Cold-Inducible RNA Binding Protein (CIRBP) contributes to quality of waking, REM sleep homeostasis and refines the molecular response to sleep deprivation (SD)

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Objectives: SD changes clock-gene expression but the underlying mechanism is unknown. We propose CIRBP because 1) its expression is sleep-wake driven, possibly through changes in cortical temperature (Tcx); 2) CIRBP mediates high-amplitude clock-gene expression. We therefore expect that sleep-wake dependent changes in clock-gene expression are attenuated in CIRBP knock-out (KO) mice, thereby altering the sleep homeostat.

Methods: We measured Tcx, EEG, sleep-wake behavior and locomotor activity in male KO and wild-type mice during two baseline days, 6h SD and two recovery days. The effects of SD on cortical gene expression was quantified in both genotypes.

Results: Tcx changes with sleep-wake state and SD sustained high Tcx. KO mice are more active, display faster theta-activity during active waking and altered sleep-wake distribution resulting in increased NREM sleep delta power (0.75-4Hz) and lost more REM sleep incurred by SD. SD induces a genotype-dependent change in Hsp90b, Hspa5/BiP, RevErba and Clock.

Conclusions: CIRBP regulates sleep-wake distribution, quality of waking and REM sleep homeostasis. Only for Rev-erbA expression was the SD-dependent change attenuated in KO mice. Other mechanism(s) are likely to link sleep pressure to clock-gene expression.

Presenting Author: Hoekstra, Marieke
**Micro-regulators of sleep homeostasis in mice**

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**Objectives:** In the current study, we first assessed whether microRNA expression is affected by sleep deprivation (SD) in mice. We then tested the functional involvement of the top microRNA candidate, miR-709, in sleep regulation.

**Methods:** We sleep deprived male C57BL6 mice for 6h and assayed by microarray which microRNAs altered their expression. Next, mice were implanted with EEG/EMG electrodes, and injected intracerebroventricularly (ICV) with either miRNA-709 inhibitors or controls. The response to a 6h SD relative to baseline was compared among the groups. Changes in predicted miR-709 targets were investigated after inhibition of miR-709 in primary cortical cultures.

**Results:** Sleep deprivation altered the cortical expression of several microRNAs with miR-709 exhibiting the most prominent changes. *In vivo* inhibition of miR-709 resulted in a larger increase in EEG delta power after periods of prolonged wakefulness, as compared to the controls. This larger increase was specific to the slow delta frequencies (0.75-2.25 Hz). Top predicted gene targets of miR-709 in the brain, such as *Gsk3b* and *Sema6a*, were validated as targets *in vitro*.

**Conclusions:** miR-709, an activity-induced microRNA, both affects and is affected by sleep processes. miR-709 might functionally link neuronal excitation during extended wakefulness to the recovery process occurring during sleep.

**Presenting Author:** Kompotis, Konstantinos
Objectives: The mechanisms regulating the microarchitecture of non-REM sleep (NREMS), in particular fluctuations in arousability levels, are critical for sleep pathophysiology. Optogenetic manipulations of specific neuronal populations trigger shifts in arousal probability, yet correlates in undisturbed NREMS are unclear. We investigated spontaneous exits from NREMS with respect to the infra-slow 0.02 Hz-oscillation in sigma power (10-15 Hz), which correlates with permissive windows for auditory stimulus-induced NREMS-wake transitions.

Methods: We performed 48 hours of polysomnographic recording (EEG/EMG) in freely-moving mice sleeping in undisturbed conditions. Their behavioral state was scored with a 4-s resolution and the temporal dynamics of specific frequency bands were analyzed with respect to beginnings or ends of NREMS bouts.

Results: Spontaneous exits from NREMS to both wake and REMS occur during the fragility period defined by the descending phase of the 0.02 Hz-oscillation in sigma power. Microarousals occur in 25% of fragility periods, after which the 0.02 Hz-oscillation continues undisturbed. After prolonged wakefulness or REMS, however, the oscillation is less pronounced and takes time to build up.

Conclusions: We propose a biological correlate for the microarchitecture of sleep, the 0.02 Hz-oscillation in sigma power. Spontaneous exits from NREMS occur preferentially during permissive windows defined by the phase of the 0.02 Hz oscillation.

Presenting Author(s): Sandro Lecci, Romain Cardis
Changes in Human Grey Matter Density during Long-Term Caffeine Consumption and Caffeine Withdrawal

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Objectives: The present study investigates changes in grey matter density (GMD) during long-term caffeine consumption and caffeine withdrawal.

Methods: Eighteen young participants took part in a double-blind within-subjects design with three conditions lasting 11 days each: caffeine (450 mg/day), placebo, and withdrawal (caffeine for nine days, followed by placebo). MR images were assessed 14h after wake-up at the 10th day, along with caffeine levels in the sweat. All reported results were significant at $p<0.05$, family-wise error-corrected.

Results: Total but not regional GMD was lower during caffeine than placebo. In contrast, total GMD did not differ between withdrawal and placebo, but was regionally increased in parietal regions, insula, and thalamus compared to both placebo and caffeine. After accounting for acute caffeine levels (by including them as covariate), GMD reductions in the caffeine condition were no longer significant, while all differences between withdrawal and placebo remained.

Conclusions: Our findings suggest that reductions of total GMD during chronic caffeine consumption do not mirror stable morphological differences, but reflect dynamic changes responding to acute caffeine intake. Together with withdrawal-related changes assessed within 24h, the results underline that GMD can flexibly change within a short time-frame, potentially due to changes in cerebral blood flow.

Presenting Author: Lin, Yu-Shiuan
Deep brain stimulation of the sleep-promoting center VLPO modulates slow wave sleep in healthy rats

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Objectives: To test whether deep brain stimulation (DBS) can reversibly modulate the activity of wake- and sleep-promoting centers and, thus, be helpful for patients with treatment-resistant severe sleep-wake disorders (SWD), we performed DBS experiments selectively targeting the sleep-promoting ventrolateral preoptic area (VLPO) in healthy rats.

Methods: Sprague-Dawley rats were bilaterally implanted into the VLPO with concentric bipolar electrodes. Electroencephalography/electromyography electrodes were implanted to record vigilance states in parallel to stimulation. Recordings were performed for 24h baseline assessment, followed by 24h stimulation (2, 10 and 125Hz). The proportions of vigilance states, along with delta power and slow wave energy were assessed under stimulation and compared to baseline.

Results: None of the stimulation frequencies produced a significant change in the vigilance states duration. At 2 and 10Hz, delta power and slow wave energy remained unchanged. However, we found a substantial ca. 36% increase of delta power, along with equal enhancement of slow-wave energy at 125Hz.

Conclusion: Our findings suggest that DBS of the VLPO at a high frequency (i.e. 125Hz) modulates vigilance states mainly by “deepening” slow wave sleep, while their relative duration remains unaffected. In other words, the intensity and the quality but not the length of sleep are modulated.

Presenting Author: Masneuf Sophie
mGluR5-dependent nuclear speckle assembly drives sleep-wake transcriptomics


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Objectives: The nucleus has been shown to be heavily compartmentalized to regulate gene expression, but the extent of its plasticity during normal daily sleep-wake rhythms still remains elusive. Here we show the importance of structural rearrangement upon sleep-wake transcriptomics and subsequent neuronal activity by the example of the RNA binding Drosophila Behavior Human Splicing (DBHS) protein family, consisting of NONO, PSPC1 and SFPQ.

Methods: C57Bl6 and DBHS knockout mice were analyzed for nuclear morphology, sleep phenotype and gene expression variations using immunofluorescence, transcriptomics, and cortical EEG recording.

Results: We show that DBHS proteins form a new type of heterogeneous clusters in neurons in vivo and in vitro whose abundance is increased in circadian and sleep-wake-dependent fashion. These clusters rearrange upon neuronal activity, which is signaled via glutamatergic pathways, mainly via mGluR5 and its downstream target PKC. We also show that DBHS proteins are important for sleep gene expression and the homeostatic response to sleep deprivation.

Conclusions: Our results identify DBHS protein clusters as plastic, intra-nuclear structures important for regulation of synaptic transmission during sleep and wake, and give an insight into possible downstream mechanisms of mGluR5 upon sleep and wake.

Presenting Author: Andrea Spinnler
Investigation of the possible effects of the *BDNF* Val66Met polymorphism on the sleep EEG in a large, homogenous sample

<table>
<thead>
<tr>
<th>Laura van Bommel¹, Diego Bauer¹², Mairav Zion-Cohen³, Sebastian Holst¹², Wolfgang Berger⁴, Peter Achermann¹², Hans-Peter Landolt¹²</th>
</tr>
</thead>
</table>

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**Objectives:** Animal studies indicated a causal link between brain-derived neurotrophic factor (*BDNF*) and sleep homeostasis. Investigation in a small human sample of the impact of the functional Val66Met polymorphism of *BDNF* (rs6265) suggested that the difference between Val/Val and Met-allele carriers on the sleep EEG resembles the effects of sleep deprivation. Here we aimed at corroborating these earlier findings in a larger sample.

**Methods:** All-night sleep EEG recordings in baseline and recovery nights after 40 hours prolonged wakefulness were available in 118 healthy young men (18-34 y; 78 Val/Val and 40 Met-allele carriers). Sleep-state-specific power spectra were calculated using FFT. Statistical analyses were conducted with PERMANOVA and linear mixed-effects models.

**Results:** Prolonged wakefulness reliably increased slow wave sleep and NREM sleep EEG power in the ~ 0.5-11 Hz range, and reduced power in the ~ 13.75-15 Hz band. By contrast, in baseline and recovery nights, sleep architecture and EEG spectra in NREM and REM sleep were strikingly similar in Val/Val and Met-allele carriers. The response to sleep deprivation did not differ between the genotypes.

**Conclusions:** These ongoing analyses indicate that the impact of rs6265 of *BDNF* on sleep and the sleep EEG is less pronounced than previously suggested.

**Presenting Author:** Van Bommel, Laura
Diurnal changes in glutamate/glutamine assessed by MRS are related to EEG sleep slow wave activity

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Objectives: The glutamatergic α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic-acid (AMPA) receptor is a key player in synaptic plasticity. Animal studies have shown 1) changes in AMPA receptor levels with sleep and wake and 2) a reduction of glutamate (GLU) during NREM sleep, which was positively correlated with sleep slow wave activity (SWA). Our Goal was to combine magnetic resonance spectroscopy (MRS) and high-density (hd) EEG to assess diurnal changes in glutamate/glutamine (GLX) and its relation to SWA in the human brain.

Methods: MRS of 16 healthy young subjects (6 female, 21.3 ± 2.2 years) were measured in the left parietal lobe in the evening and in the next morning. The night between the scans was recorded with hd EEG.

Results: Significant overnight changes were only found in GLX (-6.6 ± 1.6 %, p=.006). Further, the reduction in GLX was positively correlated with the SWA decrease from the NREM sleep episode with maximal SWA to the last NREM sleep episode (r=0.6, p=0.02).

Conclusions: Our results show that quantification of diurnal changes in GLX in the human brain is possible by means of MRS. Further, our results might support an active role of SWA in downregulating the increase in GLX levels that presumable occur during wakefulness.

Presenting Author: Volk, Carina
Influence of Habitual Caffeine Consumption and Its Withdrawal on Subjective Sleepiness, Vigilance, Caffeine Craving, and Melatonin

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Objectives: Our aim is to investigate the effects of habitual caffeine consumption and its withdrawal on subjective sleepiness, vigilance, caffeine craving, and melatonin.

Methods: Nineteen habitual caffeine consumers (26.6 ± 4.0 years, daily caffeine consumption 473.6 ± 109.4 mg) participated in a balanced, randomized, double-blind, within-subjects design comprising three conditions: a caffeine, a withdrawal, and a placebo condition each lasting 11 days. Subjective sleepiness, vigilance (lapses on Psychomotor Vigilance Task, RTs > 500 ms), caffeine craving (Visual Analogue Scale), and salivary melatonin were quantified regularly during a 43-hour laboratory study starting on day 9 of treatment.

Results: Compared to placebo, the caffeine treatment did not significantly impact on sleepiness and vigilance (p>0.1). In contrast, during withdrawal participants felt significantly sleepier compared to placebo (p<0.01) and caffeine (p<0.01). In addition, vigilance was worse and craving for caffeine stronger during withdrawal compared to placebo (p<0.05). Melatonin levels did not reveal any significant differences between the three conditions (p>0.1).

Conclusions: Our data corroborate the effects of caffeine withdrawal on subjective sleepiness, vigilance, and caffeine craving. In addition, our results so far indicate that habitual caffeine consumption does neither go along with benefits in sleepiness and vigilance nor strongly affects melatonin levels.

Presenting Author: Weibel, Janine
Sleep deprivation affects microRNA expression profile in humans

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Objectives: MicroRNAs (miRNAs) are small, non-coding RNA fragments regulating gene expression at the post-transcriptional level and playing established roles in various biological processes. Given their proposed role in sleep-wake regulation, we investigated the impact of acute sleep deprivation on blood miRNA expression in humans.

Methods: Twenty-two young (mean age: 24±3 years) and 9 older (65±1 years) healthy men completed a controlled in-lab study, consisting of 8-hour baseline sleep, sleep deprivation, and a 10-hour recovery sleep opportunity. At the same circadian time in all three conditions (at 04:23 pm ± 23 min), qPCR expression profiling of 86 miRNAs was performed in serum. Data were analyzed using mixed-model ANOVAs with the factors ‘condition’ and ‘age group’.

Results: While eight different miRNAs showed a main effect of ‘age group’, only miR-127 was reliably affected by ‘condition’ (p_{air}<0.05), such that miR-127 expression was upregulated after extended wakefulness and normalized after recovery sleep.

Conclusions: Our findings show that sleep deprivation and recovery sleep affect the blood miRNA expression profile, suggesting that MiR-127 and its target proteins may provide novel biomarkers of sleep loss in humans.

Presenting Author: Weigend, Susanne
Later school start times alleviate sleep deprivation and social jetlag in adolescent high school students

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Objectives: Early school start times (SST) clash with the late circadian phase and thus late bedtimes of adolescents. Consequently, adolescents accumulate sleep debt and “social jetlag”, impairing their health and career prospects. We studied whether delaying SST ameliorates this problem.

Methods: We monitored changes in sleep, circadian rhythms and grades, when in 2016 a high school in Aachen introduced “flexi time”, allowing senior students to choose daily between an 8- or 9-am-start. Using actimetry (N=42) and sleep diaries (N=70), we followed students aged 15-19 for 3 weeks before and 6 weeks into the flexi-system. In 2017, we conducted a 1-year-follow-up in which 106 students kept a sleep diary for 6 weeks (overlap wave 1 and 2: N=41).

Results: We found that delaying SST increased sleep length and decreased social jetlag. Independent of chronotype, participants slept one hour longer on 9-am-days: sleep onset remained unchanged but sleep offset became later. On 9-am-days, participants reported to require their alarms less often, feel more concentrated and motivated, and to sleep and learn better. Social jetlag was significantly reduced because weekend sleep timing was advanced. Results from our follow-up study corroborate these findings.

Conclusions: Based on the persistently positive effect, we recommend later SST for adolescent students.

Presenting Author: Biller, Anna; Eva, Winnebeck.
* equal contribution
Relationship between infant sleep behavior and gut microbiome beta diversity

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Objectives: In the first year of life infants’ sleep regulation undergoes rapid maturation. Simultaneously, the gut microbiota (GM) matures and increases in diversity. First studies hint towards a bi-directional relationship between sleep regulation and the GM composition. However, little is known about this relationship during early-life and infancy.

Methods: Sleep behavior was assessed longitudinally across infancy using ankle actigraphy and 24-h sleep-wake diaries (n=59 3-month-olds, n=45 6-month-olds, n=10 12-month-olds). Sleep duration, sleep fragmentation and sleep consolidation were averaged in each infant from 7.0 ± 2.1 days. Fecal samples were collected from infant diapers. Total genomic DNA was extracted and subjected to high throughput 16S rRNA gene (V3) amplicon sequencing.

Results: Preliminary results show a significant longitudinal relationship between GM distribution and infant sleep fragmentation (3-12 mo. \(p=0.002\)) that is partially explained by changes in the relative abundance of Bifidobacterium longum. Subsequent analysis indicated a particularly strong relationship when infants reached 12 month of age \((p < 0.001)\). Similar longitudinal associations were found between GM composition and sleep consolidation (3-12 mo. \(p =0.03\)).

Conclusions: These findings uncover a possible interplay between infant sleep behavior and GM composition. We propose that the GM profile may support the maturation of infant sleep regulation.

Presenting Author: Schoch, Sarah F.
Homeostatic Response to Sleep Restriction in Adolescents

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\end{tabular}

Objectives: As chronic sleep restriction is highly prevalent in adolescents, it is important to understand how adolescent sleep is regulated under such conditions. In adults, sleep intensity is homeostatically regulated: if sleep is restricted, then sleep intensity increases. Our goal was to investigate sleep regulation in adolescents undergoing different durations of sleep opportunities.

Methods: 34 subjects were divided into three groups: 5 h, 7.5 h and 10 h of sleep opportunity. Each group underwent a protocol of 9 nights mimicking a school week between 2 week-ends: 2 baseline nights (10 h sleep opportunity), 5 condition nights (5 h, 7.5 h or 10 h), followed by two recovery nights (10 h). Slow-wave activity (SWA; EEG power in 0.75-4.5 Hz range) and slow-wave energy (SWE; cumulative SWA) were calculated for frontal and central EEG derivations and extracted from simulations of the homeostatic process.

Results: The protocol was effective in restricting sleep and predictions of the two-process model were accurate, with only minor differences compared to the empirical homeostatic markers.

Conclusions: Sleep homeostasis was preserved in late adolescents undergoing chronic sleep restriction.

Presenting Author: Skorucak, Jelena
Objectives: Slow waves (SW), during deep sleep, can be systematically manipulated by acoustic stimulation: Stimulation time locked to the down-phase of SW reduces, whereas stimulation time locked to the up-phase increases SW. There is evidence that spike-wave activity (SWA) in epileptic patients with an activation of epileptiform discharges during sleep are related to these SWs. Thus, we aimed at investigating whether SWA can be systematically influenced by acoustic stimulation time locked to SW.

Methods: In 5 patients, all-night EEG were recorded, combined with real time SW detection. Throughout the night acoustic stimulation was performed in a 3 x 5-min-block design (no stimulation - stimulation - no stimulation). Tones were applied time locked either to the up (UP) or down (DOWN) phase of the detected SW alternately.

Results: Our preliminary analysis shows that the more tones were applied after the onset of the EEG negative trend the more SWA was reduced (Spearman’s Rho=-0.71, p=.058), whereas the more tones were applied after the onset of the EEG positive trend the more SWA was increased during stimulation (Spearman’s Rho=0.74, p=.046).

Conclusions: Thus, we found first evidence that SWA can be systematically influenced by acoustic stimulation, which might provide a new simple non-invasive approach to influence SWA.

Presenting Author: Fattinger Sara
Local, spindle-enriched non-REM sleep in mouse somatosensory cortex enabled through heterogeneous thalamic burst propensity

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**Objectives:** Sleep is a global vigilance state, yet its cerebral correlates are locally heterogeneous. We explore the expression of locally different sleep features and investigate their underlying cellular and circuit mechanisms, as well as their relevance for local circuit function.

**Methods:** We record in mice the palette of regional activities in-vitro within the major thalamic rhythm pacemaker (the thalamic reticular nucleus TRN), and the local variations of sleep oscillations in multiple cortical areas in-vivo.

**Results:** We identify TRN CaV3.3 calcium channels as a molecular source for cortical heterogeneity in mouse non-REM sleep. CaV3.3-channels enabled a graded form of repetitive burst discharge: strongest in somatosensory, intermediate in auditory, and weak in non-sensory sectors of the TRN. In undisturbed sleep, the corresponding somatosensory (but not auditory and prefrontal) cortices, showed fast, strong and locally synchronous sleep spindles. Without CaV3.3 channels, somatosensory areas expression in delta waves was enriched, and spindles became homogenous across sensory and non-sensory cortices. Furthermore, the tight locking of fast spindles to the upstate of cortical slow-oscillation was disrupted.

**Conclusions:** We unravel the critical role of the thalamus in shaping local heterogeneities of non-REM sleep and in imposing forms of spindle-enriched sleep in the major sensory modality of mouse.

**Presenting Author:** Fernandez, Laura
Prototype development for mobile and automated auditory sleep stimulation

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Institute of Robotics and Intelligent Systems, Mobile Health Systems Lab, D-HEST, ETH Zurich

Objectives: Non-invasive sleep stimulation methods to promote restorative processes of sleep have recently gained considerable interest. Single-night, in-lab studies show that precisely timed tones played during deep sleep can enhance slow wave activity. Whether such methods proof transformative to real-life settings remains to be investigated. We are currently developing a portable device that will enable ambulatory sleep stimulation approved for clinical and research applications.

Methods: We developed a mobile system integrating a comfortable and adjustable headband, low-power and high quality EEG, EOG and EMG amplification, SDcard recording, and wireless streaming. We added a dedicated digital signal-processing chip to perform real-time, closed-loop auditory stimulation and sleep classification. In addition, we designed multiple hardware and software safety mechanisms for preventing accidental and intentional misuse ensuring safety.

Results: Our prototype considerably decreased the set-up time compared to in-lab recording methodologies. The quality and resolution of the obtained biosignals was comparable to lab-based systems. When evaluated on two preliminary recordings from subjects (mean 60 years), real-time NREM sleep was detected with more than 90% precision.

Conclusions: Our mobile sleep stimulation prototype enables high-quality, large-scale sleep research outside the lab, which represents an important step towards applying sleep stimulation technologies to clinical and long-term studies.

Presenting Author: Ferster, Maria Laura
Acoustic modulation of slow-wave sleep in rats: effect of boosting or inhibiting delta activity in SWS on motor learning.

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*These authors contributed equally to this work.

Objectives:
Slow oscillations (SOs), hallmark of slow-wave sleep (SWS), play a major role in sleep-dependent memory formation, including learning of motor tasks. SOs consist of an upstate, where neurons present increased excitability, followed by a downstate, where neurons are silent. Previous studies in humans established that targeting auditory pulses to SOs’ upstate – in-phase modulation – constitutes a privileged time window for improvement in memory reactivation, whereas intervening SOs’ downstate – out-of-phase modulation – seems to disrupt slow oscillatory patterns and diminish recall performance. We hypothesize that in-phase acoustic stimulation in healthy rats during motor training in the single-pellet reaching task, by increasing slow-wave activity, will translate into enhanced learning of motor skills, whereas out-of-phase stimulation will offer the opposite effect.

Methods:
A newly auditory closed-loop protocol for rodents was established targeting SOs’ up- or down-state phases and deliver clicks of pink-noise (25 ms, 35 dB) within 8 ms. In our model, sleep is recorded by electroencephalography/electromyography while acoustic stimulation is applied to enhance or disrupt SOs and ultimately modulate deep sleep. For that, a real-time SWS detection feature runs alongside a predictive phase-locked loop as a function of the endogenous signal.

Results:
The software’s processing tree is running and animal experiments are ongoing.

Presenting Author: Gonçalves Moreira, Carlos
High-density EEG recordings combined with Magnetic Resonance Spectroscopy to study the relationship between sleep and diurnal changes in markers of cortical plasticity in children

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Objectives: In healthy adults, Magnetic Resonance Spectroscopy (MRS) revealed that Glutamate + Glutamine (GLX) concentration decreases from evening to morning in a parietal voxel and that this decrease correlates with the decrease in slow wave activity (SWA). A reduction in SWA during sleep is thought to reflect a reduction in overall synaptic strength, restoring the brain’s learning capacity. Because children characteristically show a larger decrease in SWA across the night compared to adults, we hypothesized that also the overnight reduction in GLX would be larger.

Methods: In an ongoing study, 6 healthy children (1 female, 13.5 ± 1.3 years) were measured in the evening and in the subsequent morning using a 3 T MRI scanner. High-density sleep EEG was recorded during the night in-between. During both scan sessions 1H-MRS spectra were acquired from a parietal voxel.

Results: Our preliminary analyses show that compared to adults, children showed increased GLX levels in the evening (p = 0.009) and in the morning (p = 0.0003). No significant overnight reduction in GLX was found (p = 0.825).

Conclusions: These results indicate, that in contrast to adults, children seem to show no clear link between the SWA decrease and GLX overnight changes.

Presenting Author: Jaramillo, Valeria
Spatio-Temporal Characterization Of Theta And Sigma Power Following Auditory Stimulation During Slow-Wave Sleep

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Objectives: In this study, we investigated the neural underpinnings and temporal dynamics of the enhancement in EEG theta and spindle activity observed during closed-loop auditory stimulation during sleep.

Methods: For this we collected high-density sleep EEG in 5 subjects (23±2y.o.) in three conditions carried out in different nights: (1)non-stimulation (baseline), closed-loop auditory stimulation in (2)the up-phase or (3)the down-phase. The stimulation/baseline contrast was calculated in the theta (4-8 Hz) and spindles (12-16 Hz) frequency bands in sensors and source space.

Results: In the sensors space, we observed an enhancement of theta and spindle power (cluster corrected p≤0.05) for stimulation condition in the left fronto-central and right centro-parietal electrodes. The generalized enhancement of theta power occurred from ~100 to ~800 ms (electrode FC3,F(1,3)=25.36,p=0.015), and from ~800 to ~1500 ms of spindles power (FC3,F(1,3)=37.64,p=0.009). Beamformer source analysis of the stimulation-induced changes in the theta range revealed involvement of the left temporal lobe, right frontal lobe and right parietal lobe. A similar source pattern was identified for the spindle range (both cluster corrected p≤0.01).

Conclusions: Our findings suggest the presence of different phases of the acoustically induced response which arise from the same functional network, which largely overlaps the default mode network.

Presenting Author: Krugliakova Elena
### How the efficiency of auditory closed-loop stimulation during deep sleep depends on the timing and morphology of slow waves

Miguel Navarrete¹, Anugrah Honesty², Helen Le Seur², Jules Schneider², Nihkil Kurian², Hong-Viet V. Ngo¹, Mario Valderrama⁴, Pennelope Lewis¹, Alex Casson².

1- Cardiff University’s Brain Research Imaging Centre, United Kingdom  
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**Objectives:** Auditory closed-loop stimulation during deep sleep has demonstrated to be effective for enhancing behavioural and physiological sleep functions by promoting particular electrophysiological rhythms. Nevertheless, as the neural mechanisms involved in the cortical response to phase-locked stimuli are not understood, the optimal placement of sound stimulus is not clearly determined. The objective of this work was to evaluate the efficiency of the timing and phase of acoustical stimulus based on the response of subsequent slow oscillations and sleep spindles.

**Methods:** We analysed the data of 21 subjects closed-loop sound stimulated during slow-wave sleep. The stimulus efficiency was examined by measuring ten different features of consequent slow wave and spindles depending on the click timing and its corresponding Hilbert phase.

**Results:** We found an increased response of slow-wave amplitude and RMS energy for stimuli applied in the intervals confined in time between 400ms and 200ms before the maximum peak of the wave and phases between $-\pi/6$ and $\pi/2$ radians. Consistently, spindle duration, amplitude and RMS energy were strengthened by stimuli in similar intervals.

**Conclusions:** Our results suggest optimal placing for closed-loop stimulation which may be the basis of real-time detection methods and the understanding of cortical response to in-phase slow-wave stimulation

**Presenting Author:** Miguel Navarrete
Glutamatergic recruitment of thalamic reticular nucleus by postsubiculum projections: role in head-direction system?

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**Objectives:** Beyond sleep rhythm pacemaking, the thalamic reticular nucleus (TRN) is involved in sensory gating and arousal state regulation through its inhibitory control over the thalamus. Curiously, its role in the subicular-thalamic circuit, which is an essential component of the head-direction and self-referenced navigation system, remains largely unexplored.

**Methods:** In vitro and in vivo electrophysiological recordings of TRN and anterior thalamic (ATN) neurons of mice were combined with AAV1-CaMKII-ChR2-YFP transfection of the postsubiculum and optogenetic stimulation.

**Results:** In vitro recordings of acute brain slices showed that TRN and ATN neurons discharge in a time-locked manner in response to postsubicular afferent activation. Subicular responses in ATN, but not in TRN cells obligatorily recruited feedforward inhibition. Both synaptic pathways showed little depression when activated repeatedly, enabling persistent membrane depolarization and repeated firing of their postsynaptic targets. In vivo data in freely moving animals showed both light-evoked excitation and inhibition of ATN units, part of which showed head-direction tuning.

**Conclusions:** Together, these data identify a faithful information transfer between postsubicular and thalamic circuits, including TRN. These findings implicate a role for TRN in shaping the tuning curves of thalamic head-direction neurons and could provide circuit substrates for replay of spatial information during sleep.

**Presenting Author:** Vantomme, Gil
## Performance on the Stroop Color-Word task in healthy adults is inversely associated with habitual sleep duration

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\textsuperscript{5} Zürich Center for Interdisciplinary Sleep Research (ZiS), University of Zürich, Switzerland

**Objectives:** To examine whether a relationship between habitual sleep duration and cognitive performance exists in healthy, non-sleep deprived adults.

**Methods:** 220 healthy participants were studied (115M, 25.2 ± 0.4 years). Cognitive functions were assessed using the Stroop task, the d2 attention task, and the random number generation test. Participants were classified by a median split on each of the tasks as higher- or lower-performers. Habitual sleep duration was assessed using the Munich Chronotype Questionnaire (n=220) and 4-weeks of wrist actigraphy (n=82) (Cambridge Neurotechnology, Cambridge, UK).

**Results:** Participants reported sleeping on average 1.2 h less on work days (7.3 ± 0.1 h) than leisure days (8.5 ± 0.1 h) ($t_{219} = 11.7, p<.001$). Shorter self-reported sleep duration on leisure days was associated with significantly better performance on all three tasks ($F_{217} = 10.77, p<.01$). Actigraphic sleep estimates corroborated this difference, but only for inhibitory control on the Stroop task ($F_{79} = 7.29, p<.01$).

**Conclusions:** The findings show a robust association between distinct measures of executive functions and possibly other cognitive abilities and habitual sleep duration. One possible interpretation of these findings is that better tolerance for high sleep pressure, as exhibited by short sleepers, would permit increased mental and attentional availability for the acquisition of cognitive processes.

**Presenting Author:** Cohen-Zion, Mairav
Objectives: A large portion of nonorganic sleep disturbances are caused by psychological factors including worrying, perceived prospective threats and negative recurrent thoughts, suggesting that sleep is strongly influenced by cognitive and affective mechanisms. We aim at testing whether healthy participants are capable of voluntarily influencing objective sleep parameters. Predicting participants can voluntarily worsen but not improve their sleep.

Methods: Eighteen volunteers participated in one adaptation night and three experimental nights with an interval of one week. Polysomnography and subjective sleep quality was measured during all nights. In the three experimental nights, participants either had to sleep “normal”, worse than normal or better than normal.

Results: Results show that subjective and objective sleep onset latency as well as the time spent awake after sleep onset could be significantly altered. There were no changes in sleep architecture.

Conclusions: We could demonstrate that it is possible to influence sleep voluntarily in a negative way. Findings show if sleep is influenceable within one’s mean.

Presenting Author: Combertaldi, Selina L.
Poor sleep quality reduces resilience - may social networks act as a buffer? A prospective daily diary study in at risk- individuals

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Objectives: Healthy sleep may promote resilience in the face of stress and adversity. Moreover, social support and social networking has been highlighted as key factor influencing reactions to stress including the development of PTSD.

Methods: Here we examined a sample of 50 medical students during their first internship representing a well described real-world stressor. Data on sleep and heartrate were continuously collected over a time frame of 12 weeks non-invasively by a wrist-worn activity monitor. Prior to starting the internship, i.e., at baseline, and mid-internship, participants filled in a weeklong sleep and stress diary, including information on social interactions, arousal and anxiety as well as other questionnaires, such as a social network index. Mixed models were calculated to examine complex relationships between sleep, stress and social resources.

Results: Results show that social safeness may buffer the detrimental impact of daily sleep and stress. Additional prospective relationships between sleep quality, social relations and resilience will also be presented.

Conclusions: Together, this longitudinal prospective data suggest sleep quality and social resources as potential targets for stress-prevention programs that could help reduce the negative influence of stress in at risk- populations and promote resilience.

Presenting Author: Yasmine Azza
A Field-Study on the Role of Sleep in Stress Resilience in Rescue Workers: First Preliminary Analyses of Polysomnographic Data

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* equal contributions

**Objectives:** Good sleep may benefit stress and emotional regulation. Here we aim at better understanding the role sleep plays in stress resilience in an at-risk group for stress disorders.

**Methods:** In this ongoing study, we will investigate a sample of 100 paramedics (male and female, 18-65 y) continuously over the course of one month. Lifestyle related variables (e.g., consumption of alcohol and caffeine, smoking) and data on psychological stress (PSS-10) and sleep-wake habits are collected by validated questionnaires and continuous wrist and heart activity (ACT). Polysomnographic (PSG) sleep recordings at baseline and in association with a stressful event are planned in a subset of 30 volunteers.

**Results:** Preliminary analyses of sleep latency and sleep efficiency derived from home-PSG revealed similar values in subjectively higher and lower stressed study participants ($n = 8$). The PSG variables corresponded well to Fitbit measures. Regression analyses will be conducted between PSG/ACT and subjective measures of sleep quality and the PSS-10 scores.

**Conclusions:** These preliminary findings may indicate inter- and intrapersonal variability in sleep profiles and stress management regarding stress resilience in paramedics, warranting further investigation.

**Presenting Author:** Clark, Ian
**Sleep and psycho-behavioral difficulties in Internally Displaced children in Georgia**

Irine Sakhelashvili, Marine Eliozishvili, Nikoloz Oniani, Nato Darchia.

*Research Centre, T. Oniani Laboratory of Sleep-Wakefulness Cycle Studies, Ilia State University, Tbilisi, Georgia.*

**Objectives:** The aim of this study was to examine the prevalence of sleep problems and associated psychological factors in Georgian Internally Displaced Children compared to their population-based controls.

**Methods:** 161 children (10.85±0.9) from ID families, escaped from Shida Kartli, Georgia, in 2008, and 161 non-ID children (10.94±0.9) were studied after 7 years of displacement. Children completed Pre-Sleep Arousal Scale (PSAS), Buss-Perry Aggression Questionnaire (BPAQ), Child’s Trauma Screening Questionnaire (CTSQ) and Children’s Depression questionnaire (CDI). Parents completed Sleep Disturbance Scale for Children (SDSC). Data were analyzed with SPSS21.

**Results:** Compared to the controls ID children revealed a significantly higher score of Physical Aggression, sleep disordered breathing, sleep hyperhidrosis, SDSC total scores. In IDs Somatic pre-Sleep arousal showed significant correlation with disorders of arousal, while cognitive pre-sleep arousal was significantly correlated with Disorders in initiating and maintaining sleep, sleep breathing disorders, disorders of arousal, sleep-wake transition disorders, disorders of excessive somnolence and total score of SDSC. Also, both pre-sleep arousals were significantly associated with CDI and CTSQ score.

**Conclusion:** Attention to the Childhood sleep disturbances following traumatic experiences and associated factors is urgently required.

**Presenting Author:** Sakhelashvili Irine
Sleep quality of medical students from the State University of Medicine and Pharmacy of the Republic of Moldova

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Objectives: To assess sleep quality of medical students in the first and sixth years of study, based on the self-assessment questionnaire.

Methods: In the study were included 102 students (73 females) (first year students (1YS) - 50, mean age 19 years and sixth year students (6YS) - 52, mean age 25 years) from the State University of Medicine and Pharmacy of the Republic of Moldova. Sleep quality assessment was based on self-report using The Pittsburgh Sleep Quality Index (PSQI).

Results: In both groups, tendencies towards low quality sleep was observed, although the quality of sleep in 1YS is lower than in 6YS (8.96 vs 7.28, P = 0.0072). This finding is due to the fact that 1YS show a voluntary sleep deprivation (sleep duration scale of the PSQI: 2.32 vs. 1.28, P = 0.0067), sleeping 2 hours less as older colleagues (average sleep duration 4.6 h vs 6.7 h, P <0.0001), this reduction being based on late bedtime. Also, students of the first year presented worse results on daytime dysfunction (1.86 vs 1.08, P <0.0001), probably due to reduced amount of sleep.

Conclusions: Medical students are exposed to sleep disorders. The 1YS reported a worse subjective quality of sleep because of voluntary sleep deprivation.

Presenting Author: Sofia Zubcu
**Automatic Snoring Detection from Respiratory Sleep Sounds in Adults and Children**

**Mustafa Cavusoglu, PhD**

*ETH Zürich, Institute for Biomedical Engineering*

**Objectives:** The possible objective measures of snoring characteristics may serve clinicians as a common ground for diagnosis. The objective of this study is to develop an effective method to detect snoring episodes, which is sufficiently fast to process full-night recordings in a reasonable amount of time.

**Methods:** Firstly, sound episodes, which can be defined as the sound activity intervals, were identified and then these episodes were classified as snore or nonsnore based on the characterization of the spectral energy distribution of snoring signals. Spectral characterization involves subband decomposition in the frequency domain.

**Results:** The proposed system was tested by using the manual annotations of an ENT specialist as a reference. The accuracy for simple snorers was found to be 97.3% when the system was trained using only simple snorers’ data. It dropped to 90.2% when the training data contain both simple snorers’ and OSA patients’ data.

**Conclusions:** The information, such as total snoring time, snore-to-sleep ratio, variation of snoring rate and regularity of snoring episodes in time and in amplitude, may be useful for the diagnosis of sleep disorders. These kinds of information can be obtained by detecting snore episodes.

**Presenting Author:** Cavusoglu, Mustafa, PhD
Cognitive impairments in obstructive sleep apnea patients depending on morning headache

Ana Diaconu¹, Victor Vovc¹,², Adrian Lupușor¹,²

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**Objectives:** To establish the relationship between morning headache (MH) and cognitive impairments (CI) in obstructive sleep apnea syndrome (OSAS) patients.

**Methods:** Our study included 17 OSAS patients (11 females, 6 men, mean age 57.8 years, SD±8,6), were investigated with the cardiorespiratory polygraph SleepDoc Porti “Dr. Fenyves und Gut”. Headache characteristics were appreciated with a personalized questionnaire for headaches. Cognitive function was assessed with the Montreal Cognitive Assessment (MoCA) tool.

**Results:** Patients were divided into two groups, first with MH (11 patients) and the second without MH (6 patients). All patients fulfilled the MoCA questionnaire, 14 patients had a total score below 26 (≥26 normal, maximum 30) and 3 patients had above 26. According to the MoCA result only the abstraction ability in OSAS patients with MH was 0.8 versus 1.6 in those without MH, p<0,05. Regarding the other domains (visuospatial/executive, naming, memory, attention, language, orientation) we did not find any statistical significant differences between groups.

**Conclusions:** In OSAS patients with MH the abstraction ability is significant diminished from those without MH. The decline of this function imply also the diminishing of the ability of complex analyzing and perception. However, for more representative results, we must rise the number of investigated patients.

**Presenting Author:** Diaconu Ana
The effect of obstructive sleep apnea on pain

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Introduction. The interaction between pain syndrome (PS) and sleep disorders (SD) is well-known, pain affecting sleep quantity and quality, whereas poor sleep quality exacerbates pain. Obstructive Sleep Apnea Syndrome (OSA) is a SD. The literature has estimated the prevalence of OSA at about 2%-25%. The pathogenetic mechanisms of OSA are also involved in pain modulation.

Objective of the study. To study the influences of OSA mechanisms on PS.

Material and methods. An analysis of the latest scientific sources has been carried out using the PubMed search engines, "HINARI" and Google Academic.

Results. Among the multiple OSA mechanisms, sleep fragmentation (SF) and nocturnal intermittent hypoxia (NIH) are two compounds involved in pain modulation. SF causes hyperalgesia, through activation of proinflammatory pathways with involvement of prostaglandins, cytokines and the serotonergic mechanism. NIH can cause PS by enhancing the oxidative stress, which results in central and peripheral sensitization to pain. NIH can lead, also, to hypoalgesia, by increasing the expression of mu and delta opioid receptors.

Conclusions. In patients with OSA, SF – enhances pain, whereas NIH can both enhance and ameliorate pain. Depending on the severity of NIH, its effect could either mask the hyperalgesia produced by sleep disruption, or even result in hypoalgesia.

Presenting Author: Spînu Doina
Anxiety and depression in patients with insomnia versus patients with obstructive sleep apnea syndrome

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Objectives: Depression and anxiety are common comorbid disorders in patients with sleep disturbances. The goal of study is to compare the degree of reactive and personality anxiety and the degree of depression in insomnia patients versus patients with obstructive sleep apnea syndrome (OSAS).

Methods: The study included 108 patients. Insomnia group – 58 patients (54%) (15/43 M/F) aged 50 ± 16 years [mean ± SD], OSAS group - 50 patients (46%) (35/15 M/F) aged 52 ± 11 years [mean ± SD] with an AHI 34 ± 24 [mean ± SD]. AHI was determined by ambulatory nocturnal cardiorespiratory polygraphy. The diagnosis was established according to the ICSD criteria. Anxiety was assessed by Spielberger-Hanini inventory, depression was assessed by Beck depression inventory. Statistical data were processed with the StatsDirect software.

Results: Reactive anxiety in the insomnia group was 39 points, in OSAS group was 32 points, (p=0.01), personality anxiety in the insomnia group was 51 points, in the OSAS group was 47 points, (p=0.03), depression in the insomnia group was 9 points, in the OSAS group was 7 points, (p>0.01).

Conclusions: Patients in the insomnia group had an increased reactive anxiety, very high personality anxiety and moderate depression, while patients in OSAS group had an almost normal reactive anxiety, an increased personality anxiety and a mild depression.

Presenting Author: Lupusor, Adrian
# Sleep stage related heart rate variability distinguishes between insomnia and normal sleep

Thorsten Mikoteit (1,2), Marcel A. Pawlowski (2,3), Eleonora Seelig (4), Stefan Bilz (5), Edith Holsboer-Trachsler (6), Axel Steiger (2), Martin Hatzinger (1)

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**Objectives:** In insomnia disorder a mismatch between subjective complaints and quite normal sleep EEG results is a common finding. The aim of this study was to evaluate the capability of heart rate variability (HRV), a correlate of autonomous nervous system activity, to objectify insomnia.

**Methods:** In a case-control study design 10 adult women (age: 49.6±7.5 years) suffering from primary insomnia according to DSM-IV criteria were compared to a control group (N = 10). Sleep was objectively assessed with polysomnography. HRV was assessed in artefact-free 5-min segments of pure sleep stages. Sleep EEG and HRV frequency domain measures were compared between patients and controls.

**Results:** Insomnia and normal sleep did not differ in regard to any of the common measures of sleep EEG except for a higher amount of N1-sleep in insomnia. HRV frequency power was blunted in early REM and adjacent N2 significantly. Furthermore, in early REM sleep there was a shift of relative HRV frequency power from high frequency to very low frequency.

**Conclusions:** Our results are in line with the hypothesis of hyperarousal in insomnia. Sleep stage related HRV analysis delivers more sensitive markers for insomnia than common sleep EEG variables.

**Presenting Author:** Mikoteit Thorsten

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**Sleep and Medical Disorders**  
**Poster No. 32**
Deep non-rapid eye movement (NREM) sleep predicts motor progression in Parkinson's disease

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Objectives: To investigate whether deep NREM sleep relates to motor progression of Parkinson’s disease (PD).

Methods: Consecutive patients with PD (n=131, 36% women, mean±SD age=62.6±10.6, mean±SD disease duration=5.2±4.5 years) with documented overnight polysomnography and clinical data at two time points ≥ 2 years apart were included in a retrospective study. Slow-wave energy (SWE), reflecting depth and duration of NREM sleep, was quantified with spectral power analysis. Progression of poorly levodopa-responsive motor symptoms from the Unified-Parkinson's-Disease-Rating-Scale part III was calculated, to estimate motor progression in patients receiving dopaminergic treatment (Evans et al., 2011). Within a general linear model framework controlling for relevant covariates, we investigated the relationship between SWE and PD progression and compared patients with high vs. low SWE, using the median of SWE as cut-off.

Results: Patients with high SWE showed slower progression compared to those with low SWE over the mean±SD observation time of 4.7±2.5 years (SWE x time interaction: F(1,128)=39.2; p<0.001, repeated-measures ANOVA). Higher SWE at baseline predicted the annual increase rate of motor progression (ß= -0.40, p<0.001).

Conclusions: Although preliminary in nature and limited by its retrospective design, this study provides novel evidence that deeper NREM sleep is associated with slower motor progression in patients with PD.

Presenting Author: Schreiner, Simon
Assessing human sleep dynamics in real-life and large numbers

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Objectives: The temporal dynamics that characterize sleep are difficult to capture outside the sleep laboratory. Therefore, longitudinal studies and big-data approaches assessing sleep dynamics are lacking.

Methods: Using longitudinal wrist movement recordings of >16,000 sleep bouts from 573 people, we developed an easy method to probe sleep structure and dynamics in humans based on non-linear conversion of locomotor activity to Locomotor Inactivity During Sleep (LIDS). After assessing the method in laboratory polysomnography (20 nights), we performed detailed analyses of human sleep dynamics in real life using mixed model regressions on the >16,000 sleep bouts with age, sex, sleep duration, work schedules and mental health status as covariates.

Results: The temporal structure of sleep is directly reflected in LIDS. LIDS oscillates in synchrony with sleep cycles and declines gradually during sleep in its levels, reminiscent of sleep homeostatic markers. Our current analyses indicate no sex differences in LIDS-derived sleep dynamics, whereas especially age but also shift work have pronounced effects, specifically on decline rates and amplitude. In contrast, ultradian period and phase emerged as remarkably stable across the tested variables.

Conclusions: Our approach and results provide the necessary quantitative sleep phenotypes for large field studies and outcome assessments in clinical trials.

Presenting Author: Winnebeck, Eva
Learning to Lucid Dream Enhances Aspects of Personal Growth

Karen Konkoly and Christopher Burke

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Objectives: Lucid dreaming is often used to promote aspects of personal growth such as enhanced creativity and problem solving. However, such benefits are evidenced by anecdotal reports and correlational studies rather than controlled experiments. Further, existing evidence is confounded by the fact that most lucid dreaming practices involve two techniques—dream journaling and a mindfulness exercise called reality checking—that may be independently associated with personal growth. We examined whether successfully inducing lucid dreams leads to personal growth benefits above and beyond those from a journaling and mindfulness practice.

Methods: Our 28-day longitudinal design compared participants in a lucid dreaming training condition to a control group that learned journaling and mindfulness practices but did not learn to lucid dream.

Results: By the end of the study, successful lucid dreamers had significantly higher self-esteem and life satisfaction than unsuccessful lucid dreamers, but we found no effect between groups. Participants also reported higher moods the day after lucid dreaming. Finally, those initially high on personal growth measures benefitted more from lucid dreaming.

Conclusions: As the first study to empirically investigate the benefits of lucid dreaming for personal growth, we found that lucid dreaming is helpful for some people but fewer overall benefits than anecdotally reported. Future studies should investigate how the effects of lucid dreaming may vary with more time.

Presenting Author: Konkoly, Karen