morning (6:00-7:00 am) after the PSG. CLOCK, BMAL1, CRY1 and PER1 protein concertation measurements were performed using ELISA.
Results: Increased level of following proteins was observed in OSA group: evening CLOCK (p=0.037), morning CLOCK (p=0.019), morning BMAL1 (p=0.0.16), evening PER1 (p=0.004), morning PER1 (p=0.029) and evening CRY1 (p=0.035). Yet, no significant difference was found between morning and evening level of any of the proteins in OSA and control group. Additionally, morning level of activator proteins CLOCK and BMAL1 had positive correlation with AHI (p=0.022, R=0.510 and p=0.010, R=0.560, respectively) and desaturation index (p=0.209, R=0.487 and p=0.009, R=0.570, respectively), while for repressor proteins PER1 and CRY1 significant correlations were found with desaturation index in the evening (p=0.025, R=0.500 and p=0.048, R=0.448, respectively), AHI in REM stage (p=0.009, R=0.569 and p=0.027, R=0.495, respectively) and AHI (for PER1 only p=0.014, R=0.540).
Conclusion: OSA patients have increased level of circadian clock proteins that corelates with severity of the disease. Further research is needed into the disruption of circadian clock should in OSA patients and possible effect of OSA treatment on concentrations of these proteins should be investigated.
Support: The study was financed by Polish National Centre Grant no. 2018/31/N/NZ5/03931.

0060

MORNING LOCUS COERULEUS ACTIVATION DURING THE PVT PREDICTS LATER-DAY SLEEPINESS

LEI, H.[1] QUAN, P.[1] LIU, W.[1] ZHANG, X.[1] CHAI, Y.[1] YANG, F.[1] DINGES, D.[2] RAO, H.[1,2]
[1]Center for Functional Neuroimaging, Department of Neurology, University of Pennsylvania, Philadelphia, PA, [2]Division of Sleep and Chronobiology, Department of Psychiatry, University of Pennsylvania, Philadelphia, PA.

Introduction: The locus coeruleus (LC) plays a key role in the regulation of arousal and autonomic function. Homeostatic sleep pressure refers to the drive for sleep that increases as a saturating exponential when we stay awake and decreases exponentially when we sleep. The current study used arterial spin labeling (ASL) functional magnetic resonance imaging (fMRI) to investigate the relationship between homeostatic sleep pressure (sleepiness) and LC activity during the psychomotor vigilance test (PVT).
Methods: We analyzed sleepiness and ASL imaging data from N=70 health adults (40 males, age range 21–50 years) who participated in a controlled in-laboratory sleep study. All participants were scanned at rest and during the PVT on the morning between 0700h-1000h after 9 hour time-in-bed (TIB) baseline sleep. LC regions-of-interest (ROI) were defined by standard templates from Keren et al. (2009). Sleepiness was assessed by the Karolinska Sleepiness Scale (KSS) every two hours from 10:30 am to 10:30 pm.
Results: Sleepiness scores gradually increased over wakefulness time and reached its peak in the evening at about 10:20pm. PVT-induced CBF changes did not correlate with sleepiness scores on the morning ($p > 0.05$), but showed significant negative correlations with sleepiness scores on later day when sleep pressure became higher, especially during the night-time ($r = -0.41$, $p < 0.001$). Specifically, LC CBF showed significant increases during the PVT scan as compared to the resting scan ($p = 0.04$) in individuals with less nigh-time sleepiness (KSS < 4), but no differences ($p > 0.1$) in individuals with greater nigh-time sleepiness (KSS ≥ 5). After controlling for age, gender, and total sleep time, PVT-induced regional CBF difference in the LC still negatively predicted sleepiness ($\beta = -0.325$, $p = 0.005$).
Conclusion: Our findings showed that individuals with greater LC CBF increases during the PVT were less sleepy during the night, supporting the key role of LC activity in promoting wakefulness and maintaining sleep homeostasis. PVT-induced LC activation may provide a non-invasive bio-marker of homeostatic sleep pressure in healthy adults.
Support: Supported in part by NIH grants R01-HL102119, R01-MH107571, R21-AG051981. CTRC UL1RR024134, and P30-NS045839.

0061

DOES COMBINING M1 M2 REFERENCE INFLUENCE AMPLITUDE OF SLOW WAVES?

Walker, N. A. Roth, H. L. Fan, Z. Vaughn, B. V.
UNC at Chapel Hill, Chapel Hill, NC.

Introduction: Slow wave amplitudes are critical to determining Stage N3 sleep yet ECG artifact frequently interferes with accurate amplitude measurement. This artifact may be lessened by using a combined M1-M2 reference however theoretically this may decrease the amplitude due to shorter inter-electrode distance (predicted 27% loss). The AASM Scoring Manual recommends scoring slow wave activity using F4-M1 channel or alternatively F3-M2, but does not recognize a combined reference. This study measures the differences in slow wave amplitude using contralateral versus combine reference.
Methods: 12 polysomnograms were randomly selected for analysis of amplitude of slow wave using contralateral and combined reference channels. Six separate EEG channels (F3-M1, F3-M2, F3-M1+M2, F4-M1, F4-M2, and F4-M1+M2) were used to analyze 25 different slow waves from each polysomnogram. Individual slow waves from Stage N3 sleep were analyzed using the Natus Sleepworks Amplitude Measurement Tool if their peak and trough were free EKG artifact. Averages and standard deviations of the waveforms were calculated for each patient and channel. Differences were normalized by dividing by the amplitude of the original wave using the contralateral reference.
Results: Subjects age ranged from 30–69 yrs, with 6 being females. Mean amplitudes were as follows: F3-M2 was 131.75μV, F3-M1+M2 125.84 μV, F4-M1 130.57 μV, and F4-M1+M2 128.22μV. The overall average difference of F4-M1 to F4-M1+M2 was 0.92% and the average difference of F3-M2 to F3-M1+M2 was 3.52% with the average standard deviation of 8.47%.
Conclusion: This study shows the average loss in amplitude of converting F4-M1 to F4-M1+M2 was less than 1% and 3.5% for F3-M2 to F3-M1+M2. Combining M1M2 reference may be a valuable alternative to reduce EKG artifact.
Support: None

0062

IMPROVED CIRCADIAN DATA ORDERING IN THE PRESENCE OF BIOLOGICAL AND TECHNICAL CONFOUNDS

Hammarlund, J.[1] Anafi, R.[2]
[1]Drexel University School of Biomedical Engineering and Health Systems, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA.

Introduction: We recently used unsupervised machine learning to order genome scale data along a circadian cycle. CYCLOPS (Anafi et al PNAS 2017) encodes high dimensional genomic data onto

an ellipse and offers the potential to identify circadian patterns in large data-sets. This approach requires many samples from a wide range of circadian phases. Individual data-sets often lack sufficient samples. Composite expression repositories vastly increase the available data. However, these agglomerated datasets also introduce technical (e.g. processing site) and biological (e.g. age or disease) confounders that may hamper circadian ordering.

Methods: Using the FLUX machine learning library we expanded the CYCLOPS network. We incorporated additional encoding and decoding layers that model the influence of labeled confounding variables. These layers feed into a fully connected autoencoder with a circular bottleneck, encoding the estimated phase of each sample. The expanded network simultaneously estimates the influence of confounding variables along with circadian phase.

We compared the performance of the original and expanded networks using both real and simulated expression data. In a first test, we used time-labeled data from a single-center describing human cortical samples obtained at autopsy. To generate a second, idealized processing center, we introduced gene specific biases in expression along with a bias in sample collection time. In a second test, we combined human lung biopsy data from two medical centers.

Results: The performance of the original CYCLOPS network degraded with the introduction of increasing, non-circadian confounds. The expanded network was able to more accurately assess circadian phase over a wider range of confounding influences.

Conclusion: The addition of labeled confounding variables into the network architecture improves circadian data ordering. The use of the expanded network should facilitate the application of CYCLOPS to multi-center data and expand the data available for circadian analysis.

Support: This work was supported by the National Cancer Institute (1R01CA227485-01)