleep pressure. Thus, treating physicians should be aware of this discrepant effect and consider MWT improvement as the main treatment outcome.
Disclosure: Nothing to disclose.

P944

The Swiss Narcolepsy Scale for the identification of patients with narcolepsy: a prospective, 'real-life', sleep-centre study in a cohort of 811 patients

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Background and objectives: The Swiss Narcolepsy Scale (SNS) is a tool for the identification of narcolepsy. The questionnaire includes five questions and a calculated value of <0 suggests the presence of narcolepsy. In two pilot studies, high sensitivity and specificity (>85%) were found. We aimed at evaluating sensitivity and specificity in a large clinical cohort with different sleep-wake-disorders and at comparing the SNS with other questionnaires typically used in evaluating the diagnosis of narcolepsy [Ullanlinna Narcolepsy Scale (UNS); Epworth Sleepiness Scale (ESS)].
Patients and methods: We prospectively studied a series of 811 consecutive patients consulting our sleep-centre from 2008 to 2013. Patients of all categories of sleep disorders were included. There were 95 patients with narcolepsy (narcolepsy with cataplexy (NC) n = 71; narcolepsy n = 24). ESS, UNS and SNS questionnaires were given to all patients, those with confirmed narcolepsy additionally received the Stanford Cataplexy Questionnaire (SCQ).
Results: The SNS had a sensitivity of 91% and a specificity of 90% in identifying patients with narcolepsy (with and without cataplexy). In patients with NC the sensitivity was considerably higher (97%) than in patients without cataplexy (70%). Sensitivities and specificities of UNS and ESS (score >14) were 85% and 87%, respectively 83% and 76%. In NC patients, there was an inverse correlation between high risk for cataplexy (SCQ) and SNS score (r = -0.74; P < 0.01).
Conclusion: This 'real-life' sleep-centre study confirms the value of the SNS as simple and accurate tool to identify and differentiate patients with narcolepsy (especially NC) from other sleep-wake-disorders, and from hypersomnias in particular.
Disclosure: Nothing to disclose.

P945

Frequency of genetic risk and protective alleles for narcolepsy with cataplexy in Estonia

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Objectives: HLA typing is not routinely used in the diagnosis of narcolepsy with cataplexy (NL). Tafti et al. (2014) showed that nearly 100% of NL patients are *HLA DQB1*06:02* positive. Several other genetic markers were found to either predispose to NL or have protective effect. This study was aimed to estimate the frequency of *HLA DQB1*06:02*, risk allele for NL in T cell receptor alpha (*TCRA*) locus and protective allele around *HLA-DQA2* locus in normal population of Estonia by using 4400 individuals from Estonian Genome Center Biobank.
Methods: Data for SNPs rs2858884 (*HLA-DQA2*), rs1154155 (*TCRA*) and rs3135388 (tag SNP for *HLA-DRB1*15:01-DQB1*06:02* haplotype) were retrieved for 4400 individuals genotyped by Illumina ExonChip data. We also use SNP2HLA tool for more precise haplotype detection in HLA region. These SNPs are also genotyped in 17 narcolepsy patients by using Sanger sequencing.

Results: We identified that 27.2% of the individuals are heterozygous and 2,7% homozygous for *HLA-DRB1*15:01-DQB1*06:02* haplotype. Among these 1315 individuals the frequency of risk genotype CC (rs1154155) in TCRA locus is 1.8% and the frequency of protective allele C rs2858884 is 12.3%. Only 24 individuals had simultaneously *HLA* risk haplotype and were homozygous for rs1154155.

HLA typing has been considered of low specificity for narcolepsy. The specificity can be increased by testing simultaneously the presence of another allele around *HLA-DQA2* locus, shown to have a protective influence. In our cohort ca 24% of individuals who were positiive for *-DRB1*15:01-DQB1*06:02* haplotype, had one or two protective alleles in rs2858884.

Disclosure: Nothing to disclose.

P946

Patterns of sleep latency in the multiple sleep latency test naps across the day in central nervous system hypersomnias

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Objectives: MSLT remains the gold standard to differentiate central hypersomnias (C-H). We aimed to determine if different C-H have different patterns of sleep latency (SL) in the MSLT naps across the day.

Methods: Adults who underwent MSLT and evaluation by a sleep specialist, divided in three groups: narcolepsy with/without cataplexy (NL), idiopathic hypersomnia (IH), depression associated hypersomnia (DH), compared regarding MSLT measures. A SL ratio between the SL in each nap and the mean SL of all naps was calculated for each patient, to demonstrate variations in the SL across naps.

Results: Thirty patients identified: 11 in NL group (54.5% female, median age 45.0 years); 9 in IH group (55.6% female, median age 52.0 years); 10 in DH group (90.0% female, median age 45.5 years). Mean SL did not differ significantly among groups: 4.08 min, 5.27 min, and 6.60 min ($P = 0.111$), while the presence of SOREMP was almost exclusive of NL patients. Regarding SL variations across naps, the DH group had significantly lower SL than the others in the second nap, without differences in the others. In DH group, SL ratio was significantly higher in the first two naps than in the third and fourth ($P = 0.001$). The same SL ratio difference throughout the day was not patent in the NL and HI groups.

Conclusions: This preliminary work points out possible circadian differences regarding sleep propensity in C-H, especially in major depression, where circadian rhythm changes were described. This data may be of clinical relevance for diagnosis as well as a more directed timing of stimulant treatment.

Disclosure: Nothing to disclose.

P947

Persistent somnolence despite adequate CPAP therapy

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Excessive daytime sleepiness (EDS) is one of the most common sleep related complaints, affecting an estimated 20% of the population [1]. Most commonly Obstructive Sleep Apnoea (OSA) is the cause of this complaint. The first line treatment for OSA is an airway therapy known as Continuous Positive Airway Pressure (CPAP), which is extremely successful at reducing symptoms of EDS. Despite CPAP's success, a select proportion of patients continue to experience EDS post CPAP therapy. This audit aims to establish a cause for the prevalence of persistent EDS despite CPAP therapy by analysing the results of nocturnal polysomnographys obtained from 64 patients presenting to Nuffield House Sleep Centre, in addition to their relevant clinical notes. It is the hope of this audit that these findings will lead to a better understanding of persistent EDS post CPAP, and that this understanding may be used to improve treatment guidelines. The findings from the audit suggest that the greatest cause of EDS in these patients is attributable to Periodic Limb Movement Disorders. While this explains the cause in those with abnormal nPSG results, further studying is needed to better identify the cause in those with normal sleep studies.

Disclosure: Nothing to disclose.

P948

The occurrence of hypnagogic hallucinations and sleep paralysis according to age and disease duration in narcolepsy with cataplexy

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Objectives: Narcolepsy with cataplexy (NC) is defined as chronic sleep disorder characterized by excessive daytime sleepiness (EDS) and cataplectic attacks often accompanied by hypnagogic hallucinations (HH), sleep paralysis (SP) and nocturnal sleep disturbances. Clinical experience suggest that some of these symptoms may disappear or get milder with age. We focused on hypnagogic hallucinations and sleep paralysis, the two in research rather neglected symptoms.

Methods: We examined 77 patients diagnosed with NC (age range 20–87 years). 26 patients were treated with stimulants only, seven with antidepressants only, 22 were on combination of stimulants and antidepressants, nine subjects took Xyrem and 13 were completely without medication. The patients were asked about life experience with HH and SP and about the occurrence of HH and SP in the last year. For the data analysis we divided the subjects into groups according to their age and to the duration of the disease.

Results: From the 77 subjects, 45 had life experience with HH and 37 with SP. Last year 33 of the subjects experienced HH and 27 SP. Although HH disappeared in 26.7% and SP in 27.0% of those subjects having life experience with these symptoms, no decrease associated with either age or disease duration was found.

Conclusions: We did not prove (nor disprove because of small number of subjects) the association of HH and SP disappearance with age or with the duration of the disease.

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Disclosure: Nothing to disclose.

Neurological disorders and sleep

P949

Sleep disorders other than parasomnias, as mimics of epilepsy

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Objectives: Next to parasomnias, other disturbances of sleep are thought to be exceptional as mimics of epilepsy. However, in our third line clinic dedicated to epilepsy and sleep disorders, these mimics are regularly encountered and are described here.

Methods: In our clinic long term (>24 h) video-EEGs always contain sensors which make global polysomnography (PSG) possible (respiration and EMG/muscle tone). In case this recording suggests a sleep disorder, a full PSG, (AASM rules) is done in order to get more details. We are aware that our patient group is a selection from the general population which may give bias in the prevalence figures.

Results: In 1650 consecutive patients video-EEG recordings suggested a serious sleep disorder in $n = 255$ (15%). During the consecutive PSG in 19 of all patients (1.1%) a sleep disorder was found with characteristics similar to the clinical description of the events during the night without any video-EEG prove of epilepsy. The final diagnoses in this group of 19 patients were obstructive or central apneas (O/CSA) in 9, sleep myoclonia in 5 and excessive periodic limb movements in the other 5 patients. In addition to these 19 patients, two patients had a status cataplecticus during day-time as part of not detected narcolepsy. Elsewhere, this was thought to be an epileptic disorder. Therapy for the sleep disorders resulted in substantial improvement.

Conclusions: In 1.2% of our population a sleep disorder other than parasomnia, proved to be a mimic of epilepsy. This finding has major impact on the therapy.

Disclosure: Nothing to disclose.

P950

Transcraneal magnetic stimulation improves sleep parameters and quality of life in patients affected with focal epilepsy

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Epilepsy is one of the most frequently cause of sleep disorders, affecting nearly 60% of epileptic patients. It has multiple etiological factors. It has been reported that EEG abnormalities in epileptics appears as a result of neural hyper-excitability. Sleep disorders like insomnia and hyper-arousals are associated with these disease. In addition, transcranial magnetic stimulation (TMS) has shown to be effective in the treatment of disorders characterized by neural hyper-excitability.

Objectives: To evaluate the effect of slow repetitive trasncraneal Magnetic Stimulation on sleep parameters, electroencephalographic abnormalities and quality of life in epileptic patients.

Method: In the present study, 24 male patients with focal symptomatic epilepsy and insomnia were submitted to slow repetitive transcranial magnetic stimulation, for 15 min daily during 10 days. Polysomnographic recordings and QOLIE-31 were performed before and after TMS.

Results: Most of the sleep parameters showed significant improvement: increase of TST (Total Sleep Time), SWS (Slow Wave Sleep), decrease of SL (Sleep latency), Arousal index, TWT (Total Wake Time) and WASO (Wake Time after Sleep on set). Also did QOLIE-31 ratings. In addiction, electroencephalographic abnormalities decrease during the second PSG study.

Conclusions: These data support the notion that TMS is a reliable therapeutic tool for patients affected with epilepsy and insomnia.

Disclosure: Nothing to disclose.

P951

Effect of the timing of acetylcholinesterase inhibitor ingestion on sleep

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Objectives: Many patients with Alzheimer's disease experience sleep disturbances, and donepezil is usually prescribed for night-time administration. However, increased acetylcholine is associated with cortical arousal. We evaluated whether subjective sleep quality differed according to the timing of medication administration.

Methods: Ninety-two patients with mild to moderate Alzheimer's disease who had taken donepezil at night ($n = 54$) or galantamine in the morning ($n = 38$) were recruited for this study. Scores on the sleep visual analogue scale (VAS) for sleep quality and daytime drowsiness were obtained.

Results: The mean sleep-quality and daytime-drowsiness VAS scores of the donepezil and galantamine groups differed significantly at baseline (44.0 ± 26.4 vs. 55.2 ± 27.3, respectively; $P < 0.001$ and 48.8 ± 28.8 vs. 38.8 ± 25.3, respectively; $P < 0.001$). The patients taking donepezil were then randomly assigned to take donepezil in the morning ($n = 24$) or at night ($n = 30$). Eight weeks later, VAS scores also differed among the three groups ($P < 0.001$ for both sleep quality and daytime drowsiness). The VAS scores of patients taking galantamine and donepezil in the morning were different from those taking donepezil at night at week 8. Significant changes in VAS scores emerged only in the group taking donepezil in the morning (4.6 ± 26.5, $P = 0.046$ for sleep quality; -7.1 ± 26.1, $P < 0.001$ for daytime drowsiness).

Conclusions: These results suggest that taking acetylchlinesterase inhibitors in the morning can improve the sleep states of patients with Alzheimer's disease.

Disclosure: Nothing to disclose.

P952

Orexin levels in patients with Niemann-Pick type C and their response to Miglustat treatment

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Introduction: The symptoms of narcolepsy can occur during the course of other neurological conditions (i.e. symptomatic, narcolepsy). Inherited disorders, tumors and head trauma were the three most frequent causes for symptomatic narcolepsy. Among inherited disorders, Niemann-Pick type C (NPC), Myotonic dystrophy type 1, and Prader-Willi syndrome were mostly reported. NPC is an autosomal recessive and congenital neurological disorder characterized by the accumulation of cholesterol and glycosphingolipids in the peripheral tissues and of the glycosphingolipids in the brain. Symptoms include hepato-splenomegaly, vertical supranuclear gaze palsy, ataxia, dystonia, and dementia. Some cases display cataplexy indistinguishable from those seen in idiopathic narcolepsy.

Recently, Miglustat that inhibits glucosylceramide synthase, an essential enzyme for the synthesis of most glycosphingolipids, was approved for the treatment for NPC.

Method: The subjects were seven patients with NPC (three male and four female). Patients or families were gave informed consent for the lumbar puncture. We checked clinical symptoms, PSG, MRI or CT, HLA and CSF orexin levels.

Result: Concerning the CSF orexin levels, two cases were low, three cases were intermediate, and two cases were normal levels. Subjects having cataplexy (n = 5) had low (n = 2) or intermediate (n = 3) levels. Interestingly, one case (6/F) treated with Miglustat was shown to reduce cataplexy and the orexin level became normal (351 pg/mL) from intermediate level (183 pg/mL).

Conclusion: Moderate or severe decreases in CSF orexin levels were observed in some cases with NPC with cataplexy. However, the degree of reduction was small in contrast to idiopathic narcolepsy-cataplexy. Miglustat may cure cataplexy and orexin deficiency.

Disclosure: Nothing to disclose.

P954

The cognitive and functional status of stroke patients are negatively affected by obstructive sleep apnoea

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Objectives: Obstructive sleep apnoea (OSA) is a common sleep disorder in stroke patients and is associated with decreased functional outcome and an increased risk of post stroke mortality. The effect of OSA on cognitive functioning following stroke has not yet been investigated. Therefore, the primary objective of this study was to compare stroke patients with and without OSA on cognitive and functional status upon admission to our rehabilitation centre.

Methods: A total of 158 patients underwent sleep examination for diagnosis of OSA. We performed a cognitive and neurological assessment, and rated their activities of daily living (ADL). We also administered questionnaires on fatigue, sleepiness and mood.

Results: Sixty-five patients were diagnosed with OSA. Stroke patients with OSA were older and had a higher BMI than non-OSA stroke patients. No difference in stroke severity was objectified. As regards to cognitive functioning, OSA patients performed worse on tasks of attention, working memory, executive functioning, visuoperception and problem solving than patients without OSA. For memory and language no difference was seen. As for functional status, OSA patients had a worse overall neurological status and showed more ADL problems than non-OSA patients. There was no difference in the reported levels of fatigue, sleepiness and depressive symptoms.

Conclusions: Stroke patients with OSA show decreased cognitive functioning, have a worse overall neurological status and encounter more difficulties in ADL as compared to stroke patients without OSA. Thus, we conclude that OSA negatively affects the cognitive and functional outcome of stroke patients.

Disclosure: Nothing to disclose.

P955

Sleep apnea and stroke

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Objectives:

Aims of this ongoing study are to investigate: (1) the prevalence of obstructive sleep apnea (OSA) among the ischemic stroke patients (ISP) in Northern Finland,

(2) to compare the prevalence of OSA and its severity among patients receiving thrombolysis (THR) and those without thrombolysis (CTRL).

Methods: We enrolled 149 over 18 years old ISP. Exclusion criteria was non-compliance. 49 patients (32/65% males) had thrombolysis and 100 (55/55% males) didn't. Sleep recording (ApneaLink®, Resmed, Sydney) was performed within 48 h after symptom onset and after a 6-month follow-up period.

Results: We obtained sleep recordings of 149 ISP. Furthermore, there were 10 drop outs and one fatal adverse event. Mean age was 65.9 years and 69.6 years in THR and CTRL, respectively. Mean Body Mass Index (BMI) in both groups was 27 kg/m^2. Groups did not differ in terms of gender distribution, age or BMI. Men had more OSA than women (64/73.6% vs. 42/67.7%, P = 0.440). Median National Institutes of Health Stroke Scale (NIHSS) score was higher in THR compared to CTRL (6 vs. 2, P < 0.001). In total, 106 (71.1%) ISP had OSA. OSA was more prevalent in THR than in CTRL (41 /83.7% vs. 65/65%, P = 0.018). There was significant correlation between NIHSS and OSA (Pearson's correlation coefficient r = 0.177; P = 0.031). THR had severe OSA than CTRL and proportions of mild (53.1% vs. 26%), moderate (8.2% vs. 20%) and severe OSA (22.4% vs. 19%) differed between THR and CTRL, respectively (P = 0.003).

Conclusions: THR had more OSA than CTRL.

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P956

Sleep spindles mixed with spikes/sharp waves in a patient with supplementary motor area epilepsy

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Objectives: Aspect of interictal sleep spindles in a 16 years old patient with supplementary motor area (SMA) epilepsy.

Methods: We analyzed the 24 h video-surface EEG (sleep and wake, 10–20 electrode placement) which registered interictal and ictal elements and the cerebral MRI which was normal, in a patient with very frequent asymmetric tonic seizures.

Results: Sleep spindles (sigma activity) together with K-complexes are hallmarks of the NREM sleep. The spatial distribution of spindles indicates predominant frontal involvement in normal individuals. The vertex regions, where spindles appear first in non-rapid eye movements sleep (NREM) stage, reflect activity from the most posterior portion of the supplementary motor region of the frontal lobe. It is well known that the spindle-generating circuit is composed of two sets of neurons: inhibitory neurons in the reticular thalamic nucleus and excitatory thalamocortical neurons in the dorsal thalamic nuclei.

Focal interictal epileptiform discharges become more frequent with increasing depth of NREM sleep (this is the gating role of slow activity of sleep in generating seizures and interictal events).

The K-complexes are frequently associated with spikes/sharp waves (interictal epileptiform discharges), whereas a mixture of spikes/sharp-waves and spindles in epileptic patients is quite rare as we registered in this young epileptic patient.

Conclusions: The IED's integrated in the interictal sleep spindles could prove a gating role of spindles in frontal lobe epilepsy patients and raise the question of the role of SMA in generating spindles.

Disclosure: Nothing to disclose.

P957

Sleep quality and pain thresholds in subjects with tension type headache and migraine compared to healthy controls

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Background: Headache patients report more sleep disturbances than healthy controls. What is the relationship between subjective and objective sleep and pain sensitivity in migraine and tension-type headache?

Methods: A blinded, controlled, cross sectional study with polysomnography, measurements of pain thresholds (PT), data from headache and sleep diaries and questionnaires. We included 34 healthy controls, 50 migraineurs and 20 patients with TTH. Migraineurs who had their sleep recording more than 2 days from an attack were classified as interictal while those registered less than 2 days from an attack were classified as either preictal or postictal. Migraineurs with attack debut time mainly during night or by awakenings was classified as sleep migraine (SM). Migraineurs without a preference for nightly attacks were classified as non-sleep-migraine (NSM).

Results: Both TTH and NSM patients had more slow wave sleep (SWS), less fast arousals, more daytime tiredness and a tendency to lover PT than healthy controls; consistent with sleep deprivation. However, the sleep diary showed no difference in sleep time between headache patients and healthy controls. Migraineurs had shorter latency to sleep onset in the preictal phase than in the inter-ictal phase. SM patients had slightly increased number of awakenings than controls and less SWS than NSM.

Conclusions: Reduced arousal level and a tendency to reduced PT among TTH and NSM patients may be related to a relative sleep deprivation. Except for the SM group, our data indicate that subjects with headache may need more sleep than healthy controls.

Disclosure: Nothing to disclose.

P958

Fatal familial insomnia: a new Spanish case of an unreported family

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Background and objective: Fatal Familial Insomnia (FFI) is an autosomal dominant disease with incomplete penetration. Change in sleep pattern can be an important clinical clue for identifying FFI, accompanied shortly after by motor signs, autonomic hyperactivation and cognitive and behavior deficits.

Our aim was to report a case of FFI in a patient- of an unreported Spanish family- with three members (mother and two brothers) affected and deceased.

Patient and methods: A woman 45 years old, with confirmed genetic diagnosis 15 years before, was referred with symptoms of depression, dizziness, weight loss, amenorrhea, mild cognitive disorder and insomnia that progressively appeared 10 month before admission.

Results: Neurological examination showed mild attention deficit, hyperreflexia, bilateral Hoffman sign, aquileus clonus, some spontaneous myoclonus, and postural and intentional tremor. She had tachycardia, hypertension and Body Mass Index of 16,3 Kg/m^2. Cranial MRI revealed hyperintensity in both thalami in FLAIR sequences; normal EEG; perfusion brain SPECT showed frontoparietal cortical, subcortical and both thalami hypoperfusion. Serial polysomnography assessment showed disrupted macro and micro sleep structure with an absence of clear sleep stages (reduction in spindles activity and slow waves); continuous central apneas-hypopneas; myoclonic jerks and PLMS. Genetic study showed a missense mutation at codon D178N of the prion-protein gene and homozygosis polymorphism at codon 129 (129M/M).

Conclusion: The patient developed a typical course with a depressive syndrome as initial symptom. The treatment with hypnotics and chronobiotics was unsuccessful. The management consisted of symptomatic treatment, genetic counseling and psychosocial support as the best standards of care.

Disclosure: Nothing to disclose.

P959

Sleep structure, associated sleep disorders, and the effects of medications on nocturnal sleep and daytime sleepiness in patients with Parkinson's disease

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Sleep problems are very frequent complaints of patients with Parkinson's disease (PD), the most common being sleep fragmentation, REM sleep behavior disorder (RBD) and excessive daytime sleepiness. The clinical significance of sleep disordered breathing (SDB) in PD remains contraversial. We have prospectively examined consecutive 51 patients diagnosed as PD based on UK Brain Bank Criteria. All participants underwent one-night standard inlab video-polysomnogram (PSG) and 25 patients had Multiple Sleep Latency Test (MSLT). Participants were instructed to take their medications at their regularly scheduled time. A total of 35 patients (68.6%) were diagnosed to have sleep disordered breathing. RBD was present in 21 patients (41.2%), while only 63.2% of these had REM without atonia in polysomnography, and 7 patients had REM without atonia but no clinical RBD symptoms. The most important risk factor determining the presence of SDB and RBD was the duration of PD ($P = 0.01$). The disease duration was negatively correlated with the duration of slow-wave sleep ($P = 0.03$), but no effect was observed regarding REM duration or latency. The most important factor affecting sleep fragmantation was found as PH-related somatic problems, nocturia and periodic leg movements in sleep ($P < 0.05$). Medications did not seem to have most of value regarding nocturnal sleep structure, but the dose of dopaminergic treatment was positively correlated with the latency of MSLT ($P = 0.04$). The mechanisms through which sleep structure is affected in patients with PD should better be delineated, sleep disorders and clinical correlates should also better be defined in this particular patient group.

Disclosure: Nothing to disclose.

P960

Brain structural abnormalities associated with rapid eye movement sleep behaviour disorder in Parkinson's disease

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Objective: Rapid eye movement sleep behavior disorder (RBD) patients are at high risk for developing Parkinson's disease (PD). We used Deformation-Based Morphometry (DBM) analyses of Magnetic Resonance Imaging (MRI) data to detect neurostructural abnormalities associated with RBD in a large sample of PD patients.

Methods: We compared DBM differences between 41 PD with RBD (PD+RBD) and 162 PD patients without RBD (PD-RBD) to identify structural alterations associated with RBD. Presence of RBD was based on the RBD Screening Questionnaire. MRI data were extracted from the Parkinson's Progression Markers Initiative (PPMI) database. DBM analyses were conducted on T1-weighted MRI images, and FDR thresholded at $t \geq 2$.

Results: RBD was associated with a volume decrease of the pontomesencephalic tegmentum (PMT), thalamus, and putamen. Volume increases were found in the superior temporal, cingulate, and lateral prefrontal cortices, as well as in the olfactory tract and bulb. RBD was not associated with any change in the substantia nigra, red nucleus or hippocampus, which contrasts with the volume decrease observed in these regions with PD.

Conclusion: The present study highlights specific neural abnormalities associated with RBD in PD, in line with the key role of nuclei in the PMT for the control of muscle tone during REM sleep. They are also in agreement with the altered olfaction and depressive symptoms observed in PD+RBD. Structural alterations of the substantia nigra were found in PD, but independently from RBD.

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P961

Arousal scoring in epilepsy

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Objective: The aim of this study was to determine the changes in the polysomnographic parameters and the cyclic alternating pattern (CAP) in generalized and partial epilepsy patients (with and without epileptiform discharges on EEG) using video-EEG-PSG recording.

Methods: 73 patients diagnosed with epilepsy and 19 healthy controls within the same age group (control group) underwent an 8-h long sleep video-EEG-PSG recording. After the first evaluation, the CAP parameters were scored in 57 patients (31 generalized and 26 partial epilepsy) and 16 healthy subjects who had no sleep diseases and the results were compared within the groups.

Results: The total sleep time and the NREM I phase were found to be longest in the partial epilepsy group and shortest in the control group, while the REM phase was found to be exactly the opposite to this. The mean CAP ratios were found to be statistically higher in the generalized epilepsy group when compared to the other two groups. This difference was also found in the control group and the generalized epileptic patients who had no abnormality on EEG. No difference was found between the partial epilepsy and the control group regarding CAP ratios.

Conclusions: Patients with generalized epilepsy have differences compared to healthy individuals regarding the macro- and microstructure of sleep, and it seems that these differences are independent from the epileptiform discharges. In partial epilepsy patients, no microstructural differences were detected, while macrostructural changes were evident.

Disclosure: Nothing to disclose.

P962

Sleep apnea and periodic leg movements in the acute phase of spinal cord injury

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Objectives: Sleep disturbances are frequently reported by patients with spinal cord injury (SCI). Different studies have shown an increased incidence of sleep-disordered breathing (SDB) and Periodic Leg Movements (PLMS) in people with stable long-term SCI.

Methods: We performed a prospective observational study in order to evaluate the features and possible predisposing factors of SDB and PLMS in a heterogenic population of consecutive SCI patients admitted at the Spinal Unit of the Niguarda Hospital within the first year after injury. Each patient underwent a clinical assessment, full polysomnography and arterial blood gas analysis before and immediately after sleep. Multiple logistic regressions were applied in order to evaluate factors associated with SDB and PLMS.

Results: Thirty-five (15 tetraplegic and 20 paraplegic) patients were enrolled. Nine patients (25.7%) had an obstructive SDB and 10 (28.6%) had PLMS. The frequency of SDB was higher in tetraplegic patients with respect to paraplegic ones (Wald stat = 7.71, $P = 0.0055$), while PLMS were significantly more frequent in patients with an incomplete motor lesion than in subjects with a complete one (Wald stat = 6.14, $P = 0.013$).

Conclusions: Our study confirms a high frequency of SDB and PLMS in SCI patients in the first year following injury. Independently from possible sub-acute and chronic clinical variables, the level and the completeness of the spinal cord lesion are the main factors associated respectively with an early development of a SDB and PLMS.

Disclosure: Nothing to disclose.

P963

A questionnaire study on the sleep-related difficulties in the children with cerebral palsy

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Objectives: Sleep disorders are often occurred in different neurological conditions. Although neurologically impaired patients have considerable increase of sleep disturbances, few studies have been devoted to children sleep difficulties with cerebral palsy (CP) coexisting with epilepsy. This work was aimed to assess the distribution of sleep complaints in children having CP with and without epilepsy.

Methods: Children aged 1-to-8 years old with CP having epilepsy ($n = 85$) and not having epilepsy ($n = 80$), and 359 age- and sex-matched subjects, were selected. A structured sleep-waking questionnaire was developed on the basis of Child Sleep Questionnaire for Parents and the Pediatric Sleep Questionnaire. The subjects were recruited from the Institute of Neurology and Neuropsychology located in Tbilisi, Georgia.

Results: In overall, 64.8% ($n = 107$) of children with CP vs. 20.3% ($n = 73$) of healthy subjects had sleep complaints. Sleep disorder breathing (SDB) was the most common problem in the children having CP [58.78% ($n = 97$)] compared to the control subjects [8.07% ($n = 29$)]. Sleep onset difficulty and sleep maintenance difficulty was identified accordingly in 41.2% ($n = 68$) and 39.4% ($n = 65$) of neurologically impaired children that was much higher than control group's corresponding indices.

Conclusions: The findings show that sleep problems are more prevalent among the neurologically impaired children. The subjects with both diagnosis of CP and epilepsy are at higher risk to develop SDB; otherwise comorbidity with epilepsy does not increase the disposition to the sleep deterioration compared to the children having only CP.

Research conducted in Georgian Ministry of Health, Labour and Social Affairs Program 'Child Care'

Disclosure: Nothing to disclose.

P964

Sleep disturbances in patients with multiple sclerosis associated fatigue

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Objective: Fatigue is the most frequent symptom in MS patients and often is profoundly debilitating. Patients with MS do not often distinguish between fatigue and sleepiness. The goal of this study was to determine sleep disturbances associated with fatigue in patients with MS and look for a correlation with the location of demyelinating lesions seen on magnetic resonance imaging (MRI).

Methods: Ten patients with RR MS who had fatigue based on fatigue questionnaire (MFIS) undergo PSG. 3 men and 7 women aged between 20–32 with EDSS. These included difficulties initiating sleep and/or frequent awakenings due to spasms in the legs (7), difficulties in initiating or maintaining sleep (4), snoring (2) and nocturia (3). All patients were screened for depression with BDI and no one had a score more then 14. MRI scans were performed on all patients on the day of polysomnography.

Results: Of the 10 fatigued patients with MS all had REM-sleep without atonia, two had REM-sleep associated motor activity in legs, seven had frequent awakenings and significantly reduced sleep efficiency, five had hypopnea. One of the patients with sleep apnoea and fatigue was especially prominent in this case. Two had snoring. All patients had MRI brain stem lesions and two of them had demyelinating lesions in pons.

Conclusion: We have noted a relationship between fatigue-associated sleep abnormalities in MS patients and MRI brain stem lesions. These abnormalities may play a role in the pathophysiology of poorly understood MS fatigue. Large-scale studies are needed to confirm our findings.

Disclosure: Nothing to disclose.

P965

Sleep quality through overnight standard polysomnography in patients with cerebral palsy

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Objectives: To evaluate the sleep by overnight polysomnography (PSG) in adult patients with cerebral palsy (CP).

Methods: 21 patients with spastic diparetic CP (11 female), mean age 28.4 $\pm$ 5.4, mean neck circumference 37.8 $\pm$ 2.55 and mean BMI 24.2 $\pm$ 2.78. The sample was classified using the Gross Motor Functional Classification Scale (GMFCS). All patients were recruited from the Special Care Clinic of the Universidade Estadual Paulista - UNESP, Brazil. The inclusion criteria were spastic diparetic CP, partially preserved cognitive function, and a statement of informed consent signed by the participant or legal guardian agreeing to voluntary participation in the study. The exclusion criteria were having undergone orthodontic or orthopedic treatment of the jaws or therapies to reduce spasticity (botulin toxin) in the six months prior to the study. This study received approval from the Brazilian National Human Research Ethics Committee (007/2011). All patients underwent the full overnight PSG exam at Sleep Disorders Laboratory, (UNINOVE) after the habituation night.

Results: The mean total time sleep (TTS) was 210 min. The heart rate maximun was 118.2 ± 34 bpm. Mean sleep stage was 10% in NREM 3 and 14% in REM. Obstructive sleep apnea (OSA) was observed in 11 patients with a mean IAH 11.68 ± 6.6.
Conclusion: This is one of the first studies that evaluated the sleep through PSG with CP patients. It was observed a decrease of TTS, a higher heart rate, considerable decrease in NREM3 and REM stages and OSA. The sleep of patients evaluated in this study was of poor quality.
Disclosure: Nothing to disclose.

P966

Central sleep apnoea in patient with hydrocephalus. A case report

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Objective: To assess the quality of sleep in patient with hydrocephalus through full overnight polysomnography (PSG).
Methods: The patient underwent to a clinical evaluation and PSG exam at Sleep disorders Laboratory (UNINOVE).
Results: ALVM with 62 years old, BMI 31 kg/m^2, active, teacher, smoker (45 pack/years) with hypertension and acute myocardial infarction 3 years ago. He was in neurological treatment for the last two years due to tremors. Echocardiogram showed a normal ejection fraction with mild concentric hypertrophy and mild ventricular relaxation deficit. No other complaints without neurological deficits on physical examination. The patient showed intense snoring and excessive daytime sleepiness. After neurosurgery with ventricular peritoneal shunt in April (2014), the CT scan showed mild cerebral atrophy with ventricular enlargement and cerebrospinal fluid with normal pressure. The MRI confirmed the CT findings. The first PSG showed AHI of 74.9 with 50% of central apnoea and remained 30% of total sleep time (TST) with O_2 saturation below 90%. The second PSG with CPAP (10cmH_2O) showed AHI 27.2 (15.5/h central events) and remained only 1.9% of TST with O_2 saturation below 90%.
Conclusion: After treatment with CPAP the patient showed good clinical improvement of snoring, daytime sleepiness and quality of life. We suggest a new PSG with servo ventilation to evaluate the decrease of central apneas.
Support: The authors thank Fundaçao de Amparo a Pesquisa do estado de Sao Paulo (Fapesp, acronym in Portuguese) and Conselho Nacional de Desenvolvimento Cientifico e tecnologico (CNPq, acronym in Portuguese) for supporting this research.
Disclosure: Nothing to disclose.

P967

Subjective and objective sleep quality in migraine: the Hypnolaus/Psycholaus study

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Objective: The aim of this study was to compare subjective and objective sleep quality between migraine patients and age and sex matched controls.
Methods: Data from participants in a population-based cohort study (Colaus/Psycholaus/HypnoLaus, Lausanne, Switzerland) was collected. The diagnosis of migraine was assigned according to International Headache Society criteria. Sleep-related complaints and habits were investigated using the Pittsburgh Sleep Quality Index (PSQI), the Epworth Sleepiness Scale, the International Restless Legs Syndrome (RLS) Study Group questionnaire, the Berlin questionnaire for sleep disordered breathing and the Horne-Ostberg morningness-eveningness questionnaire. All subjects underwent a complete polysomnography (PSG) at home.
Results: 115 subjects (mean age: 54.3 ± 10.7 years, 69.5% women) with migraine (w/wth aura) were identified. Compared to 230 controls matched for age and gender (mean age: 54.3 ± 10.7 years, 69.5% women), migraineurs reported poorer sleep quality (PSQI score: 6.1 ± 3.3 vs. 5 ± 2.8, $P = 0.006$), their estimated subjective sleep latency was higher (20.2 ± 18.8 vs. 16.2 ± 14.5 min, $P = 0.009$), they had more frequently RLS (22.6% vs. 13.9%, $P = 0.039$) and apneas were more often reported by relatives (11.3% vs. 5.2%, $P = 0.014$). No major differences were found for PSG sleep variables, but a trend was observed for longer total sleep time (415.7 ± 58.2 vs. 403.1 ± 73 min, $P = 0.10$) and lower slow wave sleep (20.4 ± 7.3% vs. 21.9 ± 8.2%, $P = 0.10$). No significant differences were found between groups concerning other sleep related parameters, neither for the intake of drugs potentially influencing sleep.
Conclusions: Compared to controls, migraine patients reported more sleep-related complaints, despite the absence of major differences in objective sleep variables measured by PSG.
Disclosure: Nothing to disclose.

P968

EEG topography alterations in wakefulness and sleep in patients with mild cognitive impairment and Alzheimer disease

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Objective: In mild cognitive impairment (MCI) and Alzheimer disease (AD) the waking EEG is characterized by a slowing phenomenon, with increase of delta and theta frequencies and decrease of alpha and beta bands. Several findings confirm that MCI/AD patients also show sleep abnormalities, such as increase of nighttime awakenings and stage 1, decrease of slow wave sleep and REM sleep. Since waking and sleep EEG are strongly related, the aim of the present study was to assess the EEG topography during sleep and wakefulness in MCI/AD patients, evaluating possible relations between their EEG alterations.
Methods: 16 AD, 24 MCI and 11 elderly healthy controls performed one-night sleep polisomnographic recording (19 cortical derivations, EOG, EMG). Moreover, waking EEG (5 min with eyes open and 5 min with eyes closed) was recorded in two different circadian phase (morning and evening).
Results: Waking EEG in clinical groups are characterized by an increase of posterior delta and anterior theta, associated with decreased beta 1 in central regions. In NREM sleep we have found decreased sigma band in clinical groups, while during REM sleep the patients show a reduction of theta band.
Conclusions: The increase of low-frequency bands in MCI/AD patients confirms the phenomenon of EEG slowing during wake. The

decrease of both beta 1 during wake and sigma during NREM suggests the existence of a similar pattern of EEG alteration between wake and sleep, albeit this conclusion cannot be extended to changes in the low-frequency activity.

Disclosure: Nothing to disclose.

P969

Interhemispheric information flow between wake- and sleep-EEG signals after cerebral ischemia

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Objectives: Neuroimaging studies have shown that large-scale cortical functional networks, especially interhemispheric connections, play a crucial role for recovery after stroke (Carter et al., Ann Neurol, 2010; Park et al, Stroke, 2011). Here we characterize interhemispheric information flow between EEG signal in the acute and in the subacute phase after cerebral ischemia, using methods from information theory.

Methods: 29 patients with unilateral acute ischemic stroke in the anterior circulation underwent a polysomnography (SAS-CARE Study) within a few days after stroke and on follow up after 3 months. Information flow was assessed with symbolic transfer entropy (STE) between bipolar derivations defining left and right hemisphere (F3-O1 vs. F4-O2), anterior (F3-C3 vs. F4-C4), and posterior (C3-O1 vs. C4-O2) regions. Asymmetries between left-to-right and right-to-left STE values were compared with lesion laterality.

Results: In the acute phase, interhemispheric information flow was significantly asymmetric, going predominantly from the non-lesional to the lesional side during wakefulness ($P = 0.044$), N3 ($P = 0.01$) and REM ($P < 0.0001$). After 3 months, asymmetries were no longer statistically significant. Interhemispheric information flow within anterior and posterior brain regions was significantly asymmetric only during REM sleep (anterior: $P = 0.041$, posterior: $P = 0.044$).

Conclusion: The significant asymmetry in interhemispheric information flow during W, N3 and REM in the acute phase, but not after 3 months, is consistent with functional imaging studies showing a transient compensatory 'over activity' of contralateral areas after stroke (Rehme et al., J Physiol, 2013). Future work will include correlation of information flow with the localization and size of lesions.

Disclosure: Nothing to disclose.

P970

Fatigue and excessive daytime sleepiness in the UK Myotonic Dystrophy Patient Registry

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Background: The UK Myotonic Dystrophy Patient Registry was launched in May 2012 and collects a core dataset, outlined in the TREAT-NMD/Marigold International Workshop Report and data is entered by both patients and clinicians.

Fatigue and excessive daytime sleepiness are major non-muscular complaints of myotonic dystrophy type I patients and we want to assess how the registry may reflect reality and give clues for future research.

Objectives: To assess the relevance of fatigue and excessive daytime sleepiness among the myotonic dystrophy type 1 (DM1) population who have registered between May 2012 and April 2014.

Results: Of the 365 patients registered with DM1 the majority report adult-onset DM1 with similar proportions of patients registered from both sexes. 75% of patients were between 21 and 60 years old, with only 15% over 60. Fatigue and/or excessive daytime sleepiness were the most commonly reported symptoms (78%). Fourteen percent of the patients take modafinil for fatigue and excessive daytime sleepiness.

Conclusions: Fatigue and excessive daytime sleepiness are a main complaint of myotonic dystrophy type I patients. We need to investigate the degree to which these symptoms impair work capacity and quality of life of these patients and how modafinil or other therapies may help. However, it is clear that modafinil use is present in this population, regardless of the recommendations from the European Medicines Agency (EMA) and the Medicines and Healthcare Products Regulatory Agency (MHRA) to cease its use in myotonic dystrophy, pointing towards an unmet medical need that warrants further investigation.

Disclosure: Nothing to disclose.

P971

Longitudinal changes in the build-up of sleep slow wave activity in young patients recovering from acquired brain injury

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Objectives: Sleep slow wave activity (SWA, 1–4.5 Hz) is known to be regulated in a use dependent manner: globally after prolonged wakefulness and locally after intensive training involving specific brain areas. After acquired brain injury, patients typically show an increase in low frequency brain activity (ALFA, 0.5–6 Hz) overlapping the frequency range of SWA. In the present study we investigate longitudinal changes in SWA in young patients recovering from acquired brain injury and, hypothesize that the build-up of SWA, rather than SWA itself, reflects use dependent brain activity.

Methods: We used high density electroencephalography (128 electrodes) to record two nights of sleep (at onset of rehabilitation and 2–4 months later) in 5 children with acquired brain injury. We calculated SWA over 2-min epochs for the first 30 min of non-rapid eye movement sleep, and quantified the build-up using a linear fitting approach.

Results: Comparing SWA and the build-up of SWA, we found electrode clusters with high SWA, but low SWA build-up, in the two most severely impaired patients. Four patients who recovered motor functions in the course of rehabilitation showed a maximal increase of the SWA build-up from the first to the second measurement over

central brain areas related to motor functions (range: 37–339% increase).

Conclusions: In children recovering from acquired brain injury, high SWA despite low SWA build-up might indicate non-regulated, use independent brain activity related to ALFA. In contrast, changes in SWA build-up in the course of rehabilitation might reflect changes in use due to neuronal reorganization.

Disclosure: Nothing to disclose.

P972

Partial sleep deprivation in patients with focal epilepsy: effect on sleep macrostructure and cyclic alternating pattern

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Objectives: The potential mechanisms underlining the promoting role of sleep deprivation (SD) for epileptic seizures and interictal epileptiform abnormalities have been extensively studied, but some issues have not been completely addressed. Epileptic phenomena are deeply sensitive to fluctuations of arousal and sleep instability, that may be related to SD. Aim of our study was to evaluate the role of cyclic alternating pattern (CAP) as a potential mechanism through which SD may exert its activating effect.

Methods: Eight patients with focal epilepsy (mean age 39 $\pm$ 19 yy; 5F, 4M) underwent in-lab polysomnography (PSG) and sleep deprived diurnal PSG after partial SD, being awake from 2 AM, performed within 7 days. Sleep macrostructural and microstructural parameters were evaluated according to standard guidelines.

Results: One subject had an epileptic attack recorded during the diurnal polysomnogram and was excluded from the analysis. Macrostructural analysis showed a decreased first REM latency for diurnal sleep (night vs. diurnal sleep: 207.0 $\pm$ 158.3 vs. 59.2 $\pm$ 42.4 min), although with a decreased REM percentage (18.0 $\pm$ 7.8 vs. 10.6 $\pm$ 10.3) and a trend in increased SWS. Microstructural analysis suggests a greater sleep instability for diurnal sleep, with significantly increased CAP rate (53.5 $\pm$ 8.2 vs. 66.0 $\pm$ 9.9), particularly for N2 (44.2 $\pm$ 9.7 vs. 57.6 $\pm$ 15.3) and CAP slow components, as reported by increased A1 index (46.0 $\pm$ 10.0 vs. 57.7 $\pm$ 17.7).

Conclusions: In diurnal sleep after partial SD of subjects with focal epilepsy, CAP and its slow components, are increased and may thus offer a favorable framework through which SD modulates interictal and ictal epileptic activity.

Disclosure: Nothing to disclose.

P973

Narcolepsy-like symptoms in Parkinson′s disease

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Objectives: Various sleep related problems, e.g. insomnia and symptoms of RBD, are common in Parkinson′s disease (PD). The prevalence of narcolepsy-like symptoms, hallucinations and RBD and their association with other symptoms were studied.

Methods: Altogether 1447 randomly selected Parkinson patients, aged 43 to 89 years, participated in a questionnaire study. A structured questionnaire with 207 items was based on the Basic Nordic Sleep questionnaire. Questions on demographics, PD, RBD, and other issues were included.

Results: The response rate was 59.0% and of these 73% had answered to all questions that were used in the analyses (n = 625).Occurrence of narcolepsy like symptoms (UNS $\geq$14) were found in 11.0% of the subjects, RBD (RBDSQ $\geq$6) was found in 39.2% of all patients with PD and in 59.4% of those with narcolepsy-like symptoms having UNS $\geq$14. In patients with PD hallucinations before going to bed in the evening occurred in 6.1%, hypnagogic hallucinations in 4.0%, hypnopompic hallucinations in 3.4%, and hallucinations during night in 8.3%. Cataplexy symptoms occurred in 46.4% of subjects with UNS $\geq$ 14. In a logistic regression analysis PD-NC was associated with RBD, all types of hallucinations, daytime sleepiness, fatigue, and intense dreaming also when adjusted for age, sex, disease duration and use of levodopa.

Conclusions: Narcolepsy-like symptoms may be present in patients with Parkinson′s disease. Symptoms of RBD associated with symptoms of narcolepsy including symptoms of cataplexy.

Disclosure: Nothing to disclose.

P974

Periodic limb movements during REM sleep in multiple sclerosis

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Objectives: There are few studies describing periodic limb movements (PLM) in REM sleep in patients with narcolepsy, restless legs syndrome, REM sleep behavior disorder, spinal cord injury and, to a lesser extent, in insomnia patients and healthy controls, but no published cases in multiple sclerosis (MS).

Methods: From our original cohort, the first cross-sectional polysomnographic trial in consecutive MS patients, we retrospectively analysed PLM during REM sleep classifying patients into two subgroups: REM-PLM greater than or equal to vs. less than ten per hour REM sleep (PLMI-R-high vs. PLMI-R-low). A univariate analysis between PLM and disability, laboratory findings and polysomnographic data was performed. Fifty-nine patients were classified in the PLMI-R-high and seven in the PLMI-R-low subgroup.

Results: We found a significant difference in the classification in one of the two subgroups and disability measured by the Kurtzke Expanded disability status scale (P = 0.023), whereas there were no differences for laboratory and other polysomnographic findings. The presence of more than 10 PLM per hour REM sleep was associated with a greater risk of disability (odds ratio 22.1; 95% - Confidence interval 3.5–139.7; P < 0.0001).

Conclusions: PLM during REM sleep were not described in MS before and we hypothesize that spinal cord or brainstem lesions may cause them. The anatomical pathways of this new finding should be investigated further.

Disclosure: Nothing to disclose.

P975

Lower quality of sleep is associated with lower quality of life in patients with epilepsy

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Objectives: Aim of study was to identify whether there is a relationship between quality of sleep and health-related quality of life (HRQOL) among patients with epilepsy.

Methods: Patients with proven diagnosis of all-cause epilepsy were enrolled in study. Quality of sleep was assessed by Pittsburgh Sleep Quality Index (PSQI) discriminating sleep quality into poor and good, HRQOL was assessed by SF-36 generic questionnaire. The latter has 8 domains (D1–D8) expressing physical, emotional and social well-being. Patients were divided into two groups according to PSQI rates: Group 1 (G1) - patients having normal quality of sleep: Group 2 (G2) - patients with low quality of sleep. T-test was used for statistics.

Results: 143 patients were enrolled in study (mean age was 34.4 years) where 89 were females (62.2%). The mean age (32.4 in G1, 36.5 in G2) and seizure frequency (G1 - 20/y, G2 - 35/y) were not significantly different in both groups G1: (n = 44) and G2 (n = 83) was not significant. Results of SF-36 for G1/G2 were: D1 = 78.7/55.3, D2 = 54.9/24.4, D3 = 58.7/24.4, D4 = 66.9/38.6, D5 = 66.8/41.2, D6 = 77.2/51.1, D7 = 79.1/50.2, D8 = 58.5/38.1. There were significant differences between all domains, showing lower quality of life in epilepsy patients with poor sleep quality - G1 ($P < 0.0001$). Differences were more obvious for D2 (Limitations due to physical health), D3 (Limitations due to emotional problems), D4 (Energy/fatigue) and D5 (Emotional well-being).

Conclusion: The results of our study show there is a relationship between lower quality of sleep and poor HRQOL in patients with epilepsy. Emotional domains being more affected.

Disclosure: Nothing to disclose.

P976

'HRV' (Heart rate variability) - a new parameter for the autonomic nervous system and correlate of normal and pathologic sleep?

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The autonomic nervous system (ANS) plays an important role not normal sleep and sleedisturbances.

Measurements of heart rate variability (HRV) are generally performed on the basis of 24 h recordings (long-term recordings) depending on gender and age.

Important variables of heart rate variability are: power intensity(HRV), parasympathetic activity, vegetative quotient (LF/HF), total variability (SDNN). heartrate (HR). HRV - a new diagnostic tool for sleep.

The heart rate variability gives a good correlation (cross-correlation coefficient: 0.78582) to the PSG (polysonogramm). Therefore we can use the parameters of the HRV to describe sleep. The best parameters to discriminate good sleepers vs. insomnia patients are total variability (SDNN) and vegetative quotient (LF/HF).

In sleep disturbed patients (n = 15; 7 males, 8 females; age 45.29 $\pm$ 6.21) a reversal of autonomic activation between day and night based on a reduced capability regulation of the autonomic nervous system is found.

Sleep disturbed patients are suffering from a lower parasympathetic activity depicted by the vegetative quotient (VQ); moreover total variability (SDNN) is lower.

Sleep of parkinson patients (n = 8; 6males, 2 females; age 60.1 $\pm$ 8.9) affects sympathovagal balance both in nREM and REM sleep, indicating an impairment of one or both branches of the autonomic nervous system. In further investigations different contributors of the pathophysiological processes in parkinson patients may be isolated.

Conclusions: Different variables of heart rate variability (HRV) may be helpful for an objective support to improve the diagnostic process of sleep in the future.

Disclosure: Nothing to disclose.

P977

Sleep/wake changes and loss of orexinergic neurons in transgenic mouse models of Alzheimer's disease

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Alterations in sleep/wake and circadian rhythms impair daily activities and memory processing of Alzheimer's disease (AD) patients. Experimental findings implicated the sleep/wake cycle and the neuropeptide orexin in amyloid-β (Aβ) accumulation in AD. We investigated sleep/wake changes and neuropathology in the PDAPP and TASTPM transgenic (Tg) mouse models of AD. Tg and matched wild-type (Wt) mice of 5 and 21 months of age were subjected to telemetric recording and the brains processed for histopathology under ethical approval. Wakefulness, rapid-eye movement and slow-wave sleep (SWS) were scored, and spectral power for specific band frequencies analyzed. Alterations in electroencephalographic power spectra, in particular a decrease in delta frequency band, were found in Tg mice of both age groups. Sleep/wake abnormalities, such as decreased wakefulness and increased SWS, were detected in the older Tg mice. A significant reduction in the number of orexin-expressing neurons was found in the hypothalamus of the older PDAPP and Wt mice, compared to younger ones. Such reduction was more marked in the Tg mice that in Wt ones. No Aβ accumulation was detected in the hypothalamus of PDAPP mice of either age group. Aβ deposition was observed in the hippocampus, in intimate association with glial cell activation, in 21 month-old PDAPP mice but not in younger ones. Analyses on TASTPM mice are in progress. The findings implicate orexinergic neuron loss in sleep/wake changes observed in AD, in the absence of Aβ deposition in the hypothalamus.

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P978

Relationship of insomnia to different nocturnal symptoms in patients with Parkinson's disease

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Objectives: To determine the relationship of different nocturnal symptoms of Parkinson's disease (PD) with insomnia.

Methods: Patients with PD (UK PD Society Brain Bank diagnostic criteria) were enrolled in study and divided into 2 groups: PD with insomnia, and PD without insomnia. They were interviewed for having nocturnal akinesia, nocturnal tremor, nocturia, vivid dreaming/parasomnia, and restless legs syndrome (RLS). Chi-square test was used for statistical analysis.

Results: Forty-four patients with idiopathic PD without cognitive symptoms aged 47–79 (mean age 63.5 years, females - 40.9%), were enrolled in the study (mean duration - 3.9 years, Hoehn and Yahr mean stage - 2). PD with insomnia group: $n = 25$, females - 44%, mean age - 63.5 years, mean duration - 4 years, mean stage - 2.1. PD without insomnia group: $n = 18$, females - 38.9%, mean age - 63.5, mean duration - 3.9 years, mean stage - 1.9. Nocturnal symptoms were distributed in PD without insomnia group vs. PD with insomnia group as follows: nocturnal akinesia - 10 of 18 (55.6%) vs. 17 of 25 (68%); nocturnal tremor - 9 of 18 (50%) vs. 13 of 25 (52%); nocturia - 10 of 18 (55.6%) vs. 18 of 25 (72%); vivid dreaming/parasomnia - 10 of 18 (55.6%) vs. 12 of 25 (48%); RLS - 4 of 18 (22.2%) vs. 3 of 25 (12%). The first three were higher in PD+insomnia; however, differences were not statistically significant ($P > 0.05$).

Conclusion: Current findings suggest that nocturnal symptoms are not associated with insomnia in our sample of PD patients.

Disclosure: Nothing to disclose.

P979

Is sleep related breathing disorder associated with REM sleep behavioural disorder in patients with idiopathic Parkinson's disease?

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Objectives: It has been controversially debated whether patients with idiopathic Parkinson's disease (PD) are prone to develop sleep related breathing disorders (SRBD). Since it has been suggested that REM-sleep behavioural disorder (RBD) might affect breathing in REM-sleep, we investigated whether RBD and SRBD are associated in patients with PD. To this end, we examined the prevalence of SRBD in PD patients with (PD+RBD) and without RBD (PD-RBD) as well as in patients with idopathic RBD (iRBD) without PD.

Methods: We examined 30 patients with PD of whom 19 had PD+RBD and 11 PD-RBD. As a further control we studied 13 patients with iRBD. All patients underwent video polysomnography. In patients with PD, daily Levodopa equivalent dose (LED) was assessed.

Results: AHI in the PD+RBD group (mean ± SD: 12,2 ± 12,5/h) was significantly higher than in the PD-RBD group (2,2 ± 2,3/h); AHI in the iRBD group was 8,4 ± 8,7/h. There was no difference in AHI between REM and NREM-sleep in all groups. LED was higher in the PD+RBD group (902 ± 770 mg) than in the PD-RBD group (660 ± 479 mg).

Conclusions: PD+RBD patients show significantly increased AHI compared to those with PD-RBD whereas patients with iRBD also have an increased AHI, though not significantly. In patients with PD, increased AHI is associated with more severe PD. It seems likely that there is a common underlying pathophysiology that affects the neuronal circuits involved in respiratory regulation as well as in inhibition of the motor system in REM-sleep independently from dopaminergic transmission as both groups of patients with RBD display SRBD.

Disclosure: Nothing to disclose.

P980

Epilepsy patients with insomnia express more severe depression compared to insomnia patients

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Objective: Chronic insomnia and epilepsy are both associated with higher rates of depression. The aim of the current study was to observe whether there is difference between severity of depression among epilepsy patients having chronic insomnia compared to patients with chronic insomnia alone. **Methods**

The study was performed among two groups of patients:: Group 1 (G1) - patients with epilepsy and co-morbid chronic insomnia, Group 2 (G2) - patients with primary chronic insomnia.

The diagnosis of chronic insomnia was made according to clinical interview utilizing International Classification of Sleep Disorders (2nd edition) criteria, and diagnosis of epilepsy was proven at a tertiary epilepsy center. The severity of depression was assessed by Hamilton Depression Rating Scale (HAMD). T-test was used for statistical analysis.

Results: Thirty-three epilepsy patients with chronic insomnia were enrolled in G1 (mean age = 40 years, F/M = 66.7%/33.3%), and 31 patients with primary chronic insomnia in G2 (mean age = 40.4 years F/M = 48.5%/51.5%). Mean HAMD score in G1 was 21.5 (12–36) and 17.8 (7–31) in G2. There was higher rate of depression in patients with epilepsy and insomnia, and this difference was statistically significant ($P = 0.009$).

Conclusion: Our findings suggest depression could be more severe in epilepsy patients with insomnia than in patients who have chronic insomnia. Although this issue is multi-factorial and the current study contributes to the further understanding of this connection.

Disclosure: Nothing to disclose.

P981

Estimation of sleep in patients with epilepsy: comparison of polysomnographic (PSG) and sleep log measures

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Objectives: Sleep logs represent a low-cost adjuvant tool in the assessment of sleep/wake disorders, scarcely used in the investigation of sleep and epilepsy. We compared subjective sleep measures as obtained from self-report and sleep logs with PSG measures in a cohort of epileptic patients unselected for sleep disorders.

Methods: Forty-eight epileptic patients (12 males/36 females, mean age 41 ± 13 year) underwent PSG preceded by 1-week sleep logs. Parameters under study were: mean 1-week sleep-logged total sleep time (TST-L), overnight PSG total sleep time (TST-PSG) and sleep latency (SL-PSG), and post-PSG self-report total sleep time (TST-SR) and sleep latency (SL-SR). A 5-point Likert scale was used to evaluate the TST-SR and SL-SR, as a measure of first night effect (FNE) on PSG. Mean monthly seizure frequency (MMSF) was modeled binomially using a cut-point of 4/month. Pearson correlations were used for normally distributed variables, Spearman's for skewed, and linear regressions for modeling. Covariates for regression included age, MMSF and number of antiepileptic drugs (AEDs).
Results: The MMSF was 2.9 ± 6.6. A positive correlation was found between TST-SR and TST-PSG (Pearson r = 0.452, $P = 0.0016$) and between SL-SR and SL-PSG after correcting for FNE (Spearman r = 0.5, $P < 0.0004$), while TST-PSG and TST-ML correlated less strongly. After adjusting for age, MMSF and number of AEDs did not predict TST-PSG.
Conclusions: This preliminary work suggests that adults with epilepsy can accurately estimate sleep time and latency recorded on PSG when considering the impact of first night effect. Further work validating sleep log data in epilepsy populations is required.
Disclosure: Nothing to disclose.

P982

Pulmonary function of myotonic dystrophy with chronic ventilatory failure

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Objectives: Chronic ventilatory failure is a common complication of neuromuscular disorders, and generally parallels the development of limb and respiratory muscle weakness. However in myotonic dystrophy (MD), ventilatory failure may occur when respiratory muscle weakness is not marked. We aimed to correlate daytime pulmonary function studies with nocturnal ventilatory status of MD patients.
Methods: MD who had applied noninvasive home mechanical ventilator (HMV) at pulmonary rehabilitation center at Gangnam Severance hospital due to ventilatory impairment during overnight capnometry and oxymetry studies became candidates. We retrospectively reviewed daytime pulmonary function data at the point of HMV application, and correlations were sought between the two.
Results: 27 MD patients (M:10, F:17, mean age 45.3 ± 13.6 years) were recruited. During overnight studies, mean maximal end tidal CO2 was 56.1 ± 10.9 mmHg, and mean nocturnal O2 saturation was 94.4 ± 3.7%. On pulmonary function, mean normal predicted forced vital capacity (FVC) in sitting position was 40.6 ± 18.0%, and nine patients presented >50% of normal predicted FVC. Mean value of maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) was 33.6 ± 18.8cmH2O and 42.7 ± 16.8 cm H_2O respectively.
Conclusions: In MD patients, the occurrence of nocturnal ventilatory failure can be difficult to predict from daytime measurement of pulmonary function. In order to find out latent ventilatory failure, nocturnal capnometry and oxymetry studies can be helpful for patients even with tolerable range of pulmonary function. Pathophysiology of ventilatory failure in MD may include other mechanism like abnormal central respiratory drive as well as respiratory muscle weakness. Further research is warranted on this issue.
Disclosure: Nothing to disclose.

P983

Polysomnography detects benign paroxysmal positional vertigo

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Objectives: Benign paroxysmal positional vertigo (BPPV) is the most common cause of dizziness. Head movements may disabling episodes of vertigo accompanied by nystagmus. Despite the availability of highly effective canalolith repositioning procedures, the condition remains underdiagnosed, which too often means unnecessary long-lasting suffering and dangerous falls. While it is well known that changes of head position in bed often elicit BPPV, video-polysomnography (PSG) has not yet been considered as a tool to detect unrecognized BPPV.
Methods: Case Report.
Results: A 59-year-old woman was admitted to our emergency department because of repeated attacks of rotational vertigo, triggered by head movements while in bed. Supine roll test to the left revealed apogeotropic horizontal nystagmus with a latency of several seconds. Supine roll test to the right caused even stronger apogeotropic nystagmus, establishing the diagnosis of left lateral canal cupulolithiasis. Since the attacks were often precipitated by changes of body position at night and thus interfering with sleep quality, we decided to perform a whole-night-PSG including electro-oculography (EOG). Six episodes of apogeotropic positional nystagmus were observed with change of body position. Several episodes with changes of head position but unaltered body position also triggered positional nystagmus.
Conclusions: This case provides the first evidence that PSG can detect BPPV in the sleep laboratory. The typical EOG pattern of positional nystagmus should therefore be brought to the attention of sleep specialists, because this cumbersome condition is highly prevalent yet often overlooked, while the diagnosis is easy and treatment is safe, inexpensive and highly effective.
Disclosure: Nothing to disclose.

P984

Reduced frequency of cortical arousals in patients with idiopathic Parkinson's disease

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Objectives: To assess the frequency and clinical correlates of arousal characteristics in patients with idiopathic Parkinson's disease (PD).
Methods: Seventy PD patients and 70 control subjects were carefully matched with regard to age, sex, body-mass-index, apnea-hypopnea-index (AHI) and periodic leg movements in sleep (PLMS).
Results: Despite all demographic and polysomnographic similarities, PD patients had significantly fewer arousals than controls (9.1 ± 7.6/h vs. 18.6 ± 22.9/h, $P = 0.001$). Arousals occurred most often from sleep stages NREM1 and NREM2, less frequently from REM sleep,

and rarely from slow-wave sleep. Twenty-one PD patients and 22 control subjects had normal numbers of both AHI and PLMS, and the frequency of arousals appeared to be similar in these subjects (6.5 ± 5.4/h vs. 8.5 ± 5.6, $P = 0.24$). In the presence of pathological numbers of AHI and/or PLMS, control subjects presented a strong elevation of the arousal index to 23.3 ± 26.1/h ($P < 0.001$). Conversely, PD patients exhibited only a mild increase of the arousal index to 10.2 ± 8.2/h. While the arousal index of PD patients with short disease duration (≤6 years, $n = 37$) was moderately associated with AHI (r = 0.383, $P = 0.02$), PD patients with long disease duration (>6 years, $n = 33$) did not show this correlation anymore (r = 0.285, $P = 0.11$). In the same line, linear regression analysis revealed a significant negative association between arousal index and Hoehn & Yahr stages ($\beta = -0.297$, $P = 0.015$).

Conclusions: Our findings suggest that the neurodegenerative process underlying Parkinson's disease causes a progressive impairment in brain structures responsible for arousal regulation. The clinical significance of our observation remains uncertain at this moment.

Disclosure: Nothing to disclose.

P985

Occurrence of restless legs syndrome is associated with higher depression and anxiety rates and nocturnal seizures in epilepsy

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Objective: Our aim was to determine possible association of restless legs syndrome (RLS) with depression, anxiety and seizure frequency in epilepsy patients.

Methods: Patients with epilepsy diagnosis proven at a tertiary center were enrolled in study and divided into two groups: RLS(+) (if fulfilling 4 essential diagnostic criteria for RLS) and RLS(-). Hamilton Depression and Anxiety Rating Scales (HAMD and HAMA respectively) were used for evaluating severity of depression and anxiety. Last year and month seizure frequencies and occurrence at night was reported by patients. Chi-square test and T-test were used for statistical analysis.

Results: Total number of enrolled patients with epilepsy was 135. Samples by groups had the following characteristics: in RLS(+) group $n = 28$ (20.7%), mean age was 42.9 (18–67), F - 46.4%; in RLS(-) group $n = 107$ (79.3%), mean age was 33.8 (18–71), F - 44.9%. HAMD and HAMA scores were higher in RLS(+) group: HAMD mean score for RLS(+) was 16.6, for RLS(-) - 12 ($P = 0.005$); HAMA mean scores: RLS(+) - 19.4, RLS(-) - 13.9 ($P = 0.006$). Patients reported higher seizure frequencies for last year and last month in RLS(-) group: RLS(-)/RLS(+) for last month - 3.24/1.86, for last year - 31.3/25.6 ($P > 0.05$). Interestingly, seizure occurrence at night (partially or exclusively) was significantly higher in RLS(+) (77.8%) than in RLS(-) group (54.6%) ($P < 0.05$).

Conclusion: Our data suggest that RLS could be an important contributor for higher depression and anxiety rates in epilepsy. Also, seizures at night seem to be more prevalent in epilepsy patients with RLS.

Disclosure: Nothing to disclose.

P986

Faster sleep spindles at the side of the epileptic focus in patients with temporal lobe epilepsy

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Objectives: To identify potential asymmetries of sleep spindles in patients with temporal lobe epilepsy (TLE).

Method: Sleep recordings of six patients with a right focus, six patients with a left focus and twelve control subjects with non-epileptic paroxysmal events were used. Sleep spindles were detected at electrode Cz using a custom computer algorithm implemented in MATLAB. Spectral analysis was performed in order to extract parameters such as spectral power, spectral centroid frequency, magnitude squared coherence and the angle (ANG), which represents phase difference between 2 electrodes, all in 10–16 Hz range.

Results: No statistically significant inter-hemispheric asymmetries were found for spectral power, centroid frequency or magnitude squared coherence. ANG from F3 to F4 was positive in all 6 R-TLE patients (mean ± SE = +0.197 ± 0.057) (implying a leading F4) and negative in 5 of 6 L-TLE patients (mean ± SE = -0.028 ± 0.025).

Conclusion: Epilepsy may promote a small but consistent phase lag between spindles recorded from left and right surface electrodes, with the side of the epileptic focus having the lead. Network cortical reorganization at the side of the epileptic focus and/or altered hippocampal-prefrontal networks that modulate sleep oscillations may underlie the observed changes. Such results also suggest that further development of sleep spindle asymmetry computational analysis methods may find a role in the indirect localization of an occult epileptic focus.

Disclosure: Nothing to disclose.

P987

Bright light therapy in restless legs syndrome: a double-blind, placebo-controlled study

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Objectives: Medications often partially alleviate the symptoms of RLS patients, emphasizing the need for finding alternative treatments. Recent studies reported an efficacy of bright light therapy (BLT) in Parkinson disease. RLS pathogenesis involves the dopaminergic system and light has been shown to influence the dopaminergic tone. Therefore, the objective of our study was to determine the therapeutic value of three weeks of BLT on RLS symptoms severity, sleep quality, daytime somnolence, circadian rhythms and mood.

Methods: Proof of concept, double blind, placebo-controlled study. Twenty-four drug-free patients were pair-matched according to age, sex and symptoms severity. The administration of BLT (10 000 Lux 30 min) or placebo light (<70 lux, >620 nm) was calculated individually according to the circadian phase of each patient in order to act through direct, non-circadian, effects of light.

Results: The circadian phase remained unchanged (sleep log, actimetry, core body temperature). Although BLT did not significantly ameliorate RLS symptoms severity (IRLS score, suggested immobilization test), the treatment improved sleep parameters such as sleep

maintenance. BDI-II score was ameliorated in patients with impaired mood at inclusion, but no statistical analyses could be done given the low number of depressed patients.

Conclusion: Even though BLT does not influence directly RLS severity, the results suggest that BLT administered at appropriate circadian time ameliorate sleep quality and mood, symptoms often associated with RLS. Thus, BLT could represent a new and innovative approach in the treatment of RLS, especially in case of mood alteration as antidepressants may worsen RLS.

Disclosure: Nothing to disclose.

P988

The prevalence of restless legs syndrome (RLS) and sleep medication use in patients with myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS)

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Objectives: The non-restorative sleep is one of the major symptoms in ME/CFS according to Canadian criteria, but RLS can co-exist as co-morbidity. RLS may cause sleep disorders and daytime symptoms such as tiredness and/or fatigue. However, little is known about the prevalence of RLS as well as use of sleep medication in patients with chronic fatigue disorders.

Methods: Ninety-seven patients referred to ME/CFS-rehabilitation completed questionnaires related to RLS (four positively answered questions are required) as well as Epworth Sleepiness Scale (ESS). The severity of RLS was also graded according to Likert 4 grade scale from mild to very difficult. Clinical records were studied in order to estimate the use of sleep medications.

Results: Of 97 patients (81% women), 57 patients were diagnosed with ME/CFS according to Fukuda and/or Canadian criteria while 40 suffered from other disorders explaining fatigue. Results showed that 40% of patients in both groups rated positively for all four questions for RLS. 2/3 of the patients graded their RLS symptoms as mild-severe. Approximately 30% of patients used sleep pills helping mostly for insomnia symptoms and only 2% were treated with dopaminreceptor agonist. There were no significant correlations between symptoms of RLS, sleepiness and use of sleep medication.

Conclusions: The prevalence of RLS in patients with fatigue was as high as 40%. One-third of patients used sleeping pills but few were treated for RLS. We suggest that patients with fatigue should be asked about the symptoms of RLS and treated adequately before the diagnosis of ME/CFS is given.

Disclosure: Nothing to disclose.

Paediatrics

P990

Sleep duration sleep at 3 years is associated with fat, lean and bone mass at 4 years of age: findings from the Southampton Women's Survey

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Objectives: To determine if sleep duration at 3 years predicts body composition at 4 years of age.

Methods: Southampton Women's Survey is a population-based cohort study of 12 583 women aged 20–34 years. Children born to those who subsequently became pregnant (n = 3159) were followed up. Mothers reported their child's total 24 h sleep time at age 3 years. Fat, bone and lean mass were derived using dual energy X-ray absorptiometry (DXA) at age 4 years in a subset of children. The relationship between sleep and body composition was assessed in multiple regression analyses with adjustment for maternal education, pre-pregnancy BMI, smoking during pregnancy, child's age, sex, height at DXA, age last breastfed, dietary quality at 3 years, TV watching and hours actively on the move.

Results: Mean 24 h sleep duration of the 898 children (475 boys) who had a DXA scan was 11.5 h. Shorter sleep duration was associated with higher BMI (β = −0.2366 kg/m^2 per hour, 95% CI −0.3724, −0.1007) and fat mass (β = −0.1188 kg per hour, 95% CI −0.2288, −0.0089), but also with lean mass (β = −0.1287 kg per hour, 95% CI −0.2142, −0.0434) and total bone mineral density (β = −0.0039 kg per hour, 95% CI −0.0075, −0.0004).

Conclusions: We confirm previous findings that shorter sleep in early childhood predicts greater BMI and fat mass but also report novel findings that shorter sleep predicts greater lean and bone mass. Our data suggest that the inverse relationship between sleep and BMI is not determined by adiposity alone.

Disclosure: Nothing to disclose.

P991

Consequences of taking risks: why adolescents choose to 'switch off' before bed

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Objectives: Technology use is ubiquitous in paediatric populations, and various mechanisms have been proposed to explain how technology affects sleep. This study investigated individual differences and the 'displacement of sleep' hypothesis by examining whether risk-taking propensity, flow state, and gaming experience influenced adolescents' self-selected bedtimes after technology use, and whether clock presence moderating such a link.

Methods: 21 adolescents (age = 17.6 ± 1.8 years) completed the Cognitive Appraisal of Risky Events and Game Engagement questionnaires, and attended two school nights (1 week apart) in the Sleep Laboratory (clock present vs. absent, counter-balanced). Adolescents played the new videogame *Bioshock Infinite* from 8 pm until they self-selected their own bedtime. Bedtimes were monitored via infrared internet protocol (IP) cameras.

Results: Flow state, gaming experience, and perceived benefits of risk-taking did not predict adolescents' bedtimes (all P > 0.05). However adolescents higher on perceived consequences of risk-taking went to bed earlier (P = 0.03), such that a 1-unit increase on the questionnaire (eg, '*moderately likely*' to '*extremely likely*' to engage in behaviour) corresponded with 38.6-min earlier bedtime. Clock presence had no significant moderating effect, despite adolescents rating their reason for bedtime due to '*conscious it was getting late*' on clock-present nights, and '*felt sleepy*' on clock-absent nights.

Conclusions: Adolescents who perceive greater consequences of risk-taking actions self-select earlier bedtimes after technology use, independent of internal (i.e., sleepy) or external cues (i.e., parents, clocktime). More research is needed to identify which adolescents are 'at risk' for delaying bedtimes, and thus displacing sleep, due to technology use.

Disclosure: Nothing to disclose.

P992

Correlation between salivary alpha amylase level and electrocardiogram (ECG) based cardiopulmonary analysis in paediatric subjects with obstructive sleep apnoea

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Objectives: The aim of this study is to confirm the association between sleep quality and sympathetic nerve activity according to the severity of sleep apnoea in the paediatric subjects.

Methods: This prospective study enrolled 63 children who underwent physical examination and overnight polysomnography (PSG). Continuous electrocardiographic (ECG) signal was taken as a part of PSG. Cardiopulmonary coupling (CPC) analysis for evaluation of sleep quality was performed using the commercially available PSG software. Saliva for evaluation of sympathetic activity was collected at night before PSG and in the early morning after.

Results: Subjects (n = 63) were divided into control (n = 24) and obstructive sleep apnoea syndrome (OSAS) groups (n = 39). There were no significant differences between the two groups in almost all parameters of CPC and salivary alpha amylase (sAA), except high frequency coupling (HFC). The OSAS group was subdivided into mild (n = 17) and moderate-severe (n = 22) groups to evaluate the change of OSA severity. HFC and low frequency coupling (LFC) showed significant differences in moderate-severe group compared to the other groups. Subtraction and ratio of sAA showed significant increase in moderate-severe group. In the correlation analysis, HFC was negatively correlated with AHI and arousal index whereas LFC was positively correlated with the AHI and arousal index. Subtraction and ratio of sAA was positively correlated with the AHI and arousal index.

Conclusion: Our study support that decreased sleep quality may be associated with increased sympathetic nerve system. Also, ECG -derived method and salivary sampling could be potentially used to assess sleep physiology in moderate-severe paediatric OSA.

Disclosure: Nothing to disclose.

P993

Analysis of cephalometry in obstructive sleep apnoea in paediatric subjects

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Objectives: Obstructive sleep apnoea (OSA) is characterized by repetitive collapse of the upper airway. Cephalometics is a simple, non-invasive technique with the ability to elucidate the upper airway structure. This study was designed to analyse the relationship between a cephalometric analysis and the apnoea-hypopnea index (AHI) in children with OSA.

Methods: A retrospective cross-sectional study was conducted. All subjects underwent otorhinolaryngologic examination and in-lab polysomnography. The children were then submitted to orthodontic evaluation and cephalometry. Cephalometry data included three segment of the upper airway: total length, upper segment and lower segment of upper airway based on the mandibular plane.

Results: Subjects were divided into control (n = 18) and OSAS group (n = 21). The OSAS group was subdivided according to the AHI (mild, 1 < AHI ≤ 5; moderate-severe, 5 < AHI). We found that subjects with OSAS had a longer upper airway length and lower segment of upper airway than control group. The significant difference was especially seen in the moderate-severe group compared to other groups. However, there were no differences in upper segment of upper airway according to the OSA severity. Thus, lower segment of upper airway could be considered to affect the OSA more significantly. AHI was statistically correlated with the lower segment of the upper airway among the three parameters (r = 0.35, P = 0.03).

Conclusion: Length of upper airway and lower segment of upper airway may help us to discriminate the moderate-severe OSA. Cephalometics is a non-invasive, inexpensive and easy method for evaluation of children with OSAS and for further treatment planning.

Disclosure: Nothing to disclose.

P994

The children sleep comic - a new self-rating tool for childhood insomnia

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Objectives: A proper diagnosis of sleep disorders in children should include self-ratings in addition to information provided by the parents. Yet, there are only few standardized self-assessment instruments for children, and these are based on verbal items. The children sleep comic provides a drawn picture for each item and response category and comprises 20 questions covering all relevant aspects for exploring insomnia in children, such as 'time to fall asleep' or 'sleeping in own bed'. First validation data and a cut-off-score are presented here.

Methods: We presented a sample of n = 127 children between 5 and 10 years of age with the children sleep comic to test its applicability in young children in a group testing setting and a sample of n = 106 children was tested in a one-on-one setting. Children also answered the Sleep Self Report (SSR-DE) and parents answered the Children's Sleep Habits Questionnaire (CSHQ-DE). Additionally a diagnosis was made by using a structured interview.

Results: Application of the children sleep comic took on average 30 min. Comparisons between the Children Sleep Comic and the SSR-DE and CSHQ-DE indicated moderate correlations. The younger the children, the more they benefited from a one-on-one setting. The children sleep comic allowed for discrimination between healthy children and children with sleep disorders.

Conclusion: The children sleep comic is an instrument appropriate for screening and exploring sleep behavior. The interactive procedure can foster a good relationship between the investigator and the child and thus, establishing the basis for successful intervention.

Disclosure: Nothing to disclose.

P995

Prospective changes in adolescents' sleep and weight across 1 year

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Objectives: A cross-sectional relationship between sleep and weight in adolescent samples is evident, however prospective evidence is mixed. The current study assessed the prospective relationship between adolescent sleep duration and sleep timing with body mass index (BMI) and weight status over a one-year period.

Methods: 106 adolescents (Time 1 age = 15.7 ± 0.9 years, Time 2 age=16.6 ± 0.9 years, 69%m) completed the School Sleep Habits Survey (incl. self-reported BMI, physical activity, SES [SEIFA]), and the CES-D during school class time, on two occasions, one year apart. 'Obese' and 'overweight' status were defined using Center for Disease Control and Prevention, the National Center for Health Statistics, and the American Academy of Pediatrics criteria.

Results: School-night sleep duration slightly decreased (8.1 to 7.9 h; P = 0.02). The percentage of adolescents overweight remained stable (17.9%); obesity showed a small decline (9.4 to 8.5%), yet overall BMI changed from 21.2 to 22.0. After accounting for demographic, depressed mood, physical activity and Time 1 weight variables, additional variance in Time 2 BMI scores explained by Time 1 school-night sleep duration was not statistically significant (B = 0.06, P = 0.14). No significant relationships occurred when testing for Time 2 overweight status in logistic regression analyses (OR = 1.20, 95% CI = 0.56–2.57). There was no evidence that sleep timing predicted BMI and overweight status (all P < 0.05).

Conclusions: This prospective study of Australian adolescents concurs with other prospective data from adolescents and young adults (Calamaro et al., 2010, JSR; Lauderdale et al., 2009, Am J Epidemiol), that shortened sleep duration during adolescence may not impact on later BMI or weight status.

Disclosure: Nothing to disclose.

P996

Does obstructive sleep apnea contribute to elevated intracranial pressure in children with syndromic craniosynostosis? A prospective cohort study

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Objectives: Children with syndromic or complex craniosynostosis have a prevalence of 68% of obstructive sleep apnea (OSA), which

has been associated with an increased risk for developing elevated intracranial pressure (ICP). The objective of this study was to evaluate how often and to what extend OSA increases the risk of elevated ICP in children with syndromic and complex craniosynostosis and to prospectively evaluate our current clinical treatment protocol.

Methods: A prospective observational cohort study of patients with syndromic or complex craniosynostosis treated at the Sophia Children's Hospital, started in January 1st 2007. All patients received repeated sleep studies and fundoscopy (to evaluate papilledema as proxy for elevated ICP), according to a standardized protocol.

Results: Sixty-two patients underwent full analysis, with a mean age at time of latest follow-up of 6.0 years. Mean age at first presentation of papilledema was 1.9 years (range 0.4–6.0). Twenty-three of 62 children (37.1%) had papilledema, of whom 13 (21.0%) pre-operative. Thirty-nine of 62 (62.9%) children had OSA. Compared to patients without OSA, papilledema was not more frequently present in patients with mild or moderate OSA. However, patients with severe OSA had pre-operatively significantly more often papilledema ($P = 0.015$).

Conclusions: Patients with syndromic craniosynostosis are at risk of elevated ICP due to a complex interaction of risk factors. The relationship between mild and moderate OSA and elevated ICP is weak, however in individual patients OSA may be the decisive factor. Severe OSA significantly increases the risk of elevated ICP.

Disclosure: Nothing to disclose.

P997

Effects of a multimodal sleep training for infants and toddlers on maternal sleep - preliminary actigraphy data

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Objectives: Sleep onset problems, problems sleeping through the night and behavioral insomnia of childhood are prevalent among young children and are correlated with maternal depression, higher parental stress level and lower quality of life. Therefore, a parent training for children from 6 months to 4 years of age with sleep disorders was developed: The Mini-KiSS training - a manualized multimodal short-term group intervention program. First studies showed positive effects on the sleep of children, e.g. higher total sleep time and less night wakings. We here present data on the effects on maternal sleep measured by actigraphy.

Methods: Before and after the training mothers ($n = 11$) took part in detailed diagnostic sessions including wearing an actigraph for one week each time. Parents participated in weekly treatment sessions à 90 min for six weeks. Therapeutical interventions were based on CBT and hypnotherapy (e.g. psychoeducation, sleep hygiene, emotional security, bedtime stories).

Results: The number of sleep disorders decreased significantly after taking part in the Mini-KiSS sleep training. Furthermore, maternal sleep improved significantly: e. g. sleep efficacy increased; sleep onset latency, number of awakenings and total wake time after sleep onset decreased.

Conclusions: The multimodal sleep training Mini-KiSS has not only effects on the sleep of the children, but also on objective parameters of maternal sleep. With its short duration it is well applicable and therefore can derive a benefit for the area of early childhood insomnia. Further investigations are necessary to consolidate these effects with a larger sample size.

Disclosure: Nothing to disclose.

P998

Delayed sleep phase disorder in an Australian school-based sample of adolescents

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Objectives: To establish the extent to which the developmental changes in sleep timing experienced by Australian adolescents meet the International Classification of Sleep Disorders (ICSD-2) diagnostic criteria for Delayed Sleep Phase Disorder (DSPD), and whether adolescents with DSPD engage in poorer lifestyle choices, and are more impaired compared to good sleeping adolescents.

Methods: Three-hundred and seventy-four Australian adolescents (mean age = 15.6 years, SD = 1.0) completed a 7-day sleep diary, wore wrist actigraphy, and completed a battery of questionnaires to assess DSPD criteria.

Results: The ICSD-2 criteria for DSPD were met by 1.1% ($n = 4$) of the adolescents sampled. The majority of adolescents (51.9%, $n = 194$) met one criterion, 14% ($n = 52$) of the adolescents met 2 criteria, while 33.2% ($n = 124$) did not fulfill any DSPD criteria. Despite having significantly delayed sleep timing, adolescents who met all criteria for DSPD reported similar lifestyle habits and daytime functioning. However, there were trends for greater alcohol and caffeine consumption, less sport participation, yet more time spent on extracurricular activities (i.e., learning to play a musical instrument) for adolescents with DSPD.

Conclusions: Despite the majority of adolescents reporting DSPD symptoms, only a small minority met full diagnostic criteria. Adolescents with DSPD reported similar lifestyle habits and daytime functioning to those with some or no symptoms. Future investigations of non-school-attending DSPD adolescents are needed to confirm the trends for lifestyle behaviors found in the present study.

Disclosure: Nothing to disclose.

P999

Prevalence of obstructive sleep apnoea in young children with Down syndrome: a domiciliary cardiorespiratory study

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Objectives: To determine the prevalence of obstructive sleep apnoea (OSA) in young children with Down syndrome (DS): a domiciliary study.

Methods: Children with DS aged 6 months to 6th birthday attended one of 3 participating research centres and were weighed and measured. Parents were trained to set up a cardiorespiratory device (Somnotouch, S-Med, Germany) at home unless they expressed a preference for sleep laboratory assessment. Measures included chest and abdominal RIP, nasal pressure flow, toe pulse oximetry,

actigraphy, body position and snore sensor. Studies recording at least 4 h of sleep were scored by an experienced sleep technologist using AASM (2012) scoring rules.

Results: To date 52/54 children (28 boys) have been successfully studied, median age 28.5 months, range 6–71 months. Two parents opted for sleep laboratory studies. Four domiciliary studies failed night one (2 < 4 h of data and 2 had no RIP). All were successfully repeated at home. Two children did not tolerate home studies and are awaiting admission. The prevalence of OSA, defined by an obstructive apnoea hypopnoea index (OAHI) $\geq$ 1 is 40/52 (77%; 95% confidence intervals 64% to 86%), and of moderate to severe sleep apnoea (OAHI > 5/h) is 12/52 (23%, 95% confidence interval 14% to 36%). OAHI did not correlate with age or BMI.

Conclusions: We believe this to be the largest study of OSA in very young children with DS and the first to successfully use unattended domiciliary monitoring. Consistent with previous studies we report a high rate of OSA.

Disclosure: Nothing to disclose.

P1000

Incidence and persistence of insomnia symptoms in the transition between childhood and adolescence

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Objectives: Cross-sectional studies show that insomnia symptoms are the most prevalent parent-reported sleep problem in childhood and that adolescents report an even higher prevalence. Little is known about the natural history of insomnia symptoms and its predictors in the transition between childhood and adolescence.

Methods: The Penn State Child Cohort is a general population sample of 700 children aged 5–12 years (8.6 $\pm$ 1.7 years) at baseline of whom 421 were followed-up during adolescence (17.0 $\pm$ 2.3 years). Subjects underwent a 9-h polysomnography, medical history and parent-reported scales at baseline. Insomnia symptoms were defined as parent-reported difficulty falling (DFA) and/or staying (DSA) asleep at baseline and as self-reported DFA and/or DSA at follow-up.

Results: The incidence of insomnia symptoms in adolescence was 31.2% and was higher in females ($P < 0.05$) and those with childhood psychiatric/behavioral problems ($P < 0.01$). Childhood externalizing and internalizing behaviors were associated with incident insomnia symptoms, with tension being the best predictor ($P < 0.05$). The persistence of insomnia symptoms was 48.2% and was higher in females ($P < 0.01$), minority ($P < 0.01$), heavier children ($P < 0.05$) and those with childhood psychiatric/behavioral problems ($P < 0.05$). Childhood polysomnographic parameters, including apnea-hypopnea index, were not associated with the natural history of insomnia symptoms.

Conclusions: The incidence and persistence of insomnia symptoms in the transition between childhood and adolescence is high and similar to that found throughout adulthood. Gender differences appear during this transitional period, while behavioral problems are an independent predictor of insomnia symptoms development and persistence.

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P1001

Does obstructive sleep apnea influence sleep quality in children with syndromic craniosynostosis?

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Objectives: Children with syndromic and complex craniosynostosis have a 68% prevalence of obstructive sleep apnea (OSA). Symptoms including apneas, snoring and difficulty in breathing are often reported, but the effect on objective sleep parameters is relatively unknown. The aim of this study was to determine whether OSA influences sleep architecture and to evaluate if OSA-treatment leads to an improvement of sleep quality.

Methods: Patients with syndromic or complex craniosynostosis treated at the Sophia Children's Hospital were prospectively enrolled. All patients underwent polysomnography, including electroencephalography. Sleep was categorized into REM-sleep and non REM-sleep (N1, N2 and N3). Sleep quality was defined as slow wave sleep (N3) and REM-sleep, indexed by total sleep time.

Results: Thirty children, with mean age at polysomnography 5.1 years (range: 0.6–15.1) were evaluated. Twenty-one children had no OSA, 6 mild and 3 moderate/severe OSA. Compared to children without OSA, those with OSA had a decreased sleep quality, 44.1% vs. 35.4% ($P = 0.04$). Patients with moderate/severe OSA additionally had fewer REM-sleep periods ($P = 0.04$) and a decreased percentage REM sleep ($P = 0.00$). Analysis of children with serial polysomnographies ($n = 6$) showed a decrease in sleep quality after worsening of symptoms, whereas after OSA-treatment in some cases the oAHI remained equal while the sleep quality did improve.

Conclusions: OSA leads to a disrupted sleep architecture with decreased sleep quality in children with syndromic craniosynostosis. While OSA-treatment usually leads to an improvement in oAHI this is not definite, nevertheless treatment can lead to an improvement of upper airway resistance leading to better sleep quality.

Disclosure: Nothing to disclose.

P1002

Meta-analysis of protective and risk factors for adolescent sleep

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Objectives: Teenagers need sufficient sleep to function well on a daily basis, yet there is an absence of consolidated evidence advising which factors protect or damage adolescents' sleep. The present study aimed to meta-analyse the existing literature.

Method: Mean weighted *r* values were calculated, to better understand protective and risk factors for 85 558 adolescents' (M ages 12–18 years.) bedtime, sleep onset latency (i.e., the time it take to fall asleep; SOL) and total sleep time (TST). Correlation coefficients were requested from authors who had not published suitable results. Forty-one, peer reviewed articles were included in the final analysis.

Results: Alcohol, tobacco, sleep hygiene, parent-set bedtime and physical activity were associated with earlier bedtimes. Technology use (video gaming, phone, computer and internet use) and evening light were related to delayed bedtimes. Sleep hygiene was negatively correlated with SOL. Alternatively, SOL lengthened as a negative family environment and pre-sleep worry increased. Substance use

(tobacco, alcohol, caffeine), evening light, a negative family environment, computer and phone use were associated with decreased TST, whereas physical activity, good sleep hygiene and parent-set bedtimes were related to longer sleep length.

Conclusions: Good sleep hygiene, parent-set bedtimes and physical activity appear to be protective factors, whereas a negative home environment, evening light, computer use and phone use seem to be risk factors. Caffeine, tobacco, alcohol, internet use, video gaming and pre-sleep worry are considered as potential risk factors. Experiments are needed to test when these factors are likely to have the largest impact on adolescents' sleep.

Disclosure: Nothing to disclose.

P1003

One hour of pre-bedtime screen light: effects on adolescents' pre-bedtime alertness, sleep and daytime functioning

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Objectives: Technology use among adolescents is increasing, however, there is a lack of empirical evidence showing how this impacts adolescents' sleep. It is possible that bright screen light, emitted by electronic devices before bed, increases alertness and inhibits sleep. The present study explored whether this short-wavelength light (i.e., blue) results in pre-bed alertness, or additionally, whether later chronotypes are hypersensitive to evening light.

Methods: This within subjects experiment analysed the pre-sleep alertness (GO/NOGO task speed, accuracy; subjective sleepiness), sleep (sleep diary, polysomnography), and morning functioning of 16 adolescents (M age = 7.4 $\pm$ 1.9 years, 56% f) who used a bright tablet screen (80 lux), dim screen (1 lux) or a filtered short-wavelength screen (f.lux; 50 lux) for 1 h before their average bedtime.

Results: No significant interactions were observed for chronotype. The GO/NOGO task produced significant effects between the bright and dim screens for speed and accuracy. Clinical significance is questionable, however, as these differences were small (e.g. GO/NOGO speed = 23 ms, accuracy = 13%). There were no significant effects found for sleep onset latency, slow-rolling eye movements, or the number of slow wave sleep (SWS) and rapid eye movement (REM) minutes in the first two sleep cycles.

Conclusions: One hour of screen light did not produce meaningful effects on adolescents' pre-bedtime alertness or sleep. Future experiments need to test longer durations of screen exposure, and cumulative effects over multiple nights, in order to determine when screen exposure begins to affect adolescents' sleep.

Disclosure: Nothing to disclose.

P1004

The effect of cystic fibrosis on sleep and its impact on daytime functioning in school-aged children

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Objectives: To examine the relationship between sleep quality and both global health and quality-of-life in children with cystic fibrosis (CF).

Methods: Parental report of sleep (Sleep Diary and Child Sleep Health and Behaviour Questionnaire), global health [Cystic Fibrosis Questionnaire-Revised (parent form)] and quality-of-life (Pediatric Quality of Life Questionnaire) were collected in 29 children with CF (mean $\pm$ SD = 11.2 $\pm$ 4.4 year) and 28 healthy controls (12.7 $\pm$ 3.0 year). Children with CF were recruited from a hospital clinic and controls from classroom peers of children with CF.

Results: Sleep diary findings indicated that children with CF had significantly more nocturnal arousals, longer periods of wake after sleep-onset, longer total sleep times and a later sleep phase preference; while sleep questionnaire findings indicated significantly more problems with sleep routine, sleep inertia, bedtime anxiety and restless sleep. All global health and quality-of-life scores were significantly reduced in children with CF. In children with CF, correlational analyses revealed that a poor sleep routine was associated with both lower global health and quality-of-life scores; conversely only a few but non-specific significant associations were observed between remaining sleep and either global health or quality-of-life scale scores.

Conclusion: The present findings indicate a strong relationship between sleep routine (i.e. regular bed and out-of-bed times) and both global health and quality-of-life in children with CF. These findings suggest that attention to good sleep-hygiene practices may play an important role in promoting global health and quality-of-life in children with CF.

Disclosure: Nothing to disclose.

P1005

A reliability and validity study of the pediatric daytime sleepiness scale among school aged children in Japan

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Objectives: A recent systematic review suggested that bedtimes were later and total sleep time was shorter in Asian adolescents than in North American and European adolescents, possibly causing daytime sleepiness in this population. We aimed to develop and validate the Japanese version of the Pediatric Daytime Sleepiness Scale (PDSS-J).

Methods: A multi-step translation methodology consisting of forward translation, back translation, expert review and cognitive debriefing interviews was used. After the linguistic validation, we conducted a psychometric validation comprising 174 students, 11–15 years old (51.7% male), using the PDSS-J, Karolinska Sleepiness Scale (KSS), and bedtimes and wake-up times at intervals of one month. PDSS-J scores were compared among three groups of sleep duration (<7 h, 7–8 h, >8 h) on school days using one-way analysis of variance.

Results: The translation and the cognitive debriefing process were performed without major translation difficulties. Internal consistency (Cronbach's alpha) of the PDSS-J was 0.880. Children who slept less than 7 h showed significantly higher scores than those who slept more than 8 h [$F(2168) = 4.27$, $P = 0.016$, mean(SD) score: 16.9 [9.5] in <7 h sleep, 13.3(5.4) in >8 h sleep]. With regard to PDSS-J score and KSS score, there was a significant linear effect (Pearson's $r = 0.42$, $P < 0.001$).

Conclusions: Given its robust psychometric properties including high reliability as well as strong concurrent validity with another measure of sleepiness, the PDSS-J is an important tool for assessing daytime sleepiness among school-aged children. Future studies should utilize the PDSS to determine relative levels of sleepiness across cultures.
Disclosure: Nothing to disclose.

P1006

Disturbances of carbohydrate metabolism at night in children with obesity, different height and sleep apnea (pilot study)

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Background: It is known that obesity in children is often accompanied by insulin resistance and disturbances of carbohydrate metabolism. In addition, 50% of children with obesity reveals obstructive sleep apnea syndrome (OSA). Episodes night hypoxia cause increased metabolic disorders, worsening of carbohydrate and lipid metabolism.
Aim: To explore the daily dynamics of glycemia in patients with obesity, high height and OSA.
Patients and methods: Examined 11 children aged 8–18 years with chronic adenotonsillar pathology: with obesity and normal height (n = 4), obesity and high height (n = 5); with normal weight and height (n = 2). Glycemic profile was investigated using a system of continuous monitoring of blood glucose (CGMS) within 72 h. All children underwent *laboratory*-based nocturnal cardiorespiratory monitoring (Embla N7000).
Results: In all cases was revealed mild to moderate OSA (mean IAH 1.5/h, nadir 91%). In two children with normal weight and height and with mild OSA was higher-normal daily level of glycemia with insufficient night decrease of BG and had not episodes of hypoglycemia. A specified threshold level of glycemia (3.3 mmol/l) was in five children, four (80%) from which - with high height. Among obese children with normal height - three cases were with decrease of daily glycemia, but not below low-normal level (3.3 mmol/l) except one case.
Conclusion: On the basis of identified episodes significant reduction of glucose in blood in night sleep, can possible to expect the same episodes of hypoglycemia in children with obesity and high height, which need to be revealed and corrected in time.
Disclosure: Nothing to disclose.

P1007

Consequences of updated AASM criteria in scoring for obstructive sleep apnea in children with syndromic craniosynostosis

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Objectives: The American Academy of Sleep Medicine (AASM) published in 2012 an updated manual for the scoring of sleep and associated events. The aim of this ongoing study is to determine whether the updated rules lead to a difference in sleep summary statistics, when evaluating polysomnography in children with syndromic craniosynostosis suspected for obstructive sleep apnea (OSA).
Methods: Polysomnographies were scored using the original 2007 and updated 2012 rules. Events scored were apneas, hypopneas (obstructive, central and mixed) and desaturations. Summary statistics calculated were obstructive apnea-hypopnea index (oAHI), oxygenation-desaturation index (ODI) and central apnea index (CAI). OSA was defined as oAHI $\geq$1, subdivided in mild (oAHI $\geq$1 and <5), moderate (oAHI $\geq$5 and <24) or severe (oAHI $\geq$25) OSA.
Results: Fourteen children (mean age: 5.0, range: 0.6–14.2) were evaluated. The difference between the 2007 and 2012 criteria for oAHI was 2.6 vs. 3.4 (P = 0.66), for ODI 2.6 vs. 4.8 (P = 0.09) and for CAI 2.7 vs. 1.3 (P = 0.02). According to the 2007 criteria 6 children had no OSA, 6 mild, 1 moderate and 1 severe OSA, whereas with the 2012 criteria 8 children had mild OSA; 2 of them had no OSA with the 2007 criteria.
Conclusions: Using the updated AASM criteria the scored respiratory variables showed only difference in the central apnea index. However, a few patients who previously were screened without OSA had mild OSA with the new rules. It is not clear if this will have clinical consequences, but prevalence statistics concerning OSA might change considerably.
Disclosure: Nothing to disclose.

P1008

Sleep disturbance in children with and without developmental coordination disorder (DCD) and links with daytime functioning

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Objectives: Our previous work, using a parent questionnaire, revealed significantly higher sleep disturbance for children with DCD compared to a control group. The current study aimed to examine sleep in DCD using more extensive and objective measures and to explore possible links with daytime psychological functioning.
Methods: 30 primary and secondary school children with DCD took part, together with 30 typically developing children matched for age and gender. The Moverment-ABC-2 Test was used to assess movement difficulties. Sleep was assessed using the Children's Sleep Habits Questionnaire, questionnaires to assess child and parent sleep-related cognitions, the Pediatric Restless Legs Syndrome (RLS) semi-structured interview plus actigraphy (one week). Child functioning assessments included the PedsQL Multidimensional Fatigue Scale and Harter's Self-Perception Scale for Children. The teacher version of the Strength & Difficulties Questionnaire was used to describe behavior at school.
Results: Objective and subjectively defined differences in aspects of sleep were seen between the DCD and control groups (especially for older DCD children), with primary and secondary age children showing slightly different profiles of disturbances. Children with DCD had more wakes (frequency and duration), more fragmented sleep and reduced sleep efficiency. Symptoms of RLS were not prominent at any age. Relationships between the sleep measures will be examined to obtain a detailed picture of sleep in each group along with relationships between sleep and other aspects of child functioning.
Conclusions: Sleep disturbance is apparent in children with DCD and clinicians should consider sleep both in assessment and intervention planning with these children.
Disclosure: Nothing to disclose.

P1009

Weighted blankets and sleep in autistic children - a randomised controlled trial

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Objective: To assess the effectiveness of a weighted blanket intervention in treating severe sleep problems in children with autism spectrum disorders (ASD).

Method: This phase III trial was a randomised, placebo controlled cross-over design.

Participants were aged between 5 years and 16 years 10 months, with a confirmed ASD diagnosis and severe sleep problems, refractory to community based interventions. The interventions were either a commercially available weighted blanket (weighted) or otherwise identical usual weight blanket (control), introduced at bedtime; each was used for a two week period before cross-over to the other blanket. Primary outcome was total-sleep-time (TST) recorded by actigraphy over each 2 week period. Secondary outcomes included actigraphically recorded sleep onset latency, sleep efficiency, assessments of child behaviour, family functioning and adverse events. Sleep was also measured using parent-report diaries.

Results: 73 children were randomized and analysis conducted on 67 children who completed the study. Using objective measures, in comparison to the control blanket the weighted blanket did not increase TST as measured by actigraphy and adjusted for baseline TST. There were no group differences in any other objective or subjective measure of sleep including behavioural outcomes. On subjective preference measures parents and children favoured the weighted blanket.

Conclusions: The use of a weighted blanket did not help children sleep for a longer period of time, fall asleep significantly faster, or wake less often. However, the weighted blanket was favoured by children and parents and blankets were well tolerated over this period.

Disclosure: Nothing to disclose.

P1010

The effect of therapist input on effectiveness of internet therapy for adolescents with insomnia

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Objectives: Research has shown that cognitive behavior therapy for insomnia (CBTi) in an ehealth setting is effective in treating adolescents. There are also indications that personalized input from a therapist during the treatment improves effectiveness of internet therapy. Less is known about the variables from therapists and patients that influence the effect of therapist input.

Methods: 39 adolescents with DSM-IV primary insomnia followed a program of internet CBTi. The therapy consisted of 6 weekly sessions with exercises of CBTi, personalized feedback from a therapist, and personalized bedtime-advice. Furthermore the participants had a 20-min chat session with their sleep therapist after the second session.

Participants' sleep variables were measured with actigraphy. At baseline and post-treatment also symptoms of chronic sleep reduction and insomnia were measured.

Therapist input was operationalized as the amount of words of feedback in each session, and the numbers of encouraging and supportive comments, empathic and caring comments, and directive and guiding comments.

Results: Results concerning sleep outcomes at baseline and post-treatment show that the CBTi internet therapy was effective. At the congress data will be presented to answer the question whether sleep improvement based on actigraphy, sleep logs, and symptoms of chronic sleep reduction and insomnia, is related to therapist feedback. Furthermore, we will explore the influence of participant characteristics (e.g. age, gender, SES) on these relations.

Conclusions: Based on the results conclusions will be drawn and discussed concerning the influence of the different characteristics of therapist feedback on the efficacy of internet CBTi.

Disclosure: Nothing to disclose.

P1011

Hand and foot distal vasodilation decreases wakefulness duration in preterm neonates

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In adults, sleep onset occurs when core body temperature is decreasing. Promoting distal vasodilation, in particular at hand and foot levels, increases sleepiness. Here, we questioned whether wakefulness duration (WD) and hand and foot temperatures are related in 9-day old preterm neonates with specific sleep/wake cycle and rhythmicity and whose circadian body temperature rhythms are not yet well established.

Overnight polysomnography was performed in 33 preterm neonates (gestational age: 29.9 $\pm$ 1.1 weeks, birth weight: 1310 $\pm$ 338 g) at the 9th day of life. Proximal (abdominal) and distal (hand, foot) skin temperatures were measured by infrared thermography every 5 min during 118 spontaneous wakefulness periods (mean WD: 16 $\pm$ 15 min). Average values of skin temperatures and proximal-to-distal differences were calculated throughout each wakefulness episode.

Linear regressions showed a significant, negative relationship between WD and the average level of distal temperatures. Also, a decrease in WD was found when hand and foot temperatures increased during the wakefulness episode, i.e. when proximal-to-distal differences decreased.

Present results suggest that distal vasodilation may lead to a decrease in WD. Although presleep behavioural and postural changes do not exist at this age, and despite large differences in circadian rhythms and sleep organization, distal hand and foot vasodilation improves sleep onset in preterm neonates as previously observed in adults.

Disclosure: Nothing to disclose.

P1012

How families sleep? - Observations from the child-sleep birth cohort study

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Objective: The aim of the CHILD-SLEEP birth cohort study is to define early development of sleep, and the effects of infant and parental sleep and family environment on the child's development.

Methods: Altogether 1667 mothers and 1602 fathers from Pirkanmaa Hospital District, Finland, participated in the study during the last pregnancy weeks in 2011–13. Questionnaires were implemented prenatally for the parents and at 3, 8, and 24 months after the birth for the parents and the baby. During the delivery, cord blood sample of infants and parental blood or saliva samples were gathered for molecular genetic studies. The cohort included several subsamples: the sleep education group (n = 178 particpants and 183 controls), home polysomnography group (n = 88) and actigraphy group (n = 446).

Results: Frequent difficulties in falling asleep, night wakings (3 or more per night), early morning awakenings, or subjective poor quality of sleep were present among 14%, 37%, 11%, and 27% of the mothers prenatally, and 8%, 44%, 8%, and 23% at the three months. The corresponding values for the fathers were 5%, 4%, 3% and 7% of the fathers prenatally, and 4%, 9%, 5% or 12%, at the three months.

Conclusion: The preliminary data analysis shows that subjective quality of sleep improves slightly in mothers from prenatal period to 3 months of postnatal age, while the sleep quality of fathers deteriorates. Despite these changes, mothers, as compared to fathers, experience more symptoms of insomnia both prenatally and postnatally.

Disclosure: Nothing to disclose.

P1013

Routine respiratory screening for children with severe motor disorders using night-time postural equipment (sleep systems): a qualitatitve study

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Objectives: To explore:
Therapist and parental views on sleep disordered breathing (SDB) in children using night-time postural equipment (NTPE)
Whether domiciliary oximetry and capnography screening impacts on:
(a) Anxiety levels and concerns
(b) Compliance and confidence in NTPE use
(c) Acceptability of respiratory screening.

Methods: Local research identified that children using NTPE are vulnerable to SDB. To identify such children, a domiciliary respiratory screening programme has been introduced. Focus groups were conducted involving paediatric physiotherapists and occupational therapists. Parents of five NTPE users were interviewed. Data were analysed thematically involving: data transcription, generating codes, identifying and reviewing themes among the codes, defining and naming themes.

Results: Several core themes emerged from the focus groups. SDB is not a priority for therapists initiating NTPE therapy unless children have pre-existing respiratory problems, rather their primary concerns relate to comfort and postural care. Local research has increased local professional awareness of the vulnerability of NTPE users to SDB and to some extent has also increased professional anxiety. A screening programme has been broadly welcomed. Parents similarly reported low levels of concern about SDB in their children using NTPE. Nonetheless both therapists and parents expressed a willingness to accept an additional investigation of potential benefit to the child.

Conclusion: Routine domiciliary oximetry and capnography in children using NTPE is generally welcomed by parents and therapists although SDB has hitherto not been a main clinical priority. Screening has the potential to increase parental confidence and compliance in using NTPE in their children.

Disclosure: Nothing to disclose.

P1014

The impact of demographics and sleep hygiene factors on sleep in children aged 2–10 years

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Objectives: Socio-cultural factors including country of origin, education and family income; and sleep hygiene factors, including sleep environment, bedding, screen time, and meals can affect children's sleep, but are rarely explored. This study investigates relationships between these variables and sleep in children aged 2- to 10-years.

Method: Participants are the primary caregivers of children aged 2- to 10-years. To date primary caregivers of 202 children aged 2- to 10-years have completed a survey including demographics, an environment-sleep questionnaire, and the Children's Sleep Habits Questionnaire (CSHQ). Group comparisons (sleep problem, no sleep problem) and correlations will be conducted as appropriate. Regression models will be used to examine predictors of children's sleep quality (CSHQ score) and total night sleep.

Results: A preliminary study of 101 children aged 2- to 5-years (28 with ASD) found that sleep quality was related to family demographics. Sleep was also related to several sleep hygiene variables. Regression found that screen time, temperature and bedcovers predicted sleep quality, while age, ASD diagnosis, screen time and sleep environment predicted hours slept. Analyses of the current cohort of 200 + , 2- to 10 year-olds will be presented here.

Conclusions: Preliminary results indicated the importance of environmental factors for sleep in young children. While there is recent attention to the impact of screens on children's sleep, other modifiable factors including the sleep environment can be ignored. It is anticipated that the previous findings will be replicated with this older cohort, supporting that simple environmental changes can lead to improved child sleep.

Disclosure: This study was funded by Australian Wool Innovation: Not for profit organisation owned by Australian woolgrowers

P1015

Effects of six-months methylphenidate treatment on sleep disturbances in children with attention-deficit/hyperactivity disorder. A pilot study

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Objective: Sleep problems, particularly difficulty initiating and maintaining sleep, are frequently reported in hildren with Attention-Deficit/Hyperactivity Disorder (ADHD) combinate type with or without methylphenidate (MPH) treatment.Th aim of the study is to evaluate sleep consistency in children with ADHD and to look for a correlation between sleep characteristics and ADHD symptom severity and general functioning.

Methods: Ten ADHD patients, ages 6–10 years, were evaluated at T0 (drug naive) and at T1 (after six months of MPH treatment; two dose/die 0.5 mg kg/die). Children sleep and habits questionnaire (CSHQ), Clinical Global Impression for Severity scale (CGI-S) and Improvement scale (CGI-I) and Children′s Global Assessment Scale (CGAS) were administered.

Results: At T0 6 out of 10 patients showed sleep disorder (CSHQ total score >41, mean value 44,3). Elevated score in CSHQ subdomain such as bad resistence and daytime sleepiness were found.CGI-S, CGI-I and CGAS score didn't correlated with sleep characteristics (p=ns).

At T1 a reduction of CSHQ mean total value (=42,3) has been registered. The normalization of sleep pattern didn't correlated with CGI-S, CGI-I and CGAS scoring.

Discussion: Clinically significant sleep problems are present in children with ADHD both drug naïve and on MPH treatment. The nature of etiology of the sleep problems in ADHD and the contributions of psychotropic treatment strategies on their evolution have still to be better characterize.

Disclosure: Nothing to disclose.

P1016

Valid methods for the estimation of children's sleep problems in clinical practice

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Objectives: Behavioral sleep problems are highly prevalent during childhood. A careful evaluation of sleep patterns is essential in clinical practice. Recently, we provided data about the interchangeable use of actigraphy, diary and questionnaire for the assessment of sleep patterns in healthy children (Werner, 2008). However, it remains unclear how well actigraphy and diary also agree in sleep-disordered, young children.

Methods: A total of 42 sleep-disordered children (age range 6–47 months) who came for out-patient sleep consultations were included. Sleep patterns were assessed by actigraphy and diary. Sleep patterns were identically defined as in Werner et al. (2008). The degree of agreement between methods was quantified using the 95% limits of agreement of Bland and Altman (1986).

Results: Parents reported bedtime struggles in 62% of the children, and night awakenings in 95%. Differences between methods were smallest for sleep start (± 25 min), sleep end (± 26 min), and assumed sleep (± 35 min). For actual sleep time, day-time sleep duration and 24-h sleep duration, differences were ± 97 min, ± 49 min, and ± 60 min, respectively.

Conclusions: On the basis of our clinical experience, we defined the agreement between methods as acceptable if differences were smaller than 30 min. This condition was satisfied for sleep start, sleep end, and assumed sleep, while for actual sleep duration and day-time sleep, it was not. Our findings suggest that at least for sleep start, sleep end and assumed sleep, the diary is a satisfactory method for the assessment of sleep patterns in sleep-disordered, young children.

Disclosure: Nothing to disclose.

P1017

Evaluation for apparent life-threatening events (ALTE) in infants - using polysomnography with simultaneous pH monitoring

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Objectives: An apparent life-threatening event (ALTE) is an acute, unexpected change in an infant's breathing, appearance, or behavior that is frightening to parent or caretaker with various cause. To assess the cause of ALTE, we evaluated the patient by polysomnography with simultaneous pH monitor.

Methods: Infants who visit Bundang CHA Medical Center with experiencing ALTE without definite cause were tested. Detailed history, physical examination, pH monitor, polysomnography, EEG, brain study and echocardiography were done, case by case. Feeding incoordination was defined as skipped respiration during feeding, feeding hypopnea was as decreased amplitude of nasal flow during feeding and GER was as positive history of regurgitation or less than pH 4 during pH monitor after feeding.

Results: Among 13 infants, nine (80%) have REM periodic breathing less than 90% saturation, seven (58%) have GER during and after feeding, five (46%) have feeding incoordination, and five (46%) have hypopnea with feeding. Only one infant have cardiac problem which didn't provoke cyanosis. One infant have interictal activity in EEG without clinical seizure activity. Central apnea which meets the criteria of premature apnea was not noted.

Conclusions: Polysomnography with simultaneous pH monitoring was very useful for evaluating the unknown cyanosis in infants, especially in infants with feeding problems. Besides of relatively well-known etiologies of ALTE such as apnea, seizure and GER, feeding incoordination and hypoxia or REM periodic breathing can be a trigger or major factor of ALTE in neonate.

Disclosure: Nothing to disclose.

P1018

Child and carer sleep quality in paediatric hospital wards

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Objectives: To compare sleep of children in hospital and their resident parents/carers, with sleep at home after hospital discharge and investigate sound levels across the two sleep environments.

Methods: Sleep duration and quality was measured using Actiwatches (AMI, New York), specifically total sleep time (TST) and sleep efficiency (SE). Sound levels were measured using a sound

level meter (Bruel & Kjaer 2236), with results in median decibels. Sleep was measured for up to 5 nights in hospital and 5 nights at home, sound levels for 2 nights in each setting.

Results: Data collection is ongoing. Preliminary sleep data from 23 children and 11 parents are reported. Results were normally distributed and analysed using parametric tests. Children's mean TST was 79 min longer at home (552 min, 95% confidence intervals 516 to 588 min) than in hospital (473 min, 95% confidence interval 430 to 516 min), $P < 0.005$. Children's SE was higher at home (86%, 95% confidence interval 82 to 89%) than in hospital (75%, 95% confidence interval 70 to 80%), $P < 0.001$.

Co-sleeping carers' TST did not differ between settings but mean sleep efficiency was lower in hospital (75%, 95% confidence interval 65 to 86%) than at home (88%, 95% confidence interval 82 to 93%), $P < 0.005$.

Median sound levels, monitored for 9 children, were significantly higher in hospital (49.5 dB) than at home (32.6 dB), $P < 0.001$.

Conclusions: Preliminary data indicate that children have poorer sleep in hospitals, which are noisier environments. Further data from ongoing patient recruitment will be presented.

Disclosure: Nothing to disclose.

P1019

Prospective polysomnographic study in children with monosymptomatic nocturnal enuresis and polyuria

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Objectives: To explore the impact of sleep fragmentation in children with primary MNE and nocturnal polyuria. Secondly, we were interested in the comparison of the registered PLMS to previous findings in children with refractory NE. (Dhondt et al; JU 2009).

Methods: Children (6–16 years) with primary MNE and polyuria were recruited from the nephro-urology clinic. Fluid intake was evaluated by a daytime diary (4 days); NE enuresis by 14 consecutive nights, bladder capacity during one day of forced drinking. Maximal voided volume and 24 h concentration profile were determined. Uroflow ultrasound and determination of residue after micturition were performed.General demographic questionnaire was completed. All subjects participated in one polysomnographic study.

Results: Thirty children with MNE and nocturnal polyuria (23 boys and seven girls: mean 10.43 years $\pm$ 3.08 SD) participated. The mean PLMS-index was increased: 10,83 $\pm$ 4,99 SD. The mean arousal index and awakening index were 6.433 $\pm$ 3.310 SD respectively 8.720 $\pm$ 3.757 SD, both positively correlated with the PLMS-index ($P < 0.001$). There was no significant correlation between the sleep and the enuretic parameters. Children with refractory NE from the pilot study showed a significant higher PLMS-index compared to the children from the actual study group($P < 0.001$).

Conclusions: PLMS and cortical arousals in sleep are increased in children with MNE and nocturnal polyuria. No correlation was found with the enuretic parameters. The presence of PLMS probably constitutes a comorbid phenomenon, driven by a common but independent pacemaker. We hypothesize the autonomic system, its sympathetic branch, and the dopaminergic system as a candidate.

Disclosure: The study was financially supported by Ferring.

P1020

Effects of a dietary intervention on the sleep patterns in children with autistic spectrum disorders

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Background: There is growing interest in possible dietary involvement in the etiology and treatment of Autistic Spectrum Disorders (ASD). Some parental reports postulated that sleep quality in ASD improves after the intake of some alimentary complements. The aim was to examine the effects of a food complement formula in children with ASD on their sleep structure.

Methods: Two overnight PSGs were carried out in two groups of ASD children aged 3–13 years, belonging to a specialized school. The diet group (DG) took 20 grams of the formula twice a day during 3 months, ($n = 19$); PSGs were done at the beginning and 3 months after continuous intake of the formula. A no diet group (NDG) of ASD children ($n = 21$), and a control group (CG) of 30 matched healthy children with one PSG were included for comparative purposes.

Results: TST, SEI, N3 and REM sleep duration, as well as O2 saturation values were shorter in DG and NDG compared to CG. These parameters improved in DG after 3 months of the formula intake. Sleep latencies to N1 and REM sleep, wakefulness, WASO, N1 and N2 duration, as well as sleep apnea index were higher in DG and NDG compared to CG. Again these values showed a significant improvement in DG according to the second PSG.

Conclusions: We found significant differences in sleep architecture in ASD children compared to healthy children. The intake of a formula based in protein and micronutrients improved some sleep parameters affected in ASD children.

Disclosure: The study was supported by grant 196483, Consejo Nacional de Ciencia yTecnología (CONACYT), México

P1021

Improvement of sleep architecture in down syndrome children after a nutritional complement

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Background: Down syndrome (DS) is generally accompanied by sleep-disordered breathing. Many predisposing factors, including overweight and obesity have been described. The possible dietary involvement in the expression of chronic diseases is under study. Some reports postulated that sleep quality in DS improves after dietary interventions.The aim was to examine the effects of a dietary intervention in children with DS on their sleep structure.

Methods: Two overnight PSGs were done in two groups of DS children aged 4–13 years, belonging to a specialized school. Diet group (DG) took 20 grams of the formula twice a day during 3 months, ($n = 24$); PSGs were completed at the beginning and 3 months after continuous intake of the formula. A no diet group

(NDG) of DS children (n = 18), and a control group (CG) of 30 matched healthy children with one PSG were included.

Results: SL, TST, SEI, N3 and REM sleep duration, and O2 saturation values were shorter in DG and NDG compared to CG. These parameters improved in DG after 3 months of the intervention. Wakefulness, WASO, N1 and N2 duration, as well as sleep apnea index were higher in DG and NDG compared to CG. Sleep apnea index was severe in DS patients, and in spite of a significant improvement, it continued severe. Sleep improved in DG after the dietary intervention.

Conclusions: Differences in sleep parameters in DS children were found compared to healthy children. The dietary intervention improved the sleep architecture in DS children.

Disclosure: The study was supported by grant 196483, Consejo Nacional de Ciencia yTecnología (CONACYT), México

P1022

Tobacco smoke exposure increases gastro-oesophageal reflux occurrence during active sleep in neonates

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Environmental tobacco smoke (ETS) exposure is probably one of the most important neonatal risk environmental factors for health in occidental countries. The present study aimed to assess the influence of pre- and/or postnatal ETS exposure on the occurrence and characteristics of gastro-oesophageal reflux (GOR) as regards to sleep stages in human neonates.

Twenty three neonates (post-conceptional age: 42 $\pm$ 5 weeks, body weight: 3.6 $\pm$ 1.1 kg) underwent simultaneous, synchronized 12-h polysomnography and combined multichannel intraluminal impedance (MII, GOR-imp) and pH monitoring (pH, GOR-pH). Two groups were studied according to whether they either were exposed (ETS group, urinary cotinine: 57 $\pm$ 89 ng/mL) or not (control group, urinary cotinine: 0 ng/mL) to ETS pre- and/or postnatally.

All the parameters describing the GOR-pH and GOR-imp events were higher in the ETS group than in the control group but significance was reached for the frequency of GOR-imp events only (1.2 $\pm$ 1.1 vs. 3.2 $\pm$ 2.7/h, P = 0.031). When considering vigilance states, the effect of ETS was significant during active sleep only for the time spent in GOR-imp (% of total sleep time) (0.2 $\pm$ 0.2 vs. 0.8 $\pm$ 0.8%, P = 0.033) and the frequency of GOR-imp events (0.54 $\pm$ 0.48 vs. 2.28 $\pm$ 1.98/h, P = 0.031).

These preliminary results suggest that ETS increases the occurrence of GOR with retrograde migration of the refluxate (to the proximal oesophagus) in neonates in a sleep stage-dependent manner. ETS may increase the vulnerability of neonates since the reflexes that protect the airways against aspiration are depressed during active sleep.

Disclosure: Nothing to disclose.

P1023

Ready, Set, Snooze! An interactive, web-based treatment program for pediatric behavioral sleep problems

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Up to 70% of children under the age of 10 experience sleep problems yet the number of professionals with training pediatric sleep medicine is vastly limited. Behavioral interventions have proven efficacious for insomnia of childhood but these interventions remain highly underutilized. Internet-based sleep interventions for adults have emerged in recent years reducing cost and access barriers to treatment. However online sleep interventions for school-age children have been unavailable. *Ready, Set, Snooze!* is an newly-developed, innovative, web-based program for children 7 to 11 years with behavioral insomnia. The current study examined the feasibility, acceptability and initial efficacy of *Ready, Set, Snooze!* A pilot sample of 20 families with children with behavioral sleep problems completed an in-person diagnostic assessment followed by the 3-week intervention at home on their own computer. Specific elements of the program include:

(1) child and parent-focused educational videos about sleep and principle of behavior modification; (2) knowledge checks; (3) experiential rehearsal scenarios for practicing specific intervention techniques; and

(4) embedded sleep-based games to increase child motivation and engagement in the program.

Following completion of the program, children and parents provided feedback about *Ready, Set, Snooze!* and changes in sleep child patterns and behaviors. Findings suggest the program to be highly feasible and acceptable and preliminary examination of child sleep patterns/behaviors indicate positive changes in sleep from pre to post intervention. Computer-based interventions therefore offer an important means of disseminating empirically-supported behavioral treatments directly to families. *Ready, Set, Snooze!* is a comprehensive, engaging treatment with promise for broad dissemination.

Disclosure: Nothing to disclose.

P1024

European survey on polysomnography in patients with Robin sequence

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Objective: To provide a European overview of the use of polysomnography (PSG) in children with Robin Sequence (RS), a congenital malformation classically characterized by mandibular hypoplasia, glossoptosis and upper airway obstruction.

Methods: An online survey among European clinics on the use of PSG in children with RS executed between June and November 2013.

Results: Surveys from 101 different clinics of 24 European countries were included in the analysis. All respondents were involved in the management of RS children. Seventy-one percent of the respondents used PSG to assess the severity of the airway obstruction in children with RS. The number of respondents that used PSG in individual countries (with n > 5 respondents) differed: France 8/8 (100%), Germany 7/12 (58%), the Netherlands 7/11 (63%), Sweden

3/6 (50%) and the UK 19/26 (73%). About half of the respondents only performed PSG on indication. Most respondents used type I (56%) and type IV (33%) systems, in contrast to the type II (13%) and type III (13%) systems.

Conclusions: Our results showed that the use of PSG is not well integrated in RS care. A type I PSG system, the gold standard to diagnose obstructive sleep apnea was only used by about half of the respondents, which may lead to underestimation of the obstructive pathology. This first European survey study on PSG use in children with RS shows that there are considerable differences within Europe concerning use and type of PSG and emphasizes the need for a European guideline.

Disclosure: Nothing to disclose.

P1025

Sleep deprivation impact upon adolescents′ health and quality of life

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Objective: This study aims to evaluate the influences of sleep duration, sleep deprivation, weekend variability of sleep upon other adolescents' health and health related quality of life.

Methods: The Health Behaviour in School-Aged Children (HBSC) survey is a self-completed questionnaire completed by 3476 students (53.8% girls), attending the 8th and 10th grades. Subjective sleep duration during the week and weekends was collected; sleep deprivation (SD) was considered whenever their difference was higher than 2 h; health complaints frequency (headaches, backaches, fatigue, sadness, irritability, anxiety and difficulty to fall asleep) and Kidscreen10 (health related quality of life).

Results: SD was present in 18.9% of the students; SD was negatively correlated with sleep duration in weekdays; there were no gender differences but SD increased with age and grade; a considerable number of adolescents had sleep problems (37.2%); 25.5% had difficulties in sleep initiation, which was more prevalent in SD adolescents; the week days hours of sleep were decreased in the SD group; the BMI, higher in SD teens, was negatively correlated with sleep duration and positively correlated with SD; the average health related quality of life was reduced in SD adolescents; the frequency of headaches, fatigue, irritability, nervousness, shoulder pain and dizziness was higher is SD adolescents, in those with reduced sleep duration and higher variation between week and weekends; in SD the general health was poorer.

Conclusions: Sleep quality and sleep duration affect the perception of health-related quality of life and perceived physical and mental health.

Disclosure: Nothing to disclose.

P1026

A case of adolescent with severe non-24-h sleep-wake disorder due to lack of time cues

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Objective: The circadian regulatory system is one of the key central nervous system processes modulating the timing and quality of sleep and wakefulness. Its ability to facilitate the proper timing of physiological processes is dependant on periodic input of timing signals or zeitgebers (time cues). We present a case of an adolescent with severe non-24-h sleep-wake disorder due to lack of time cues.

Methods: Careful history and 3-week actigraphy were performed in the patient.

Results: 14-years old girl presented with headache, episodes of syncope and excessive sleepiness. She was admitted to a local hospital were extensive laboratory work-up was completely normal. She performed also a psychological exam revealing attention deficit. Due to excessive sleepiness in school she dropped out of school. From that point on she stayed in her bed with a fiend for the whole day. The girls ate, slept and talked in an almost constantly illuminated bedroom. 3-week actigraphy revealed severe non-24-h sleep-wake disorder with clear periods of free-running of the rhythm. She was put on melatonin treatment with strict schedule of light exposure to maintain entrainment.

Conclusion: Bad sleep hygiene and a complete lack of time cues can result in severe non-24-h sleep-wake disorder in adolescent that can be successfully treated with melatonin and strict schedule of light exposure.

Disclosure: Nothing to disclose.

P1027

Polysomnography is a useful tool in the decannulation procedure of children with a tracheostomy tube

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Introduction: The decannulation procedure of tracheostomized children depends on the underlying pathology. It starts with a speaking valve followed by downsizing of the tracheostomy tube which can be completely blocked during daytime. If these procedures are successful an overnight polysomnography (PSG) is done with a blocked tracheostomy tube. This study aims to evaluate the use of PSG in the decannulation procedure.

Methods and patients: Retrospective study of children with a tracheostomy tube who got a PSG at the end of the decannulation procedure.

Results: Sixteen children (F5/M11) were studied (period 2009–2014). Age at PSG, 3 months to 27 years. Underlying cause were severe obstructive breathing in craniofacial syndromes (n = 5), tumors (n = 4), chronic lung disease (n = 2), vocal cord paralysis (n = 2), subglottic stenosis (n = 2). PSG showed a normal breathing pattern in 6 children, 5 were successfully decannulated, in 1 child decannulation was postponed because of intubation difficulties (McCormack 4). In 5 children a respiratory arrhythmia related to upper airway resistance was seen, all were successfully decannulated. In 5 children clear PSG abnormalities were seen (in 2 severe desaturations and CO2 retention, in 1 severe obstructions, in 1 frequent arousals and inspiratory stridor and in 1 central apneas); in 4 decannulation was postponed, only 1 child with central apneas was decannulated.

Conclusion: Overnight PSG with a blocked tracheostomy tube at the end of a decannulation procedure showed in a number of children clear abnormalities and was therefore useful in the decision whether to decannulate or not.

Disclosure: Nothing to disclose.

P1028

The value of pre-operative polysomnography with a palatal plate in predicting the risk of respiratory distress following palatal closure in patients with Robin sequence

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Objective: To assess the value of pre-operative polysomnography (PSG) with a palatal plate in predicting respiratory distress following palatal closure in children with Robin Sequence (RS).

Methods: Children with palatal closure between 2009–2012.

Results: Seventy-one eligible children: 41 non-RS patients and 30 RS patients. After birth 26 of the 30 RS children were treated by prone positioning, four needed additional treatment. Mean age at closure non-RS vs. RS children: 10.9 vs. 12.4 months (P = 0,05). Twenty-eight of the 30 RS children underwent pre-operative PSG with a custom-made palatal plate: 26 were scheduled for closure and two were postponed and were rescheduled later after a second PSG. None of the non-RS group and nine of the 28 RS children developed post-operative respiratory distress (8 < 48 h and 1 > 7 days). Four children required a nasopharyngeal tube (<2 days). In the other cases the obstructive problems resolved spontaneously within a few days. There was a significant difference between pre-operative PSG results of the 9 RS children with post-operative respiratory distress vs. those who did not regarding ODI 2.88 $\pm$ 2.6 vs. 1.38 $\pm$ 1.34 and absolute number of desaturations 24.8 $\pm$ 26.5 vs. 11.9 $\pm$ 12.5 (both $P < 0.05$). Of the four children who initially needed additional treatment in two postoperative respiratory distress occurred.

Conclusion: RS children are at risk to develop temporary respiratory distress following palatal closure and pre-operative PSG can be useful in selecting children who are at risk. This study emphasizes the need of close post-operative monitoring after palatal closure.

Disclosure: Nothing to disclose.

P1029

Sleep characteristics in children with autism spectrum disorder

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Objectives: To describe sleep characteristics in children with diagnosis of Autism Spectrum Disorder, because sleep disruption, especially of the microstructure, could have an important role in the behaviour, development and evolution in these patients.

Methods: 25 children (19 boys and 6 girls) with 3–5 years old, diagnosed of Autism Spectrum Disorder, normal MRI, without epileptiform discharges in EEG and without diagnosis of other disorders. Children participated in a polysomnographic (PSG) sleep recording. Sleep disorders like Obstructive Sleep Apnea Pediatric (OSAP), Periodic Limb Movement Disorder (PLMD) parasomnias, and sleep characteristics like sleep stages percentage, microarousal index, sleep efficiency and awakenings episodes were analyzed.

Results: We found OSAP only in two patient, and parasomnias in three patients. However, it was relevant data about PLMD, because 72% present this disorder with an average index of 9.42. We found an average of 5.09% of stage 1, 39.76% of stage 2, 25.43% of stage 3, 25.63% of stage REM, 3.15 awakening episodes $\geq$5 min, 84.56 of sleep efficiency, 36.78 of microarousal index (82.9% with microarousal index $\geq$30).

Conclusion: We observed that although the sleep architecture in terms of the macrostructure, appears to be not consistently altered in relation with normal values, it is very important the analysis of sleep microstructure because specific features would be altered in these patients and could be in relation with the problem of behavior, learning and memory in these patients. Treatment to stabilize sleep structure, and for specific sleep disorders could improve the symptomatology in these patients.

Disclosure: Nothing to disclose.

P1030

Sleep quality in infants at the age of three months

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Objectives: The aim of this study was to evaluate sleep habits and quality in infants aged three months and describe how they are related.

Methods: The study is a part of the CHILD-SLEEP birth cohort consisting of 1667 mothers and 1602 fathers. Parents filled out several questionnaires regarding the infant sleep quality, family environment and parental well-being when the infant was three months of age.

Results: Sleep onset took >30 min in 25% of the infants, night wakings (between 24-06) were reported in 83%, waking up more than two times/four times per night in 49%/9%. Most of the infants slept in their own cots while 35% were at least occasionally taken to parents bed due to sleeping problems; 12% were taken to parental bed every night. Ability for self-soothing was observed frequently in 31%, occasionally in 24% and never in 18% of the infants. Ability for self-soothing was related to shorter sleep onset and moderately lower frequency of nocturnal awakenings. A fifth of the parents considered that the infant had sleeping difficulties (mild 18%, moderate 4% and severe 0.3%). Parental reports of sleeping difficulties reflected both sleep onset problems and night wakings, the latter being by far the most typical behavior considered problematic (42% vs. 76%, $P < 0.001$).

Conclusions: This study evidenced the large inter-individual variation in sleep quality at 3 months of age. Future studies are needed to characterize both genetic and environmental factors that influence the early sleep development.

Disclosure: Nothing to disclose.

P1031

Automated EEG amplitude variability parameters during non-REM sleep: differences between normal weight, overweight and obese children

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Objective: To compare automated EEG amplitude variability parameters during nonREM sleep between normal weight (NW), overweight (OW) and obese (OB) children.

Methods: Polysomnographic recordings were obtained from 63 participants (10.3 $\pm$ 0.2 years) belonging to a follow-up study since

infancy. Besides OW or OB, all were healthy. NW (n = 29), OW (n = 15) and OB (n = 19) categories were established using body-mass index percentiles according to WHO criteria. Sleep stages were scored following standard criteria. During nonREM sleep stages 1, 2 and slow-wave sleep (SWS), an automatic analysis of the EEG amplitude variability was performed [1]. Differences between groups were evaluated by a mixed model including potential covariates such as age, sex, sleep efficiency and respiratory disorder index.

Results: All participants were free from sleep breathing disorders and the groups presented similar conventional sleep stage architecture. Relatively to the NW and OW groups, the OB group showed higher total variability time and SWS variability time, longer variability events duration, and shorter inactivation time duration (time without variability) (all $P < 0.05$). No differences were found for duration or proportion of the fast or slow types of EEG amplitude variability events.

Conclusions: Automated EEG amplitude variability parameters during nonREM sleep in OB children differed from those of NW and OW children. These results suggest that these EEG parameters relate to subtle sleep changes associated to obesity before the appearance of other overt sleep disorders commonly associated with it.

Support: Fondecyt 1110513 and NIH HD33487 grants.

Reference: [1] Ferri R et al, J Sleep Res 2012; 21(2):212–20

P1032

Automated EEG amplitude variability parameters during non-REM sleep correlate with their corresponding cyclic alternating pattern (CAP) parameters in healthy children

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Objective: To perform a correlation analysis between automated EEG amplitude variability parameters and Cyclic Alternating Pattern (CAP) parameters during non-REM sleep.

Methods: Nighttime polysomnographic recordings were obtained from 63 healthy children (10.3 + 0.2 years). Sleep stages were scored following standard criteria. The automatic analysis of EEG amplitude oscillations [1] and the visual detection of CAP parameters during non-REM sleep [stages 1(S1), 2(S2), and slow-wave sleep (SWS)], were carried out using software Hypnolab.

Results: All EEG amplitude variability parameters correlated positively with their corresponding CAP parameters ($P < 0.05$), but variability cycle duration (with CAP cycle), and number and percentage of fast variability events (with CAP A3 number and percentage, respectively). Higher correlation values were found for SWS variability time (with SWS CAP time; r = 0.67, P = 0.000), total events (with total CAP events; r = 0.51, P = 0.000), and S1 & S2 variability time (with S1 & S2 CAP time; r = 0.50, P = 0.000). Concordance analyses showed the highest intraclass correlation coefficient (ICC) for SWS variability time with SWS CAP time (ICC:0.66, P = 0.000), S1 & S2 variability time with S1 & S2 CAP time (ICC:0.51, P = 0.000), and total events with total CAP events (ICC:0.5, P = 0.000).

Conclusions: These data show that most automated EEG amplitude oscillation parameters during non-REM sleep have good correlation and concordance with their corresponding CAP parameters in children. Given that this quantitative analysis of the EEG amplitude variability is completely automatic, it offers several benefits for studying non-REM sleep microstructure in childhood.

Support: Fondecyt 1110513 and NIH HD33487 grants.

Reference: [1] Ferri R et al, J Sleep Res 2012,21(2):212–220

P1033

Narcolepsy in school-aged children. A case report

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Narcolepsy is a lifelong neurologic disorder of rapid eye movement sleep with attacks of irresistible daytime sleepiness, cataplexy, hypnagogic hallucinations, sleep paralysis, and fragmented night sleep.

The highest incidence is in the second decade of life but it has been found that 34% of all subjects had onset of symptoms prior to the age of 15 years, 16% prior to 10 years, and 4.5% prior to 5 years.

Daytime sleepiness is the most disabling feature of narcolepsy, with background drowsiness and sleep attacks superimposed. The daytime sleepiness is associated with impaired concentration and consolidation of memory, executive dysfunction and school-related learning problems.

Its etiology is autoinmune; the target is the hypothalamic neuropeptide hypocretin-1, and there's a strong association with HLA-DQB1*0602 antigen.

Case report: Nine year old boy who presents daytime hypersomnia with sleep attacks during he dreams, since 3 months ago. One month later, he suffers brief episodes of sudden loss of cervical and lower extremities muscle tone.

The suspected diagnosis of narcolepsy-cataplexy was confirmed with a nocturnal polysomnography and multiple sleep latency test. The immunochemical study was positive for HLA -DQB1 * 0602. We take a sample of cerebrospinal fluid for hypocretin-1 determination, (pending results).

We perform treatment with planned naps, methylphenidate and imipramine, with improvement in daytime sleepiness and cataplexy attacks, althought sleep paralysis and hypnagogic hallucinations are added to the symptoms.

Conclusions: Narcolepsy is rare but may be underdiagnosed in childhood. It should be included in the differential diagnosis in children with learning and mood disorders.

Disclosure: Nothing to disclose.

P1034

Evaluation of two projects on sleep education: 'Sleep Schools Project' and 'Sleep more to Read better'

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Objectives: The present work aims to present sleep education and sleep awareness activities, whenever an educational model is assumed: a three-dimensional model about sleep, addressing sleep habits, personal and environmental factors with nine subcategories, together with associated community projects and scientific research activities. Two projects are evaluated: Sleep Schools Project (SSP) and Sleep more to Read better (SMRB).

Methods: In spite of somewhat different objectives, both projects used similar methodologies and therefore are evaluated together. The observation period is 5 years (from 2009 to 2014) and includes private and public schools with every age levels. The number of target involved, educational and awareness actions was computed along project evolution and trends were measured. Idem for community projects around sleep, research presentations, education materials and media dissemination (direct and indirect impacts). Furthermore the accuracy and efficiency of the model was assessed (Chi square, regression and trend analysis were applied).
Results: During this 5 years, the number of sessions increased exponentially (105). The project targets were teachers (1711), parents (3395), students (7943), health professionals. Schools participated in different ways, in a total of 469. There were 37 scientific communications; while 7 questionnaires and 1 model were validated. Presently, there are 46 community projects ongoing. The number of communications in the media (TV, radio and newspapers) also increased significantly.
Conclusions: The present data are clear indicators of significant awareness raising, but future work must deal with measurement of impacts upon Portuguese sleep behaviors.
Disclosure: Nothing to disclose.

P1035

Sleep habits, personal factors and environmental factors: a three-dimensional sleep model for Portuguese adolescents

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Objectives: This study characterizes sleep's adolescents considering habits, self-perceptions, and knowledge, explores the factors that underline their self-perceptions, and proposes a model to an integrative approach of sleep as framework of future researches and interventions.
Methods: Participated 400 students (54.8% girls 45.3% boys), with a mean age of 15.33 years, attending the 9th and 11th grades, of two schools in Lisbon. They were assessed by the Questionnaire About Sleep for Adolescents (Rebelo-Pinto, 2010), which addresses 18 questions about sleep habits and routines, 5 about self-perceptions, and 20 about knowledge.
Results: Quantitative results focused on: (i) sleep duration, regularity and autonomy, verifying a marked irregularity in rise (4 h04) and bedtime (2 h18) hours, or total sleep time (2 h06) comparing week and weekend; (ii) on organization and functionality of the room and eating habits, whereas the main causes attributed to insufficient sleep are 'noises in the room', 'watch TV until late', and 'being at the internet for hours'; and, (iii) factors of cognitive and emotional nature such as knowledge and concerns, since the majority deemed to have 'average' (45.5%) and 'good' (23.0%) knowledge. From the qualitative exploration of self-perceptions, emerged in the environmental factors the daily activities in relation with sleep, and in the personal factors the knowledge and problems related to sleep.
Conclusions: Results raised the possibility of developing a proposal for a three-dimensional model about sleep that addresses sleep habits, personal factors and environmental factors, and that can be used as a generator matrix of objectives for clinical and educational interventions.
Disclosure: Nothing to disclose.

Sleep and gender

P1036

Sensitivity and specificity of the neck circumference in predicting obstructive sleep apnea syndrome in male

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Objectives: To assess the ability of the neck circumference (NC) to predict the diagnosis of obstructive sleep apnoea syndrome (OSAS) in a population group from Timisoara, Romania.

Methods: We included 836 consecutive male patients (18 years old) referred to be polysomnographic evaluated for OSAS, October 2005 - April 2013. At initial visit anthropometric data including NC were recorded. With the area under curve (AUC) derived from the receiver-operating characteristic (ROC) curve we assessed the ability of NC for the diagnostic of OSAS. Sensitivity, specificity, positive predicted value (PPV), negative predicted value (NPV), positive likelihood ratio (LR+) and negative likelihood ratio (LR-) were calculated for different cut-off points.

Results: Age 19 - 83 years (median 52), NC 30–62 cm (median 45). 778 (93.1%) patients diagnosed with OSAS, apnoea - hypopnea index (AHI) >5/h, median AHI 38.75/h (interquartile range 22.85 - 57.72). A significant correlation was found between NC and AHI ($\rho = 0.35$, $P < 0.001$). The AUC of 0.71 (95% CI 0.63–0.79, $P < 0.001$) indicates that 71% of OSAS diagnosed subjects had a higher NC than no OSAS patients. The optimal NC was 41 cm with a sensitivity of 0.8099, specificity of 0.5185, PPV of 0.9588 and NPV of 0.1647. The LR+ 1.68 indicates that a male with NC >41 is 1.68 times more likely to have OSAS.

Conclusions: NC is a reliable measurement in OSAS patients. Low NPV indicates that NC needs a additional predictors for screening an OSAS population. Patients with NC >41 cm should have a priority for sleep study.

Disclosure: Nothing to disclose.

P1037

The impact of CPAP treatment on life satisfaction and close relationships in patients with sleep apnea

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Introduction: The present study investigates life satisfaction and close relationships in male and female patients with Obstructive Sleep Apnea, before and after 1 year of CPAP-treatment.

Material and methods: Study design: Consecutive inclusion of male ($n = 150$) and female ($n = 46$) patients with OSA scheduled for treatment with CPAP. After informed consent the patients were asked to fill out a questionnaire on two different occasions: before start of CPAP-treatment and after 1 year of CPAP-treatment. We selected four questions from LiSat-11; one investigating general satisfaction (Life as a Whole) and three investigating closeness (Family Life, Partner Relation and Sexual Life). Epworth Sleepiness Scale was used to investigate daytime tiredness.Results within the groups and between genders are shown.

Results: With respect to life satisfaction we found no significant difference. When looking at the three questions on closeness, we only found a significant improvement in Sexual Life in the male group after one year in CPAP treatment.No other items showed any significant improvement.In both groups daytime tiredness was reduced after one year of CPAP- treatment.

Conclusion: Except for improved sexuality in male patients, no significant change can be seen in life satisfaction and close relationships in our patients after one year of CPAP-treatment. Although no improvement is seen in these items, the results indicate that CPAP-treatment per se does not have a negative impact on life satisfaction and close relationships. This is important information to patients who finds CPAP-treatment cumbersome and stigmatizing.

Disclosure: Nothing to disclose.

P1038

Gender differences in obstructive sleep apnea

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Introduction: Reviewing recent research on the roles of gender in obstructive sleep apnea syndrome (OSAS), female patients experience sleep apnea at an older age and with higher body-mass-index. Female OSAS patients report atypical symptoms more frequently.

Objectives: This study investigated gender differences in a patient's cohort with sleep apnea.

Methods: A retrospective review of patients referred to our sleep laboratory during 2006–2011 was done.

Results: We studied 146 patients, 98 males (67%) and 48 women (33%). Women were slightly older (58 years $\pm$ 12.3 vs. 56 years $\pm$ 13.1, p 0.2), had higher body mass index (36.6, SD 8.6 vs. 30.7, SD 4.7; p 0.01), and lower apnea/hipoapnea index (AHI) at the time of diagnosis (20.2, SD 18 vs. 29, SD 21, p 0.042). Insomnia was more prevalent in the women (31% vs. 16%, p 0.01). Daytime sleepiness (Epworth sleepiness scale) appeared more raised in men (15.09 $\pm$ 4.2 vs. 10.53 $\pm$ 5.5; p 0.02). The proportion of positive diagnoses was similar (60.4% in women and 63.3% in men). There was similar prevalence of HTA, DM, ischemic heart disease and depression in men and women.

Conclusions: Women reported significantly less subjective daytime sleepiness, more insomnia, a higher body mass index, as well as a minor AHI. Some of these findings have been described before. Clinicians need to be aware of these differences when assessing women for the possibility of sleep apnea in order to allow a correct management of the disease.

Disclosure: Nothing to disclose.

P1039

Effect of mother-infant separation on sleep habits of mothers

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Objective: Sleep habits of mothers after delivery are largely affected by conditions related to baby care. The aim of the study was to identify the sleep habit of mothers who experienced mother-infant separation immediately after delivery.

Subjects and methods: Twenty nine mothers who were separated from the infants due to the admission to the neonatal intensive care unit (NIUC) were included in the study. Sleep habit of mothers were asked using a questionnaire on two occasions; two weeks after delivery (under regular milking with 3 h interval while the baby was in NICU) and two month after delivery (under brestfeeding at home), and the parameters were compared.
Results: Mean bedtime, wake time and sleep duration did not show any statistical difference between 2 weeks and 2 months after delivery. Percentage of mothers who require more than 20 min before falling asleep was 42.4% at 2 weeks, and the percentage significantly decreased to 15.4% at 2 months after delivery. Mean number of naps did not show any difference, but the duration of each nap significantly decreased from 70.0 min to 32.4 min at two months after delivery.
Discussion: Our subjects continued regular milking during the period of mother-infant separation which may have influenced the sleep pattern of mothers resulted in similar sleep habits compared to the sleep during brestfeeding. Shorter duration before falling asleep and decreased nap duration may be caused by the sleep deprivation due to the baby care.
Disclosure: Nothing to disclose.

P1040

Upper airway flow limitation during sleep in normal pregnancy

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Objectives: The frequency of snoring increases from 7.9% during the 1st trimester to 21.2% during the 3rd trimester of pregnancy. This increase is associated with sleepiness, higher initial BMI and higher prevalence of edema, but not with weight gain during pregnancy. Self-reported snoring is a surrogate of upper airway flow limitation which can be objectively measured with nasal prongs and transcutaneous carbon dioxide ($tcCO_2$) monitor. Our aim was to characterize the patterns and occurrence of sleep-induced upper airway flow limitation during normal pregnancy.
Methods: Sixteen healthy women went through a standard polygraphic sleep recording in a sleep laboratory when pregnant for 31–33 weeks. The respiratory effort was monitored with thoraco-abdominal belts, nasal airflow with nasal pressure cannula and the gas exchange with pulse oximeter and transcutaneous carbon dioxide.
Results: Severe continuous flow-limitation with $tcCO_2$ increases was observed in 3/16 (19%) women. A new, previously undescribed pattern of oscillating flow limitation with transient $tcCO_2$ changes occurred in 9/16 (56%) women. Overall, 75% of women presented with sleep-induced upper airway flow-limitation with $tcCO_2$ changes.
Conclusions: Pregnancy markedly predisposes to upper airway flow-limitation during sleep, which may affect maternal or fetal well-being. Flow limitation during sleep may also play a role in the previously described associations between habitual snoring, gestational hypertension and preeclampsia.
Disclosure: Nothing to disclose.

Sleep changes in aging: causes and consequences

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Age-related changes in the molecular and cellular mechanisms of sleep homeostasis

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Aging is associated with changes in sleep -wake homeostasis. Staying awake puts pressure on the neurons of the brain's various arousal systems, such as on the cortically projecting neurons of the basal forebrain. During wakefulness, these neurons are active and excite the cortex, thereby enhancing behavioural arousal. The price of continuous neural and synaptic activity is the accumulation of sleep pressure, which dissipates with time spent asleep. Age-related alterations have been observed in many of the molecular and cellular processes that couple changes in wake duration and quality to changes in sleep. These processes include for example changes in energy metabolism, cellular stress and synaptic plasticity. This lecture aims to summarize current knowledge of the age-related changes in sleep-wake homeostasis, with a focus on the molecular and cellular mechanisms of sleep pressure.

Disclosure: Nothing to disclose.