SLEEP 2023

Late Breaking Abstracts

LBA 001
Chronobiotic Use of Melatonin Improves DaT-Binding in iRBD

Authors and Institutions: Dieter Kunz[1,2], Jan de Zeeuw[1,2], Sophia Stotz[1,2], Michail Plotkin[3], Frederik Bes[1,2]
[1]Institute of Physiology, Sleep Research & Clinical Chronobiology, Charité–Universitätsmedizin Berlin, Germany; [2]Clinic for Sleep- & Chronomedicine, St. Hedwig-Hospital, Berlin, Germany; [3]Institute of Nuclear Medicine, Vivantes Clinics Berlin, Berlin, Germany

Introduction: Isolated REM-sleep behavior disorder (iRBD) is recognized as a prodromal state of clinical α-synucleinopathies such as Lewy-body dementia and Parkinson's disease. A pathophysiologic hallmark of α-synucleinopathies is nigrostriatal dopaminergic impairment, with dopamine-transporter (DaT)-SPECT imaging considered the best available prognostic and monitoring marker. DaT binding is reported to decrease with healthy aging by 4-10% per decade, being accelerated to 4-12% per year in patients with iRBD. We have introduced melatonin as a treatment option for iRBD. The aim of the study was to evaluate effects of melatonin on DaT-SPECT imaging in patients with iRBD.

Methods: In a prospective, longitudinal, observational, single-center study until December 2022, we performed at least two DaT-SPECTs in 78 patients with iRBD being treated with melatonin as a chronobiotic (i.e. administration always-at-the-the-same-clock-time; 10-11p.m. - corrected for chronotype); 23 patients were excluded mainly due to change of psychotropic drugs known to influence DaT.

Results: After a mean follow-up of 3.3yrs, only 12 of 55 patients [7 female; mean age 70±7yrs] showed specific binding ratios (SBR) in most affected region (MAR, predominantly right posterior putamen) comparable to usually reported declines with iRBD. In contrast, 7 had declined SBR at a rate comparable to healthy aging, while 36 had actually improved SBR. Improvement after one year (SBR of MAR; $F_{1,25}=20.874; p>0.001$) and two years was significant ($F_{1,21}=10.083; p=0.005$). After four years more than half of the patients showed a higher SBR than at baseline (20 vs. 16 patients), though this was not significant. 31/55 of our patients at baseline met established criteria for an advanced state. Instead of expected 10-19 patients converting to clinical α-synucleinopathy (n=31, FU-mean 3.1yrs), only three patients in our cohort had converted by the end of the observation period.

Conclusion: To the best of our knowledge, the present data give first evidence for a consistent increase in DaT-binding ratios in nigrostriatum over time in a cohort of patients with iRBD. In addition, the low conversion rate reported here and a previously reported persisting effect of melatonin on RBD symptoms suggest that melatonin, when used as a chronobiotic, may have a disease-modifying effect in prodromal α-synucleinopathies.

LBA 002
Diurnal Variation in Suicidal Ideation and Behavior in Youth

Authors and Institutions: Anastacia Y. Kudinova [1,2], Leslie Brick[2], Jennifer Wolff [1,2], Sarah Ryan[1,2], Nicole Nugent[1,2], Michael Armey[2], Micaela Maron[1,2], and Mary A Carskadon[1,2,3].
[1]Emma Pendleton Bradley Hospital; [2]Department of Psychiatry and Human Behavior, Alpert Medical School of Brown University; [3]Sleep Research Laboratory

Introduction: Suicide risk may follow a diurnal pattern, increasing at night. Most studies focused on a single event in adults, leaving critical gaps in the short-term time-variant effects of time on youth suicide risk. Suicidal ideation (SI) is a significant predictor of suicidal behavior; thus, characterizing its diurnal patterns and potential modifiers is essential for informing early intervention. We aimed to 1) extend prior findings of greater frequency of suicide attempts in youth at nighttime in a sample of psychiatrically hospitalized adolescents and 2) examine the association between time of day and SI in youth recruited after a partial hospitalization program. We also explored whether self-referential processes, such as self-critical rumination (repetitive thinking focused on negative self-evaluation) and self-reassurance (providing compassion to self), moderated the link between time of day and SI.

Method: We asked psychiatrically hospitalized youth (n=165; 72% assigned F at birth; ages 11-18; mean 14.95; sd = 1.65 yr) about the time of day of their most recent suicide attempt. We used ecological momentary assessment (EMA) 3 times/day over 2 weeks in discharged partial hospital patients for the timing of SI assessed at home (n=61; 61% assigned F at birth; ages 12-15; mean 13.5; sd 2.26 yr).

Results: We found that the majority of psychiatrically hospitalized adolescents reported their most recent suicide attempt in the evenings and nights (57.6%), followed by daytime (35.2%) and mornings (7.3%). A series of generalized linear mixed models showed that youth in the second sample experienced significantly more frequent SI later in the day (B=0.41,SE =0.01,p<0.01). There was also a significant moderating effect of self-criticism (B=-0.08,SE =0.02,p<0.01), but not self-reassurance (p>0.05), such that more self-critical youth evidenced the highest levels of SI later in the day.

Conclusion: These preliminary findings highlight the clinical relevance of diurnal variation in SI and the importance of the availability of support during evenings and nights to reduce suicide risk in youth. The findings can also inform future research on targeting self-critical rumination to reduce SI via mobile, just-in-time interventions.

LBA 003
Intracranial Electrical Stimulation of Corticolimbic Sites Modulates Sleep-Wake Levels in Humans

Authors and Institutions: Joline M. Fan[1,2], Andrew M. Lee[2,3], Kristin K. Sellers[4], Cara Woodworth[3], Ghassan S. Makhoul[3], Tony X. Liu[3], Catherine Henderson[3], Daniella Astudillo[3], Ankit N. Khambhati[4], Vikram R. Rao[1,2], Leo P. Sugrue[5], Katherine W. Scangos[2,3], Edward F. Chang[4], Andrew D. Krystal[2,3]
[1]Department of Neurology, University of California, San Francisco, CA; [2]Weill Institute for

Neurosciences, University of California, San Francisco, CA; [3]Department of Psychiatry, University of California, San Francisco, CA ; [4]Department of Neurosurgery, University of California, San Francisco, CA ; [5]Department of Radiology, University of California, San Francisco, CA

Introduction: Humans routinely shift their sleep-wake levels in response to emotional factors. The coregulation of mood and arousal suggests that the ascending arousal network may be more distributed than previously appreciated and linked with networks that mediate mood. In this study, we tested the hypothesis that electrical stimulation of corticolimbic sites can differentially modulate sleep-wake levels.

Methods: We performed intensive stimulation-response mapping of sleep-wake levels in two individuals (participating in a clinical trial for treatment resistant depression, NCT04004169). Both individuals were implanted with sixteen-contact depth electrodes, targeting the bilateral amygdala, hippocampus, subgenual cingulate (SGC), orbital frontal cortex (OFC), and ventral capsule (VC). Sleep-wake behavior was quantified using two subjective survey scores (Stanford Sleepiness Score, SSS, and Visual analog scale of energy) and a bedside clinical score of arousal. Resting-state electrophysiology and behavioral scores were collected for biomarker assessment. Spectral power was computed for each region using wavelet analysis and segmented into canonical frequency bands. Pearson correlations were computed to compare SSS to spectral power bands of each region. Finally, pre- and post-stimulation changes in the identified biomarkers were quantified in response to wake and sleep-promoting stimulation.

Results: Across two patients undergoing intensive stimulation mapping, three sites differentially modulated arousal levels, which include the OFC, SGC, and, most robustly, VC. Low frequency (1 Hz) stimulation of the OFC led to increased sleepiness, while high frequency (100 Hz) stimulation of the SGC, OFC, and VC led to increased wakefulness. Spectral power in the gamma frequency band was associated with decreased sleepiness/increased wakefulness across a variety of regions. In contrast to 1Hz OFC stimulation, stimulation of the VC (100Hz) led to increased gamma frequency power across biomarker regions.

Conclusions: Our findings provide supporting mechanistic evidence for the overlapping circuitry between sleep-wake function and mood regulation in humans. These findings support the strong clinical and behavioral associations between arousal and mood. In addition, our findings may open the door to new treatment targets and the consideration of therapeutic neurostimulation for sleep-wake disorders.

LBA 004
Suppressed 24-h Rest-Activity Rhythms Linked to Higher Stroke Risk and Adverse Stroke Outcome

Authors and Institutions: Sarah N. Baker B.A.[1,2], Xi Zheng M.S.[2], Peng Li Ph.D[2,3,4], Frank A.J.L. Scheer[3,5], Lei Gao M.B.B.S.[1,2,3,4], Kun Hu Ph.D.[2,3,4]
[1]Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; [2]Medical Biodynamics Program, Division of Sleep and Circadian Disorders, Brigham and Women's Hospital, Boston, MA, USA; [3]Division of Sleep Medicine, Harvard Medical School, Boston, MA, USA; [4]Broad Institute of MIT and Harvard,

Cambridge, MA, USA; [5]Medical Chronobiology Program, Division of Sleep and Circadian Disorders, Brigham and Women's Hospital, Boston, MA, USA

Introduction: Almost all biological processes are controlled by circadian clocks and display ~24-hour rhythms. Interfering with this circadian regulation is linked to adverse health outcomes. We tested whether participants with disrupted/suppressed 24-h rest-activity rhythms (RAR) — actigraphy-based circadian disturbance measures — would have higher risk for stroke and whether stroke patients with RAR disturbances would have more adverse outcomes.

Methods: We studied ~100,000 participants in the UK Biobank (baseline age: ~44-79 years old; ~57% females) who underwent an actigraphy assessment (for up to 7 days) between 2013-2015 and were followed up for a median of 5 years. We analyzed actigraphic recordings and derived the following RAR measures: (1) activity counts of the most active 10 hours (M10) across the 24-h cycle; (2) activity counts of the least active 5 hours (L5); (3) relative amplitude (RA) = (M10-L5)/(M10+L5). Cox proportional hazard models were performed to determine the associations of these RAR measures with (i) stroke incidence during the follow-up in those with no history of stroke or transient ischemic attack at baseline (n=92,485); and (ii) adverse events (depression, disability, dementia, and death) in those stroke patients (n=1,652).

Results: Lower RA was associated with a higher risk for stroke ($p<0.0001$), i.e., as compared to those in the top quartile [Q4], the risk for stroke was 1.25 times higher in the third quartile [Q3] (HR: 1.25; 95% confidence interval [CI]: 1.04,1.51; $p=0.018$), 1.4 times higher in the second quartile [Q2] (HR: 1.40; 95% CI: 1.17-1.68; $p=0.0002$), and 1.6 times higher in the lowest quartile [Q1] (HR: 1.62; 95% CI: 1.36-1.93; $p < 0.0001$). Consistently, lower M10 ($p<0.0001$) and higher L5 ($p=0.011$) were also associated with a higher risk for stroke. In participants with stroke, lower RA and lower M10 were associated with a higher risk for depression, dementia, disability, or death) ($p=0.00032$, $p=0.02$). All the associations were independent of age, sex, race, obesity, sleep disorders, cardiovascular diseases or risks, and other morbidity burdens.

Conclusion: Suppressed 24-h rest-activity rhythm may be a risk factor for stroke and an indicator of worse outcomes after stroke.