0194

SOURCES OF VARIATION IN THE SPECTRAL SLOPE OF THE SLEEP EEG

Nataliia Kozhemiako[1], Dimitris Mylonas[2], Jen Pan[3], Michael Prerau[1], Susan Redline[4], Shaun Purcell[4]

Brigham and Women's hospital, Harvard medical school [1] Massachusetts General Hospital, Harvard Medical School [2] Stanley Center for Psychiatric Research, Broad Institute of MIT and Harvard [3] Brigham and Women's Hospital, Harvard Medical School [4]

Introduction: The 1/f spectral slope of the electroencephalogram (EEG) estimated in the gamma frequency range has been shown to reflect neural excitation/inhibition ratio and synchronization level within local neural populations. It was proposed as an arousal marker that differentiates wake, non-rapid eye movement (NREM) sleep, and rapid eye movement (REM) sleep. These stages exhibit progressively steeper 30-45 Hz slopes, interpreted in terms of increasing cortical inhibition. Here we sought to replicate these findings in a larger sample and provide a comprehensive characterization of how slope changes with age, sex, and its test-retest reliability as well as potential confounds that could affect the slope estimation.

Methods: After stringent exclusions and quality control, our final sample included 10,255 whole-night polysomnograms (PSGs) on 7,312 individuals 2,943 of whom had a second PSG, from the National Sleep Research Resource (NSRR). All preprocessing steps were performed using an open-source Luna package and the spectral slope was estimated by fitting log-log linear regression models on the absolute power from 30 to 45 Hz separately for wake, NREM and REM stages. We described sources of variation in the spectral slope (both within and between individuals) and its relationship to other sleep parameters including power and interhemispheric coherence.

Results: There was unambiguous statistical support for the hypothesis that, within individuals, the mean spectral slope grows steeper going from wake to NREM to REM sleep. We found that the choice of mastoid referencing scheme modulated the extent to which electromyogenic or electrocardiographic artifacts were likely to bias 30-45 Hz slope estimates, as well as other sources of technical, device-specific bias. Nonetheless, within individuals, slope estimates were relatively stable over time. Both cross-sectionally and longitudinal, slopes tended to become shallower with increasing age, particularly for REM sleep; males tended to show flatter slopes than females across all states. Although conceptually distinct, spectral slope did not predict sleep state substantially better than other summaries of the high-frequency EEG power spectrum (>20 Hz, in this context) including beta band power, however. In contrast to the common conception of the REM EEG as relatively wake-like (i.e. 'paradoxical' sleep), REM and wake were the most divergent states for multiple metrics, with NREM exhibiting intermediate profiles. Under a simplified modeling framework, changes in spectral slope could not, by themselves, fully account for the observed differences between states, if assuming a strict power-law model.

Conclusion: Although the spectral slope is appealing, theoretically inspired parameterization of the sleep EEG, we underscore some practical considerations that should be borne in mind when applying it in diverse datasets. Future work will be needed to fully characterize state-dependent changes in the aperiodic portions of the EEG power spectra, which appear to be consistent with, albeit not fully explained by, changes in the spectral slope.

Support (If Any):

0195

INTEGRATED ACTIGRAPHY-BASED BIOMARKER FOR THE RISK OF ALZHEIMER'S DEMENTIA

Hui-Wen Yang[1], Peng Li[1], Haoqi Sun[2], Matthew Maher[3], Jacqueline Lane[3], Andrew Lim[4], David Bennett[5], Lei Yu[5], Richa Saxena[3], Aron Buchman[5], Kun Hu[1]

Brigham and Women's Hospital [1] Harvard Medical School and Massachusetts General Hospital [2] Broad Institute [3] Sunnybrook Health Sciences Centre [4] Rush University [5]

Introduction: Many physiological measures derived from actigraphy including physical activity, sleep, circadian/daily rhythm, and temporal correlations have been shown to predict Alzheimer's dementia (AD). This study aimed to combine these actigraphy-based measures to develop an integrated actigraphy biomarker (IAB) for AD and to test its link to the genetic risk for AD.

Methods: We analyzed data of 1107 participants (age 80.9±7.3(mean±SD)) from the Rush Memory and Aging Project who were non-demented and had actigraphy (~10 days) at baseline, and had annual cognitive assessment during the follow-up (1-15 years). 270 developed AD (mean = 7.4 years). To construct the IAB for the AD's risk, we trained a random forest survival model, in which time to incident AD was the outcome, and inputs included 10 features derived from actigraphy data: physical activity level, 3 features for sleep (sleep duration, sleep fragmentation, activity fragmentation), 4 features for circadian rhythmicity (amplitude, acrophase, interdaily stability, and intradaily variability of 24-hr rhythms), and 2 features for temporal correlations (at timescales between 1-90 min and 120-480 min). Polygenic risk score (PRS) was calculated using 457 independent SNPs strongly associated with Alzheimer's disease ($p<0.001$). Cox proportional hazard ratio models were performed with different combinations of IAB, PRS, age, sex, and education, and the concordance score (C-score) was used to evaluate model performance.

Results: The derived IAB was 0.6 SD larger in the AD group as compared with the controls. The IAB alone achieved a C-score = 0.61 in predicting AD, with a hazard ratio=1.5 for 1-SD increase in IAB. The IAB and PRS were not correlated ($r2=0.0004$, $p=0.25$), and both significantly contributed to the prediction (both $p<=0.0001$) when included in one model, giving a C-score of 0.65. C-score was 0.7 in the model using only age, sex and educations yielded, and increased to 0.74 after including IAB and PRS (both effects remained significant $p<0.0001$).

Conclusion: The integrated actigraphy biomarker may provide complementary information for early prediction and detection of AD, independent of the known demographic and genetic risk factors.

Support (If Any): NIH (RF1AG064312, RF1AG059867, R01AG56352, R01AG17917, T32GM007592, and R03AG067985); The BrightFocus Foundation (A2020886S).

0196

RETINAL RESPONSIVITY IS ASSOCIATED WITH CIRCADIAN PHASE AND CIRCADIAN ALIGNMENT BUT NOT SLEEP TIMING

Delainey Wescott[1], Alison Klevens[1], Brant Hasler[1], Peter Franzenn[1], Kathryn Roecklein[1]

University of Pittsburgh [1]

Introduction: Light entrains the central circadian clock, with projections from the retina to the SCN through melanopsin-containing retinal ganglion cells (ipRGCs). Altered responsivity to light