Canadian Sleep Society | Société Canadienne du Sommeil

CANADIAN SLEEP SOCIETY

ABSTRACT BOOK

OCTOBER 28 TO 30, 2021 | 28 AU 30 OCTOBRE 2021

SOCIÉTÉ CANADIENNE DU SOMMEIL

LIVRE DES RÉSUMÉS

TABLE OF CONTENTS

SAMPLE ANNOTATION:

Luke R, Peever J, Fraigne, J. Alpha-synuclein pathology in the REM sleep circuit triggers REM sleep behaviour disorder in mice. *Vigilance* (S), 2021 October, p. 28.

ORAL SESSION 1: Neural Control of Sleep and Wakefulness

DATE: 10/29/2021

START TIME: 2:15 PM END TIME: 3:45 PM

SESSION TITLE:

Circuit control of theta oscillations during REM sleep

PRESENTING AUTHOR: *Taksokhan, Anita*[3]

CO-AUTHORS: *Fraigne, Jimmy*[1]*; Peever, John*[1, 2]

AFFILIATIONS: *1 Cell and Systems Biology, University of Toronto; 2 Physiology, University of Toronto; 3 University of Toronto*

DESCRIPTION:

Introduction: One of the many features of REM sleep includes theta oscillations, which is described as firing of neurons within a 4-8 Hz range frequency. Theta oscillations during REM sleep have significant implications in episodic and emotional memory formation, spatial navigation, and have been shown to be correlated with the level of learning impairments in patients with autistic spectrum disorder. Although the functional importance of theta oscillations is well described, the anatomical and synaptic bases by which theta oscillations are regulated during REM sleep remain unclear.

Theta oscillations recorded by EEG electrodes during REM sleep are regarded to originate from the pyramidal cells of the hippocampus. However, generation of theta oscillations requires a bidirectional connection between the medial septum nucleus (MS) and the hippocampus. Specifically, the GABAergic neurons of the MS target hippocampal interneurons and pace theta oscillations by periodic disinhibition of hippocampal pyramidal cells. In return, hippocampal interneurons provide rhythmic feedback to the MS to regulate theta oscillations. Moreover, it has been proposed that the septo-hippocampal pathway is triggered by excitatory inputs from the brainstem. Our lab has recently shown that a brainstem nucleus named the sublaterodorsal tegmental nucleus (SLD), plays a role in theta oscillation modulation. However, whether the SLD is able to regulate theta oscillations specifically during REM sleep, and which neurons are responsible for this regulation is yet to be determined. One SLD neuronal population that has not yet been investigated in this field is the glutamate neurons. These neurons are crucial in generating muscle atonia and REM sleep itself, hence it is highly likely that in addition to these roles, they also regulate theta oscillations during REM sleep.

Thus, the objectives of this study are to determine whether the glutamate SLD neurons are responsible for REM sleep theta generation, and whether they do so by sending projections to the GABA MS neurons.

Experimental approach: To examine the nature of connection between the SLD and MS (i.e. monosynaptic vs. indirect), we used viral tracing methods. Injection of an anterograde virus into the SLD and a retrograde virus into the MS resulted in co-staining of all intermediary regions. Next, a retrograde virus was injected into these nuclei to further confirm that these regions receive projections from the SLD. Finally, an anterograde tracer was injected into the intermediary nuclei to determine pathways by which they potentially regulate theta oscillations.

Results: We found that the glutamate SLD neurons do not send direct projections to the MS. However, these neurons send dense projections to the parabrachial nucleus (PB), a major hub for regulation of theta oscillations during wakefulness. These glutamate PB neurons then project to many theta-regulating nuclei, including the basal forebrain, thalamus, and the MS.

Conclusion: Our results indicate that although there is no direct connection between the SLD and MS, the glutamate PB neurons may act as a relay center to connect these two nuclei and regulate theta oscillations. Interestingly, the glutamate PB neurons send a wide range of projections to many theta-regulating centers, including the MS.

ORAL SESSION 1: Neural Control of Sleep and Wakefulness

DATE: 10/29/2021

START TIME: 2:15 PM END TIME: 3:45 PM

SESSION TITLE:

Implication of GABAergic synaptic adhesion molecules in the regulation of sleep and wakefulness

PRESENTING AUTHOR: *Leduc, Tanya*[1, 2]

CO-AUTHORS: *Mongrain, Valérie*[1,2]

AFFILIATIONS: *1 Département de neurosciences, Université de Montréal, QC; 2 Centre d'études avancées en médecine du sommeil, Recherche – Centre intégré universitaire de santé et services sociaux du Nord-de-l'Île-de-Montréal, QC*

DESCRIPTION:

Chronic sleep restriction has been linked to many health issues such as diabetes, obesity, mood disorders, cognitive impairment, and immune dysfunctions. Sleep thus appears as a crucial physiological process, yet its molecular regulation remains poorly understood. Synaptic adhesion molecules (SAMs) modulate sleep/wake parameters, possibly via their involvement in neurodevelopment, neurotransmission and neuroplasticity (1). GABAergic neurotransmission plays an important role in sleep/wake regulation, but also in the physiological response to sleep loss (2). Neuroligin-2 (NLGN2) and the immunoglobulin superfamily member 21 (IgSF21) are two GABAergic SAMs showing different patterns of expression in the brain. Our group has shown that the knockout (KO) of Nlgn2 in male mice decreases time spent asleep and consolidates wakefulness in baseline (BL) conditions (3). This project now aims to determine how NLGN2 and IgSF21 are implicated in sleep/wake regulation by verifying whether the manipulation of their expression in mice will impact vigilance state variables under both BL and sleep-deprived conditions.

The expression of Nlgn2 and Igsf21 will be manipulated using genetic KO and adeno-associated viruses. Viral-mediated overexpression, rescue, and downregulation are planned in the cerebral cortex using a neuron-specific promoter (i.e., human synapsin 1). Adult male and female mice will undergo surgical implantation of electrodes for electrocorticography (ECoG) and electromyography (EMG), and the ECoG/EMG signals will be recorded during 24 h of BL, 6 h of sleep deprivation (SD) starting at light onset, and 18 h of recovery (REC). SD will be achieved by gentle handling, and vigilance states (wakefulness, slow-wave sleep [SWS], paradoxical sleep [PS]) will be manually identified on 4-sec epochs. Analyses will include sleep/wake architecture, ECoG spectral activity, and SWS individual slow wave parameters.

Preliminary data shows that Nlgn2 KO males spend less time asleep and have more consolidated sleep/wake states after SD in comparison to wild-type (WT) littermates. Igsf21 KO and WT males have similar vigilance state duration/distribution in both BL and SD/REC conditions, but their ECoG spectral activity differs in BL. However, observations of epileptic seizures in the Igsf21 KO and WT cohort and possible developmental compensation in Nlgn2 KO mice emphasizes the need for the currently undergoing viral strategy to define the involvement of NLGN2 and IgSF21's in the control of vigilance states.

This study will bring a deeper insight concerning SAM-specific GABAergic sleep regulation, which might help alleviating the negative effects of poor sleep in the future. Given that trans-synaptic

ligands of NLGN2 and IgSF21 (e.g., neurexins) are frequently implicated in neurodevelopmental disorders, our research shows potential to help understanding sleep disturbances observed in patients suffering from these diseases.

FUNDINGS:
Canada Research Chair in Sleep Molecular Physiology, fellowship from the department of Neuroscience of the Université de Montréal, and fellowship from the J.A. DeSève organization.

REFERENCES:

1. O'Callaghan EK et al. Neurosci Res. 2017.
2. Jones BE. Neuropsychopharmacology. 2020.
3. Seok BS. Mol Brain. 2018.

ORAL SESSION 1: Neural Control of Sleep and Wakefulness

DATE: 10/29/2021

START TIME: 2:15 PM END TIME: 3:45 PM

SESSION TITLE:

Rhynchophylline, a derivative of traditional Chinese medicine, modifies sleep in male and female mice

PRESENTING AUTHOR: *Ballester Roig, Maria Neus*[1,2]

CO-AUTHORS: *Leduc, Tanya*[1,2]*;Dufort-Gervais, Julien*[1]*;Maghmoul, Yousra*[1, 3]*;Mongrain, Valérie*[1, 2]

AFFILIATIONS: *1 Center for Advanced Research in Sleep Medicine, Recherche CIUSSS-NIM, Montreal, QC; 2 Department of Neuroscience, Université de Montréal, Montreal, QC; 3 Department of pharmacology and physiology, Université de Montréal, Montreal, QC*

DESCRIPTION:

Some drugs of traditional Chinese and Japanese medicines containing Uncaria plants increase sleep duration and quality in humans. One of Uncaria principal components is the alkaloid rhynchophylline (RHY). Although treatment with RHY alone has not been tested in humans, rodent studies show that it may modulate synaptic components including ion channels, receptors and kinases that have been shown to be involved in sleep and wake regulation. Interestingly, RHY can inhibit the EphA4 receptor and our group showed that EphA4 knockout (KO) mice have less rapid eye movement (REM) sleep and modifications in electrocorticographic (ECoG) activity during non-REM (NREM) sleep. Here we aimed at determining the effects of RHY administered at two different times on sleep and molecular pathways linked to sleep regulation.

The ECoG was recorded during a full 24 h (12 h light:12 h dark) in adult male and female mice receiving intraperitoneal injections of RHY (50 or 100 mg/kg) or saline at light onset and 1 h before light offset. ECoG analyses include sleep architecture and spectral activity measurements. Brains were sampled the next morning at light onset to examine protein expression of known targets of RHY (e.g., EphA4, glutamate receptors, CDK5) in the cerebral cortex, thalamus/hypothalamus, hippocampus, and striatum. An additional group of mice was sacrificed 3 h after each RHY administration (i.e., at light onset or 1 h before light offset) to assess changes in the transcriptome with a high spatial resolution.

Preliminary results show that, in both males and females, RHY decreases the time spent in wakefulness during the dark phase, which is accompanied by an increase in NREM sleep. RHY also reduces REM sleep during the light phase, and increases the number but decreases the duration of individual bouts of NREM sleep and wakefulness (indicative of more fragmentation of wake/sleep episodes) in both sexes. In males, RHY enhances activity in slow frequencies during wake, and modifies the time course of NREM sleep delta and sigma activity. Spectral activity in females is currently being analyzed. RHY did not significantly affect the protein levels of EphA4 and other downstream effectors (e.g., glutamate receptors, CDK5, glial glutamate transporter 1) in the cerebral cortex or thalamus/hypothalamus. The effect of RHY on protein level and gene expression in other brain regions is under investigation.

This research reveals that RHY modifies sleep in a manner similar to the EphA4 KO phenotype. Nevertheless, some effects differing from KO mice (such as the increased fragmentation) may suggest EphA4-independent effects of RHY. These findings will provide further knowledge of the impact of RHY on brain functioning, and increase the understanding of molecular pathways contributing to sleep regulation.

FUNDING: NSERC discovery grant, VANIER fellowship, and Canada Research Chair in Sleep Molecular Physiology

ORAL SESSION 1: Neural Control of Sleep and Wakefulness

DATE: 10/29/2021

START TIME: 2:15 PM END TIME: 3:45 PM

SESSION TITLE:

Role of sublaterodorsal tegmental nucleus GABA neurons in sleep-wake control

PRESENTING AUTHOR: *Lee, Hanhee*[1]

CO-AUTHORS:

Fraigne, Jimmy[1]*; Peever, John*[1]

AFFILIATION: *1 University of Toronto*

DESCRIPTION:

INTRODUCTION: The sublaterodorsal tegmental nucleus (SLD) is a brain region located in the dorsal pons of the brainstem. It is well documented that the SLD plays an important role in controlling REM sleep. The SLD is composed of different subtypes of neurons including the glutamate and GABA-releasing neurons. We previously showed that glutamate SLD neurons play a central role in controlling both REM sleep and REM sleep atonia; however, the question regarding the functional role of GABA SLD neurons yet remains unclear. Here, we used in vivo optogenetic strategies to determine the functional role of GABA SLD neurons in sleep-wake control.

METHOD: We used optogenetics to manipulate the activity of GABA SLD neurons. Firstly, we drove the expression of light-gated ion channel called opsin (either inhibitory (eArch3.0) or excitatory (CheTA)) into the GABA SLD neurons using viral vector and cre-lox recombinase mechanism (n=10). Then, we bilaterally implanted optic fibers above the SLD to deliver light stimuli and implanted electrodes onto the cortex and muscles to record its activity (polysomnography) for sleep-wake identification. Moreover, we used genetically assisted track tracing to identify the axonal projections of GABA SLD neurons.

RESULTS: First, we demonstrated that optical inhibition of GABA SLD neurons during both REM and NREM sleep promotes transition into wakefulness ($p<0.001$) and prolonged inhibition of these neurons sustains wakefulness ($p<0.001$). Second, we demonstrated that optical activation of GABA SLD neurons decreases the time spent in wakefulness ($p<0.05$) while increasing the time spent in NREM sleep ($p<0.005$). Last, we demonstrated that these neurons send axonal projections to various brain nuclei including medial septum (MS), median raphe (MnR), dorsal raphe (DR), tuberomamillary nucleus (TMN) and vestibular nucleus (VN).

CONCLUSIONS: Our data suggests that the function of GABA SLD neurons is to suppress wakefulness. Although the primary function of GABA SLD neurons may be to suppress wakefulness, these neurons also seem to play a crucial role in sustaining REM sleep because inhibition of these neurons almost instantaneously terminated REM sleep. Overall, our previous and current studies suggest that the glutamate neurons in the SLD are involved in promoting REM sleep while the neighboring GABA neurons are involved in suppressing wakefulness. From this, we propose that a glutamate-GABA microcircuit contained within the SLD may function in a cohort to promote a stable and undisturbed state of REM sleep

ORAL SESSION 1: Neural Control of Sleep and Wakefulness

DATE: 10/29/2021

START TIME: 2:15 PM END TIME: 3:45 PM

SESSION TITLE:

Survival of the fittest: Long versus short sleep in Drosophila melanogaster in three separate environments

PRESENTING AUTHOR: *Harbison, Susan*[1]

CO-AUTHORS: *Singh, Akanksha*[1]*; Hansen, Nancy*[1]*; Serrano Negron, Yazmin* [1]

AFFILIATIONS: *1 National Heart Lung and Blood Institute*

DESCRIPTION:

High levels of variation in sleep duration are maintained both within and among species. Why this variation exists in a trait broadly conserved across species is not known. Our previous work, which used artificial selection to breed for very long and very short night sleep duration in flies suggested that short-sleeping flies have lower overall fitness. To test this hypothesis experimentally, we pitted an extremely long-sleeping inbred line of the Drosophila Sleep Inbred Panel (SIP), SIP_L1_9 (697.13 min per night), against an extremely short-sleeping inbred line, SIP_S2_8 (68.61 min per night). We combined the SIP genotypes in three different 'doses': 1) equal numbers of long and short sleepers; 2) 3 to 1 long sleepers to short sleepers; and 3) 1 to 3 long sleepers to short sleepers. We maintained flies of each dose for 30 generations in each of three different environments: 1) a standard laboratory environment, 2) a constant light environment, and 3) a low-nutrient food environment. Every 5th generation we measured sleep in each population and collected DNA. Across 30 generations, each of the three environmental treatments had profound effects on night sleep ($P < 0.0001$), and night sleep was also different across sleep dose ($P < 0.0001$), leading to a significant sleep dose-by-environment interaction ($P < 0.0001$). After 30 generations, flies in the constant light environment slept the least (202.2 min ± 14.9 SE), flies in the standard environment were in the middle (290.5 ± 6.9 SE), and flies in the low nutrient environment slept the most (443.6 ± 56.0 SE). Increases in night sleep over generation were observed under restrictive food conditions for all but the highest 'dose' of short sleepers. The implications of these findings as well as the underlying changes in the corresponding DNA polymorphisms over time will be presented and discussed.

ORAL SESSION 2: Insomnia: Updates on Treatments

DATE: 10/29/2021

START TIME: 4:00 PM END TIME: 5:30 PM

SESSION TITLE:

Effectiveness and Safety of the Dual Orexin Receptor Antagonist Lemborexant in Subjects Previously Treated with Placebo for 6 Months

PRESENTING AUTHOR: *Moline, Margaret [4]*

CO-AUTHORS: *Yardley, Jane [1]; Inoue, Yuichi [2]; Pinner, Kate[1]; Perdomo, Carlos[3]; Filippov, Gleb[3]; Kubota, Naoki [4]; Moline, Margaret [4]*

AFFILIATIONS: *1 Eisai Ltd., Hatfield, UK.; 2 Tokyo Medical University; 3 Eisai Inc., Woodcliff Lake, NJ; 4 Eisai Co., Ltd, Tokyo, Japan*

DESCRIPTION:

Introduction: Lemborexant (LEM) is a dual orexin receptor antagonist approved in the United States, Japan, and Canada for the treatment of adults with insomnia. In phase 3 study E2006-G000-303 (Study 303; SUNRISE-2; NCT02952820), LEM demonstrated significant benefit compared with placebo (PBO) on patient-reported sleep diary assessments of sleep onset and sleep maintenance over 6 months. However, some improvement on sleep outcomes was also observed in the subjects treated with PBO. Here, we report sleep outcomes from the PBO-treated subjects who were rerandomized to LEM for the last 6 months (Treatment Period 2) of Study 303.

Objectives: To assess the impact of LEM on sleep onset and sleep maintenance outcomes in Treatment Period 2 for subjects previously treated with PBO during the first 6 months (Treatment Period 1) of Study 303.

Methods: Study 303 was a randomized, double-blind, global phase 3 study in adults ages ≥18 years with insomnia disorder. During Treatment Period 1, subjects received nightly PBO or LEM (5mg [LEM5]; 10mg [LEM10]). During Treatment Period 2, PBO subjects were rerandomized to LEM5 or LEM10, while LEM subjects continued their originally assigned treatment. Changes from the 6-month baseline (calculated after PBO completion at the end of Treatment Period 1) in subjective sleep onset latency (sSOL), subjective sleep efficiency (sSE), and subjective wake after sleep onset (sWASO) are reported for PBO subjects rerandomized to LEM.

Results: At study baseline for PBO subjects (n=318), median sSOL (min) was 55.9, mean (SD) sSE (%) was 61.3 (17.8) and sWASO (min) was 132.5 (80.2). For rerandomized PBO-LEM5 (n=133) and PBO-LEM10 (n=125) subjects, the 6-month baseline values, respectively, were: median sSOL, 31.2, 34.3; mean (SD) sSE, 70.5 (20.2), 71.1 (18.0); and mean (SD) sWASO, 105.1 (80.6), 100.1 (84.6). Median sSOL further decreased (improved) from the 6-month baseline after 1 month (PBO-LEM5, −3.2; PBO-LEM10, −2.9) and 6 months (PBO-LEM5, −2.7; PBO-LEM10, −5.0) of treatment with LEM. Mean (SD) sSE further increased (improved) from the 6-month baseline after 1 month (PBO-LEM5, 3.9 [12.1]; PBO-LEM10, 3.5 [8.1]) and 6 months (PBO-LEM5, 3.9 [13.6]; PBO-LEM10, 4.5 [13.0]). Mean (SD) sWASO further decreased (improved) after 1 month (PBO-LEM5, −8.5 [49.4]; PBO-LEM10, −5.7 [36.1]) and 6 months (PBO-LEM5, −8.2 [49.0]; PBO-LEM10, −10.0 [58.8]) of LEM treatment. For these subjects, the incidence of treatment-emergent adverse events (TEAEs) during Treatment Period 1 was 62.7%, and remained consistent during Treatment Period 2 with LEM treatment (PBO-LEM5, 54.9%; PBO-LEM10, 57.7%). The TEAEs

reported during Treatment Period 2 for subjects rerandomized to LEM were consistent with those recorded during Treatment Period 1 for the subjects who were originally randomized to LEM.
Conclusion: Rerandomization to LEM was associated with additional and sustained improvement in sleep onset and sleep maintenance parameters following the response related to PBO treatment. LEM benefit was observed as assessed at 1 month following rerandomization, and persisted over 6 months. LEM was well tolerated.
Support: Eisai Inc.

ORAL SESSION 2: Insomnia: Updates on Treatments

DATE: 10/29/2021

START TIME: 4:00 PM END TIME: 5:30 PM

SESSION TITLE:

Safety and Efficacy of Lemborexant Over the Long-term in Subjects with Irregular Sleep-Wake Rhythm Disorder and Alzheimer's Disease Dementia

PRESENTING AUTHOR: *Moline, Margaret*[1]

CO-AUTHORS: *Bsharat, Mohammad*[1]*; Cheng, Jocelyn Y.*[1]

AFFILIATIONS: *1 Eisai Inc., Woodcliff Lake, NJ*

DESCRIPTION:

Introduction: Circadian rhythm sleep disorders, such as Irregular Sleep-Wake Rhythm Disorder (ISWRD), are common among individuals with Alzheimer's disease dementia (AD-D). Lemborexant (LEM), a dual orexin receptor antagonist, has been approved in the US, Japan, and Canada for the treatment of insomnia in adults, and is under investigation as a treatment for ISWRD. This Phase 2 proof-of-concept and dose-finding clinical study (E2006-G000-202 [Study 202]; NCT03001557) explored the impact of LEM treatment on ISWRD clinical measures in patients with mild-moderate AD-D. Over 1 month in the Core phase, LEM was found to improve circadian variables and help consolidate nighttime sleep. LEM was also well tolerated.

Objectives: To evaluate safety and efficacy outcomes over the Core and long-term open-label Extension Phases for those subjects who participated in the Extension Phase of this Phase 2 study.

Methods: Study 202 was a randomized, double-blind, multicenter, global, placebo-controlled parallel group study. Eligible subjects were 60-90y of age who met the DSM-5 criteria for ISWRD and also had mild-moderate AD-D. During the Core Phase, randomized subjects received treatment for 28 days with placebo or LEM (2.5mg, 5mg [LEM5], 10mg [LEM10], or 15mg [LEM15]). Subjects who entered the Extension Phase first received open-label LEM10, with the option of titrating the dose to LEM5 or LEM15. The Sleep Disorders Inventory (SDI), which assesses sleep-related disturbances, was completed by caregivers. SDI total score (SDI-ts) was defined as the product of the average of the frequency ratings and the average of the severity ratings (range: 0–12 [worst]).

Results: A total of 25 subjects entered the Extension Phase of Study 202. Over the Core and Extension Phases (1-14 months), treatment-emergent adverse events (TEAEs) were reported in 16/25 (64%) subjects. Serious TEAEs were reported in 3/25 (12%) subjects and no deaths occurred. Dose adjustment due to TEAEs occurred in 4/25 (16%) subjects. Nasopharyngitis (n=4; 16%), fall (n=3; 12%), and somnolence (n=3; 12%) were the most common TEAEs (incidence >10%). In subjects who received LEM10 as their modal dose (Core and Extension Phases [n=17]), baseline mean (SD) SDI-ts (n=12) was 0.72 (0.75) and mean (SD) change from baseline in SDI-ts was −0.14 (0.63) at Day 29 (n=12). During the Extension Phase, mean (SD) change from baseline in SDI-ts was −0.37 (0.50) at Day 133 (n=14) and −0.12 (0.81) at Day 223 (n=12).

Conclusions: In this study of subjects with AD-D and ISWRD, treatment with LEM10 demonstrated moderate improvement in SDI-ts, which continued to be seen over time. LEM was well tolerated over 1-14 months.

Support: Eisai Inc.

ORAL SESSION 2: Insomnia: Updates on Treatments

DATE: 10/29/2021

START TIME: 4:00 PM END TIME: 5:30 PM

SESSION TITLE:

Effects of cognitive-behavioral therapy for insomnia on sleep misperception in chronic primary insomnia

PRESENTING AUTHOR: *Perrault, Aurore A.*[1,2]

CO-AUTHORS: *Maltezos, Antonia*[1]*; Gong, Kirsten*[1]*; Hillcoat, Alexandra*[1]*; McCarthy, Margaret*[1,3]*; Smith, Dylan*[1]*; Pomares, Florence B.*[1,2,3]*; Gouin, Jean-Philippe*[2,3,4]*; Dang-Vu, Thien Thanh*[1,2,4]

AFFILIATIONS: *1 Sleep, Cognition and Neuroimaging Lab, Department of Health, Kinesiology and Applied Physiology & Center for Studies in Behavioral Neurobiology, Concordia University, Montreal, Quebec, Canada; 2 Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal, CIUSSS Centre-Sud-de-l'Ile-de-Montréal, Québec, Canada; 3 Stress, Interpersonal Relationship and Health Lab, Department of Psychology & Centre for Clinical Research in Health, Concordia University, Montreal, Quebec, Canada; 4 PERFORM Center, Concordia University, Montreal, Quebec, Canada*

DESCRIPTION:

Individuals with chronic insomnia frequently present with sleep state misperception (SSM), i.e. underestimate sleep duration (TST), overestimate latency to sleep onset (SOL) and time spent awake after sleep onset (WASO). This study aims at characterizing SSM change before and after a psychological intervention (cognitive-behavioral therapy for insomnia; CBTi) in adults with chronic insomnia.

Methods: 46 adults with chronic primary insomnia (52.15 ± 15.15 y.o.; 34 females) came to the lab to perform a baseline (T1) sleep assessment including polysomnographic (PSG) recording along with subjective sleep assessments and the Insomnia Severity Index (ISI). They were then randomized to either a 3-months CBTi program (CBT group - N=25) or a 3-months wait-list (WL group - N=21). They performed another sleep assessment after 3 months (T2) and those in the WL group came back again after completion of the CBTi (T3). Whole night PSG recording included 17 scalp-EEG, EOG, EMG and were sampled at 512 Hz (Somnomedics, Germany). Sleep stages were scored offline according to the AASM rules. Sleep misperception index (SMI: subjective TST/objective TST*100) as well as SSM scores (subjective minus objective measures in minutes) were calculated for TST, SOL, WASO. Mixed-models ANOVAs with age as covariate were used to assess Group*Time interaction on SSM measures at T1 and T2. ANCOVAs testing the effect of CBTi (N=44) were used on SSM measures before (T1) and after CBTi (pooled T2 for CBT group and T3 for WL group).

We used cluster analysis (K means algorithm) on the basis of SMI at baseline and created 3 subgroups of sleep duration estimators: normo-estimators (>92%, N=17), under-estimators (71-92%; N=16) and extreme under-estimators (<71%; N=11). Mixed-models ANOVAs were used to assess Subgroup*Time interaction on SSM measures after CBTi (N=44).

Results: We found an effect of Group ($F(1,87)=6.52$, $p=0.01$) and a trend Group*Time interaction ($F(1,87)=2.9$, $p=0.09$) on SSM TST due to a better perception of sleep duration after CBTi in the CBT group compared to the WL group at T2. Once pooled together, participants exhibited less misperception on SSM TST ($F(1,84)=6.94$, $p=0.009$) by 40min on average after CBTi compared to baseline. Similar results were found for SMI at T2 (interaction: $F(1,87)=3.7$, $p=0.06$)) and Post-CBTi ($F(1,84)=6.35$, $p=0.01$). While change in SMI did not correlate with change in ISI ($r=-0.11$,

p=0.5), we found that high misperception (low SMI) at baseline predicted change in SMI (F= 10.88; p=0.0019; r2=0.18).
Analyses on subgroups of sleep duration estimators revealed a Time*Subgroup interaction (F(2,81)=4.54, p=0.013) and main effects of Time (F(1,81)=10.21, p=0.0019) and Subgroup (F(2,81)=23.22, p<0.001) on SMI as only extreme under-estimators revealed less misperception after CBTi (p<0.001). Similar results were found for SSM TST.
We found no change in perception of sleep onset latency or wake duration at T2 or Post-CBTi (all p>0.05).
Conclusion: These findings, using PSG and subjective sleep assessments, show the beneficial effects of CBTi on sleep misperception in chronic insomnia. Those who exhibited the largest mismatch between their objective sleep duration and subjective sleep duration at baseline revealed a better perception of sleep duration after CBTi.

ORAL SESSION 2: Insomnia: Updates on Treatments

DATE: 10/29/2021

START TIME: 4:00 PM END TIME: 5:30 PM

SESSION TITLE:

Video-Conference Delivery Of Cognitive Behavioural Therapy For Insomnia During the COVID-19 Pandemic: Comparison of Pre-Pandemic and Pandemic Cohorts

PRESENTING AUTHOR: *Stenstrom, Philippe*[1]

CO-AUTHORS: *La Rocque, Cherie*[1] *; Araújo, Taís*[1]*; Denesle, Régine*[1]

AFFILIATIONS: *1 HALEO Clinic*

DESCRIPTION:

Introduction: Research has shown increased sleep difficulties in the general Canadian population during the COVID-19 outbreak. It is unknown whether these increased sleep difficulties are evident among insomnia sufferers specifically, and whether cognitive behavioural therapy for insomnia (CBT-I) is as effective relative to pre-pandemic times. To address these questions, we compared the effectiveness of CBT-I on insomnia symptom severity in a pre-pandemic versus pandemic cohort. Methods Participants were recruited from a single Canadian employer and took part in the HALEO Telehealth CBT-I Program. The pre-pandemic group (n = 130) completed therapy between April 2019 and January 2020, and the pandemic group (n = 168) completed therapy between April 2020 and January 2021. The groups were similar on age (pre-pandemic: M = 44.84, SD = 9.79; pandemic: M = 41.41, SD = 11.78) and sex (% female: pre-pandemic = 73.3; pandemic = 70.1). The CBT-I program consisted of five weekly 30-min video-conference-enabled sessions with a registered therapist, supported by a digital platform. Insomnia symptom severity was assessed with the Insomnia Severity Index (ISI). We also examined cohort differences in self-reported use of medication and alcohol as sleep aids at baseline. Results The pre-pandemic and pandemic cohorts did not differ significantly on baseline ISI scores (M = 16.52, SD = 4.57 vs. M = 16.94, SD = 3.87; t(296) = 0.85, p = .40). A mixed-model ANOVA showed a significant cohort by time interaction, $F(1, 254) = 6.04$, $p = .015$, $\eta p^2 = .023$, and main effect of time, $F(1, 254) = 748.88$, $p < .001$, $\eta p^2 = .747$, such that participants experienced a significant reduction in ISI scores from pre- to post-therapy. A follow-up analysis showed that the reduction was significantly greater in the pandemic (M = -9.45, SD = 4.41) versus pre-pandemic cohort (M = -7.89, SD = 5.55; t(254)= -2.46, p = .023, Cohen's d = 0.32). The cohorts did not differ in terms of baseline medication use (pre-pandemic = 48.4% vs. pandemic = 58.9%; $\chi 2[1, N = 296] = 3.22$, $p = .073$) but a significantly greater proportion of those in the pandemic group (64.3%) reported using alcohol as a sleep aid compared to the pre-pandemic group (10.3%; $\chi 2$ [1, N = 294] = 86.59, p > .001). Conclusion The results suggest that, at baseline, the pre-pandemic and pandemic cohorts did not differ in terms of insomnia symptom severity but those in the pandemic group reported being more likely to use alcohol as a sleep aid. Interestingly, although both groups experienced significant reductions in ISI scores from pre- to post-therapy, the pandemic group experienced a greater treatment effect. These results suggest that the deployment of CBT-I via a video-conferencing digital platform is a viable solution to insomnia treatment during a global pandemic.

ORAL SESSION 3: Sleep Across the Lifespan

DATE: 10/29/2021

START TIME: 4:00 PM END TIME: 5:30 PM

SESSION TITLE:

NREM sleep fast delta activity is a more sensitive marker of age-related changes in homeostatic sleep pressure than slow delta in mice

PRESENTING AUTHOR: *Dubé, Jonathan[3]*

CO-AUTHORS: *Lahmimsi, Hamza[1]; Timofeev, Igor [2]; Lina, Jean Marc[3]; Carrier, Julie[4]; Bukhtiyarova, Olga[2]; Soltani, Sara[2]; Mongrain, Valérie[5]*

AFFILIATIONS: *1 McGill University; 2 CERVO Brain Research Center - Laval University; 3 Centre d'études avancées en médecine du sommeil - Hôpital du Sacré-Coeur de Montréal; 4 Département de psychologie, Université de Montréal; 5 Departement de neurosciences, Université de Montréal*

DESCRIPTION:

Introduction: NREM sleep delta activity (0.5- 4 Hz) is a marker of sleep homeostasis. In mice, NREM sleep delta activity usually decays during the light period (LP) and builds-up during the dark period (DP). This dynamic is more prominent in brain regions most active during wake (e.g., the frontal cortex). A recent study reported that compared to slow delta (Δ1: 0.5-1.75 Hz), fast delta (Δ2: 2-4 Hz) show a stronger rebound after sleep loss and a steeper decay across NREM sleep in frontal brain areas (Hubbard et al., 2020). The impact of age on the dynamic and topography of Δ1 and Δ2 is unknown. We investigated age-related changes in the dynamics and topography of Δ1 and Δ2 during NREM in 5 cortical areas and in the hippocampus of young and older mice across 24 h using local field potential (LFP).

Methods: LFP electrodes were implanted in frontal, motor, primary/secondary somatosensory and visual cortex and in the CA1 hippocampal layer (10 young and 10 old, mean age = 6.5 and 14.5 months), and signals were recorded for 24 h (12 h light and 12 h dark). States of vigilance (i.e., wake, NREM sleep, REM sleep) were semi-automatically detected and spectral analysis was performed during NREM sleep. Each epoch was visually screened for artifacts and assigned to intervals containing an equal number of epochs across the light/dark cycle (12 intervals during LP, 6 in DP). Δ1 and Δ2 power were normalized relative to the last interval of the light period. Mixed models were computed separately for light and dark periods and each sub-band.

Results : During the LP, Δ1 decayed on all electrodes and power curves were similar between young and old mice. However, mean Δ1 power (across LP intervals) was lower in the primary somatosensory cortex in old compared to young mice. In the DP, Δ1 did not vary across intervals in young mice, but old mice showed significant minima in the second and last intervals. There was no age-related difference in mean Δ1 power in the DP. During LP, Δ2 decay curves on all electrodes were smoother in older as compared to young mice. Mean Δ2 power (across LP intervals) was lower in the primary somatosensory cortex in old as compared to young mice. During DP, Δ2 power showed significant and similar buildup between young and old mice. As compared to young mice, older mice showed lower mean Δ2 power in frontal and primary somatosensory cortices but higher mean Δ2 power in the visual cortex. Conclusion: Δ1 topography and dynamics shows fewer age-related differences than Δ2 across a 24 h period. While there are no age-related changes in mean Δ1 power during the DP, old mice show lower Δ2 power in anterior and higher Δ2 power in posterior areas. Old mice also show a lower Δ2 decay in the LP, while there are no age-related differences in Δ1 decay. Overall, our data suggest that Δ2 is a better marker of age-related changes in sleep homeostasis in mice.

ORAL SESSION 3: Sleep Across the Lifespan

DATE: 10/29/2021

START TIME: 4:00 PM END TIME: 5:30 PM

SESSION TITLE:

The lost benefit of sleep for memory trace consolidation: Impact of age

PRESENTING AUTHOR: *Toor, Balmeet[1]*

CO-AUTHORS: *Van Den Berg, Nicholas[1]; Pozzobon, A.[1] ; Stewart, M[1] ; Ray, L.B.[1] ; Fang, Zhuo [1] ; Toor, H[1] ; Fogel, S.M.[1,2,3]*

AFFILIATIONS: *1 School of Psychology, University of Ottawa, Ottawa, Canada; 2 Sleep Unit, The Royal's Institute of Mental Health Research, University of Ottawa, Ottawa, Canada; 3 University of Ottawa Brain and Mind Institute, University of Ottawa, Ottawa, Canada*

DESCRIPTION:

Introduction:

Sleep is known to enhance the realization of novel solutions to problems1. As we age, both the quantity and quality of sleep are reduced[2]. Evidence suggests that problem solving skills are compromised as we age, impacting cognitive function and quality of life[4]. This reduced capacity for problem solving skills may be due to age-related changes in sleep[5,6,7]. However, the role of sleep in the realization of the solution to a novel problem, the changes in brain activity that accompany this process, and how these sleep-memory relationships evolve with age remain to be investigated. Despite intact learning, older adults seem to benefit less from retention intervals that contain sleep as compared to young adults, suggesting age-related deficits in latent/offline learning processes8. Here, we sought to investigate the functional consequences of age-related changes in sleep for acquiring novel cognitive strategies to solve problems. Groups of young and older adults were scanned using fMRI while practicing a classic cognitively complex procedural task (e.g., the Tower of Hanoi; ToH) that requires the acquisition of a novel cognitive strategy (e.g., recursive logic) in order to improve performance. ToH training and re-testing took place on two separate sessions, before and after a retention interval filled with either sleep or wake. We hypothesized that: (1) older adults will derive a reduced benefit of sleep for problem-solving skills relative to young adults, and, (2) following a period of sleep, older adults that slept will have a reduced change in BOLD activation as compared to young adults that slept, in brain regions known to support problem solving skills9 such as the dorsolateral prefrontal cortex, hippocampus and caudate.

Methods:

40 healthy young adults (20-25 years), and 30 healthy older adults (60-85 years) participated, and were assigned to either the nap [young-nap (YN), older-nap (ON)] or wake [young-no-nap (YNN), older-no-nap (ONN)] conditions. Participants were trained on the ToH in the AM, followed by either a 90-minute nap opportunity or a period of wake, and were retested afterward. Functional MRI scans were obtained at 3T to examine differences ($pFDR<0.05$) in brain activation from training to retest in young vs. older groups as a function of sleep [(YN-YNN)-(ON-ONN)].

Results:

Consistent with previous work conducted in our lab9, sleep significantly benefitted the young but not the older participants (speed and accuracy) on the ToH. A bilateral difference in activation of the hippocampus was observed from training to retest between young and older

subjects. Specifically, YN displayed decreased activation, whereas YNN showed increased activation. The older groups showed the opposite pattern whereby ON displayed increased activation whereas ONN showed decreased activation. The same pattern was observed for the middle temporal gyrus and medial prefrontal cortex. By contrast, the opposite pattern among the groups was observed in the premotor area, inferior and superior parietal cortex.

Conclusions:

These results suggest that sleep differentially contributes to the realization of a novel cognitive strategy in young vs. older individuals, consistent with the notion that as the consolidation of a newly formed memory trace progresses, the hippocampus becomes less involved over time; especially so when sleep occurs during that time, however, the nature of the memory trace transformation is dependent on age. Our results suggest that sleep preferentially contributes to this process in the young, but not in older individuals.

ORAL SESSION 3: Sleep Across the Lifespan

DATE: 10/29/2021

START TIME: 4:00 PM END TIME: 5:30 PM

SESSION TITLE:

Feasibility testing of the ABCs of SLEEPING for Babies mobile application as an intervention to improve sleep in infants aged 6 to 12 months

PRESENTING AUTHOR: *Keys, Elizabeth*[1]

CO-AUTHORS: *Corkum, Penny*[2]*; Keating, Sarah*[2]*; Weiss, Shelly*[3]

AFFILIATIONS: *1 University of British Columbia; 2 Dalhousie University; 3 The Hospital for Sick Children/University of Toronto*

DESCRIPTION:

Introduction: Nearly 80% of families experience difficulties with their infant's sleep behaviours at some point during the first year of life. A mHealth intervention (i.e., using mobile or wireless technologies for health services and interventions) could provide parents access to consistent, credible, evidence-based information that they could use to improve infant sleep behaviors. We recently developed an adaptation of the ABCs of SLEEPING app for parents of children aged 6 to 12 months who are experiencing sleep difficulties.

Objective: To evaluate the feasibility, usability (acceptability and implementation), and preliminary effectiveness of the ABC's of SLEEPING for Babies mobile app in parents of 6 to 12-month-old infants who are experiencing sleep difficulties.

Methods: In this single-group pre-post study, Canadian parents of typically developing infants aged 6 to 12 months who were experiencing sleep difficulties were recruited via social media and email networks. Parents completed a week of actigraphy and sleep diary to measure infant sleep, as well as an online study questionnaire, at baseline and outcome. The study questionnaire included the (1) Brief Infant Sleep Questionnaire-Revised, (2) the Maternal Cognitions about Infant Sleep Questionnaire, (3) the Patient-Reported Outcomes Measurement Information System (PROMIS) Sleep Disturbance Short Form and the (4) PROMIS Sleep-Related Impairment Short Form. During the 4-week intervention period parents had unlimited access to the app and completed a weekly implementation questionnaire. Acceptability data was collected with the outcome study questionnaire. Descriptive statistics will be used to describe the feasibility (i.e., recruitment and retention), acceptability (i.e., satisfaction, suitability ratings) and implementation (i.e., parental report of use of the Sleep Tips) of the intervention. Paired t-tests will be used to compare pre- and post-intervention values for subjectively and objectively measured infant sleep behaviours. Qualitative data collected from open-ended items will be analyzed using content analysis.

Results: Over a 1-month recruitment period, 356 potential participants "clicked-in" to the online eligibility survey. Of these potential participants, 37 provided informed consent and were enrolled. As of February 24, 2021, 31 participants completed the baseline questionnaire and 5 participants had withdrawn. Based on preliminary baseline descriptive statistics, most participants were White (90.3%), mothers (93.5%), on parental leave (71.0%), with a university-level education (66.8%), and living with a partner (93.5%). Just over half the infants (M = 9.9 months; SD = 1.98) were female (54.8%) and nearly 60% were the youngest child in the home. Parent-reported night wakings per night at baseline ranged from 0 to 5 (M = 3.12; SD = 1.45),

60% of parents reported their infant's sleep was a moderate/severe problem, and 42.5% of parents were somewhat or very unsure about how to manage their infant's sleep. Outcome data collection will be completed on April 15, 2021.
Conclusion: To our knowledge, this is the first Canadian mHealth evidence-informed mobile app intervention designed to help parents improve their infant's sleep. Finding from this study will be used to refine the ABCs of SLEEPING for Babies app and inform a future randomized controlled trial.

ORAL SESSION 3: Sleep Across the Lifespan

DATE: 10/29/2021
START TIME: 4:00 PM END TIME: 5:30 PM
SESSION TITLE:

Long-term Efficacy and Safety of Lemborexant Versus Placebo For the Treatment of Insomnia in Elderly Adults

PRESENTING AUTHOR: *Moline, Margaret*[1]
CO-AUTHORS: *Inoue, Yuichi*[2]*; Pinner, Kate*[3]*; Perdomo, Carlos*[1]*; Filippov, Gleb*[1]*; Kubota, Naoki*[4]*; Yardley, Jane*[3]
AFFILIATIONS: *1 Eisai Ltd., Hatfield, UK.; 2 Tokyo Medical University; 3 Eisai Inc., Woodcliff Lake, NJ; 4 Eisai Co., Ltd, Tokyo, Japan*
DESCRIPTION:
Introduction: Lemborexant (LEM) is a dual orexin receptor antagonist that is approved for the treatment of insomnia in adults in the United States, Japan, and Canada. Compared with placebo (PBO), treatment with LEM provided significant benefit on subjective sleep parameters over 6 months in the overall population of Study E2006-G000-303 (Study 303; SUNRISE-2; NCT02952820). Additionally, these benefits continued up to 12 months.
Objective: To examine efficacy and safety outcomes for LEM vs PBO in the subgroup of elderly (≥65y) subjects over 12 months.
Methods: Study 303 was a 12-month, randomized, double-blind, PBO-controlled (first 6 months [Treatment Period 1]), global phase 3 study that enrolled adults age ≥18y. During Treatment Period 1, subjects received treatment with PBO or LEM (5mg, [LEM5]; 10mg, [LEM10]). During Treatment Period 2 (the second 6 months), PBO subjects were rerandomized to treatment with LEM5 or LEM10 (data reported separately), and LEM subjects remained on their original dose. Sleep diary data were used to assess patient-reported (subjective) sleep onset latency (sSOL), sleep efficiency (sSE), and wake after sleep onset (sWASO). Mixed-effect model repeated measurement analysis was used to evaluate changes from baseline for LEM vs PBO at 6 months.
Results: The Full Analysis Set included 949 subjects; 262 were in the ≥65y subgroup (PBO, n=89; LEM5, n=87; LEM10, n=86). In elderly (≥65y) subjects, significantly greater reductions from baseline in median sSOL (min) were observed vs PBO (−10.8) for LEM5 (−21.7; P<0.0001) and LEM10 (−26.0; P<0.01) at 6 months; reductions persisted at 12 months for LEM5 (−29.3) and LEM10 (−34.3). Significantly greater increases from baseline in mean (SD) sSE (%) were observed for LEM5 (16.9 [13.6]; P<0.001) and LEM10 (14.9 [15.9]; P<0.01) vs PBO (8.5 [13.3]) at 6 months; increases persisted at 12 months for LEM5 (18.1 [12.5]) and LEM10 (18.0 [16.8]). Significantly

greater mean (SD) reductions from baseline in sWASO (min) were observed vs PBO (−26.5 [52.9]) for LEM5 (−54.8 [64.4]; P<0.01) and LEM10 (−51.4 [69.3]; P<0.05) at 6 months; reductions persisted at 12 months for LEM5 (−58.6 [46.0]) and LEM10 (−60.9 [80.4]). In the LEM5 and LEM10 groups, the most frequent treatment emergent adverse events (>5% in either group) were somnolence (8.1%, 19.0%) and headache (9.3%, 1.2%), respectively, during Treatment Period 1, and headache (1.4%, 6.3%) and urinary tract infection (1.4%, 6.3%), respectively, during Treatment Period 2.
Conclusion: In this subgroup of subjects age ≥65y, LEM demonstrated significant benefit on subjective sleep parameters at 6 months compared with PBO. These benefits persisted for an additional 6 months. LEM was also well tolerated.
Support: Eisai Inc.

POSTER SESSION 1

DATE: 10/29/2021
START TIME: 6:45 PM END TIME: 8:00 PM

PS1: F100
ABSTRACT TITLE:

A Systematic Literature Review of Insomnia Treatments and On-The-Road Driving Performance

PRESENTING AUTHOR: *Tahami, Amir*[2]
CO-AUTHORS: *McElroy, Heather*[1], *O'Leary, Beth*[1]; *Adena, Michael*[1]; *Campbell, Renee*[2]; *Meier, Genevieve*[2]
AFFILIATIONS: *1Datalytics, Kingston ACT, Australia; 2Eisai Inc., Woodcliff Lake, NJ 07677, USA*
DESCRIPTION:
Background: Insomnia, which involves difficulty falling asleep, staying asleep or premature awakening, is a common sleep problem. People with insomnia may experience increased fatigue and decreased quality of life. Next-day driving performance may be impaired by some insomnia treatments. The dual orexin receptor antagonist (DORA) lemborexant is approved for the treatment of insomnia in adults.
Objectives: To compare the effects of lemborexant and other insomnia treatments on next-day driving performance via a systematic literature review (SLR).
Methods: Searches in Medline and Embase were performed through May 2019. Clinical trial registries were also searched. We included randomized controlled trials (RCTs) that fulfilled the following criteria: measured performance on a standardized on-road driving test, enrolled healthy volunteers or people with insomnia, published in English, and had ≥1 group randomized to a recommended dose of the following 16 treatments: benzodiazepines (flunitrazepam, estazolam, triazolam, temazepam, brotizolam, etizolam, alprazolam, lorazepam), z-drugs (zolpidem, eszopiclone, zaleplon, zopiclone), trazodone, ramelteon or DORAs (lemborexant, suvorexant). The National Institute for Health and Care Excellence (NICE) checklist for RCTs was used to assess trial quality. The difference between each active treatment and placebo in standard deviation of lateral position (SDLP) was evaluated by pairwise random-effects meta-analyses. Interpretation of clinical significance was based on the established benchmark equating a difference in SDLP versus placebo of +2.4 cm with a 0.05% blood alcohol concentration.
Results: Fourteen studies involving eight treatments, with dates of publication ranging from 1984 to 2019, were included in this SLR. Clinically significant differences in SDLP vs placebo were shown for zopiclone (10/10 studies) and ramelteon (1/1 study) in healthy volunteers, and for flunitrazepam in people with insomnia (2/3 studies). Early driving test termination was reported most often for zopiclone (5/10 studies). No statistically or clinically significant difference from placebo in SDLP was found for lemborexant 5 mg or 10 mg, and no early terminations of the driving test were reported (1/1 study).
Conclusion: The z-drug zopiclone, ramelteon, and the benzodiazepine flunitrazepam were associated with impaired driving performance, comparable to driving under the influence of alcohol. Early termination of the driving test was reported most often for zopiclone. No significant effect on driving performance and no premature test terminations were found with lemborexant 5 mg or 10 mg.
Support: Eisai Inc.

PS1: F101

ABSTRACT TITLE:

A test of predictions of the emotional regulation theories of dream function

PRESENTING AUTHOR: *Turpin, C*[1]

CO-AUTHORS: *Barbeau, K.* [1] *; Ben Massaoud, H*[1]*; Lafrenière, A.* [1]*; Campbell, E.* [1]*; De Koninck, J.* [1]

AFFILIATIONS: *1 School of Psychology, University of Ottawa*

DESCRIPTION:

Introduction: A prevailing modern theory of dream function is one of mood regulation. It would be achieved through desensitization to negative events replayed within dreams. It has been supported by the observation that dreamers tend to evaluate emotions felt in their dreams more positively than independent judges from dream narratives (i.e., positivity bias).The present study aimed to examine the relationship between evening, dream, and morning mood and the potential desensitization function of dreams and its effects on morning mood.

Methodology: Male and Female participants (N = 175) between the age of 12-24 years old (Mean age = 19.23, SD = 2.87) recorded at least two dreams (dreams N = 350) over a period of ten days and self-reported their mood at bedtime, during their dream retrospectively, and upon waking. An independent judge trained in dream content scoring also evaluated the subjects' dream mood. The dream emotions were derived from Hall and van de Castle using a 1 to 4 scale. Additional emotions were assessed at bedtime and upon waking in the morning. Subjects' positivity bias of their dreams was defined as the difference between the subjects and an independent judge's evaluation of positive emotions in the dream.

Results: As expected, on average, subjects evaluated their dream emotions as more positive than negative. Interestingly, the distribution was bimodal with many having more negative (n = 171; 49%) or positive dreams (n = 164; 47%), and a few reporting neutral dreams (n = 15; 4%). A t-test revealed that subjects were more likely to perceive their dreams as more positive than an independent judge (p = < .001) but not less negatively (p = .88). Results of a structural equation model (SEM) demonstrated that bedtime mood was the strongest predictor of morning mood, with positive bedtime mood leading to positive morning mood and negative bedtime mood leading to negative morning mood. Subjects' perception of dream mood, but not judge's evaluation of dream mood, was positively associated with morning mood. Subjects' perceived positive dream mood was positively associated with positive morning mood, while perceived negative dream mood was positively associated with negative morning mood. Only in the case of negative mood was the relationship between bedtime mood and morning mood mediated by dream mood. Results of the second SEM where subjects were divided into two groups based on the valence of their dream (i.e., positive or negative) demonstrated that bedtime mood was still the strongest predictor of morning mood; however, the second strongest predictor of morning mood, specifically positive morning mood, was subjects' positivity bias. This positivity bias explained why positive dreams can lead to positive morning mood above and beyond the objective positivity of the dream. The relationship between dream positivity bias and positive morning mood was strongest in those who had negative dreams.

Conclusion: These results support the notion of a desensitization function of dreams and its potential for mood regulation. However, the results are correlational in nature. Experimental manipulation of dream mood would be required to test this theory.

PS1: F102

ABSTRACT TITLE:

Acute Cognitive Effects of the Dual Orexin Receptor Antagonist Lemborexant Compared with Suvorexant and Zolpidem in Recreational Sedative Users

PRESENTING AUTHOR: *Moline, Margaret*[1]

CO-AUTHORS: *Landry, Ishani*[1] *; Hall, Nancy* [1]*; Aluri, Jagadeesh*[1]*; Filippov, Gleb*[1]*; Reyderman, Larisa*[1]*; Setnik, Beatrice*[2]*; Moline, Margaret*[1]

AFFILIATIONS: *1Eisai Inc., Woodcliff Lake, NJ; 2Altasciences, Laval, Quebec, Canada*

DESCRIPTION:

Introduction: The acute cognitive effects of lemborexant (LEM; dual orexin receptor antagonist approved to treat insomnia in the US, Canada and Japan), were assessed while examining the abuse potential of LEM.

Objectives: To examine changes in cognitive performance following LEM compared with zolpidem (ZOL), suvorexant (SUV), and placebo (PBO).

Methods: Healthy adult (aged 18-55y), nondependent, recreational sedative users were enrolled in a single-center, single-dose, randomized, double-blind, 6-way crossover study, Study 103 (E2006-A001-103; NCT03158025), to assess the abuse potential of LEM. Cognitive performance was evaluated for LEM (10mg [LEM10]; 20mg [LEM20]; 30mg [LEM30]) versus PBO, ZOL 30mg and SUV 40mg. Choice Reaction Time (CRT) and the Divided Attention Test (DAT) were evaluated pre-dose and at pre-specified time points post-drug. CRT includes: recognition reaction time (RRT), motor reaction time (MRT), and total response time (TRT). Higher scores indicate greater impairment for all assessments. DAT is a visual/manual tracking test that includes percentage of target hits (lower scores indicate greater impairment) and number of false alarms (higher scores indicate greater impairment).

Results: Thirty-two subjects completed all treatments. Mean maximum change from baseline (CFBmax) in RRT was significantly greater vs PBO (82.4ms) for all LEM doses (LEM10, 164.8ms; LEM20, 172.8ms; LEM30, 181.8ms; all P<0.001), and for ZOL (164.2ms; P<0.001) and SUV (143.6; P=0004); no LEM dose was significantly different versus ZOL or SUV. Mean CFBmax in MRT versus PBO (44.3ms) was significantly greater for all LEM doses (LEM10, 86.6ms; LEM20, 102.9ms; LEM30, 97.9ms; all P<0.001), and for ZOL (227.4ms; P<0.001) and SUV (83.0ms; P<0.001). All LEM doses had significantly lower mean CFBmax (smaller increase in MRT) versus ZOL (all P<0.001), but not versus SUV. For TRT, mean CFBmax was significantly greater versus PBO (99.3ms) for all LEM doses (LEM10, 229.5ms; LEM20, 246.7ms; LEM30, 258.7ms; all P<0.001), and for ZOL (359.4ms; P<0.001) and SUV (197.7ms; P<0.001). Mean CFBmax in TRT for LEM30 was significantly greater versus SUV (P=0.025). All LEM doses had significant lower mean CFBmax in TRT versus ZOL (all P<0.001).

For DAT target hits, the mean minimum CFB (CFBmin) vs PBO (−17.8%) was significantly lower for all LEM doses (LEM10, −43.3%; LEM20, −43.8%; LEM30, −45.6%; all P<0.001), and for ZOL (−62.1%; P<0.001) and SUV (−36.7%; P<0.001). All LEM doses had significantly greater CFBmin versus ZOL (all P<0.001). Compared with SUV, LEM20 and LEM30 had significantly greater decreases in percentage of target hits (P=0.028 and P=0.003, respectively). Mean CFBmax in number of DAT false alarms was lowest with LEM (LEM10, 5.8; LEM20, 4.5; LEM30, 7.4),

followed by SUV (7.5), PBO (9.2), and ZOL (10.5); all LEM doses were significantly different versus ZOL (P=0.002, P=0.001, P=0.025, respectively) but not SUV.
Conclusion: Results of the CRT suggest that for all doses of LEM, reaction time was less delayed versus ZOL but generally similar to SUV. Divided attention capabilities were found to be significantly better with all LEM doses versus ZOL. Findings from this study suggest that ZOL has a greater negative impact on cognitive performance versus LEM and SUV in this subject population.
Support: Eisai Inc.

PS1: F103

ABSTRACT TITLE:

Alpha-synuclein pathology in the REM sleep circuit triggers REM sleep behaviour disorder in mice

PRESENTING AUTHOR: *Luke, Russell*[1]

CO-AUTHORS: *Peever, John*[1]*; Fraigne, Jimmy*[1]

AFFILIATIONS: *1 University of Toronto*

DESCRIPTION:

Introduction: REM sleep behaviour disorder (RBD) is a neurological condition marked by a loss of REM sleep muscle atonia, which releases aggressive motor behaviours during REM sleep. However, the most concerning aspect of RBD is that 80-90% of patients eventually develop a synucleinopathic neurodegenerative disease such as Parkinson's disease, Lewy body dementia or multiple system atrophy. The tight association between RBD and the synucleinopathies suggests that RBD itself could result from alpha-synuclein mediated degeneration of the neural circuits that normally control REM sleep atonia. This idea is well substantiated by basic science and clinical evidence, yet it remains unknown whether RBD and synucleinopathies are caused by the same degenerative mechanisms. Here, we test the hypothesis that degeneration in the REM sleep atonia circuit causes RBD in mice.

Methods: We used an adeno-associated virus vector-based approach to drive the overexpression of human alpha-synuclein in the ventromedial medulla (vmM) of wild-type mice, which is in the core brainstem circuit that generates REM sleep atonia. From 12-24 weeks later, we assessed if these interventions 1) induced degenerative processes in these cells; and 2) if they affected motor activity during REM sleep. Sleep-wake behaviours and motor activity were assessed by EEG and EMG recordings as well as real-time video monitoring.

Results: First, immunohistochemical analysis revealed that the viral delivery of alpha-synuclein caused the accumulation of pathologic aggregates of phosphorylated alpha-synuclein within vmM cells. This pathological aggregation of alpha-synuclein was associated with astro- and microgliosis in the vmM (Unpaired t-tests, $n = 8$, $p<0.05$). Second, we found that alpha-synuclein pathology induced apoptosis in vmM neurons (Unpaired t-test, $n=5$, $p<0.01$) and led to cellular loss in the vmM (Unpaired t-test; $n=4$, $p<0.05$). Third, we found that alpha-synuclein pathology in vmM cells was associated with an increase in muscle activity during REM sleep (One-way ANOVA; $n=8$; $p<0.01$). This was characterized by exaggerated muscle twitching (One-way ANOVA; $n=8$, $p<0.05$) as well as higher muscle tone during REM sleep (One-way ANOVA; $n=8$; $p<0.05$). Third, we found that vmM pathology had no effect on overall amounts of sleep or wakefulness (Unpaired t-tests; $n=8$; $p>0.05$).

Conclusions: Our findings demonstrate that alpha-synuclein pathology in the REM sleep atonia circuit induces an RBD phenotype in otherwise healthy mice, which suggests that RBD in humans could also result from a synucleinopathic mechanism.

PS1: F104

ABSTRACT TITLE:

Attitudes toward sleep, sleep quality, and academic performance in undergraduate students

PRESENTING AUTHORS: *Hood, Suzanne[1]; Cooper, Megan[1]*

CO-AUTHORS: *Gooding, G.[1]; Roy, M.[1]; Muthiah, G.[1]; Paradis, P.O.[1]*

AFFILIATIONS: *1 Bishop's University*

DESCRIPTION:

Objective: Quality, duration, and regularity of nightly sleep are associated with academic performance in undergraduate students (e.g., Phillips et al, 2017). Recent evidence suggests that sleep quality and quantity in this population may be predicted in part by individual attitudes towards sleep (that is, the degree to which one enjoys and prioritizes sleep) (Windred et al, 2021; Peach et al, 2018). A deeper understanding of the associations between sleep attitudes, the experience of sleep, and academic performance could inform interventions targeting health and performance outcomes in students. In the present study, we examined whether attitudes towards sleep predicted sleep quality and, separately, academic performance in undergraduate students. Importantly, we collected these data mid-way through the academic term when students may be experiencing a heavy workload.

Methods: 45 full-time undergraduates (mean age 21.4 years ± 3.6; 89% female) completed a questionnaire at a single time point. Questions assessed attitudes and beliefs towards sleep using the Charlotte Attitudes Towards Sleep (CATS) scale, comprising two subscales: the Benefits/Enjoyment subscale measuring attitudes toward sleep as a beneficial or enjoyable activity, and the Time Commitment subscale measuring attitudes toward sleep as a time commitment. Additional scales included the Morningness-Eveningness Questionnaire Self-Assessment Version (MEQ-SA); the Perceived Stress Scale (PSS); and the Pittsburgh Sleep Quality Index (PSQI). Academic performance was assessed with one question pertaining to self-evaluated overall academic performance with five possible answers ranging from 'Well Below Average' to 'Excellent (well above average)'.

Results: A multiple linear regression model indicated that sleep attitude, reflected by the total score from the CATS scale, did not predict global PSQI score (b = –0.77, 95% CI (–1.85, 0.10)), whereas perceived stress score did (b = 0.23, 95% CI (0.10, 0.36); t = 3.57; p = <0.001). In a separate linear model, total CATS score significantly predicted self-reported academic performance, but negatively so (b = –0.50, 95% CI (–0.78, –0.21), t = 3.49, p < 0.001). Greater morningness score on the MEQ-SA significantly and positively predicted academic performance (b = 0.46, 95% CI (0.12, 0.80), t = 2.71, p = 0.01), whereas global PSQI score was not a significant predictor (b = –0.02, 95% CI (–0.11, 0.06)).

Conclusions: In contrast to recent literature, sleep attitudes assessed using the CATS scale did not significantly predict sleep quality in our sample. With respect to academic performance, we found that a more 'positive' attitude toward sleep (as being enjoyable and requiring prioritization in one's schedule) was associated with poorer self-reported academic performance. Eveningness preference was also associated with poorer academic performance, whereas overall sleep quality was not. Taken together, our findings are inconsistent with the view that sleep attitudes and sleep quality are linked and suggest that more negative sleep attitudes are in fact associated with better academic standing. Given the time of year when our data were collected, our results could reflect that, for some students, increased academic pressure undermines healthy attitudes and beliefs toward sleep as a means of supporting high-quality performance.

PS1: F106

ABSTRACT TITLE:

Can evening light exposure promote circadian adaptation to night shifts? A systematic review

PRESENTING AUTHOR: *Artenie, Despina Z.*[1]

CO-AUTHORS: *Cyr, Marième*[2]*; Albikaii, Alain*[3]*; Olson, Jay A.*[4]

AFFILIATIONS: *1 Department of Psychology, University of Quebec in Montreal; 2 Faculty of Medicine and Health Sciences, McGill University; 3 McGill University Health Centre; 4 Department of Psychology, Harvard University*

DESCRIPTION:

Introduction. Working night shifts is associated with higher risks of workplace errors and health issues. A potential moderator of these outcomes is the circadian misalignment caused by the desynchrony between work times and the sleep-wake cycle. Bright light interventions have been shown to reduce circadian misalignment as well as improve fatigue, sleep, and work performance. However, such interventions generally have low feasibility since they often take place at night, the optimal time for light exposure to improve alignment. Such light exposure during the night shift requires institutional buy-in and can interfere with work. Furthermore, light at night has been linked to adverse health effects such as obesity and cancer. The use of evening light exposure may therefore be a more feasible and safer alternative to help workers adapt to their night shifts.

Objective. Our goal was to conduct a systematic review of the effects of evening bright light exposure on adaptation to night shifts. We aimed to determine whether light exposure during the evening can improve workers' circadian alignment to night shifts as measured by biological, psychological, and behavioural measures.

Methods. We searched five databases (i.e., Medline, PsychINFO, Embase, Web of Science, and the Cochrane Library). The search terms were designed to identify experimental studies conducted on human participants which assessed the impact of light exposure in shift workers (or travelers) on circadian-related outcomes during shift work (or when crossing multiple time zones). We identified 993 unique articles and included in our review those that featured a light exposure intervention between 16:00 and 23:00 during real or simulated shift work in healthy populations.

Results. Only 4 articles featured evening light exposure that stopped before midnight, with a total of 53 participants. Three studies were comprised of simulated night shifts in healthy populations, and one looked at shift working nurses in hospital settings. Results are largely consistent with evening bright light exposure facilitating adaptation to night shifts. Studies reported both physiological (dim light melatonin onset, urinary melatonin, core body temperature), psychological (fatigue, mood, alertness, sleep quality), and behavioural indicators of circadian delays (sleep duration, work related errors).

Conclusion. Although the small number of studies prevents us from drawing strong conclusions, these results support the potential of evening light exposure as a promising circadian intervention for night shift workers. Given that this timing of exposure may be more feasible and safe than light at night, more research is warranted on the circadian effects of evening light.

PS1: F108

ABSTRACT TITLE:

Cognitive status combined with relative spectral power at baseline improves the prediction of conversion in idiopathic REM sleep behaviour disorder

PRESENTING AUTHOR: *Hernandez, Jimmy*[1]

CO-AUTHORS:

Gagnon, J.F.[1]*, Lina, Jean Marc* [1]*, Postuma, Ronald B.*[1]*, Carrier, Julie*[1]

AFFILIATIONS: [1] *Université de Montréal*

DESCRIPTION:

Introduction: Idiopathic rapid-eye movement (REM) sleep behaviour disorder (iRBD) is a parasomnia characterized by a loss of muscle atonia in REM sleep. iRBD is recognized as a prodromal stage of a-synucleinopathies (a-syn), including Parkinson's disease and Lewy body dementia, with a conversion rate as high as 81% after 14 years (Postuma et al., 2019). Several biomarkers have been proposed to identify iRBD patients with a higher risk of conversion. Hence, higher spectral power in theta bands (4.0-8.0 Hz) during waking electroencephalogram (EEG) at the baseline allows to discriminate iRBD patients who converted toward a-syn on average 3.5 years later from patients who were still a-syn-free (Rodrigues-Brazète, 2016). Other studies have indicated that the presence of a mild cognitive impairment (MCI) at the time of an iRBD diagnosis enhances the risk of conversion to a-syn (Génier Marchand et al., 2017; Postuma et al. , 2019). Although some studies have shown associations between spectral power and cognitive status in iRBD in relation with a-syn conversion, most of them had relatively small samples and were cross-sectional (Iranzo et al., 2010; Sasai et al., 2013).

Objective: Here, we aim to determine if the combination of wake EEG spectral power and cognitive status at the baseline is more sensitive than only a spectral power marker to predict conversion toward a-syn in iRBD patients. We hypothesize that the combination of these two markers will enhance the sensitivity to detect iRBD individuals who will convert to a-syn.

Methods: A baseline wake EEG recoding was performed in 83 iRBD patients a-syn-free. Of these patients, 49 (38M; mean age 64.77 ± 6.65; 15 with MCI) were still a-syn-free after a mean follow-up of 5.6 ± 2.9 years whereas 34 (24M; mean age 68.24 ± 7.77; 14 with MCI) converted to a a-syn (17 PD, 14 DLB and 3 MSA) after a mean follow-up of 3.56 ± 2.22 years. A comprehensive neuropsychological assessment following recording was conducted to diagnose MCI. A mixed-design ANOVA was used for each cortical region to identify which spectral bands of the baseline EEG better discriminated the patients who converted from those still a-syn-free [i.e. relative temporal theta ($p = .006$) and relative occipital theta ($p = .002$), both higher in the converted group]. A logistic regression with conversion as dependent variable and two distinct models (1: temporal theta*occipital theta; 2: temporal theta*occipital theta*cognitive status) was performed to compare the sensitivity of the prediction models 1 and 2.

Results: Although the model containing only spectral power in temporal theta and occipital theta was significantly reliable to predict conversion ($\chi2(1) = 7.806$, $p < .01$), the addition of cognitive status to spectral power data significantly improved the model predicting conversion from iRBD towards an a-syn ($\chi2(1) = 5.075$, $p < .05$; odds ratio = 4.55 (95% CI [1.14-18.15])).

Conclusion: The combination of a higher relative temporal and occipital theta spectral power with MCI at the baseline improves the prediction of conversion in iRBD patients towards an a-syn compared to spectral power biomarkers alone.

PS1: F109

ABSTRACT TITLE:

Difficulty Initiating or Maintaining Sleep and Insomnia in PAP Adherent and Non-adherent Individuals with OSA: A Prevalence Study

PRESENTING AUTHOR: *Fichten, Catherine[1,2]*

CO-AUTHORS: *Rizzo, Dorrie[1] ; Libman, E.[1] ; Creti, Laura[1]; Bailes, Sally[1]*

AFFILIATIONS: *1 Jewish General Hospital, McGill University; 2 Dawson College*

DESCRIPTION:

Objectives

Our study addresses the following questions: (1) Are there gender differences in adherence and non-adherence to PAP (positive airway pressure) treatment in OSA (obstructive sleep apnea)? (2) How does self-reported PAP adherence compare with objective PAP machine chip data? (3) What is the frequency of Difficulty Initiating or Maintaining Sleep (DIMS) and Insomnia Disorder (as opposed to the typically reported insomnia severity) in individuals with OSA? (4) Is adherence and non-adherence to PAP treatment associated with insomnia-related disorder?

Method

Participants were 80 older primary care patient volunteers (47 females, 33 males) diagnosed with OSA who were recommended PAP therapy.

Adherence for both self-report and PAP chip was defined as using the PAP device at least 4 hours, 70% of nights, for 90 days. Twenty-four participants (30%) were adherent by self-report and 56 (70%) were non-adherent. PAP chip data were available for 21 participants.

Prior to nocturnal polysomnography, participants completed a sleep questionnaire to assess DIMS and Insomnia Disorder.

Sleep onset latency (SOL) DIMS was defined as more than 30 minutes of undesired wakefulness at least 3 times a week for a minimum of 3 months. Sleep maintenance difficulty (WASO) DIMS was defined as more than 30 minutes of undesired middle of the night wakefulness. Terminal DIMS was defined as wakefulness and inability to return to sleep at least 31 minutes earlier than desired wake time at least 3 times a week. Insomnia Disorder was diagnosed by meeting the criteria for DIMS and a complaint of insomnia.

Results

Chi Square analysis did not reveal significant differences between female and male participants for treatment adherence, $X2(1,80) = .89$, $p=.346$. Pearson correlations show that self-reported and PAP chip based number of nocturnal PAP hours were significantly correlated, $r(21) = .724$, $p<.001$, and a 2x2 Chi Square test (self-reported adherent, nonadherent) x PAP chip-adherent, non-adherent) was not significant $X2(1, 21) = 3.18$, $p = .075$.

Percentage of SOL DIMS was similar for adherent and non-adherent participants. However, WASO and Terminal DIMS were higher among non-adherent than adherent participants.

Adherence	DIMS - SOL	DIMS - WASO	DIMS - Terminal	Insomnia Disorder
Adherent	25%	20%	25%	17%
Non-adherent	21%	37%	40%	24%

In addition, 48% of adherent and 50% of non-adherent participants had similar rates of “mixed insomnia” scores (i.e., DIMS with no insomnia complaint, insomnia complaint with no DIMS).

Conclusions

The literature typically shows more severe insomnia in individuals who are PAP adherent than those who are non-adherent. Contrary to such results, here we found no substantial difference in Insomnia diagnosis between the two groups, and we found that WASO and Terminal DIMS were more frequent in the non-adherent group. This may be due to a discrepancy between severity and frequency scores.

Male and female participants were not different in their adherence to PAP therapy, suggesting that adherence data from males and females may be combined.

Our findings also indicate that self-reported hours of PAP machine use were highly correlated with objective chip data. This suggests that self-reported PAP use is a reliable measure.

PS1: F110

ABSTRACT TITLE:

Effects of amyloïde-bêta on sleep architecture and electroencephalographic activity

PRESENTING AUTHOR: *Hector, Audrey*[1,2]

CO-AUTHORS: *Provost C*[1]*; Mongrain V*[1,3]*; Brouillette J*[1,2]

AFFILIATIONS: *1 Axe Neurophysiologie Recherche CIUSSS-NIM, Hôpital du Sacré Cœur, Montréal; 2 Département de pharmacologie et physiologie, Faculté de Médecine, Université de Montréal; 3 Département de Neurosciences, Faculté de Médecine, Université de Montréal*

DESCRIPTION:

Synapse loss and ensuing neuronal death are the best predictors of memory deficits in Alzheimer's disease (AD). Hippocampus-dependent memory for recent facts and events (explicit memory) is the first type of memory that is affected in the disease because of the neurodegenerative process that takes place in the hippocampus of early AD patients. There is mounting evidence from recent studies that soluble low-molecular-weight amyloid-beta oligomers (Aβo), especially oligomers derived from Aβ1-42 peptides, are the most neurotoxic species and correlate extensively with memory deficits in AD patients and animal models1. It is also well-established that sleep loss impairs the function of the hippocampus, and that sleep alterations are among the first clinical symptoms observed in AD2. Moreover, the effect of Aßo on sleep are poorly understood.

The main objective of this project is to determine the impact of soluble Aβo-induced neurodegeneration on sleep architecture and electroencephalographic (EEG) activity in rats. We also aim at identifying molecular mechanisms underlying Aβo-driven hippocampal neurodegeneration.

Chronic hippocampal injections of soluble Aβ1-42 oligomers were performed in rats3,4, and combined to EEG measurements to assess alterations in sleep variables. Wake/sleep states were visually identified on 4-s epochs of EEG traces, and spectral analysis was conducted using fast Fourier transform. The effects of Aβo on specific signaling pathways (Il1ß, TNF-alpha, NMDA, ...) were analyzed by Western blot and immunofluorescence.

Six days of Aβo injections in the hippocampus did not significantly changed time spent in wakefulness, non-rapid eye movement (NREM) sleep or rapid eye movement (REM) sleep. However, preliminary results suggest that EEG activity in theta (4-8 Hz) and beta (12,5-30 Hz) frequencies is increased in NREM sleep after six days of Aβo injection. Sleep architecture and EEG spectral analyses will be investigated across the six days of injection to determine how the progression of Aβ pathology affects sleep, and whether it associates with the progressive increase of hippocampal neuroinflammation.

Identifying the specific signature of hippocampal neurodegeneration on sleep features could serve as a non-invasive marker of early AD. A better understanding of the molecular mechanisms underpinning the effects of neurodegeneration and sleep disturbances on cognitive decline in AD will help developing novel effective treatments at the onset of the disease.

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Funding: CIHR grant, Canada Research Chair in Sleep Molecular Physiology

Bourse JA DeSève, Centre de recherche du CIUSSS-NIM, Montréal

PS1: F111

ABSTRACT TITLE:

Effects of cognitive behavioral therapy for insomnia on sleep quality and cognitive function during benzodiazepine withdrawal among older adults

PRESENTING AUTHOR: *Barbaux, Loïc[1,2]*

CO-AUTHORS: *Cross, Nathan E.[1,2]; Perrault, Aurore A.[1,2]; Zhao, Jean-Louis[1,2,3]; Adoutoro, Jeannick[1, 2]; Desrosiers, Caroline[2]; Essouni, Mehdi[2]; Guimond, Anik[2]; Doris Clerc[2]; Andriamampionona, Francis[2]; Tannenbaum, Cara[2]; Gouin, Jean-Philippe[4]; Dang-Vu, Thien Thanh[1, 2, 3]*

AFFILIATIONS: *1 Sleep, Cognition and Neuroimaging Lab, Department of Health, Kinesiology and Applied Physiology, PERFORM Center & Center for Studies in Behavioural Neurobiology, Concordia University, Montreal, Quebec, Canada; 2 Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal, CIUSSS Centre-Sud-de-l'Ile-de-Montréal, Québec, Canada; 3 Département de Neurosciences, Université de Montréal, Montréal, Québec, Canada; 4 Department of Psychology, Concordia University, Montréal, Québec, Canada*

DESCRIPTION:

Introduction: Chronic insomnia affects up to 20% of older adults. Benzodiazepines and benzodiazepine receptor agonists are commonly prescribed hypnotics for insomnia, especially in Canada. However, their long-term use is associated with negative cognitive side effects. Therefore, withdrawal is encouraged in older individuals, although insomnia symptoms may re-emerge. Cognitive behavioral therapy for insomnia (CBT-I) is the recommended first-line treatment for chronic insomnia. The aim of this study is to investigate the effect of CBT-I on both sleep quality and cognitive function during benzodiazepine withdrawal in older individuals with chronic insomnia.
Methods: 41 participants (69 ± 6.6 y.o; 31 females) with chronic insomnia and chronic use of benzodiazepines or benzodiazepine receptor agonists (9.62 ± 14.06 yrs) completed polysomnography for assessment of total sleep time (TST), wake after sleep onset (WASO), sleep onset latency (SOL), and sleep efficiency (SE). They also completed two weeks of sleep diaries (self-reported TST, WASO, SOL, SE) and a neuropsychological assessment for general cognitive function (Mini Mental State Examination, MMSE), executive function (Stroop Colour-Word interference Test, SCWT), verbal memory (Free and Cued Selective Reminding Test, FCSRT) and visuospatial abilities (Modified Taylor Complex Figure, MTCF). Participants were randomized into 2 groups: CBT-I and Waitlist (WL). The CBT-I group (N= 23, 71.70 ± 6.98 y.o; 17 females) was assigned a 16-week withdrawal program during which 8 CBT-I sessions were administered by a licensed psychologist. The WL group (N=18, 66.4 ± 5.48 y.o; 14 females) was assigned a similar weaning program without CBT-I, and served as a control group. Sleep and cognitive assessments were repeated after the withdrawal program in both groups. The effect of CBT-I on sleep quality and cognitive function within and between groups was tested using a mixed effects model, controlling for age and medication dose.
Results: 60,9% of CBT-I participants achieved complete withdrawal compared to 61,1% of WL. There was no significant main effects of group or time on any of the polysomnographic and cognitive variables (All variables: p>0,05). However, there was a significant interaction between group and time for self-reported WASO (F=5.38; p=0.01) and SE (F=3.3; p=0.049), with CBT-I improving more over time than WL (WASO: - 7.5±19 min in CBT-I, + 13.8±19.3 min in WL, t=3.14, p=0.004; SE: + 5.7±8.5% in CBT-I, - 3.5±13.2% in WL, t=-2.26, p=0.03).
Conclusion: These preliminary findings show that CBT-I during withdrawal from benzodiazepines in older chronic insomniacs improves self-reported sleep quality. Our findings support the use of CBT-I during the tapering of hypnotics in older individuals with chronic insomnia.

PS1: F112

ABSTRACT TITLE:

Exploring the effect of auditory stimulation on sleep spindles

PRESENTING AUTHOR: *Jourde, Hugo*[1]

CO-AUTHORS: *Ujevco, Arina*[1]*; Merlo, Raphaelle*[1]*; Greenlaw, Keelin*[1]*; Coffey, Emily BJ*[1,2]

AFFILIATIONS: *1 Concordia University; 2 McGill University*

DESCRIPTION:

Faulty memory consolidation during sleep might be a contributing factor to age-related memory decline. Slow oscillations (SOs) and sleep spindles are elements of sleep physiology thought to be important in this process. Several studies suggest that the co-occurence of SOs and spindles is important in memory consolidation, and de-coupling occurs in older adulthood. SO amplitude can be enhanced using precisely timed auditory stimulation, which in turn improves participants' memory consolidation. This line of work offers a means of causally manipulating brain processes to clarify their role in memory processing and in age-related decline, and offers hope for therapeutic interventions. However, to date, no one has successfully stimulated spindles or their co-occurrence with slow oscillations with high accuracy, and it is not clear whether sleep spindles can even be manipulated with sound.

The aim of our work is to characterize the effect of auditory stimulation on sleep spindles, and identify its optimal timing.

We first obtained simultaneous magnetoencephalography (MEG) and electroencephalography (EEG) recordings during a 3 hour nap opportunity from 15 healthy young adults with quiet binaural auditory stimulation. Spindles were detected using an offline detector and the effect of the auditory stimulation was assessed depending on (a) the spindle's oscillatory phase, (b) the spindle's development (e.g. beginning, middle, end), and (c) the presence of a coupled slow oscillation at sound occurrence. To further explore the coupling relationship between SOs and spindles, we obtained EEG recordings from twenty healthy young adults who received sound stimulation timed to hit peaks of SOs. We once again explore the effects on spindles of the precise timing of sound occurrence. Together, the findings from both studies provide a comprehensive view of the feasibility of modulating spindles with non-invasive auditory stimulation, and offer precise targets for future work. These results will form the basis for clarifying the role of spindles in memory decline in aging, using gentle causal manipulations, with a long-term view towards potential therapeutic intervention for older adults.

PS1: F113

ABSTRACT TITLE:

Frequency and predictors of obstructive sleep apnea in a cognitively impaired clinic population

PRESENTING AUTHOR: *Colelli, David R.*[1,2]

CO-AUTHORS: *Black, Sandra*[1,2]*; Masellis, Mario*[1,2]*; Lam, Benjamin*[1,2]*; Lim, Andrew*[1,2]*; Boulos, Mark I.*[1,2]

AFFILIATIONS: *1 L.C. Campbell Cognitive Neurology Research Unit, Sunnybrook Health Sciences Centre, Heart and Stroke Foundation Canadian Partnership for Stroke Recovery, Hurvitz Brain Sciences Research Program, Sunnybrook Research Institute, Toronto, Canada; 2 Department of Medicine, Division of Neurology, University of Toronto, Toronto, Ontario, Canada*

DESCRIPTION:

Introduction: Obstructive sleep apnea (OSA) is a common sleep disorder which results in repeated pauses in breathing during sleep and is associated with an increased risk of developing cognitive impairment. OSA is prevalent in the general population and its prevalence increases in patients who have dementia. However, the frequency and predictors of OSA have not been well-established in Alzheimer's disease and other related conditions such as vascular dementia.

Objectives: (1) To assess the frequency and predictors of OSA in patients with cognitive impairment due to a neurodegenerative and/or vascular etiology in a tertiary care clinic population. (2) To assess the correlation of OSA with cognitive impairment and actigraphy-derived sleep quality.

Methods: Patients with cognitive impairment primarily attributable to an underlying neurodegenerative and/or vascular etiology were enrolled. Patients completed various assessments and questionnaires related to sleep, cognition and mood. A home sleep apnea test (HSAT) was used to assess patients for OSA.

Results: Sixty-seven patients had complete HSAT recordings (i.e. ≥4 hours of analyzable HSAT data). Patients had a mean age (±SD) of 72.8 (±10.1) years, 44.8% were male and the mean (±SD) body mass index was 25.6 (±5.5). OSA was detected in 52.2% of the study population. Logistic regression demonstrated that OSA was significantly associated with a lower Montreal Cognitive Assessment score (OR: 0.40, p=0.048). Severity of OSA was correlated with degree of cognitive impairment and actigraphy-derived sleep variables (lower total sleep time, greater sleep onset latency, lower sleep efficiency, and greater awakenings)

Conclusion: Our study demonstrated that OSA is common in patients with cognitive impairment and is correlated with lower cognition and poorer sleep quality. Future research should examine OSA prevalence in larger cohorts and assess predictors in specific neurodegenerative and/or vascular etiologies for cognitive impairment.

PS1: F114

ABSTRACT TITLE:

Individual differences in the effect of poor sleep on sensitivity to aggression in faces

PRESENTING AUTHOR: *Gauvreau, Cidney*[1]

CO-AUTHORS: *Lustig, Kari*[1] *; McCormick, Cheryl* [1] *; Cote, Kimberly*[1]

AFFILIATIONS: *1 Brock University*

DESCRIPTION:

Insufficient sleep results in poor emotion functioning and regulation, including altered processing of emotional facial expressions, especially negative ones (1). We examined the role of sleep quality in perception of aggression in faces presented to 62 young adults (20 men, 42 women). The Aggression Perception Task required participants to rate perceived aggressiveness on a 7-point scale in 43 male faces displaying a neutral expression. Stimuli were presented twice at random in two consecutive blocks. The stimuli varied in facial width-to-height ratio (fWHR), which has been shown to relate to both perceived and actual aggression, with wider faces being more aggressive (2,3). fWHR is the width between the zygomatic bones, divided by the distance between the brow and upper lip. We calculated a correlation between the fWHR and the aggression rating of each stimulus as an index for individuals' sensitivity to aggression.

RESULTS: Poor sleep on the Pittsburgh Sleep Quality Index (PSQI) and shorter sleep duration (from weekly average of sleep diary) were both significantly associated with increased sensitivity to aggression in faces, but in men only (p's<.01). Further investigation of trait affect measures as moderators of the relation between sleep and aggression sensitivity were carried out in the full sample, and in men and women separately. In the full sample, factors of impulsivity as measured by Barratt Impulsiveness Scale (BIS-11), such as motor-perseverance and non-planning cognitive complexity were significant moderators of the relation between sleep and aggression sensitivity. Specifically, poor sleep was associated with increased sensitivity to aggression in faces for those with high levels of motor perseverance ($p<0.05$), and those with moderate and high levels of non-planning cognitive complexity ($p<.05$). Other sex-specific moderators of the relationship between sleep and sensitivity to aggression emerged in men such as trait anxiety measured by the State Trait Anxiety Inventory (STAI-T) and perspective taking measured by the Interpersonal Reactivity Index (IRI) which measures empathy. Specifically, poor sleep was associated with increased sensitivity to aggression in faces for men with moderate or high levels of trait anxiety (p's<.01), and for men with low or moderate perspective taking on the IRI (p's<.01).

CONCLUSION: Poor sleep was associated with heightened sensitivity to aggression in faces, for men, reflecting a negativity bias in emotion. It is important to consider the role of sex, and individual differences in trait affect and personality, in understanding the role of poor sleep in the perception of aggression and emotion regulation.

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Acknowledgement: NSERC

PS1: F115

ABSTRACT TITLE:

Insomnia disorder predicts self-reported cognitive decline in middle-aged and older adults

PRESENTING AUTHOR: *Zhao, Jean-Louis*[*1,11]

CO-AUTHORS: *Cross, Nathan E*.[1-4]; Yao, Chun W.[4-6]; Carrier, Julie[1,4,7,9]; Postuma, Ronald B.[4,7,8]; Gosselin, Nadia[4,7,9]; Kakinami, Lisa[2,10]; Dang-Vu, Thien Thanh[1-4,11]*

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DESCRIPTION:

Introduction: Sleep complaints increase with aging and have been shown to be associated with cognitive impairment in older adults. In older individuals, the presence of self-reported 'subjective' cognitive decline (SCD) (e.g., a complaint of decreased memory) confers an elevated risk of progression to mild cognitive impairment (MCI) or dementia (~40.7% over 4-years). Such conversion to MCI and dementia in individuals with SCD may occur progressively over 10-15 years, depending on numerous factors, including sleep quality. However, no study to date has evaluated the association between insomnia disorder and SCD in older adults. This is important to understand the impact insomnia has amongst other risk factors involved in the earliest stages of cognitive decline. The aim of this study is to examine the longitudinal risk of self-reported cognitive decline in middle-aged and older adults with probable insomnia disorder (PID), insomnia symptoms only (ISO) or no insomnia symptoms (NIS).

Methods: A total of 26,363 participants, aged 45 years and older, completed baseline and 3-year follow-up assessments from the Canadian Longitudinal Study on Aging (CLSA), which included self-reported evaluations of sleep and memory. The CLSA is a national, 20-year, prospective cohort study that collects information on the biological, medical, cognitive, psychological, social, lifestyle, and economic aspects of middle-aged and older adults. Participants were categorized as having PID, ISO, or NIS using an eight-question instrument assessing participants' sleep. The questions were selected to reflect standardized DSM-V diagnostic criteria for insomnia disorder. Participants were further grouped based on the progression from baseline to follow-up, either 1) the progression from NIS to ISO vs. NIS to PID, or 2) the worsening (i.e., NIS to ISO, ISO to PID, NIS to PID) vs. improvement (i.e., PID to ISO, ISO to NIS, PID to NIS) of their sleep status. The risk of self-reported memory worsening at follow-up was assessed for each group via the questions: "Do you feel like your memory is becoming worse?" and "Has a doctor ever told you that you have a memory problem?", using logistic regression models, adjusted for lifestyle and clinical factors.

Results: Participants who had NIS and developed PID at follow-up (NIS to PID) showed greater risk (OR 1.95; 95% CI 1.49 – 2.55; P < 0.0001) of self-reported memory worsening compared to those who developed ISO (OR 1.24; 95% CI 1.14 – 1.35; P < 0.0001) or remained NIS, after adjusting for lifestyle and medical outcomes. Participants whose sleep worsened from baseline to follow-up displayed greater risk (OR 1.28; 95% CI 1.18 – 1.39; P < 0.0001) of self-reported memory worsening at follow-up compared to those who improved their sleep or remained without insomnia symptoms, after adjusting for lifestyle and medical variables.
Conclusion: These findings demonstrate an increased risk of subjective memory decline in middle-aged and older adults with insomnia disorder, compared to adults with insomnia symptoms alone or without any sleep complaints. Subjective memory complaints are often a precursor to mild cognitive impairment (MCI) and dementia, and our findings suggest that insomnia disorder contributes to the early stages of cognitive decline.

PS1: F116

ABSTRACT TITLE:

Investigating Changes in Cognition associated with use of CPAP in Cognitive Impairment and Dementia: An Exploratory Study

PRESENTING AUTHOR: *Costa, Yakdehikandage* [1,2,3]

CO-AUTHORS: *Black, Sandra , Dr.* [1,2,3]*; Lim, Andrew , Dr.* [1,2,3]*; Boulos, Mark I., Dr.* [1,2,3]

AFFILIATIONS: *1 Hurvitz Brain Sciences Research Program, Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada; 2 Department of Medicine, Division of Neurology, University of Toronto, Toronto, Ontario, Canada; 3 Sleep Laboratory, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada*

DESCRIPTION:

Dementia is a devastating illness affecting over 747 000 Canadians, with combined medical costs and indirect costs being $33 billion annually. Cognitive impairment and dementia can have neurodegenerative and/or vascular etiologies, however, other conditions are known to play a role. Obstructive Sleep Apnea (OSA) is one such condition that manifests as recurrent obstruction of the upper airway during sleep resulting in hypoxia. OSA is highly prevalent in patients with cognitive impairment and is an independent risk factor for the development of cognitive impairment and dementia. OSA is typically treated with Continuous Positive Airway Pressure (CPAP) administering pressurized air to keep the airway open. Though CPAP use has been linked to improvements in attention, executive function, memory, and global cognition in elderly populations without cognitive impairment, the limited studies which have examined the role of CPAP in cognitively impaired populations have had small sample sizes and yielded conflicting results on CPAP's efficacy in improving cognition when comparing CPAP adherent and nonadherent patients. Furthermore, we are unable to meta-analyze the results from existing studies due to heterogeneous cognitive measures used, variability in follow-up periods, differences in OSA definitions, and differences in measuring CPAP compliance. The aim of our study is to determine i) whether CPAP adherence is associated with changes in global cognition as measured by the Montreal Cognitive Assessment (MoCA) and ii) whether specific cognitive domains change based on CPAP adherence in patients with Alzheimer's Disease (AD), mild cognitive impairment (MCI) or vascular cognitive impairment (VCI). Eligible patients will be those with (i) a clinical diagnosis of AD, MCI, or VCI, (ii) OSA diagnosis confirmed through polysomnography or home sleep apnea testing, (iii) prescription of CPAP after the OSA diagnosis, and (iv) completion of baseline and 3-6 month follow-up assessments. Patients using CPAP ≥4 hr/night, 7 days/week at the 3-6 month follow-up will be considered CPAP adherent. To examine changes between CPAP adherent vs. CPAP non-adherent patients, interarm differences in global cognition (as assessed by the MoCA and our other secondary cognitive assessments) will be evaluated using two-sample t-tests. Previous literature has indicated that the Minimally Clinically Important Difference for the MoCA is 2.0. Currently, 55 patients have been found to be eligible for our analysis, with additional eligible patients expected to be included from ongoing studies and a retrospective chart review toward a sample size goal of 88 (calculated based on the MoCA). This longitudinal study will help elucidate which cognitive domains demonstrate improvement with CPAP therapy and whether OSA-related decline in some cognitive domains can be reversed by CPAP use as evaluated by the MoCA. The findings of this study will aid in motivating patients to use CPAP as adherence rates to CPAP therapy are generally low. The results of this study would also support a sufficiently powered randomized controlled trial examining the impact of CPAP on cognitive outcomes in patients with AD/MCI/VCI.

PS1: F117

ABSTRACT TITLE:

Middle-aged women with surgical menopause show nocturnal hypoxia and reduced prefrontal cortical thickness

PRESENTING AUTHOR: *Gravelsins, Laura*[1]

CO-AUTHORS: *Gervais, Nicole*[2]*; Brown, Alana*[1] *; Laird, Kaz*[1]*; Almey, Anne* [1]*; Reuben, Rebekah*[1]*; Perovic, Mateja*[1]*; Karkaby, Laurice* [1]*; Grady, Cheryl*[1,2,4]*; Einstein, Gillian*[1],[2,3]

AFFILIATIONS: *1 Psychology, University of Toronto, Toronto, ON, Canada; 2 Rotman Research Institute at Baycrest Health Sciences and University of Toronto; 3 Tema Genus at Linköping University; 4 Psychiatry, University of Toronto*

DESCRIPTION:

Introduction

Early loss of 17β-estradiol (E2), as experienced by women with bilateral salpingo-oophorectomy (BSO; removal of the ovaries and fallopian tubes), is associated with an increased prevalence of sleep disorders (Huang et al., 2018) and greater Alzheimer's disease (AD) risk (Rocca et al., 2007). In older adults, poor sleep heightens AD risk; hypoxia increases markers for incipient AD, including circulating neurotoxic amyloid-beta (Aβ; Sharma & Varga et al., 2017), and is linked to prefrontal cortical thinning (Joo et al., 2013). Thus, we wondered: 1) if this at-risk population of middle-aged women with BSO had nocturnal hypoxia, measured by oxygen desaturation, and 2) whether this related to decreased prefrontal cortical thickness in women taking and not taking estradiol therapy (ET).

Methods

Sleep and percent oxygen desaturation (SPO2%) were measured via at-home polysomnography (TEMEC) using EEG (Fp1, Fp2) and pulse oximetry respectively from one night of recorded sleep. T1-weighted structural images were acquired on a Siemens 3.0 Tesla scanner and prefrontal cortical thickness was obtained using the CIVET pipeline. We recruited middle-age women ages 35-60 with BSO-induced menopause, some of whom were taking ET (BSO+ET; n=15), and some not (BSO; n=15). We compared their sleep and cortical thickness with that of premenopausal controls (AMC; n=18) matched on age, education, and body mass index.

Results

Women with BSO (BSO, BSO+ET) had minimum SPO2% values that were significantly lower than AMC, and significantly thinner right medial orbitofrontal (rmOF) cortices. Analyses separating groups based on ET therapy status (BSO vs BSO+ET vs AMC) revealed trending differences between groups, such that the BSO group without ET tended to have lower minimum SPO2% and thinner rmOF cortices than AMC.

Conclusion

These preliminary results suggest early and abrupt loss of E2 due to BSO may drive greater drops in sleep SPO2% in middle-age women, and may be related to reduced prefrontal cortical thickness. This study is the first to show nocturnal hypoxia in middle-age women with BSO-induced menopause, and suggests hypoxia may be one mechanism that contributes to increased AD risk in this population.

PS1: F118

ABSTRACT TITLE:

Next-dose Transition From Zolpidem to Lemborexant: Results From a 14-Week Multicenter Open-label Pilot Study

PRESENTING AUTHOR: *Moline, Margaret[1]*

CO-AUTHORS: *Rosenberg, Russell[2]; Kumar, Dinesh[1]; Perdomo, Carlos[1]; Moline, Margaret[1]; Malhotra, Manoj[1].*

AFFILIATIONS: *1 Eisai Inc., Woodcliff Lake, New Jersey; 2 NeuroTrials Research, Inc., Atlanta, Georgia*

DESCRIPTION:

Introduction: In clinical practice, patients may need to change their insomnia medication; however, there is a paucity of information regarding methods for transitioning patients between insomnia medications of different drug classes. In this open label pilot study, E2006-A001-312 (Study 312; NCT04009577), pre-specified dosing paradigms for transitioning patients with insomnia disorder from the GABA-ergic agonist zolpidem (ZOL) to the dual orexin receptor antagonist lemborexant (LEM) were examined.

Objectives: To evaluate the proportion of adult subjects with insomnia disorder taking ZOL (immediate release [IR] or extended release [ER] formulations) who successfully transitioned to LEM (5 mg [LEM5] or 10 mg [LEM10]), while also assessing the safety and tolerability of LEM in this population of subjects.

Methods: Study 312 enrolled adults (≥ 18 years) with insomnia disorder, who used ZOL (IR or ER) intermittently (3-4 nights/week) or frequently (≥5 nights/week). This study included a 3-week Screening Period (subjects continued ZOL), followed by a 2-week Titration Period (TITR), 12-week Extension Period (EXT), and 4-week Follow-up Period. Cohort-1 included subjects who were intermittent ZOL users and also included those with one week each of intermittent and frequent use of ZOL. Cohort-1 subjects began TITR with LEM5. Cohort-2 included subjects who were frequent ZOL users, and these subjects were randomized 1:1 to LEM5 or LEM10 at the start of TITR. If subjects successfully transitioned to LEM during TITR, they had the option to enter EXT. Subjects could change LEM dose during TITR (one dose change permitted) and EXT. The primary endpoint was the proportion of subjects who transitioned successfully to LEM following TITR. Treatment-emergent adverse events (TEAEs) were evaluated according to dose at time of TEAE.

Results: A total of 53 subjects were enrolled in Study 312, with n=10 in Cohort-1 and n=43 in Cohort-2. Of these 53 subjects, 43 (81.1%) transitioned to LEM at the end of TITR; all 43 (100.0%) entered EXT, and 41 of the 43 received treatment. During EXT, 3 subjects discontinued treatment. Overall, 38 of 41 (92.7%) subjects entered EXT, received treatment, and completed EXT. At the end of EXT, 25 of 41 subjects (61.0%) were receiving LEM10 and 16 of 41 subjects (39.0%) were receiving LEM5. Median time to first dose change, which was based on modal dose (most frequent dose taken during TITR and EXT combined) groups, was 14.5 days for LEM5 and 36.0 days for LEM10. The majority of TEAEs were mild/moderate in severity. Across both the TITR and EXT Periods, TEAEs occurred more frequently with LEM10 than LEM5. Somnolence (n=4) and abnormal dreams (n=4) were the most commonly reported TEAEs.

Conclusion: The potential for successful direct transition of patients from ZOL to LEM is supported by the results of this study. The safety profile of LEM was consistent with the safety profile reported in previous phase 3 studies and LEM was generally well tolerated.

Support: Eisai Inc.

PS1: F119

ABSTRACT TITLE:

Odds ratio product as a correlate of sleep fragmentation, cognition, and daytime sleepiness in Parkinson's disease

PRESENTING AUTHOR: *Gu, Yusing*[1]

CO-AUTHORS: *Younes, M.*[2,3] *;Lajoie, Annie*[1] *;Gerardy, Bethany*[3]*;Lafontaine, Anne-Louise*[4] *; Robinson, Ann*[1] *;Benedetti, Andrea*[5]*;Kimoff, R. John*[1]*;Kaminska, Marta*[1]

AFFILIATIONS: *1 Respiratory Epidemiology and Clinical Research Unit, Research Institute of the McGill University Health Centre; 2 Sleep Disorders Centre, University of Manitoba; 3 Younes Respiratory Technologies Ltd.; 4 Department of Neurology, Montreal Neurological Hospital ; 5 Department of Medicine and Department of Epidemiology, Biostatistics & Occupational Health, McGill University*

DESCRIPTION:

INTRODUCTION: Sleep disruption is a major non-motor component of Parkinson's disease (PD) that may predispose these patients to daytime sleepiness and cognitive impairment. The Odds-Ratio-Product (ORP) is a novel electroencephalographic (EEG)-derived metric that measures sleep depth continuously, thereby evaluating sleep architecture with greater resolution than traditional staging. Derivations of ORP also provide information on mechanisms of poor sleep, adequacy of sleep, and uniformity of sleep depth in the right and left hemispheres.

OBJECTIVE: Measure ORP metrics in PD patients to help understand the mechanism(s) and associated outcomes of sleep disruption in these patients.

METHODS: Overnight polysomnographic data were extracted from patients in the COPE-PAP trial (Cognition & Obstructive Sleep Apnea in PD, Effect of Positive Airway Pressure Therapy; NCT02209363). Baseline EEG was analyzed in 3-second segments for ORP. The following were also measured: 1) ORP-9, an index of speed of progression to deep sleep following arousals, ranging 0.8-1.56 in normal subjects (1.15±0.23); 2) Epoch-by-epoch agreement between ORP in right and left hemispheres (R/L correlation), an index that declines with insufficient sleep; 3) deltaORP, the increase in ORP from the start to the end of sleep, which theoretically evaluates the adequacy of sleep (decrease in sleep pressure) across the night. Spearman's correlations were calculated between ORP variables and traditional sleep fragmentation measures (sleep efficiency, wake after sleep onset (WASO), total arousal index). Multivariable linear regression with stepwise regression (AIC) models were constructed to assess predictors of ORP and its derivations from age, sex, body mass index (BMI), levodopa equivalent dose (LED), PD duration, Unified PD Rating Scale part III – motor (mUPDRS) score, and respiratory disturbance index (RDI). Multivariable linear regression was also used to assess relationships between ORP variables and Montreal Cognitive Assessment (MoCA) or Epworth Sleepiness Scale (ESS) scores.

RESULTS: 89 patients (64.7±10.8 years, 67% male) were analyzed, with average PD duration 6.4±4.9 years, RDI 43.6±17.4, MoCA 23.9±4.1, and ESS 10.1±4.3. The main abnormality was a high ORP-9 (1.30±0.39) along with significant correlations between ORP-9 and sleep efficiency (r=-0.383; 95%CI [-0.551,-0.187]), WASO (r=0.402; 95%CI [0.208,0.566]), and arousal index (r=0.290; 95%CI [0.083,0.473]). There were no significant associations between ORP-9 and demographic variables, PD duration, LED, mUPDRS, or RDI. deltaORP was significantly associated with MoCA (β=4.98; 95%CI [1.71, 8.26]), adjusting for age, sex, and BMI). R/L correlation was significantly associated with both MoCA (β=14.67; 95%CI [3.54,25.80], adjusted) and ESS (β=-14.45; 95%CI [-28.14,-0.76], adjusted).

CONCLUSION: In patients with PD, low sleep efficiency and excessive sleep fragmentation are related to high ORP-9, indicating that slow progression from wake to deep sleep significantly correlates with poor sleep quality. The associations between deltaORP, R/L correlation and MOCA suggest that insufficient sleep leads to cognitive decline, or that both sleep changes and cognitive dysfunction independently result from PD neurodegeneration. ORP-9 may be a centrally mediated trait that determines sleep quality, while global ORP measures across the night (deltaORP, R/L correlation) may reflect outcomes of poor sleep. Ongoing work with ORP may help understand pathophysiology and outcomes of poor sleep in patients with PD.

PS1:F120

ABSTRACT TITLE:

Solriamfetol titration & administration: physician titration strategies in a hypothetical patient with obstructive sleep apnea

PRESENTING AUTHOR: *Singh, Haramandeep*[1]

CO-AUTHORS: *Hyman, Danielle*[2] *; Parks, Gregory*[2] *; Chen, Abby*[2]*; Baldys, Beth*[3]*; Ito, Diane*[4]*; Thorpy, Michael J.*[5]

AFFILIATIONS: *1 Sleep Medicine Specialists of California; 2 Jazz Pharmaceuticals, Inc.; 3 InVibe Labs; 4 Stratevi; 5 Albert Einstein College of Medicine*

DESCRIPTION:

Introduction: Solriamfetol (Sunosi®) is a dopamine/norepinephrine reuptake inhibitor approved (US and EU) to treat excessive daytime sleepiness (EDS) in adults with narcole (75-150 mg/d) or obstructive sleep apnea (OSA) (37.5-150 mg/d).

Objective: To understand factors physicians consider when initiating solriamfetol titration strategies for a hypothetical patient were analyzed.

Methods: This virtual, descriptive, cross-sectional, qualitative survey of solriamfetol titration and administration (START) enrolled US-based physicians treating patients with ED due to OSA/ narcolepsy. Responses to 4 open-ended questions on a hypothetical patient were recorded. Patient scenario: 48-year-old man with OSA, obesity (body mass index=and hypercholesterolemia, who uses continuous positive airway pressure ≥6 hours/night and has taken modafinil (400 mg/d) for 2 years which no longer controls his EDS (Epw Sleepiness Scale [ESS]=13). Content analysis of the recordings identified themes in the responses; a trained linguist captured language patterns.

Results: Twenty-six physicians (neurologists, 7 [27%]; internists, 7 [27%]; pulmonologists, 6 [23%]; psychiatrists, 5 [19%]; otolaryngologists, 1 [4%]) treating OSA for a mean 16.3± years and representing 781 patients stable on solriamfetol participated; 19 (73%) were board-certified in sleep medicine. All physicians thought the hypothetical patient would be appropriate for solriamfetol, citing his lack of EDS symptom control (65%), high modafinil dose (31%), and ESS level (27%). To start solriamfetol, most suggested switching from modafinil (21 [81%]); 4 (15%) would add solriamfetol to modafinil and 1 (4%) felt the initiation strategy depended on other factors. Fourteen (54%) would not titrate solriamfetol the label, of whom 86% would start at 75 mg. Ten (39%) would discontinue modafinil abruptly; others would taper while (5 [19%]) or before starting solriamfetol (5 [19%]), taper discontinue while starting solriamfetol (4 [15%]),or use another approach (2 [8%]). Current modafinil dose (23%), likelihood of an adverse reaction (15%), similar mechanism of action (12%), EDS severity (4%), and other (12%) influenced physicians' titration decisions; 42% cited no factors influencing their decision. If the patient was not taking modafinil, 11 (42%) physicians would titrate solriamfetol per the label starting at 37.5 mg; 15 (58%) would use an alternative approach. Controlled hypertension would not change most physicians' (81%) approaches.

Conclusion: Most physicians cited lack of symptom control on modafinil as the rationale for recommending solriamfetol for the hypothetical patient. Most physicians consider specific factors when titrating (most commonly the dose of prior medication), but some did not consider any. Most would not change their approach in a patient with controlled hypertension.

PS1:F121

ABSTRACT TITLE:

Value of Neck Circumference in the STOP-Bang Questionnaire

PRESENTING AUTHOR: *Waseem, Rida*[1]

CO-AUTHORS: *Chung, Frances*[1]*; Salama, Yasser*[2]

AFFILIATIONS: *1 University Health Network, 2 University of Toronto*

DESCRIPTION:

Introduction - Obstructive sleep apnea (OSA) is a common sleep disorder. OSA has significant associated morbidity and mortality and is often underdiagnosed. The STOP-Bang questionnaire is a widely used tool to screen individuals at high risk of OSA. One parameter assessed in the questionnaire is neck circumference. This study examines the diagnostic performance of the STOP-Bang questionnaire with or without neck circumference. We hypothesise that the diagnostic performance of STOP-Bang will be higher with than without the neck circumference parameter.

Methods - A retrospective study was conducted which included patients from preoperative clinics of two hospitals in Toronto. The inclusion criteria of the study involved patients ≥18 years undergoing surgery for elective procedure. All consented patients completed the STOP-Bang questionnaire [S: Snoring, T: Tiredness, O: Observed apnea, P: Pressure, BMI (> 35 kg/m2), age (> 50 years), neck circumference (> 40 cm), and gender (male)] and underwent overnight polysomnography at the sleep laboratory. The diagnostic parameters were calculated for STOP-Bang and STOP-Bag questionnaires.

Results - There were 203 patients with mean age of 56.5 ± 12.7 years and 51.2% were male. The STOP-Bang questionnaire had a significantly higher area under receiver operating curve than the STOP-Bag questionnaire (0.782 vs. 0.758, $P<0.05$).

Similarly, McNemar test showed that the STOP-Bang questionnaire had significantly higher sensitivity when compared to the STOP-Bag questionnaire (85.5% vs 81.3%, $p<0.05$).

Conclusion - This study identified that the inclusion of neck circumference in the STOP-Bang assessment tool provides significantly better diagnostic value compared to when excluding the parameter. Despite the parameter often being overlooked in clinical assessment, these findings signify the importance of its inclusion in OSA assessment.

PS1:F122

ABSTRACT TITLE:

Associations between obstructive sleep apnea, cerebral small vessel disease, and cognition in patients with ischemic stroke and TIA

PRESENTING AUTHOR: *Muir, Ryan[1]*

CO-AUTHORS: *Murray, Brian[2,3,4]; Colelli, David[5,6]; Gao, Fuqiang[7]; Ramirez, Joel[7]; Dharmakulaseelan, Laavanya[7]; Boulos, Mark I.[7]; Swartz, Richard[7]; Black, Sandra[7]; Boulos, Mark I.[7]*

AFFILIATIONS: *1 University of Toronto, 2 Hurvitz Brain Sciences Research Program, Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada; 3 Department of Medicine, Division of Neurology, University of Toronto, Toronto, Ontario, Canada; 4 Sleep Laboratory, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada; 5 L.C. Campbell Cognitive Neurology Research Unit, Sunnybrook Health Sciences Centre, Heart and Stroke Foundation Canadian Partnership for Stroke Recovery, Hurvitz Brain Sciences Research Program, Sunnybrook Research Institute, Toronto, Canada; 6 Department of Medicine, Division of Neurology, University of Toronto, Toronto, Ontario, Canada; 7 Sunnybrook Health Sciences Centre*

DESCRIPTION:

Introduction: Cerebral small vessel disease (SVD) is the most common cause of vascular dementia. On MRI SVD manifests as White Matter Hyperintensities (WMH), lacunes, enlarged perivascular spaces (ePVS) and microbleeds. Identifying novel and treatable risk factors could facilitate stroke and vascular dementia prevention. Obstructive Sleep Apnea (OSA) is the most common sleep disorder and meta-analytic data supports a relationship between OSA and WMH. However, few studies investigate other measures of SVD, such as microbleeds, and few examine regional relationships and potential associations with cognition.

Objectives: (1) To examine the relationship between OSA severity and SVD in patients with ischemic stroke/TIA. (1a) To assess whether these associations may be present only in select brain regions with specific types of SVD. (2) To examine the relationship between OSA, SVD and cognition.

Methods: In this cross-sectional study, patients with ischemic stroke/TIA were prospectively recruited across three independent cohort studies between 2012 -2018. Years of education, vascular risk factors, stroke severity and Montreal Cognitive Assessment scores were collected. All patients completed MRI and either an in-laboratory polysomnography (PSG) or Home Sleep Apnea Test (HSAT). OSA severity was quantified using the Apnea Hypopnea Index (AHI) and Respiratory Disturbance Index (RDI). The burden of microbleeds, WMH, lacunes and basal ganglia ePVS was quantified using validated and published visual rating scales by a trained neuroimaging analyst. Ordinal logistic regression models were constructed to examine relationships between OSA severity and metrics of SVD and, while controlling for covariates.

Results: 237 patients met inclusion criteria. Increasing AHI was associated with a greater burden of periventricular WMH (pWMH) OR=1.02 (CI:1.01 to 1.04, p=0.02), deep microbleeds OR=1.03 (CI:1.01 to 1.05, p=0.002) and lobar microbleeds OR=1.02 (CI:1.01 to 1.04, p=0.03). In 96 subjects with PSG data, increasing RDI was associated with pWMH OR=1.03 (CI:1.01 to 1.05, p=0.03), deep microbleeds OR=1.06 (CI:1.03 to 1.10, p<0.001), and lobar microbleeds OR=1.03 (CI:1.01 to 1.06, p=0.02). While AHI and RDI were not associated with lacunes or basal ganglia ePVS, they did predict a greater severity of total global SVD disease burden. Finally, in an ordinal logistic regression model, lower cognitive scores were related to fewer years of education OR=0.87 (CI:0.80 to 0.95, p=0.001), greater stroke severity OR=1.41 (CI:1.21 to 1.64, <0.001), strategic stroke location OR=3.57 (CI:1.85 to 6.90, p<0.001) and cerebral microbleeds OR=1.09

(CI:1.01 to 1.18, p = 0.03). All models controlled for age, sex and vascular risk factors, including hypertension.
Conclusion: OSA severity is associated with greater small vessel disease burden, pWMH and cerebral microbleeds. The regional relationship between OSA and pWMH, may reflect differential regional vulnerability to injury in the cerebral white matter. Furthermore, cerebral microbleeds are an important clinical entity; even while accounting for the strong effect of stroke severity and location, microbleeds are predictive of lower cognitive scores. The relationship between OSA and both lobar and deep microbleeds could suggest possible relationships between OSA and nocturnal hypertension and impaired cerebral amyloid clearance. Overall, this study supports the relationship between OSA and microbleeds and suggests that microbleeds are an important predictor of cognition.

PS1:F123

ABSTRACT TITLE:

Oximetry-derived nocturnal hypoxemia is associated with postoperative cardiovascular events in patients with unrecognized obstructive sleep apnea

PRESENTING AUTHOR: *Waseem, Rida*[1]

CO-AUTHORS: *Yin Wan, Chew*[2]*; Suen, Colin*[3]*; Chung, Frances*[1]*; Chan, Matthew*[4]*; Tam, Stanley*[5]

AFFILIATIONS: *1 University Health Network, 2 University of Malaya, 3 University of Toronto, 4 The Chinese University of Hong Kong, 5 Scarborough Health Network*

DESCRIPTION:

Background: Obstructive sleep apnea (OSA) is known to be associated with postoperative cardiovascular events in patients undergoing major non-cardiac surgery. OSA is underdiagnosed in the surgical population due to the complexity of polysomnography. Overnight oximetry can identify those at risk of sleep apnea by detecting nocturnal hypoxemia. The objective of the study is to determine whether overnight oximetry can identify those at risk of sleep apnea and its association with 30-day postoperative cardiovascular events.

Methods: The study was a planned post hoc analyses of a multicenter prospective cohort study involving 1,218 at-risk surgical patients without a prior risk of sleep apnea. The inclusion criteria were patients ≥45 years old undergoing non-cardiac surgery with 1 or more risk factors for postoperative cardiovascular events. All patients underwent pulse oximetry (PULSOX-300i, Konica Minolta Sensing, Inc) before surgery. Severity of sleep apnea were classified based on oxygen desaturation index (ODI) (<5 as no, ≥5 to <15 as mild, ≥15 to <30 as moderate, ≥30 events/hour as severe OSA). ODI is defined as the number of events per hour with at least 4% decrease in saturation from the average saturation in the preceding 120s for at least 10s. Multivariable Cox regression analysis was used to examine the association between cardiovascular events and sleep apnea severity. Cardiovascular events were a composite of myocardial injury, cardiac death, congestive heart failure, thromboembolism, atrial fibrillation, and stroke within 30 days of surgery.

Results: Of 1,218 patients, the mean age was 68 ± 9 years and body mass index was 27 ± 5 kg/m2. The rate of postoperative cardiovascular events was 6.3% (33/523) for patients with ODI ≥5 to <15 events/hour, 14% (34/246) for patients with ≥15 to <30 events/hour, 21.5% (26/121) for patients with ODI ≥30 events/hour. Adjusting for age, gender, ethnicity, type of surgery, and pre-existing conditions, multivariable analysis showed that ODI ≥15 to ODI <30 (adjusted hazard ratio, aHR 2.65 [95% confidence interval (CI): 1.47-4.79]} and ODI ≥30 (aHR 4.18 [95% CI: 2.25-7.80]) lowest SpO2 ≤ 85 % (aHR 2.06 [95% CI: 1.12-3.78]), CT90 ≥ 20 minutes (aHR 2.50 [95% CI: 1.69-3.70]), CT80 ≥ 10 minutes (aHR 3.30 [95% CI: 2.16-5.04]) were independent predictors of 30-day postoperative cardiovascular events (Table 1).

Conclusions: Moderate (ODI ≥15 to <30 events per hour) and severe OSA (ODI ≥30 events per hour), lowest SpO2 ≤ 85 %, CT90 ≥ 20 min and CT80 ≥ 10 min are associated with increased risk of 30-day postoperative cardiovascular events in patients undergoing major non-cardiac surgery. Preoperative screening using oximetry will help in risk stratification and optimizing earlier treatment for those that are at high risk of sleep apnea and postoperative cardiovascular morbidity.

PS1:F124

ABSTRACT TITLE:

Who Sleeps Well in Canada? The Social Determinants of Sleep Health Among Middle-Aged and Older Adults in the Canadian Longitudinal Study on Aging

PRESENTING AUTHOR: *Rodrigues, Rebecca[1]*

CO-AUTHORS: *Guaiana, Giuseppe[1]; Reid, Graham[1]; Zou, Guangyong[1]; Gilliland, Jason[1]; Nicholson, Kathryn[1]; Anderson, Kelly[1]; Wilk, Piotr[1]; Alonzo, Rea[1]; Stranges, Saverio[1]*

AFFILIATIONS: *1 Western University*

DESCRIPTION:

Introduction: Disruptions in sleep quality or duration affect over half of the older adult population. Poor sleep health is associated with increased risk of mortality and chronic conditions. Inequities in sleep health likely contribute to disparities in poor health outcomes. Our objective was to identify the social determinants of sleep health among middle-aged and older adults in Canada.

Methods: We used cross-sectional baseline data from the Canadian Longitudinal Study on Aging, a survey of 30,097 community-dwelling adults, aged 45-85. Self-reported sleep measures included sleep duration, sleep satisfaction (vs dissatisfied/neutral), and sleep continuity (vs problems initiating or maintaining sleep). We selected social determinants a priori based on literature. We used modified Poisson regression to estimate prevalence ratios for sleep satisfaction and sleep continuity, and linear regression for sleep duration. Using block-wise adjustment, estimates were adjusted for all social determinants and further adjusted for lifestyle and clinical covariates.

Results: In analyses adjusted for social determinants, groups with better sleep included older age groups, higher household income, higher education level, and South Asian groups, with a higher prevalence of sleep satisfaction and/or sleep continuity. Female sex was associated with a lower prevalence of both sleep satisfaction and sleep continuity. Unemployment (vs retired) was associated with a lower prevalence of sleep satisfaction. For sleep duration, employed or unemployed (vs retired), Black, East Asian, and other/mixed race groups (vs white) had shorter sleep duration, while older age groups, home owners, sexual minorities, and higher education groups had longer sleep duration. Adjusting for lifestyle and clinical variables, effects for household income, unemployment, and education were attenuated, while all other associations persisted.

Conclusion: Our findings highlight sleep health disparities among Canadian middle-aged and older adults across socioeconomic gradients and ethnic/racial minority groups. Poor sleep health in disadvantaged groups warrants increased attention as a public health problem in Canada.

PS1:F125

ABSTRACT TITLE:

Genome-wide analysis of sleep in Drosophila melanogaster in constant darkness reveals context-dependent effects of genes on sleep

PRESENTING AUTHOR: *Patel, Surina*[1]

CO-AUTHORS: *Wadhwa, Anna*[1]*; Harbison, Susan*[1]

AFFILIATIONS: [1] *NHLBI*

DESCRIPTION:

Both age and environmental conditions, such as light, affect sleep in humans. Age impacts sleep in humans through changes such as increased sleep fragmentation and decreased arousal threshold. These changes in sleep also occur in the fruit fly, Drosophila melanogaster. In humans, the presence or absence of light also impacts sleep; however, the effects of light on sleep in flies are not well understood. We calculated 16 sleep parameters from previous data measuring circadian behavior in the Drosophila Genetic Reference Panel in constant darkness (DD) for 14 days. Our goal was to compare these data to a study measuring sleep in a normal light: dark (LD) cycle for 6 days. Compared to flies in LD, flies in DD had markedly different sleep. For example, we observed a significant difference in the 24 hour average bout length between flies in DD and flies in LD ($P = 0.0002$). On average, flies in DD took shorter naps. Furthermore, when we partitioned our data into two age groups, young (Days 1-6) and old (Days 7-13), sleep differed based on when it was measured. For example, the 24 hour average bout length for older female flies was significantly less than younger females ($P = 0.01$).

To determine whether these changes are orchestrated by corresponding changes in the underlying genetic architecture, we associated the line means of each sleep trait with 1,920,276 polymorphisms which implicated 2,510 polymorphic variants within 938 genes. Genes associated with the 16 sleep traits differed between LD and DD flies and between young and old sleep measures, with only a 9.7% and 19.9% overlap, respectively. These results imply a plastic response in the underlying genetic architecture of sleep that changes depending upon both environmental exposure and age. We chose 17 genes with the largest combined-sex effect sizes for average day and night bout length in younger and older flies for further study. Interestingly, all of these genes had human homologs and 4 have known associations with sleep phenotypes in humans. We are testing mutations in these candidate genes in their appropriate age and environmental context to confirm the GWAS predictions.

PS1:F126

ABSTRACT TITLE:

Multimodal assessment of sleep state misperception in insomnia disorder

PRESENTING AUTHOR: *Maltezos, Antonia*[1]

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DESCRIPTION:

Introduction: Individuals with insomnia (INS) may present sleep state misperception (SSM) by underestimating their TST and overestimating their SOL and WASO. In this study, SSM in INS and good sleepers (GS) was assessed using polysomnography (PSG) and actigraphy, along with subjective reports.

Methods: 51 INS (ISI = 17.26 ± 4.14; 49.75 ± 13.83 years old; 39 females) and 25 GS (ISI = 2.84 ± 3.20; 42.92 ± 15.48 years old; 15 females) were given an actigraphy device with a sleep diary for 11(± 2) days and came to the lab for a PSG and completed a sleep questionnaire. The misperception of SOL, WASO and TST was calculated by subtracting objective (PSG and actigraphy) from subjective data (in-lab self-assessment and at-home sleep diaries). Group differences in SSM were assessed using a one-way ANOVA with age and sex as covariates or Kruskal-Wallis test. A pairwise t-test or Wilcox test assessed the differences between subjective and objective measures within each group.

Results: The misperception of SOL differed between groups both in-lab ($F(1, 72) = 5.01$, $p = 0.03$) and at-home ($F(1, 72) = 4.47$, $p = 0.04$), with INS overestimating their SOL in lab ($p < 0.001$) and accurately perceiving their SOL at home ($p = 0.50$), and GS accurately perceiving it in lab ($p = 0.050$) and at home ($p = 0.07$). No group difference was seen in the perception of WASO in-lab. There was a significant difference for actigraphy ($\chi2(1) = 13.60$, $p < 0.001$) where INS accurately perceived WASO ($p = 0.53$) and GS underestimated their WASO ($p < 0.001$). Finally, both groups differed for their perception of TST in-lab ($\chi2(1) = 16.24$, $p < 0.001$) and at-home ($F(1, 72) = 23.34$, $p < 0.001$), with INS underestimating their TST in-lab and at home (all $p < 0.001$) and GS overestimating their TST ($p = 0.01$) in lab, yet accurately perceiving it at home ($p = 0.21$).

Conclusion: These results demonstrate that both groups perceive their sleep differently. Many differences were seen across both methods within each group, which raises the question of reliability in SSM assessment.

ORAL SESSION 4: Daytime Sleepiness and Hypersomnolence Disorders

DATE: 10/30/2021

START TIME: 12:15 PM END TIME: 1:45 PM

SESSION TITLE:

Cataplexy-Free Days in a Phase 3, Placebo-Controlled, Double-Blind, Randomized Withdrawal Study of Lower-Sodium Oxybate in Adults With Narcolepsy With Cataplexy

PRESENTING AUTHOR: *Foldvary-Schaefer, Nancy*[3]

CO-AUTHORS: *Bogan, Richard K.*[4]*; Šonka, Karel*[5]*; Thorpy, Michael J.*[6]*; Dauvilliers, Yves*[1,2]

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DESCRIPTION:

Introduction: Sodium oxybate (SXB; Xyrem®) is a standard of care for the treatment of cataplexy and excessive daytime sleepiness in narcolepsy. Lower-sodium oxybate (LXB; Xywav™; formerly designated JZP-258) is an oxybate medication with 92% less sodium than SXB. The US Food and Drug Administration approved LXB in July 2020 for the treatment of cataplexy or excessive daytime sleepiness in patients 7 years of age and older with narcolepsy.

Objective: This analysis evaluated cataplexy-free days/week, as a measure of treatment impact, in a placebo-controlled randomized withdrawal study of LXB treatment in participants with narcolepsy.

Methods: Treatment for cataplexy at study entry included 1) SXB (SXB-only); 2) SXB plus other anticataplectics (SXB+other); 3) anticataplectics other than SXB (other anticataplectics); or 4) cataplexy treatment-naive (anticataplectic-naive). Participants (aged 18–70 years with narcolepsy with cataplexy) began LXB treatment during a 12-week, open-label, optimized treatment and titration period (OLOTTP), followed by a 2-week stable-dose period (SDP). Participants were then randomized to receive placebo or continue LXB treatment during a 2-week, double-blind, randomized withdrawal period (DBRWP).

Results: Of 201 enrolled participants, 134 comprised the efficacy population (placebo, n=65; LXB, n=69). Median (1st quartile [Q1], 3rd quartile [Q3]) cataplexy-free days/week at first week of OLOTTP (while initiating LXB) by prior treatment were higher in participants entering taking SXB: SXB-only (n=41), 5.8 (2.0, 7.0); SXB+other (n=14), 6.4 (5.0, 7.0); other anticataplectics (n=21), 4.0 (1.8, 6.0); anticataplectic-naive (n=57), 3.5 (0, 5.8). At end of SDP (on stable dose of LXB), median (Q1, Q3) cataplexy-free days/week were similar in all treatment groups (6.0 [3.5, 7.0], 6.1 [1.4, 7.0], 6.0 [2.6, 7.0], and 6.2 [4.0, 7.0], respectively). Prior to randomization, there was no difference in median cataplexy-free days/week between participants to be randomized to placebo (6.0 [3.5, 7.0]) or LXB treatment (6.0 [3.0, 7.0]); during DBRWP, median cataplexy-free days/week decreased in participants randomized to placebo (3.5 [0, 5.8]) but remained similar in participants randomized to continue LXB treatment (5.6 [2.8, 7.0]). Common (≥10%) treatment-emergent adverse events were headache, nausea, and dizziness.

Conclusion: Number of cataplexy-free days/week increased with LXB treatment in participants previously naive to oxybate. Number of cataplexy-free days/week decreased during placebo exposure in participants randomized to placebo. The overall safety profile of LXB was similar to that of SXB.

ORAL SESSION 4: Daytime Sleepiness and Hypersomnolence Disorders

DATE: 10/30/2021

START TIME: 12:15 PM END TIME: 1:45 PM

SESSION TITLE:

Accurately Screening Obstructive Sleep Apnea During Wakefulness is Possible

PRESENTING AUTHOR: *Elwali, Ahmed*[1]

CO-AUTHORS: *Moussavi, Zahra*[1,2]

AFFILIATIONS: *1 Biomedical Engineering, University of Manitoba, Winnipeg, Canada; 2 Electrical and Computer Engineering, University of Manitoba, Winnipeg, Canada*

DESCRIPTION:

OSA is a common disorder that affects more than 10% of the US and Canada population and up to 1 billion people globally. Despite the severity of this disorder, it is underdiagnosed. Lacking OSA diagnosis prior to conducting a surgery that requires full anesthesia might lead to severe perioperative comorbidity and/or after-surgery mortality. Therefore, promptly and accurately screening this disorder would reduce these probable complications and help provide OSA treatment fast. Current screening tools, such as Questionnaire, suffer from low specificity (~20%) with overall low accuracy (~60%). Our developed AWakeOSA diagnostic algorithm previously achieved 81.4% testing accuracy [1]. In this study, we enhanced the feature extraction and reduction part of the AWakeOSA algorithm by creating AHI prediction models with highly AHI correlated features followed by selecting the best feature models with least redundancy, minimalizing the overlapping between the predicted OSA severity groups, to improve OSA severity prediction. The tracheal breathing sounds of 199 individuals (109 with apnea/hypopnea index (AHI) <15 as non/mild-OSA and 90 with AHI ≥15 as moderate/severe-OSA) were recorded during wakefulness in supine position. The data were divided into two groups: 60% for training and 40% for blind testing. The sound features sensitive to OSA were extracted from the training set (n=100). The extracted features were reduced using a series of correlation, modeling, and overlapping minimizer techniques, and then used in AWakeOSA diagnostic algorithm. The developed technique resulted in 90.6%, 89.7%, and 91.3% classification accuracy, sensitivity and specificity, respectively, on the blind-test dataset. The enhanced AWakeOSA algorithm could be the new accurate, reliable and quick OSA screening tool that can be done in less than 10 minutes during wakefulness.

References

[1] Elwali, A.; Moussavi, Z. A novel Decision Making procedure during Wakefulness for Screening obstructive Sleep Apnea using Anthropometric information and tracheal Breathing Sounds. Scientific reports 2019, 9, 1-12.

ORAL SESSION 4: Daytime Sleepiness and Hypersomnolence Disorders

DATE: 10/30/2021

START TIME: 12:15 PM END TIME: 1:45 PM

SESSION TITLE:

Driving Drowsy: A single night of mild sleep restriction negatively impacts EEG and driving behaviour

PRESENTING AUTHOR: *Gibbings, A.* [1,2]

CO-AUTHORS: *Ray, L.B..*[1] *; Shahidi, Zandi* [1,3] *; Comeau, F.J.E.*[3] *; Fogel, S.M..*[1,2,4]

AFFILIATIONS: *1 Sleep Research Unit, The Royal's Institute of Mental Health Research, Ottawa, K1Z 7K4, Canada; 2 School of Psychology, University of Ottawa, Ottawa, K1N 6N5, Canada; 3 Alcohol Countermeasures Systems Corp (ACS), Toronto, M9W 6J2, Canada; 4 University of Ottawa Brain & Mind Research Institute, Ottawa, K1H 8M5, Canada*

DESCRIPTION:

Background

Losing a few hours of sleep infrequently is common but is generally thought to be innocuous. However, recent studies have shown that even one night of mild sleep loss can seriously impact one's ability to perceive and react to stimuli, especially during a prolonged monotonous task. It is particularly important to understand how mild sleep restriction can affect driving behaviours because lapses while driving can have dangerous, even lethal, consequences.

Methods

Here, 22 participants (Mage±SD=24±5yrs, 13 female) completed a monotonous driving task that required quick reaction times (i.e., braking events to avoid rear-end collisions) in a driving simulator after a full night of sleep (i.e., 9 hours; 00:00–09:00) and after one night of mild sleep restriction (i.e., 5 hours; 01:00–06:00). While driving, EEG was recorded from 23 scalp electrodes and EOG, EMG, and ECG channels.

Results

After only a single night of mild and acute sleep restriction participants reported feeling more tired ($F(1,21)=64.20$, $p<0.001$, $\eta 2>0.99$), crashed more often ($t(22)=2.30$, $p=0.031$), had significantly slower reaction times ($F(1,22)=10.84$, $p=0.003$, $\eta 2=0.33$), and more often missed braking altogether ($t(22)=2.35$, $p=0.029$) than when normally rested. Also, after sleep restriction, participants' brain activity showed significant increases in both the amplitude ($F(1,18)=6.89$, $p=0.017$, $\eta 2=0.70$) and number ($F(1,18)=4.73$, $p=0.043$, $\eta 2=0.54$) of alpha bursts – an electrophysiological indicator of drowsiness/inattention – that occurred while driving.

Conclusions

These results suggest that even a single night of mild sleep restriction has serious, detrimental effects on both behavioural and neural measures of attention and vigilance. The current study underscores the importance of getting a full night's sleep, and in particular, demonstrates that drowsy driving can be dangerous or potentially fatal.

ORAL SESSION 4: Daytime Sleepiness and Hypersomnolence Disorders

DATE: 10/30/2021

START TIME: 12:15 PM END TIME: 1:45 PM

SESSION TITLE:

Sex Differences in Obstructive Sleep Apnea after Stroke or TIA

PRESENTING AUTHOR: *Dharmakulaseelan, Laavanya*[1,2,3]

CO-AUTHORS: *Black, Sandra E.* [1,2,3] *; Swartz, Richard H.* [1,2,3] *; Murray, Brian J.* [1,2,3] *; Boulos, Mark I. I.* [1,2,3]

AFFILIATIONS: *1 Hurvitz Brain Sciences Research Program, Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada; 2 Department of Medicine, Division of Neurology, University of Toronto, Toronto, Ontario, Canada; 3 Sleep Laboratory, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada*

DESCRIPTION:

Introduction: Obstructive sleep apnea (OSA) is prevalent after stroke and transient ischemic attack (TIA) and associated with decreased functional recovery and recurrent stroke. Sex differences in post-stroke/TIA OSA remain underexplored.

Objectives: The objectives of this study were to evaluate sex differences in functional outcomes, stroke severity, OSA severity, and clinical manifestations in patients with post-stroke/TIA OSA.

Methods: Study patients had sustained a stroke or TIA and underwent either diagnostic in-laboratory polysomnography or home sleep apnea testing within one year of their stroke/TIA that demonstrated OSA (apnea-hypopnea index [AHI] ≥5). Linear regression models were used to evaluate study outcomes.

Results: 178 participants with post-stroke/TIA OSA (121 males [68.0%] and 57 females [32.0%]) were included. Females and males had differing mean AHIs of 14.4±12.3 and 21.4±15.6, respectively (p= 0.003). Female sex was the only identified independent predictor for increased stroke severity on the NIH Stroke Scale (p= 0.028) and greater functional impairment on the modified Rankin Scale (p= 0.005). Female sex (p= 0.048) and lower age (p= 0.025) were independent predictors for increased post-stroke/TIA depressive symptoms. Male sex (p= <0.01) and BMI (p= <0.01) were independent predictors for an increased risk of OSA, as measured by the STOP-Bang questionnaire.

Conclusions: Women with post-stroke/TIA OSA had more severe strokes and poorer functional outcomes compared to men, despite having lower OSA severity. Women with post-stroke/TIA OSA also exhibited more depressive symptoms and presented atypically, in that they were less likely to score high on predictive scales such as the STOP-Bang questionnaire. This study suggests that there needs to be a lower threshold for referring women for diagnostic testing for OSA after a stroke/TIA. This is especially true since women are greatly impacted by the negative effects of post-stroke/TIA OSA yet present atypically. Understanding sex differences in patients with post-stroke/TIA OSA will likely facilitate better recognition of OSA and potentially improve clinical outcomes.

ORAL SESSION 4: Daytime Sleepiness and Hypersomnolence Disorders

DATE: 10/30/2021

START TIME: 12:15 PM END TIME: 1:45 PM

SESSION TITLE:

Association of Idiopathic Intracranial Hypertension with Obstructive Sleep Apnea

PRESENTING AUTHORS: *Bingeliene, Arina[1,2,3]*

CO-AUTHORS: *Tyndel, Felix[1,2,3] ; Jairam, Trevor ; Girgis, Patrick[1,2,3] ; Sundaram, Arun[1,2,3] Murray, Brian[1,2,3]; Boulos, Mark I.[1,2,3]*

AFFILIATIONS: *1 Hurvitz Brain Sciences Research Program, Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada; 2 Department of Medicine, Division of Neurology, University of Toronto, Toronto, Ontario, Canada; 3 Sleep Laboratory, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada*

DESCRIPTION:

Introduction: Idiopathic intracranial hypertension (IIH) is characterized by increased intracranial pressure of unknown etiology. The consensus is that IIH predominantly affects obese women of childbearing age, with the male to female ratio ranging from 1:4 to 1:8 in the 14 to 60-year-old age group. Males with IIH are four times more likely to have obstructive sleep apnea (OSA) compared to age and body-mass index (BMI) matched controls.

Objective: To objectively examine the association of IIH with markers of OSA severity in a large cohort of patients who completed overnight in-laboratory polysomnography.

Methods: Our sample consisted of 2982 patients who completed in-laboratory polysomnography; 48 patients had IIH (15 male and 33 female) and the remainder (n=2934) did not have IIH. We investigated the relationship between IIH and markers of OSA (i.e. apnea-hypopnea index [AHI], respiratory-disturbance index [RDI], mean O2 saturation, and lowest O2 desaturation) using multivariable linear regression analyses adjusted for age, sex, and BMI. Regression analyses were also performed using interaction terms for IIH with age, sex, and BMI.

Results: For the entire study population, mean age(±SD) was 55.1±16.5 years, 51% were female, and the mean BMI was 29.1±6.6 kg/m2. An AHI of ≥5 events per hour and an oxygen desaturation of <88% was seen in 48.3% (1441/2982) and 3.5% (105/2982) of our study patients, respectively. After adjusting for age, sex, and BMI, there were no significant associations between IIH and markers of OSA such as the AHI (p=0.58), RDI (p=0.18), average O2 saturation (p=0.053), or lowest O2 desaturation (p=0.091). Furthermore, there were no significant interactions of age, sex, or BMI with IIH and markers of OSA.

Conclusions: These results demonstrate that the presence of IIH was not associated with more severe markers of OSA after controlling for age, sex, and BMI compared to other patients referred to a sleep laboratory for assessment of sleep apnea. Our study suggests that there may not be an indication for routinely referring IIH patients to a sleep clinic for assessment of OSA.

ORAL SESSION 5: Sleep and Neurodegenerative Diseases

DATE: 10/30/2021

START TIME: 2:15 PM END TIME: 3:45 PM

SESSION TITLE:

Disturbed sleep and reduced hippocampal integrity at midlife: Implications for AD risk in women with early surgical menopause

PRESENTING AUTHOR: *Gervais, Nicole[1,2]*

CO-AUTHORS: *Brown, Alana[2] ; Gravelsins, Laura[2] ; Olsen, Rosanna[1] ; Laird, Kaz[2] ; Reuben, Rebekah[2] ; Perovic, Mateja[2] ; Karkaby, Laurice[2] ; Gosselin, Nadia[3] ; Grady, Cheryl[1] ; Einstein, Gillian[1,2,4]*

AFFILIATIONS: *1 Rotman Research Institute at Baycrest Health Sciences and University of Toronto; 2 University of Toronto; 3 Département de psychologie, Université de Montréal; Centre d'études avancées en médecine du sommeil, CIUSSS Nord-de-l'Île-de-Montréal; 4 Tema Genus at Linköping University*

DESCRIPTION:

Background: Women bear the greatest burden of Alzheimer's disease (AD), and early (< 45 years) ovarian hormone deprivation via surgical menopause further increases risk (Rocca et al., 2007). Given that sleep disturbance is implicated in AD progression (Lim et al., 2013), an important area of investigation is determining whether younger women with early surgical menopause demonstrate disturbed sleep at midlife, and whether this may confer additional risks by contributing to changes in hippocampal integrity. Thus, we investigated whether middle-aged women with bilateral salpingo-oophorectomy (BSO) not taking hormone therapy demonstrate sleep disturbance, and reduced hippocampal volume and memory. Additionally, we assessed whether sleep and hippocampal volume predict memory performance.

Method: Women with an early BSO that were either taking estradiol-based hormone therapy (BSO+ET: age= 45 ± 4.68 years; n = 22), or not taking ET (BSO: age = 46.67 ± 6.18 years; n = 18) were recruited to the study, and were compared to age-matched premenopausal (AMC: age = 43.05 ± 3.40 years n = 24) and spontaneously postmenopausal women who were ~10y older (SM: 55 ± 4.00 years; n = 20). Sleep was assessed via portable polysomnography (Vitaport-5/REMbo-234, Temec Technologies) for 1-3 nights, and sleep staging was acquired using automated scoring (Z3score, Neurobit technologies) and manually corrected following guidelines set by the American Academy of Sleep Medicine (version 2.4). High-resolution T2-weighted scans (TR/TE = 3000/66 ms; no skip, FOV = 220 mm; voxel size: 0.4 X 0.4 X 3 mm) were acquired using a Siemens 3T Prisma scanner, and hippocampal subfields (CA1, Subiculum, combined region: DG, CA2/3), were manually segmented (Olsen et al., 2017) in FSLView. Estimated Total Intracranial Volume (eTIV) was obtained via FreeSurfer (6.0) using T1-MPRAGE scans (TR=2000ms, TE = 2.6ms, flip angle = 9°, 160 sagittal slices, 1 mm3 isometric voxels; FOV = 256 mm2), and used to calculate relative volume for each ROI. The interference match-to-sample (IMTS) task was used to asses and recognition memory for scenes (Watson et al., 2013).

Results: Both hormone-deprived groups demonstrated increased sleep latency (BSO vs AMC: $p < .05$, $d = 0.74$; SM vs AMC: $p < .05$, $d = 0.69$) and decreased sleep efficiency (BSO vs AMC: $p < .05$, $d = 0.79$; SM vs AMC: $p < .05$, $d = 0.67$). Only the BSO group demonstrated reduced volume in the anterior CA1 and DGCA23 relative to AMC ($p<.05$, $d = 0.96$-1.06) and BSO+ET ($p < .05$, $d = 0.67$-0.84). Additionally, the BSO demonstrated reduced efficiency (accuracy/RTcorrect) on

scene recognition memory ($p < .05$, $d = 0.70$-0.86). Multiple regression analyses show that DGCA23 volume and group membership predict scene recognition memory performance. Conclusion: While both hormone-deprived groups demonstrated disturbed sleep, women with early BSO also showed reduced hippocampal integrity, despite being ~10 years younger than SM women. These findings are consistent with the elevated AD risk among women with BSO. It remains to be seen whether sleep disturbance at a younger age exacerbates risk.

ORAL SESSION 5: Sleep and Neurodegenerative Diseases

DATE: 10/30/2021

START TIME: 2:15 PM END TIME: 3:45 PM

SESSION TITLE:

Signs and Symptoms of Irregular Sleep Wake Rhythm Disorder (ISWRD) Reported Directly from Patients with Dementia and Their Caregivers

PRESENTING AUTHOR: *Pokrzywinski, Robin*[1]

CO-AUTHORS: *Abel, Cristina*[1] *; Lenderking, William R.*[1]*; Yardley, Jane*[2] *; Cheng, Jocelyn Y*[3]*; Moline, Margaret*[3]

AFFILIATIONS: *1 Evidera, Bethesda, MD; 2 Eisai Ltd., Hatfield, UK; 3 Eisai Inc., Woodcliff Lake, NJ*

DESCRIPTION:

Introduction: Sleep-wake disturbances occur early in the course of Alzheimer's disease (AD) and other dementias. Such disturbances are commonly associated with circadian rhythm disruptions, as seen with Irregular Sleep-Wake Rhythm Disorder (ISWRD; ICD-10 code G47-23). ISWRD is also associated with behavioral and functional symptoms. Here, we report results from Study E2006-A001-111 (Study 111; NCT04300569), which was conducted to identify features of ISWRD that are important to patients with dementia and their caregivers. These data informed the development of a novel questionnaire specific to patients with dementia and ISWRD for evaluating ISWRD symptoms.
Objectives: To identify signs and symptoms of ISWRD important to patients and caregivers of patients with dementia and ISWRD, as reported by patients and caregivers.
Methods: In this prospective, cross-sectional, qualitative, non-interventional study, patients and their caregivers were interviewed via telephone call. Patients were interviewed with their caregiver present; caregivers were interviewed alone. All interviews were conducted in English or Spanish, and all subjects were from the United States. ATLAS.ti software was used to analyze interview transcripts.
Results: In total, 15 patient/caregiver dyads and 5 caregiver-only subjects were interviewed. For the patient group (n=20; 5 not interviewed), mean (standard deviation [SD]) age was 79.0 (8.3) years and 75% were male. For the caregiver group (n=20), mean (SD) age was 67.5 (14.5) years and 20% were male. Both caregivers and patients reported fragmented nighttime and daytime sleep-wake patterns, and functional consequences of ISWRD. Examples of nighttime features included waking, wandering, and refusing to return to sleep. Examples of daytime features included falling asleep at inappropriate places; appearing sleepy; losing concentration due to sleepiness; sleepiness interfering with personal care and leisure activities; needing to postpone, change, or avoid activities due to sleepiness; adverse emotional impacts; and sundowning. There were few differences in terms, or their meaning, identified between the languages (English or Spanish) used for interviews. Because of differences in the quality of patient and caregiver reports, the potential for patient anosognosia, and caregiver ability to observe signs and behaviors, the data indicated that a caregiver-completed observer-reported outcome (ObsRO) measure is most suitable for the evaluation of ISWRD.
Conclusion: Concepts reported by patients and caregivers revealed signs, symptoms, and functional consequences specific to ISWRD that are appropriate to include in a novel ObsRO measure that can be used in future studies of ISWRD.
Support: Eisai Inc.

ORAL SESSION 5: Sleep and Neurodegenerative Diseases

DATE: 10/30/2021

START TIME: 2:15 PM END TIME: 3:45 PM

SESSION TITLE:

Endogenous Expression Levels of α-Synuclein as a Cellular Vulnerability in REM Sleep Behaviour Disorder

PRESENTING AUTHOR: *Dugan, Brittany*[1]

CO-AUTHORS: *Fraigne, Jimmy*[1]*; Peever, John*[1]

AFFILIATIONS: *1 University of Toronto*

DESCRIPTION:

Introduction: To maintain skeletal muscle atonia during REM sleep, glutamate cells of the sublaterodorsal tegmental nucleus (SLD) excite GABA/glycine neurons of the ventromedial medulla (vmM), resulting in inhibition of motor neurons located in the spinal cord. In REM sleep behaviour disorder (RBD), however, patients lose typical muscle paralysis during REM sleep, and consequent motor behaviours frequently result in self-injury and injury to bedpartners. Most importantly, 91% of individuals diagnosed with RBD will develop a synucleinopathy such as Parkinson's disease, multiple system atrophy, or dementia with Lewy bodies. With such a strong relationship, RBD is not only considered the best predictor of synucleinopathy, but also a prodromal stage of these disorders.

Although all synucleinopathies are caused by the aggregation of pathologic α-synuclein (α-syn) protein, each disease differs in temporal staging, affected brain structures, and clinical symptoms. Still, the REM sleep atonia circuit demonstrates vulnerability across synucleinopathies, suggesting a unique vulnerability despite disease differences. One notable cellular risk factor for α-syn aggregate invasion is the amount of α-syn protein expressed in a given cell under baseline conditions, as healthy α-syn protein is recruited into pathological aggregates. As such, our objective is to determine whether glutamate SLD neurons and GABA/glycine vmM neurons express high endogenous levels of α-syn in healthy conditions, helping elucidate why the REM sleep atonia circuit exhibits a consistent predisposition to α-syn pathology.

Methods: To assess α-syn levels in specific neuronal cell types, we used RNAScope® Technology to stain for both α-syn as well as either VGLUT2 or VGAT mRNA in wildtype mice. Given that α-syn protein is presynaptically located, mRNA (rather than protein) quantification allows for co-staining of α-syn along with glutamate or GABA/glycine markers within regions of interest. In brain slices containing the SLD, both α-syn and VGLUT2 probes were used, while α-syn and vGAT probes were applied to slices containing the vmM. Additionally, glutamate neurons of the locus coeruleus and GABA neurons of the gigantocellular reticular nucleus were used as controls for the corresponding cellular subtypes in the SLD and vmM, as these regions are reported to contain low levels of α-syn protein in mice.

Results: We found that glutamate SLD neurons and vmM GABA/glycine neurons both express significantly more α-syn mRNA compared to their respective neuronal cell type in control regions. Moreover, in both the SLD and vmM, α-syn mRNA expression was significantly higher within glutamate or GABA neurons, respectively, compared to other neuronal subtypes within the same region.

Conclusion: Our results indicate that neurons involved in REM sleep atonia contain high baseline levels of α-syn compared to the same neuronal cell types in regions known to express negligent levels of α-syn protein. Interestingly, our results also demonstrate that REM sleep atonia neurons specifically express higher levels of α-syn compared to other neurons within their respective region, suggesting that high baseline levels of α-syn is a significant contributor to the REM sleep atonia circuit's vulnerability across synucleinopathies.

ORAL SESSION 5: Sleep and Neurodegenerative Diseases

DATE: 10/30/2021

START TIME: 2:15 PM END TIME: 3:45 PM

SESSION TITLE:

Reduced spindle density is associated with cognitive decline in individuals with moderate-severe OSA

PRESENTING AUTHOR: *Guadagni, Veronica*[1,2,3,5]

CO-AUTHORS: *Pun, M.* [1,2,3] *; Almousawi, A.*[1,2,3] *; Yang, K.*[1,2,3] *; Hanly, P.J.*[7,8] *; Younes, M.*[9] *; Poulin, M.*[1-6]

AFFILIATIONS: [1] *Department of Physiology & Pharmacology, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada;* [2] *Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada;* [3] *Department of Clinical Neurosciences, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada;* [4] *Libin Cardiovascular Institute of Alberta, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada;* [5] *O'Brien Institute for Public Health, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada;* [6] *Faculty of Kinesiology, University of Calgary, Calgary, Alberta, Canada;* [7]*Department of Medicine, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada;* [8]*Sleep Centre, Foothills Medical Centre, Calgary, AB, Canada;* [9] *Sleep Disorders Centre, Winnipeg, Manitoba, Canada*

DESCRIPTION:

Introduction: There is evidence that Obstructive Sleep Apnea (OSA) is a risk factor for cognitive decline, likely due to the effects of inflammation and oxidative stress on amyloid and Tau metabolism and to the cerebrovascular effects of hypoxia. Previously we observed that lower spindle density was associated with lower cognitive scores in older adults. Here, we hypothesized that in older participants with OSA, a reduction in sleep spindles density would be associated with cognitive decline.

Methods: 125 participants (age±SD=66.0±6.4, 64 females) underwent one night of in-home polysomnography (PSG), and were assessed with an extensive neuropsychological battery. An automatic system with manual editing was used to score PSG data and detect spindle characteristics in both NREM stages 2 and 3, and in frontal and central electrodes. The Apnea-Hypoxia-Index (AHI) was used to distinguish those with mild OSA (n= 46, AHI>5 and <15, mean 8.6±2.9) from those with moderate-severe OSA (n= 57, AHI>15, mean 34.6± 18.5). We compared spindle characteristics between the two OSA groups (paired t-tests) and assessed their association with cognitive function (Pearson correlation). Stratified analyses were conducted to quantify sex differences.

Results: Although there were no differences in average spindle characteristics between the two groups, in individuals with moderate-severe OSA, spindle density during stage 2 NREM was associated with verbal fluency in both central (r53=0.365, p=0.007) and frontal electrodes (r53=0.326, p=0.017), and fast spindle density was associated with processing speed in the central electrodes (r53=0.357, p=0.009). Furthermore, females had greater density of fast spindles compared to males; however, only males with greater density of fast spindles showed better processing speed (r29=0.468, p=0.010).

Conclusion: Reduced spindle density, especially in the fast frequency range, may be a biomarker of cognitive decline in severe OSA and sex may play a role in modifying this relationship.

ORAL SESSION 5: Sleep and Neurodegenerative Diseases

DATE: 10/30/2021

START TIME: 2:15 PM END TIME: 3:45 PM

SESSION TITLE:

The effects of exercise on sleep quality in persons with Parkinson's Disease: a systematic review with meta-analysis.

PRESENTING AUTHOR: *Cristini, Jacopo[1,2]*

CO-AUTHORS: *Weiss, Maxana[1,2]; de Las Heras, Bernat[1,2]; Medina-Rincón, Almudena[1,3]; Dagher, Alain[4]; Postuma, Ronald B.[4]; Huber, Reto[5]; Doyon, Julien[4]; Rosa-Neto, Pedro[6]; Carrier, Julie[7]; Amara, Amy W.[8]; Roig, Marc[1,2]*

AFFILIATIONS: *1 Memory and Motor Rehabilitation Laboratory (MEMORY-LAB), Feil and Oberfeld Research Centre, Jewish Rehabilitation Hospital, Montreal Center for Interdisciplinary Research in Rehabilitation (CRIR), Laval, Quebec, Canada ; 2 School of Physical and Occupational Therapy, Faculty of Medicine, McGill University, Montreal, Quebec, Canada. ; 3 Universitat Internacional de Catalunya, Barcelona, Catalonia, Spain. ; 4 Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada. ; 5 Child Development Center, University Children's Hospital and Department of Child and Adolescent Psychiatry and Psychotherapy, Psychiatric Hospital, University of Zurich. 6 Department of Psychiatry, McGill University, Montreal, Quebec, Canada. ; 7 Université de Montréal, Montréal, Quebec, Canada. ; 8 University of Alabama at Birmingham, Alabama, USA.*

DESCRIPTION:

We conducted a systematic review with meta-analysis to determine the evidence in support of exercise to improve sleep quality assessed subjectively and objectively in Parkinson's Disease (PD). Standardized mean differences (SMD) comparing the effects of exercise and control interventions on sleep quality with 95% confidence intervals (CI) were calculated. Data from 10 randomized and 2 non-randomized controlled trials, including a total of 690 persons with PD were included. Exercise had a significant positive effect on sleep quality assessed subjectively (SMD = 0.53; 95% CI = 0.16-0.90; p = 0.005). However, the methodological quality of the studies showing positive effects on sleep quality was significantly poorer than the studies showing no effects. Only one study assessed the impact of exercise on objective sleep quality, showing improvements in sleep efficiency assessed with polysomnography (SMD = 0.94; 95% CI = 0.38-1.50; p = 0.001). Exercise performed at moderate to maximal intensities (SMD = 0.46; 95% CI = 0.05-0.87; p = 0.03) had significant effects on subjective sleep quality. In contrast, exercise performed at mild to moderate intensities showed non-significant effects (SMD = 0.76; 95% CI = 0.24-1.76; p = 0.14). These results support the use of exercise to improve sleep quality in persons with PD and reinforce the importance of achieving vigorous exercise intensities. Biases, limitations, practice points and directions for future research are discussed.

ORAL SESSION 6: Sleep, Emotional Regulation and Insomnia

DATE: 10/30/2021
START TIME: 2:15 PM END TIME: 3:45 PM
SESSION TITLE:

A Systematic Review of Insomnia Symptoms in School Teachers

PRESENTING AUTHOR: *Jackowich, Robyn* [1]
CO-AUTHORS: *Gierc, Madelaine*[1]*; Davidson, Judith*[1]

DESCRIPTION:

Although the demands and stress of teaching are generally recognized, little is known about the prevalence and nature of insomnia symptoms in teachers. We conducted a systematic review to address three questions: How prevalent are insomnia symptoms in teachers? What biopsychosocial variables are associated with insomnia symptoms in teachers? What, if any, interventions for insomnia symptoms in teachers have been studied? We searched Medline, PsycInfo, Embase, CINAHL, Education Source and ERIC for original peer-reviewed research on school teachers (kindergarten through high school) and insomnia symptoms (self-reported trouble falling or staying asleep). We identified 33 relevant articles from 15 countries. The literature was highly heterogeneous and generally of low quality with respect to the measurement of insomnia. Based on studies that met validity and reliability criteria, 36-61% of teachers reported insomnia symptoms. Associated factors included being female, work hours, workplace violence, low job satisfaction, pain, depression, and rumination. One online intervention, which included stimulus control, sleep restriction and techniques for reducing rumination, provided evidence of efficacy. High-quality research focused on insomnia symptoms in teachers is needed, including studies over the school year, identification of antecedents of insomnia, and development of interventions with the ultimate goals of understanding, preventing, and treating insomnia symptoms in teachers.

ORAL SESSION 6: Sleep, Emotional Regulation and Insomnia

DATE: 10/30/2021

START TIME: 2:15 PM END TIME: 3:45 PM

SESSION TITLE:

An open-label study on sleep spindle density in people with depression after 8 weeks of melatonin agonist intake

PRESENTING AUTHOR: *Porteous, Meggan[1,2]*

CO-AUTHORS: *Fogel, S.M.[1,2]; Ray, L.B.[1,2] ; Hickie, Ian[3] ; Carpenter, Joanne[3] ; Louati, Khaoula[2] ; Robillard, Rebecca[1,2]*

AFFILIATIONS: *1 Sleep Research Unit, The Royal Institute for Mental Health Research, Ottawa, ON, Canada; 2 School of Psychology, Faculty of Social Sciences, University of Ottawa, Ottawa, ON, Canada; 3 Brain & Mind Centre, the University of Sydney, Camperdown, NSW, Australia*

DESCRIPTION:

Depression is often associated with sleep disturbances and reductions in sleep spindles. Sleep spindles are known to play a protective role for sleep, and there are indications that melatonin agents can enhance spindles in healthy people. It is unknown if agomelatine, a melatonin agonist used in the treatment of depression, may increase spindle density sufficiently to impact sleep continuity in people with depression. This proof-of-concept study investigated changes in spindles following agomelatine intake in young adults with depression and assessed how they may relate to potential changes in sleep continuity and depressive symptoms. This study was based on an open-label design. Fifteen participants between 17 and 28 years of age (mean =22; SD=3.8) with a diagnosis of a depressive disorder underwent polysomnography before and after an intervention including sleep psychoeducation and an 8-week course of agomelatine (25–50 mg) with a guided sleep phase advance. Fast spindle density significantly increased from pre to post-intervention. This increase in spindle density significantly correlated with a reduction in wake after sleep onset, and a similar trend was found with increased sleep efficiency. There was no significant correlation between spindle parameters and depressive symptoms. Agomelatine may enhance sleep consolidation through the modulation of spindle production. Larger randomized control trials are needed to confirm these findings but they offer promising information about the impact of agomelatine on significant sleep symptoms associated to depression.

ORAL SESSION 6: Sleep, Emotional Regulation and Insomnia

DATE: 10/30/2021

START TIME: 2:15 PM END TIME: 3:45 PM

SESSION TITLE:

Dream Enactment Behavior and Trauma-associated Sleep Disorder in those Experienced Childhood Maltreatment: a Population-based Study in the CLSA

PRESENTING AUTHOR: *Yao, Chun*[1]

CO-AUTHORS: *Yao, Chun*[1,2] *; Baltzan, M.*[2-6] *; Pelletier, Amélie*[2,7]*; Postuma, Ronald B.*[2,7,8]

AFFILIATIONS: *1 Integrated Program in Neuroscience, McGill University; 2 Research Institute of the McGill University Health Centre; 3 Faculty of Medicine, Department of Epidemiology Biostatistics and Occupational Health, McGill University; 4 Centre Intégré Universitaire des Soins et Services Sociaux du Nord de L'île de Montréal; 5 Centre Intégré Universitaire des Soins et Services Sociaux du Centre-ouest de L'île de Montréal, Mount Sinai Hospital; 6 Institut de Médecine du Sommeil ; 7 Research center of the Hôpital du Sacré-Coeur de Montréal; 8 Department of Neurology and Neurosurgery, McGill University.*

DESCRIPTION:

Introduction: Dream enactment behavior is best known for its presence in REM sleep behavior disorder, the strongest prodromal predictor of parkinsonism. In recent years, dream enactment behavior has also been reported in a few psychiatric case-series among patients with post-traumatic stress disorder.

Study Objectives: To assess the associations between the occurrence of dream enactment behavior (with or without PTSD) and childhood maltreatment.

Methods: We included those aged 45-85 years, living in one of 10 Canadian provinces in between 2012-2015 (at the baseline), recruited via three population-based sampling methods. Dream enactment behavior was assessed using the RBD-1Q single-question questionnaire. Post-traumatic stress disorder (PTSD) was screened using the primary-care PTSD. Trauma-associated sleep disorder was defined as a positive screen on both RBD-1Q and PC-PTSD. A panel of questions were queried to assess the frequency of childhood maltreatment. Associations between the affected groups and the symptom naïve groups were assessed, adjusting for age and sex via logistic regression.

Results: Overall, 1,503/30,097 participants screened positive for post-traumatic stress disorder and 3,328 for dream enactment behavior. Of these, 271 participants endorsed both post-traumatic stress disorder and dream enactment behavior. Those with post-traumatic stress disorder and/or dream enactment behavior were slightly younger. Post-traumatic stress disorder was more common among females than males, whereas, dream enactment behavior was more common in males. No clear difference in the prevalence of trauma-associated sleep disorder was found between sexes. On average, experiences of childhood maltreatment were more common in those with dream enactment behavior and/or post-traumatic stress disorder. Of the three symptom groups, the association was stronger in those with either post-traumatic stress disorder or trauma-associated sleep disorder.

Conclusions: Childhood maltreatment was associated with post-traumatic stress disorder, trauma-associated sleep disorder and dream enactment behavior in later life.

ORAL SESSION 6: Sleep, Emotional Regulation and Insomnia

DATE: 10/30/2021

START TIME: 2:15 PM END TIME: 3:45 PM

SESSION TITLE:

The prevalence and predictors of postpartum anger and depression in the context of maternal-infant sleep problems.

PRESENTING AUTHOR: *Ou, Christine*[1]

CO-AUTHORS: *Hall, Wendy*[1]*; Rodney, Patricia*[1]*; Stremler, Robyn*[2]

AFFILIATIONS: *1 School of Nursing, University of British Columbia; 2 Lawrence Bloomberg Faculty of Nursing, University of Toronto*

DESCRIPTION:

Introduction: Maternal anger has been overlooked as a postnatal mood disturbance. The empirical literature supports a strong relationship between sleep and mental health. Proportions of women experiencing anger and whether maternal-infant sleep problems are associated with anger as a postpartum mood disturbance are unknown.

Objectives: 1) Examine relationships between anger, maternal-infant sleep characteristics, and depressive symptoms for women in the first postnatal year. 2) Explain the development and management of maternal anger about maternal-infant sleep.

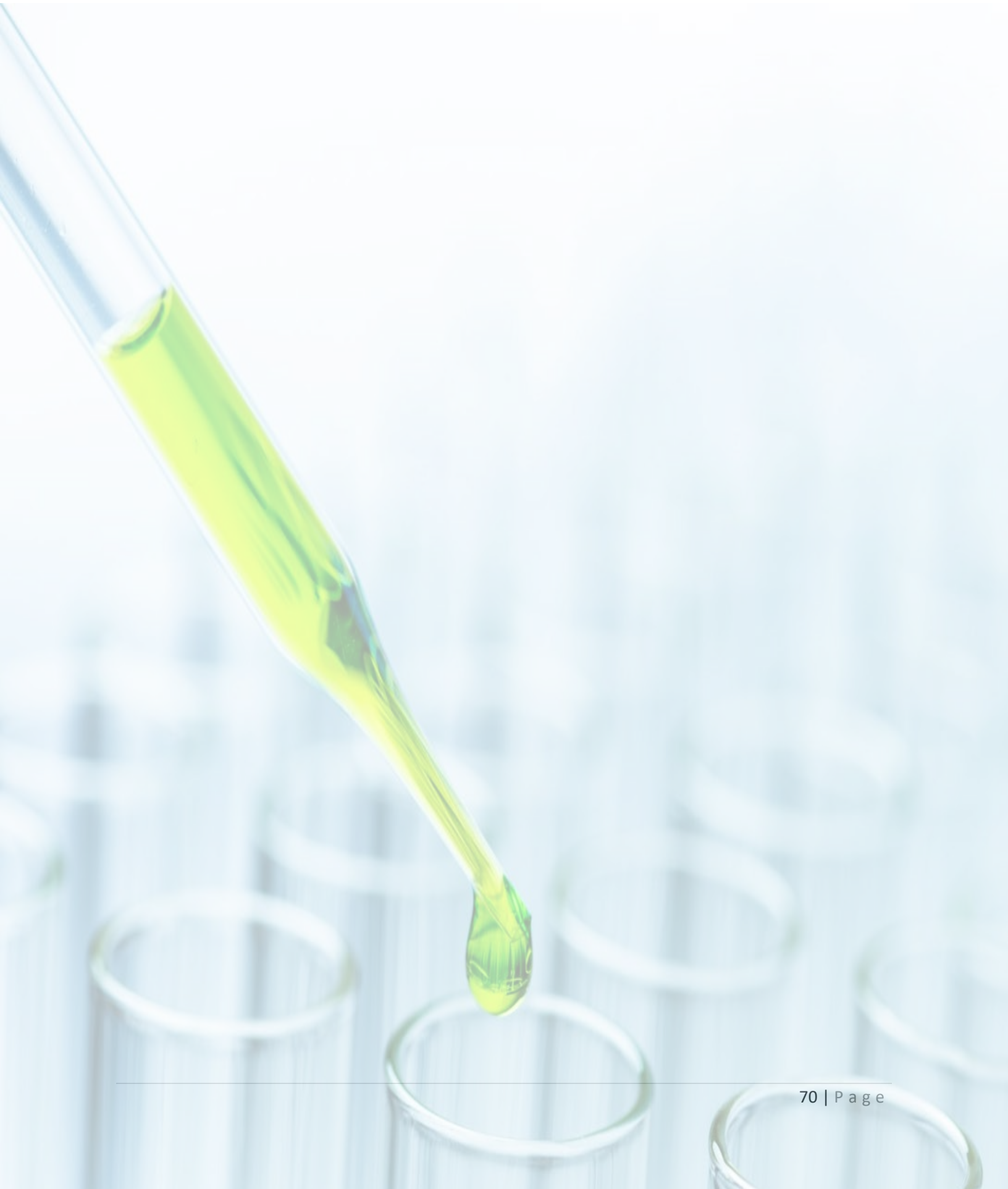
Methods: Social media was used to recruit Canadian mothers of infants between 6 and 12 months of age to complete an online survey about maternal-infant sleep after receiving ethical approval. The survey inquired about maternal-infant sleep quality, maternal fatigue, cognitions about infant sleep, support, anger, and depressive symptoms. A subset of women completing the online survey participated in telephone interviews, with the goal of generating a theory about anger after childbirth. Phone interviews were transcribed and data were analyzed using grounded theory methods.

Results: Of the 278 women who completed the survey, 70% perceived their infant's sleep as problematic. Regarding mood, 31% had high levels of anger and 26% had depressive symptoms above the cut-off score. Robust regression analysis revealed that parity ($b = 1.93$, $p < .001$), depression ($b = .50$, $p = .008$), and anger about infant sleep ($b = .46$, $p < .001$), predicted maternal postpartum anger. An interaction term between anger about infant sleep and infant age also predicted maternal anger ($b = 0.13$, $p < .001$).

Eighteen mothers described their experiences of anger in their first two postpartum years. Mothers' violated expectations and compromised needs around sleep, and being on edge contributed to feeling angry. Appropriate support from partners, family, and others, helped women manage their anger. Absent and inappropriate support prolonged maternal anger about violated expectations and compromised needs, particularly about infant sleep issues. Participants expressed or suppressed their anger with differing effects on support, relationships, and control.

Conclusion:

Anger in the postpartum period has negative effects for women and families; it can be comorbid with insomnia and depression symptoms. Clinician support around evidence-based strategies to promote maternal-infant sleep and family members' support to help meet womens' psychosocial and physical needs can reduce anger. Women require screening for anger and sleep problems after childbirth. Policy change required include structural support for women and families in the postnatal period.



POSTER SESSION 2

DATE: 10/30/2021
START TIME: 3:45 PM END TIME: 5:00 PM

PS2:S200
ABSTRACT TITLE:

Parents' Sleep-Related Practices and Perceived Pressure: An Exploratory Study

PRESENTING AUTHOR: *Lannes, Émilie[1,2]*
CO-AUTHORS:
Kenny, Samantha[1,2]; Burdayron, Rebecca[1,2]; Dubois-Comtois, Karine[2,3]; Béliveau, Marie-Julie[2,4]; Pennestri, Marie-Hélène[1,2]
AFFILIATIONS:
1 McGill University, 2 Hôpital en santé mentale Rivière-des-Prairies (CIUSSS-NÎM), 3 Université du Québec à Trois-Rivières, 4 Université de Montréal

DESCRIPTION:

Introduction
Throughout the postpartum period, parents are exposed to a lot of information about infant sleep. Unfortunately, this information is sometimes contradictory, which can leave parents feeling confused and with a heightened sense of pressure to follow certain practices. In studies investigating parenting, this perceived pressure is often associated with higher levels of stress; yet, pressure about sleep-related practices has seldom been investigated in both mothers and fathers. This study aimed to 1) assess the proportion of mothers and fathers of six-month-old infants who report feeling pressure about their sleep-related parenting practices and 2) evaluate the associations among this perceived pressure, demographic factors and sleep-related parenting practices in both mothers and fathers.
Methods
One hundred parents (54 mothers) of 6-month-old infants completed the Sleep Practices Questionnaire (SPQ) and a demographic questionnaire. To assess perceived pressure about sleep-related parenting practices, parents were asked the question "Have you ever felt pressure about your parenting choices and practices related to your child's sleep?". Responses ranged from "Never" to "Always". Linear regressions were used to measure the associations among levels of perceived pressure and 1) demographic factors (education level, age, parity) and 2) parental sleep-related practices (feeding method, frequency of bed-sharing, picking up or not picking up the infant when he/she cries at night), separately for mothers and fathers.
Results
Analyses revealed that 26.0% of mothers reported feeling pressure constantly or quite often, 46.3% reported feeling pressure sometimes, and about a quarter (27.7%) reported feeling pressure rarely or never. In fathers, 8.7% reported feeling pressure constantly or quite often, 28.3% reported feeling pressure sometimes, and 63.0% reported feeling pressure rarely or never. Lower maternal education and the presence of breastfeeding were associated with feeling more pressure about sleep-related parenting practices ($p < .05$). Furthermore, mothers reporting that they (or their partner) pick up their infant when he/she cries at night were more likely to report feeling pressure ($p < .01$). First-time fathers were more likely to report feeling pressure ($p < .01$) than non-first-time fathers, but this was not the case for mothers ($p > .05$).

However, paternal education and paternal reports of picking the infant when he/she cries at night were not associated with feeling pressure about sleep-related parenting practices ($p > .05$). Mothers' and fathers' age and frequency of bed-sharing were not associated with feeling pressure ($p > .05$).

Conclusion

The majority of mothers (72.3%) in our sample reported feeling pressure about their sleep-related parenting practices at least sometimes, suggesting that this experience is quite common. In contrast, only 37% of fathers reported feeling pressure at least sometimes. Factors associated with higher perceived pressure were not necessarily the same in mothers and fathers. Future studies should examine feelings of pressure about sleep-related parenting practices in larger samples of parents and investigate the reasons behind the discrepancy between mothers' and fathers' experiences. Interventions targeting perceived pressure could alleviate some of the stress new parents feel related to their parenting practices, and in turn, could positively impact their general well-being.

Support

Social Sciences and Humanities Research Council (SSHRC), Fonds de recherche du Québec – Santé (FRQS)

PS2:S201

ABSTRACT TITLE:

Placebo-Controlled, Double-Blind, Randomized Withdrawal Study of Lower-Sodium Oxybate in Adults With Idiopathic Hypersomnia

PRESENTING AUTHOR: *Foldvary-Schaefer, Nancy[4]*

CO-AUTHORS: *Arnulf, Isabelle[3]; Chandler, Patricia[5]; Parvataneni, Rupa[5]; Chen, Dan[5]; Skobieranda, Franck[6]; Bogan, Richard K.[7]; Dauvilliers, Yves[1,2]*

AFFILIATIONS: *1 Sleep and Wake Disorders Centre, Department of Neurology, Gui de Chauliac Hospital, Montpellier, France; 2 University of Montpellier, INM INSERM, Montpellier, France; 3 Sleep Disorder Unit, Pitié-Salpêtrière Hospital and Sorbonne University, Paris, France; 4 Cleveland Clinic Lerner College of Medicine, Cleveland, OH, USA; 5 Jazz Pharmaceuticals, Inc., Palo Alto, CA, USA; 6 Jazz Pharmaceuticals, Inc., Philadelphia, PA, USA; 7 University of South Carolina School of Medicine, Columbia, SC, USA*

DESCRIPTION:

Introduction: Idiopathic hypersomnia (IH) is a central hypersomnolence disorder characterized by excessive daytime sleepiness, prolonged nighttime sleep, and sleep inertia. No Canadian/US/EU medication is approved for treatment of IH. Lower-sodium oxybate (LXB; Xywav™; formerly designated JZP-258) is a novel oxybate medication with 92% less sodium than sodium oxybate (Xyrem®). The US Food and Drug Administration approved LXB in July 2020 for the treatment of cataplexy or excessive daytime sleepiness in patients 7 years of age and older with narcolepsy.

Objective: The efficacy and safety of LXB was evaluated in adults with IH.

Methods: Eligible participants aged 18–75 years with IH began once- or twice-nightly LXB treatment in an open-label titration and optimization period (10–14 weeks), followed by a 2-week, open-label, stable-dose period (SDP), and were then randomized to placebo or to continue LXB treatment during a 2-week, double-blind, randomized withdrawal period (DBRWP). The primary efficacy endpoint was change in Epworth Sleepiness Scale (ESS) score; key secondary endpoints were proportion of participants who reported worsening (minimally/much/very much worse) on Patient Global Impression of Change (PGIc) and change in Idiopathic Hypersomnia Severity Scale (IHSS) score, all from end of SDP to end of DBRWP.

Results: The study enrolled 154 participants (mean±SD age, 40±14 years; 68% female; mean±SD ESS, 16±3.6); mean±SD dose was 6.0±1.6 g/night. Mean±SD ESS score (n=115) decreased over open-label titration/optimization (15.7±3.8 at baseline, 9.8±4.5 at week 4, and 6.1±4.0 at the end of the SDP). At the end of the DBRWP, significant worsening was observed in participants randomized to placebo, compared with maintenance of improvement in participants randomized to continue LXB, in ESS scores (n=115; LS mean difference [95% CI] in change from SDP, −6.51 [−7.99, −5.03]; P<0.0001), in the PGIc (88.1% for placebo vs 21.4% for LXB; P<0.0001), and in IHSS scores (estimated median difference [95% CI], −12.00 [−15.0, −8.0]; P<0.0001). Common adverse events (AEs) included nausea (21.4%), headache (16.2%), dizziness (11.7%), anxiety (10.4%), and vomiting (10.4%). Serious AEs occurred in 4 participants (non-cardiac chest pain, rhabdomyolysis, syncope, and nephrolithiasis/pyelonephritis); none were reported as related to study drug.

Conclusion: In participants with IH, LXB demonstrated a clinically meaningful effect on excessive daytime sleepiness, self-reported global change, and overall IH symptom severity. The overall safety profile was consistent with that of LXB in narcolepsy.

PS2:S203

ABSTRACT TITLE:

Daily associations between sleep and physical activity: A systematic review and me-ta-analysis

PRESENTING AUTHOR: *Atoui, Sarah[1,2]*

CO-AUTHORS: *Chevance, G.[3]; Romain, A.J.[2,4]; Kingsbury, C.[1,2]; Lachance, J.P.[2]; Bernard, P.[1,2]*

AFFILIATIONS: *1 Department of Physical Activity Sciences, Université du Québec à Montréal, Montréal, Québec, Canada; 2 Research Center, University Institute of Mental Health at Montreal, Montréal, Quebec, Canada; 3 Center for Wireless & Population Health Systems, Department of Family Medicine and Public Health, UC San Diego; 4 École de kinésiologie et des sciences de l'activité physique, Faculté de Médecine, Université de Montréal, Montréal, Québec, Canada*

DESCRIPTION:

Introduction: The day-to-day variations of sleep and physical activity are associated with various health outcomes in adults, and previous studies suggested a bidirectional association between these behaviors. The daily associations between sleep and physical activity have been examined in observational or interventional contexts. Objectives: The current systematic review and meta-analysis's primary goal was to summarize existing evidence about daily associations between sleep and physical activity outcomes at the inter-and intra-individual level in adults. Methods: A systematic search of records in eight databases from inception to July 2019 identified 33 peer-reviewed empirical publications that examined daily sleep – physical activity association in adults. Results: The qualitative and quantitative analyses of included studies did not support a bidirectional daily association between sleep outcomes and physical activity. Multilevel meta-analyses showed that three sleep parameters were associated with physical activity the following day: sleep quality, sleep efficiency, and wake after sleep onset. However, the associations were small and varied in terms of direction and level of variability (e.g. inter- or intra-individual). The daytime physical activity was associated with lower total sleep time the following night at an inter-person level with a small effect size. Conclusion: From a clinical perspective, care providers should monitor the effects of better sleep promotion on their patients' physical activity behaviours. Future studies should examine sleep and physical activity during a longer period and perform additional sophisticated statistical analyses.

PS2:S204

ABSTRACT TITLE:

Relationship between Gastroesophageal Reflux Disease and Objective Sleep Quality: a Retrospective Cohort Study

PRESENTING AUTHOR: *Gurges, Patrick, MSc[1,2,3]*

CO-AUTHORS: *Murray, Brian, MD[1,2,3]; Boulos, Mark I. MD MSc[1,2,3]*

AFFILIATIONS: *1 Hurvitz Brain Sciences Research Program, Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada; 2 Department of Medicine, Division of Neurology, University of Toronto, Toronto, Ontario, Canada; 3 Sleep Laboratory, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada*

DESCRIPTION:

Introduction:

Gastroesophageal reflux disease (GERD) is a common disorder characterized by recurring reflux of stomach contents into the esophagus. Previous literature examining the link between GERD and sleep quality has primarily relied on self-reported sleep questionnaires or involved small sample sizes. We sought to objectively characterize the relationship between GERD and sleep quality using a large database of patients who had completed in-laboratory polysomnography.

Methods:

We retrospectively analyzed first-night diagnostic in-laboratory polysomnography data for 3770 patients (mean age 54.7 years; 52% male). Medication use and medical comorbidities were obtained through self-reported patient questionnaires. We considered a patient to have GERD if they reported the presence of this condition and were also using a proton-pump inhibitor (PPI) or H2-blocker. Associations between sleep quality and the presence of GERD were analyzed using multivariable linear regression models.

Results:

The presence of GERD with concomitant PPI/H2-blocker use was reported by 6.9% of patients (244/3770; mean (±SD) age 62.8±14.0 years; 36% male). After adjusting for age, sex and BMI, the presence of GERD was significantly associated with a 16.9 minute decrease in total sleep time (95% CI: -27.5 to –6.4, p=0.002), 3.8% decrease in sleep efficiency (95% CI: -6.1 to –1.5, p=0.001), 9.7 minute increase in wake after sleep onset (95% CI: 1.72 to 17.60, p=0.017), 1.39% increase in the duration of N3 sleep (95% CI: 0.07 to 2.7, p=0.039), 1.68% decrease in the duration of rapid eye movement (REM) sleep (95% CI: -2.69 to –0.67, p=0.001), and a 26.7 minute increase in REM latency (95% CI: 15.4 to 38.0, p<0.001). There were no significant associations between GERD and the duration of either N1 or N2 sleep.

Conclusion:

The presence of GERD was associated with a reduction in total sleep time, sleep efficiency, and duration of REM sleep, and an increase in wake after sleep onset, duration of N3 sleep, and REM latency, as objectively measured by in-laboratory polysomnography. These findings reinforce the need for physicians to recognize the potential for poor sleep quality in patients with GERD.

PS2:S205

ABSTRACT TITLE:

REM sleep EEG activity and clinical correlates in adults with autism

PRESENTING AUTHOR: *Gagnon, Katia*[1]

CO-AUTHORS: *Bolduc, Christianne*[1] *; Bastien, Laurianne*[1]*; Godbout, Roger*[1]

AFFILIATIONS: *1 Université de Montréal*

DESCRIPTION:

We tested the hypothesis of an atypical scalp distribution of electroencephalography (EEG) activity in autism during rapid eye movement (REM) sleep. EEG spectral activity and ratios along the anteroposterior axis and across hemispheres were compared in 15 neurotypical (NT) young adults and 17 individuals with autism spectrum disorder (ASD). EEG spectral power was lower in the ASD group over the bilateral central and right parietal (beta activity) as well as bilateral occipital (beta, theta, and total activity) recording sites. The NT group displayed a significant posterior polarity of intra-hemispheric EEG activity while EEG activity was more evenly or anteriorly distributed in ASD participants. No significant inter-hemispheric lateralization of EEG was found. Correlations between ASD symptom severity and EEG distribution showed that a higher posterior ratio was associated with better Autism Diagnostic Interview-Revised (ADI-R) score on communication skill, whereas a higher anterior ratio was related to more restricted interests and repetitive behaviors on the same questionnaire. EEG activity thus appears to be atypically distributed over the scalp surface in autism during REM sleep within cerebral hemispheres. This suggests an atypical organization and/or functioning of the thalamo-cortical loop during REM sleep in autism.

PS2:S206

ABSTRACT TITLE:

Self-reported changes in sleep and psychological distress among older adults during the COVID-19 pandemic

PRESENTING AUTHOR: *Gong, Kirsten [1,2,3,4]*

CO-AUTHORS: *Vasiliadis, Helen-Maria[5]; Grenier, Sébastien [6] Dang-Vu, Thien Thanh[1,3,4,7]; Gouin, Jean-Philippe [2,3,7]*

AFFILIATIONS: *1 Sleep, Cognition and Neuroimaging Lab, Department of Health, Kinesiology and Applied Physiology, Concordia University, Montreal, Quebec, Canada; 2 Stress, Interpersonal Relationship and Health Lab, Department of Psychology, Concordia University, Montreal, Quebec, Canada; 3 PERFORM Center, Concordia University, Montreal, Quebec, Canada ; 4 Center for Studies in Behavioral Neurobiology, Concordia University, Montreal, Quebec, Canada; 5 Université de Sherbrooke, Longueuil, Quebec, Canada ; 6 Université de Montréal, Montreal, Quebec, Canada; 7 Centre de recherche de l'Institut universitaire de gériatrie de Montréal (CRIUGM), CIUSSS Centre-Sud-de-l'île-de-Montréal, Montreal, Quebec, Canada*

DESCRIPTION:

Introduction:

Sleep difficulties, including insomnia, are common in older adults. Although stressful life events can negatively impact sleep, it is unclear if the prolonged COVID-19 pandemic has led to an increased prevalence of sleep disturbances and psychological distress among older adults.

Research Objectives:

The study aimed at examining if there were changes in sleep and psychological distress in older adults during the COVID-19 pandemic.

Methods:

In mid-April (T1), mid-June (T2), and September (T3) of year 2020, 331 older adults (78.55 ± 5.21 years; 237 females) completed online questionnaires: Insomnia Severity Index (ISI), Pittsburgh Sleep Quality Index (PSQI), and Kessler Psychological Distress Scale (K10).

Results:

There was no main effect of time on total ISI scores, $F(1.935, 638.683) = 0.458$, $p = .626$, $\eta_p^2 = .001$. There was no main effect of time on PSQI items about sleep latency, sleep quality, sleep efficiency, and sleep or nap duration (all $p > .05$). However, older adults felt less rested at T2 than at T1 and spent more time awake after sleep onset at T3 than at T1 (35.387 ± 2.788 vs. 28.851 ± 2.325 minutes). Women had more difficulty falling asleep, napped less, and felt less rested than men across the three timepoints (all $p < .05$). There was no main effect of time on total K10 scores, $F(2, 660) = 0.997$, $p = .369$, $\eta_p^2 = .003$. Nevertheless, older adults felt more depressed at T1 than at T2 ($p = .021$). Women had more psychological distress symptoms than men at all timepoints ($p < .001$).

ISI scores were positively correlated with K10 scores at all timepoints ($r(329) = .338–.468$, $p < .001$). Older adults with more psychological distress (i.e., K10 > 19) at T1 obtained higher total ISI scores than those with less psychological distress (i.e., K10 ≤ 19) at all timepoints ($p < .001$). They had more difficulty falling or staying asleep, early awakenings, and sleep dissatisfaction (all $p < .05$). Their sleep problems were more noticeable to others and they were more worried about their sleep ($p < .001$). Only those who had more psychological distress at T1 reported that their sleep problems interfered more with their daily functioning at T1 than at T2 and T3 ($p = .008$). Older adults with greater insomnia severity (i.e., ISI > 7) at T1 obtained higher total K10 scores than those with no clinically significant insomnia (i.e., ISI ≤ 7) at all timepoints ($p < .001$). They

felt more tired, nervous, restless, depressed, sad, and worthless (all $p < .05$). Everything also felt more of an effort ($p < .001$). Only those who had greater insomnia severity at T1 felt more hopeless at T3 than at T1 and T2 ($p = .001$).

Conclusion:

Overall, there was a relation between sleep disturbances and psychological distress in older adults. Women had more sleep difficulties and psychological distress than men. Thus, future research should be aimed at developing effective strategies for older adults to reduce sleep disturbances and psychological distress associated with the pandemic.

PS2:S207

ABSTRACT TITLE:

Sleep and Hippocampal Function during an Associative Memory Task are Influenced by Surgical Menopause at Midlife

PRESENTING AUTHOR: *Brown, Alana[1]*

CO-AUTHORS: *Gervais, Nicole[1,2]; Gravelsins, Laura[1]; Nicoll, Gina[1]; Rieck, Jenny[2]; Almey, Anne[1]; Leqi-Sun, Dorothy[1]; Ge, Jennifer Xiangnin[1]; Laird, Kaz[1]; Grady, Cheryl[1,2]; Einstein, Gillian[1,2,3]*

AFFILIATIONS: *1 University of Toronto; 2 Rotman Research Institute at Baycrest Health Sciences; 3 Tema Genus at Linköping University*

DESCRIPTION:

Introduction and objectives: 17β-estradiol loss is related to Alzheimer's disease (AD) risk factors, including disordered sleep and associative memory decrements (Gervais et al., 2017; Rentz et al., 2017). Women have higher risk for AD than men, and those with mid-life 17β-estradiol loss due to surgical menopause, including bilateral salpingo-oophorectomy (BSO) before age 48, have even higher risk (Rocca et al., 2007). Our objective was to investigate whether sleep and associative memory in women with BSO (mean age 44-46) would be comparable to those with spontaneous/natural menopause (SM; mean age 57), and whether 17β-estradiol-based hormone therapy (ET) might mitigate these effects.

Methods: We assessed sleep using the average of three nights of portable polysomnography (Temec) in women with BSO either taking ET (BSO+ET; n=16), or not (BSO; n=18), and in older spontaneously menopausal women (SM; n=14). Using EEG (Fp1-Fp2), we obtained sleep staging automatically (Neurobit Technologies). Participants also completed a face-name associative memory task during functional magnetic resonance imaging. Recognition accuracy and brain activation during encoding were measured.

Results: BSO exhibited reduced sleep efficiency compared to BSO+ET. For BSO, there was no relationship between percent of total sleep time in N3 and hippocampal activation during associative encoding, even though percent of total sleep time in N3 was negatively associated with hippocampal activation during associative encoding in BSO+ET. For all groups, including BSO, lower latency to consolidated N3 correlated with better associative memory accuracy. There were no group differences in associative memory accuracy. In contrast to BSO, SM showed significantly longer latency to consolidated N3 than BSO+ET.

Conclusion: Younger women with BSO have comparable sleep to older women in SM. In younger women with BSO, ET improves sleep efficiency. Further, while associative memory may be disrupted by increased latency to consolidated N3 in all women, BSO and BSO+ET showed similar associative memory accuracy and latency to consolidated N3. Only BSO+ET exhibited a significant correlation between hippocampal activity during associative encoding and time spent in N3, indicating that ET may support the negative relationship between N3 and hippocampal function. Overall, ET in younger women with BSO potentially ameliorates poor sleep and associative memory decrements.

PS2:S208

ABSTRACT TITLE:

Sleep instability correlates with attentional impairment in boys with attention deficit hyperactivity disorder.

PRESENTING AUTHOR: *Gagnon, Katia*[1]

CO-AUTHORS: *Gingras, Marc-André*[1]*; Labrosse, Melanie*[1]*; Godbout, Roger*[1]

AFFILIATIONS: *1 Université de Montréal*

DESCRIPTION:

Introduction. Theoretical models of sleep and attention deficit hyperactivity disorder (ADHD) suggest that symptoms of ADHD are associated with daytime somnolence but it has received little support. Consequently, it is expected that ADHD could lead to. Our study aimed at testing an alternative model involving the association of attentional instability with sleep instability.
Method. Twelve ADHD and 15 healthy control (HC) boys aged between 8 and 12 years old underwent two nights of polysomnography and attentional testing. Children with ADHD had no comorbidity and were withdrawn from psychostimulant medication for 48 hours before sleep recording and attention testing. Participants underwent two nights of polysomnography to mitigate the first night effect. The microarousal index, the number of awakenings and the number of stage shifts between stages 1, 2, 3, 4 and REM through the night were computed as sleep stability parameters. Attentional functioning was assessed using the Continuous Performance Test-II. Student-t tests were used to test between group differences on sleep stability. The association between sleep stability variables and attention measures were tested with Pearson's correlations.
Results. We found a significantly higher microarousal index in stage 1 ($t(25)=-2.25$; $p = 0.03$), more transitions from stage 4 to 3 ($t(25) =-2.08$; $p = 0.048$) and more transitions between stages 2 and REM ($t(25) = -2.12$; $p = 0.04$) in ADHD compared to HC. Stage 1 micro arousal index in ADHD positively correlated with higher omissions ($r = 0.78$; $p = 0.007$) and commission scores ($r = 0.77$; $p = 0.005$) on the Continuous Performance Test-II. Higher omission scores were associated with more transitions from stage 4 to 3 ($r = 0.69$; $p= 0.02$) in ADHD. HC had significantly more transitions between stage 2 and 4 ($t(25) =2.14$; $p = 0.04$) than ADHD. No association whatsoever was found between sleep instability and attentional functioning in HC.
Conclusion. The results show that sleep instability is associated with lower attentional performance in boys with ADHD, but not in HC. This supports a model according to which attention and sleep stability share a common neural substrate in ADHD.

PS2:S209

ABSTRACT TITLE:

Sleep Problems as a Predictor of Emotional and Behavioral Difficulties in Gifted and Twice Exceptional Children

PRESENTING AUTHOR: *Théoret, Rachel*[1]

CO-AUTHORS:

Bastien, Laurianne[1,2] *; Godbout, Roger*[1,3]

AFFILIATIONS: *1 Sleep Laboratory & Clinic, Hôpital en santé mentale Rivière-des-Prairies, CIUSSS du Nord-de-l'Île-de-Montréal, Montreal, Canada; 2 Department of Psychology, Université de Montréal, Montreal, Canada; 3 Department of Psychiatry, Université de Montréal, Montreal, Canada*

DESCRIPTION:

Introduction:

There is an asynchrony between intellectual development and social-emotional development in gifted (G) children. G children with a neurodevelopmental disorder (NDD) are identified as twice exceptional (2e). Sleep plays a regulatory role on daytime functioning. Children with a NDD tend to have more sleep difficulties than typically developing peers (TD) and some differences have been reported between G and TD children. Objectives: assess the relationship between sleep problems and emotional and behavioral difficulties in G, 2e and TD children and seek for group differences.

Method:

Sixty-seven children were studied: 36 G (10.1±1.3 years old), 15 2e (10.7±1.7 years old) and 16 TD (10.6±1.9 years old). Giftedness was diagnosed by a clinician based on Renzulli's criteria. Sleep problems were assessed with the Children's Sleep Habit Questionnaire (CSHQ). Emotional/behavioral difficulties were assessed with the Child Behavior Checklist (CBCL). One-way ANOVAs with Bonferroni post-hoc tests were used to compare group means for the CSHQ's eight subscales and total score. One-way ANOVAs were used to compare group means for the CBCL's eight syndrome scales, internalizing, externalizing and total problems, and its six DSM-oriented scales. Linear regression were used to assess the relationship between sleep problems and emotional/behavioral difficulties for each group, with the CSHQ's total score as the independent variable and each CBCL scale as dependent variables.

Results:

For the CSHQ scales, significant differences were found for Sleep Onset Delay (SOD; $F(2,64) = 4.27$, $p < 0.05$) and Sleep Duration (SD; $F(2,64) = 3.40$, $p < 0.05$). Post-hoc tests showed that TD children had significantly more SOD problems and less SD problems than G ($p < 0.05$). For the CBCL scales, there was significant differences for Anxious/depressed (AD; $F(2,64) = 3.79$, $p < 0.05$), Withdraw/depressed (WD; $F(2,64) = 4.66$, $p < 0.05$), Thought problems (TP; $F(2,64) = 4.20$, $p < 0.05$), Attention problems (AP; $F(2,64) = 7.34$, $p < 0.01$), Internalizing problems (IP; $F(2,64) = 8.67$, $p < 0.001$), Externalizing problems (ET; $F(2,64) = 8.66$, $p < 0.001$), Total problems (TotP; $F(2,64) = 10.96$, $p < 0.001$) and ADHD problems ($F(2,64) = 17.50$, $p < 0.001$). G children had significantly more AD, WD, TP, IP, EP, TotP and ADHD problems than TD children ($p < 0.05$). 2e children had significantly more TP, AP, EP, TotP and ADHD problems than TD children ($p < 0.05$). 2e children had significantly more AP and ADHD problems than G children ($p < 0.05$). For G children, linear regressions were significant for CSHQ total score and each CBCL scale except WD,

TP, rule-breaking behavior and ADHD ($p > 0.05$). For 2e children, linear regressions were significant only for CSHQ total score and AD, TP and anxiety problems ($p < 0.05$). No linear regression was significant for CSHQ total score and any CBCL scale for TD children.

Conclusion:

Sleep problems seem to be associated with several emotional and behavioral difficulties in gifted children but not in typically developing children, while sleep problems seem to be associated with only a few emotional and behavioral difficulties in twice exceptional children.

PS2:S210

ABSTRACT TITLE:

Sleep-related changes in Functional Connectivity within the Consolidation Network of Procedural Strategies

PRESENTING AUTHOR: *Van Den Berg, Nicholas[1]*

CO-AUTHORS: *Gibbings, [1] ; Pozzobon, A.[1]; Smith, Dylan[1]; Fogel, S.M.[1,2] ; Fang, Zhuo[1]*

AFFILIATIONS: *1 University of Ottawa; 2 Royal's Institute for Mental Health Research*

DESCRIPTION:

Introduction: Sleep consolidates procedural memories that comprise both simple motor skills and cognitive strategies (Schmid et al., 2020). Sleep-related consolidation of procedural memory is associated with greater activity in a hippocampal-striatal-cortical network, when compared to an equivalent period of wake (Urbain et al., 2013). Changes in this "consolidation network" occur as the memory becomes more stable. For example, as memory for simple motor skills improves, the hippocampus is uncoupled from the putamen (Albouy et al., 2013), while the putamen shows greater functional coupling to the motor cortex (Vahdat et al., 2017). Still, less is known about procedural memories that involve a cognitive strategy. We recently demonstrated that sleep benefits the cognitive strategy via activation in the caudate (van den Berg et al., submitted), however, it remains unclear how functional connectivity of the consolidation network differs for the strategy per se, rather than its accompanying motor skills.

Objectives: Here, we investigated how sleep influences functional connectivity in the hippocampal-striatal-cortical consolidation network following strategy learning, after controlling for the motor skills required to execute the strategy.

Methods: Participants (n=40) were trained on a procedural strategy task, the Tower of Hanoi (ToH), and a motor control task, both while undergoing functional Magnetic Resonance Imaging (fMRI). The ToH involves both a cognitive strategy and motor movements, whereas the control task involves only motor movements. After either a full night of sleep (n=20) or a full day of wake (n=20), participants were retested on the two tasks in the fMRI. Resting state activity was acquired after the training session, and before the retest session.

Results: Behavioural performance demonstrated that the sleep group showed greater improvement compared to the wake group on the ToH via improved accuracy ($t(38) = 2.08$, $p = 0.04$, $d = 0.66$) and speed ($t(38) = 6.69$, $p < 0.001$, $d = 2.12$). Next, functional connectivity analysis consisted of seed to whole-brain analyses, using seed regions associated with strategy learning (i.e., the caudate), and regions associated with motor sequence learning (i.e., the putamen, hippocampus). Compared to the Wake condition, the Sleep condition showed increased connectivity between the caudate and the motor cortex ($t(38)=3.32$, $p =0.04$ FDR, $\beta = 0.17 +/- 0.04$), from immediately after the training session to immediately before the retest session (i.e., across the retention interval filled with either sleep or wake). In addition, the hippocampus showed increased functional connectivity with the left occipital cortex ($t(38) = 4.91$, $p < 0.001$, $\beta = 0.19$, +/- 0.08), and marginally in the right cuneus $t(38) = 3.99$, $p = 0.085$ FDR, $\beta = 0.17 +/- 0.10$) and right orbitofrontal cortex ($t(38) = 5.13$, $p = 0.07$ FDR, $\beta = 0.19 +/- 0.08$). Functional connectivity was not observed when using the putamen as a seed region.

Conclusion: Sleep enhances functional connectivity in brain areas associated with strategy-learning (i.e., the caudate, hippocampus), but not in areas associated with motor skills (i.e., the putamen). In this way, we conclude that sleep preferentially enhances memory for a cognitive strategy via distinct changes in the hippocampal-striatal-cortical network.

PS2:S211

ABSTRACT TITLE:

Social jetlag, chronotype and COVID-19 in adolescents and young adults

PRESENTING AUTHOR: *Ramos Socarras, Laura*[1]

CO-AUTHORS: *Potvin, Jérémie*[1]*; Forest, Geneviève*[1]*, Ph.D.*

AFFILIATIONS: *1 Université du Québec en Outaouais*

DESCRIPTION:

Introduction and objectives: In March 2020, the world experienced a global pandemic, resulting in the shutdown of schools or a transition to remote teaching in most countries. Recent studies have shown that this led to, among other things, important changes in sleep habits in youth. The objective of this study was to investigate the relationship between chronotype and changes in social jetlag during the pandemic in adolescents and young adults.

Methods: This study was conducted during the first wave of the pandemic. 490 teenagers and young adults (22.6% boys and 76.3% girls; mean age = 18.17 ± 3.72 years old) completed online the Reduced Morningness-Eveningness Questionnaire and an adapted version of the Pittsburgh Sleep Quality Index. Participants were divided into morning (n = 63), intermediate (n = 253) and evening (n = 174) chronotypes. A repeated measures ANOVA COVID-19 (Pre vs During) X Chronotypes (morning, intermediate, evening) was conducted on social jetlag. Post hoc t-tests were used to identify significant differences.

Results: Results show a significant main effect of COVID-19 ($F(1, 487) = 152.56$, $p < .001$, $np2 = .24$) and a significant COVID-19 X Chronotypes interaction ($F(2, 487) = 3.36$, $p = .036$, $np2 = .01$). All participants showed a significant reduction in social jetlag during the pandemic compared to before, but this reduction was larger in evening chronotypes. Social jetlag decreased by 1 hour and 5 minutes in morning chronotypes ($t(62) = -3.93$, $p < .001$), 1 hour and 11 minutes in intermediate chronotypes ($t(252) = -10.91$, $p < .001$) and 1 hour and 39 minutes in evening chronotypes ($t(173) = -9.70$, $p < .001$). Further post hoc t-tests analyses showed that pre-pandemic, evening chronotypes had a significantly higher social jetlag than intermediate ($t(426) = -4.72$, $p < .001$) and morning ($t(235) = -3.48$, $p < .01$) chronotypes. However, during the pandemic, no significant differences in social jetlag between all chronotypes were found.

Conclusions: These results support the idea that when social restrictions and school demands are removed or reduced, adolescents and young adults tend to adopt sleep patterns that are closer to their natural rhythm. These changes appear to have a strong effect in reducing social jetlag, particularly in evening chronotypes. Since social jetlag has been associated with mental health and academic issues in adolescents and young adults, this study highlights the importance of considering the contribution of society and school to sleep disturbances and their consequences in youth.

PS2:S212

ABSTRACT TITLE:

Socioeconomic inequalities in pediatric obstructive sleep apnea

PRESENTING AUTHOR: *Park, Ji Woon[1,2] **

CO-AUTHORS: *Hamoda, Mona[1] **; Almeida, Fernanda[1] ; Huynh, N.[3,4] ; Conklin, Annalijn I.[5,6]*

***** Both authors contributed equally to this work.***

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6 Collaboration for Outcomes Research and Evaluation (CORE), Faculty of Pharmaceutical Sciences, University of British Columbia, 2405 Wesbrook Mall Vancouver, BC, V6T 1Z3, Canada

DESCRIPTION:

Socioeconomic status (SES) influences the occurrence and characteristics of obstructive sleep apnea (OSA) in children. Although SES is a powerful determinant of health disparities, previous research on pediatric OSA and SES are mostly retrospective studies that have the potential of bias and the diagnosis of OSA is typically obtained from self-reporting of parents and medical history records. The results of this prospective study, based on polysomnography, showed that maternal education and geographic location showed strong and consistent relationships with the occurrence of pediatric OSA. Results indicate the need to incorporate screening of SES in the diagnostic process of pediatric OSA to provide targeted intervention and patient-centered care to reduce disease burden and prevent the progression of OSA in children.

PS2:S213

ABSTRACT TITLE:

Solriamfetol titration & administration: dosing and titration strategies in patients with obstructive sleep apnea starting solriamfetol

PRESENTING AUTHOR: *Singh, Haramandeep*[1]

CO-AUTHORS: *Hyman, Danielle*[2] *; Parks, Gregory*[2] *; Chen, Abby*[2] *; Foley, Catherine*[3] *; Ito, Diane*[4]*; Thorpy, Michael J.*[5]

AFFILIATIONS: *1 Sleep Medicine Specialists of California, San Ramon, CA, USA; 2 Jazz Pharmaceuticals, Palo Alto, CA, USA; 3 Stratevi, Boston, MA, USA; 4 Stratevi, Santa Monica, CA, USA; 5 Albert Einstein College of Medicine, Bronx, NY, USA*

DESCRIPTION:

Introduction: Solriamfetol (Sunosi®) is a dopamine/norepinephrine reuptake inhibitor approved (US and EU) to treat excessive daytime sleepiness (EDS) in adults with narcolepsy (75-150 mg/d) or obstructive sleep apnea (OSA) (37.5-150 mg/d). Previous research examined the use of solriamfetol in clinical trial settings, but research in real-world settings was not previously conducted.

Objective: This study characterized real-world dosing and titration with solriamfetol.

Methods: This virtual, descriptive study of solriamfetol titration and administration (START) included a quantitative retrospective patient medical chart review among US-based physicians prescribing solriamfetol. Target enrollment was 25 physicians treating patients with EDS associated with OSA or narcolepsy. Titration strategies were classified as de novo (no prior EDS medication), transition (switched/switching from existing EDS medications to solriamfetol), or add-on (adding solriamfetol to current EDS medication).

Results: Twenty-four physicians provided data for patients with OSA. Data for 50 patients with OSA were analyzed (mean age, 51.9±9.1 years; 62% male; 90% overweight/obese); EDS was primarily moderate (56%) or severe (36%). Solriamfetol initiation was de novo for 22 (44%) patients, transition for 26 (52%), and add-on for 2 (4%). Patients primarily started at the 37.5-mg (n=24, 48%) or 75-mg (n=24, 48%) dose, and 2 (4%) started at 150 mg. The final/stable dose was 75 mg for 56% (n=28) of patients, 150 mg for 40% (n=20), and 112.5 mg for 2% (n=1) (the final dose for 1 patient was unknown). Most patients (64%) had 1 dose adjustment to reach their final dose; 10% had 2 adjustments, 2% had 3 or 4 adjustments, and 22% had none. Median (range) time to reach a stable dose was 14 (1, 74) days overall, 18 (3, 45) days with de novo treatment, 14 (1, 74) days for transition, and 7 (7, 7) days for add-on. The factor physicians most often considered when titrating onto solriamfetol was EDS severity (n=16, 32%), but more frequently, physicians stated that they did not consider any specific patient factors (n=22, 44%). Among patients transitioning, 17/18 (94%) taking a wake-promoting agent and 6/9 (67%) taking a stimulant discontinued it abruptly. Physicians were overall likely (n=24, 48%) or very likely (n=23, 46%) to recommend their titration approach for similar patients.

Conclusion: In a real-world study, the majority of patients prescribed solriamfetol for EDS associated with OSA reached a final dose of 75 or 150 mg after 1 adjustment from their starting dose. Physicians were overall confident in recommending their titration strategy for similar patients.

PS2:S214

ABSTRACT TITLE:

Strengthening Oropharyngeal Muscles as a Novel Approach to Treat Obstructive Sleep Apnea after Stroke: A Randomized Feasibility Study

PRESENTING AUTHOR: *Marzouqah, Reeman*[1]

CO-AUTHORS: *Dharmakulaseelan, Laavanya*[1] *; Jairam, Trevor*[1] *; Xiong,Kathy*[1] *; Colelli, David*[1] *; Yunusova,Yana*[1]*; Boulos, Mark I.*[1]

AFFILIATIONS: *1 Department of Medicine (Neurology) University of Toronto; 2 Hurvitz Brain Sciences Research Program, Sunnybrook Research Institute*

DESCRIPTION:

Introduction:

Obstructive sleep apnea (OSA) is characterized by recurrent obstruction of the upper airway during sleep due to intermittent loss of tone in the throat muscles. Post-stroke OSA is prevalent and has a significant impact on the health of stroke survivors. Continuous positive airway pressure(CPAP), the standard therapy for OSA, is generally poorly tolerated. Oropharyngeal exercises (OPEs) are commonly used to improve tongue/throat muscle strength and might be a promising alternative approach to treat OSA.

Objective:

To determine whether oropharyngeal exercises (OPEs) are feasible as a novel intervention for obstructive sleep apnea (OSA) after stroke.

Methods:

Forty stroke patients with OSA (AHI≥10/hr) who are unable to tolerate CPAP will be recruited and randomized (1:1) to an OPEs vs sham exercise protocol. They will be asked to perform the exercises for 6 weeks, 5 days per week, for 50 minutes per day. Feasibility will be ascertained by the proportion of enrolled patients who complete >80% of the exercises. OSA severity (assessed by the apnea-hypopnea index (AHI) and lowest oxygen desaturation and oropharyngeal physiology (e.g., tongue strength) will be collected at baseline, post-training (6-week follow-up) and retention (10-week follow-up).

Results:

The sample to-date includes 16 participants (11 males, 5 females; age 68.7±9.6 years) who have completed the study (n=8 per study group). The overall adherence was 88.3%. Preliminary analyses revealed that the OPE group had a reduced AHI after training (-18.9%change) compared to sham (-4.3% change). In addition, oxygen desaturation was more likely to increase in the OPE group compared to the sham group (4.6% vs -0.5%, respectively). There was a small increase in tongue strength in the OPE group (5.83% change) compared to the sham group (-1.7% change). The results are still exploratory at this time.

Conclusions:

Based on this initial sample, a full trial is feasible and results appear to be promising.

PS2:S215

ABSTRACT TITLE:

Systematic Review: The role of actigraphy in the diagnosis of sleep apnea

PRESENTING AUTHOR: *Huang, Ray (Kuo-Jui)*[1]

CO-AUTHORS: *Dr. Christopher-James Harvey*[2]

AFFILIATIONS: *1 University of Oxford; 2 Imperial College London*

DESCRIPTION:

The purpose of this systematic review is to provide supporting evidence on the clinical use of actigraphy in conjunction with other home sleep apnea testing (HSAT) for the diagnosis of sleep apnea in the adult population. A systematic review was conducted to identify studies that compared the apnea hypopnea index (AHI) derived from the combine use of respiratory polygraphy (RP) and actigraphy, peripheral arterial tonometry (PAT) and/or polysomnography (PSG). Statistical analysis was performed to compare the correlation between the indexes. From the thirteen studies that met the inclusion criteria: ten studies compared PAT and actigraphy with PSG, two studies compared RP and actigraphy with PSG and one study compared the use of actigraphy alone with RP. From these data, actigraphy alone failed to identity symptomatic individuals with OSA. When applied with either PAT or RP, there were significant correlations between the derived apnea-hypopnea index (AHI) with the AHI from PSG. However, inconsistences with the exclusion criteria, AHI scoring criteria for PSG, actigraphy algorithm, and the testing environment contributed to the limitations of the reported evidences. Overall, the results suggest that using actigraphy's ability to measure the total sleep time (TST) can help increase the accuracy of HSAT in the diagnosis of sleep apnea.

PS2:S216

ABSTRACT TITLE:

The gender differences in the prevalence of sleep deficits in British Columbia adolescents

PRESENTING AUTHOR: *Zhang, Kexin*[1]

CO-AUTHORS: *Conklin, Annalijn*[1,2,3]

AFFILIATIONS: *1 Food, Nutrition and Health, Faculty of Land and Food Systems, University of British Columbia, Vancouver, BC; 2 Collaboration for Outcomes Research and Evaluation, Faculty of Pharmaceutical Sciences, University of British Columbia; 3 Centre for Health Evaluation and Outcome Sciences, Providence Health Research Institute*

DESCRIPTION:

Introduction:

Adolescence is one of the fast-developing stages of a person's lifespan, and is marked by physiological, psychological and social changes that make this population vulnerable to poor sleep patterns. Sleep deficits can arise from poor sleep quantity, quality, and timing and differ between boys and girls due to sex and gender. Social jetlag is a novel concept describing the discrepancy between sleep timing on weekdays and free days (typically weekends), but is rarely assessed among teens.

Objective:

This study examined the prevalences of self-reported sleep quantity, quality, and social jetlag, by gender, using a population-based cohort in BC of 1031 ethnically diverse youth (13 – 18 years).

Methods:

Means and standard deviations (SD), or frequencies and percentages were calculated. ANOVA was used for obtaining p-values for sleep duration and social jetlag, and chi-square test was used for sleep quality.

Results:

The mean sleep duration during weekdays for girls (mean: 8.39h (SD: 0.96)) was significantly lower than boys (8.64h (0.97)) (p-value: <0.0001), and 16% of girls and 12% of boys had less than 8h of sleep on average. Twenty-five percent of girls and 16% of boys reported having restless sleep more than 3 days in a typical week (p-value: <0.001). The mean social jetlag of girls (1.64h (0.72)) was significantly higher than of boys (1.52h (0.75)) (p-value: <0.01).

Conclusion:

Results revealed that teen girls had higher social jetlag, more frequent restless sleep occurrence, and shorter sleep duration than boys in BC, highlighting a need for gender-specific sleep hygiene education.

PS2:S217

ABSTRACT TITLE:

The relationship between changes in training duration during the pandemic and sleep habits in adolescent athletes

PRESENTING AUTHOR: *Caron, Jean-François*[1]

CO-AUTHORS: *Forest, Geneviève Ph.D.*[1]

AFFILIATIONS: *1 Université du Québec en Outaouais, Gatineau, Qc, Canada*

DESCRIPTION:

During adolescence, sleep goes through modifications, such as a delay in the sleep-wake patterns and a reduction in sleep duration. Studies have shown that during the pandemic teens tended to adopt sleep patterns closer to their natural rhythm, which was characterize by a shift to later bedtimes and wake times. On the other hand, social distancing and other restriction measures implemented during the pandemic have resulted in major disruptions of training schedules in many athletes. The aim of the present study was to investigate the relationship between the changes in training duration during the pandemic and sleep habits in young athletes.

211 young Canadian athletes (aged 12 to18 years old; 30.4% boys) completed questions on sleep and sports training habits several months into the COVID-19 pandemic (January and February 2021). Participants had to be enrolled at a competitive level in a sport. The survey was administered online in an English or French version. Separate two steps hierarchical regression analyses were conducted in order to examine the contribution of changes in the number of training hours per week to sleep duration and each sleep habits variables (weekdays and weekends wake times and bedtimes). To control for age and for the number of training hours per week before the pandemic, they were added as covariables in each of the regression analyses.

Results showed that weekday bedtimes and wake times were significantly predicted by age ($\beta = .57$, $p < .001$, and $\beta = .38$, $p < .001$, respectively) and by the number of training hours per week ($\beta = -.24$, $p = .001$, and $\beta = -.40$, $p < .001$, respectively). Those models explained 40% and 30.3% of the variance for bedtimes and wake times respectively, suggesting that older teenagers had later bedtimes and wake times on weekdays, but also that less training was associated with later bedtimes and wake times on weekdays. Models were not significant for weekend bedtimes and wake times and for sleep duration.

As expected, age is associated with sleep habits, older teens showing a shift to later sleep patterns compared to their younger peers. However, training duration in young athletes also seems to be an important factor that is associated with sleep habits during the pandemic. Athletes that have been subject to more restrictions in their training schedules are those who have shifted to later bedtimes and wake times on weekdays, probably to a time closer to their natural rhythm. On the other hand, they were no association between changes in training duration and sleep duration. Since recent studies have shown associations between sleep and sports performance in athletes, further studies are needed to verify whether these changes in sleep habits are beneficial for young athletes.

PS2:S218

ABSTRACT TITLE:

Transplanting immortal orexin cells in narcolepsy.

PRESENTING AUTHOR: *Pintwala, Sara*[1]

CO-AUTHORS: *Belsham, Denise*[1]*; Fraigne, Jimmy*[1]*; Peever, John*[1]

AFFILIATIONS: *1 University of Toronto*

DESCRIPTION:

INTRODUCTION: Narcolepsy is a sleep disorder caused by a loss of orexin neurons in the lateral hypothalamus. This results in symptoms such as excessive sleepiness and cataplexy, a sudden and involuntary loss of muscle tone during wakefulness. The objective of cell replacement therapy is to treat disease by replacing lost neurons. However, testing this for narcolepsy is dependent on the availability of a reliable source of orexin neurons. Here, we describe the character of a novel immortal orexin cell line and determine the outcome on behaviour when these cells are transplanted into a mouse model of narcolepsy.

METHODS: To do this, we used an immortal cell line from adult (A) transgenic mice (m) expressing green fluorescent protein (GFP) in orexin (ORX) neurons, isolated from hypothalamus (Hypo); the mHypoA-ORX/GFP4 cell line. First, we performed immunocytochemistry against GFP and orexin to validate the phenotype of cultured cells. We then performed a live cell secretion assay coupled with enzyme immunoassay to determine orexin release. Next, we aimed to find a way to remotely control the activity of cells in vitro and exposed cultured cells to a viral vector expressing the excitatory Designer Receptor Exclusively Activated by a Designer Drug (DREADD) hM3Dq (rAAV8-hSyn-hM3Dq-mCherry). Next, we transplanted cells to the dorsal raphe (AP: 4.4/ML: ±0/DV: 3.5) in a mouse model of narcolepsy (orexin-knockout, KO) and determined the outcome on behaviour, specifically cataplexy.

RESULTS: Using immunostaining, we found that a majority of GFP-tagged cultured cells co-expressed orexin (97.78±0.22%; n=3; #cells=984). When live cells were stimulated under physiological conditions (hypoglycemia) there was significant increase in orexin release by cultured cells (0.337±0.031ng/ml; n=3) when compared to basal neurotransmitter release (hyperglycemia; 0.276±0.030ng/ml; n=3; t-test; *p<0.01). When cultured cells were exposed to a viral vector carrying hM3Dq (rAAV-hSyn-hM3Dq-mCherry) we found efficient transduction of hM3Dq as 97.47±0.97% (n=3; #cells=1158) of all cells expressed mCherry. When exposed to the ligand clozapine-N-oxide (CNO), we found a significant increase in c-Fos expression (67.5±13.0%) and orexin release (0.071±0.01ng/mL; n=3) by cultured transfected cells when compared to baseline c-Fos expression (36.5±1.9%; n=3; 2-way ANOVA, **p<0.01) and basal neurotransmitter release (0.050±0.01ng/mL; n=3; 2-way ANOVA, *p<0.05). Transplantation of mHypoA-ORX/GFP4 cells to the DR significantly reduced the number of cataplexy episodes (unpaired t-test; ***p=0.0002; n=7) and the amount of cataplexy (unpaired t-test; **p=0.0014), but not the duration of cataplexy episodes (unpaired t-test; p=0.9479 when compared to DR sham transplant (vehicle) controls (n=8). In these subjects, 309±159 orexin-expressing cells were present in the dorsal raphe.

SIGNIFICANCE: This project explores the potential of cell replacement therapy as a novel therapeutic strategy for narcolepsy, and specifically using an immortal orexin cell line to this end.

PS2:S219

ABSTRACT TITLE:

Validating a portable, open science tool for closed-loop auditory stimulation of sleep spindles

PRESENTING AUTHOR: *Jourde, Hugo*[1]

CO-AUTHORS: *Coffey, Emily BJ*[1] *; Beltrame, Giovanni*[2]*; Valenchon, Nicolas*[2] *; Bouteiller, Yann*[2]

AFFILIATIONS: *1 Concordia University; 2 Polytechnique Montreal*

DESCRIPTION:

Auditory closed-loop stimulation, in which sounds are introduced to the brain to manipulate and enhance ongoing neural oscillations, is a promising tool for investigating the mechanisms of sleep and memory. However, currently available tools are unable to accurately stimulate oscillations in frequency ranges higher than those of slow oscillations. Via an interdisciplinary collaboration between neuroscience and computer engineering teams, we have created a portable electroencephalography (EEG) system capable of stimulating sleep spindles (11-15 Hz), known as the Portiloop. It is intended as an open science tool to facilitate research on the functional roles of neural oscillations, and must therefore be inexpensive, easy-to-use, and capable of accurately detecting oscillatory events early in their evolution. As a demonstration of its effectiveness, we validate its use on the Montreal Archive of Sleep studies (MASS), an open-access and collaborative database of laboratory-based polysomnography (PSG) recordings. Specifically, we evaluate a machine learning-based spindle detection algorithm running on the Portiloop in a simulated online paradigm, to quantify the trade-offs in sensitivity (i.e. success at detecting true positives) and specificity (i.e. success avoiding false positives) at different delays relative to spindle onset. We also evaluate its stability across population demographics. In a follow-up study, we use the Portiloop to stimulate sleep spindles in 20 healthy young adults, and evaluate the accuracy of the online stimulation by comparing it to a commonly used offline spindle detection algorithm. By validating the Portiloop's effectiveness in detecting and stimulating sleep spindles and quantifying the trade-offs in detection parameters, we will maximize experimental flexibility, allowing the researcher to selectively target specific oscillations and therefore explore their causal links to health and cognitive processes. In the future, the Portiloop will be released as an open science tool, and can be extended to detect and stimulate other neural oscillations across states of consciousness.

PS2:S220

ABSTRACT TITLE:

Validation de la version française du Sleep Health Index : l'Index sur la santé du sommeil

PRESENTING AUTHOR: *Vézina-Im, Lydi-Anne*[1-4]

CO-AUTHORS: *Morin, Charles M.*[1,4]*; Desroches, Sophie*[1,2]

AFFILIATIONS: *1 École de nutrition, Université Laval, Québec, Québec, Canada; 2 Centre Nutrition, santé et société (NUTRISS), Institut sur la nutrition et les aliments fonctionnels (INAF), Université Laval, Québec, Québec, Canada; 3 École de psychologie, Université Laval, Québec, Québec, Canada; 4 Centre d'étude des troubles du sommeil, Université Laval, Québec, Québec, Canada.*

DESCRIPTION:

Introduction : L'objectif de l'étude était de valider une version française du Sleep Health Index de la National Sleep Foundation, l'Index sur la santé du sommeil (ISS), auprès d'un échantillon d'adultes francophones avec et sans diabète.

Méthode : Des adultes âgés de 18 à 64 ans étaient invités à compléter sur le Web des questionnaires sur le sommeil, soit l'ISS et des versions françaises validées de l'Index de qualité du sommeil de Pittsburgh (IQSP) et de l'Index de sévérité de l'insomnie (ISI). Les femmes enceintes et les personnes avec un horaire de travail rotatif étaient exclues de l'étude.

Résultats : Un total de 151 adultes (80,1% de femmes), parmi lesquels 54 vivaient avec un diabète (type 1: 30 et type 2: 24), a complété les questionnaires sur le sommeil. L'analyse de la structure factorielle de l'ISS a permis de confirmer la présence de trois facteurs (qualité, durée et troubles du sommeil) comme dans l'instrument original. L'ISS avait une consistance interne acceptable ($\alpha = 0,67$), ainsi que pour deux des trois facteurs qu'il mesure. La validité convergente de l'ISS était appuyée par des corrélations significatives ($p < 0,0001$) avec la mauvaise qualité du sommeil (IQSP: $r = -0,59$) et la sévérité de l'insomnie (ISI: $r = -0,66$).

Conclusions : L'ISS aurait des propriétés psychométriques adéquates puis est court et simple à compléter pour évaluer la santé du sommeil chez la population générale, incluant chez des adultes vivant avec le diabète, ce qui en fait un outil d'intérêt pour la santé publique.

Financement : La première auteure est financée par une bourse de post-doctorat en transfert des connaissances d'Action diabète Canada.

PS2:S221

ABSTRACT TITLE:

How has the COVID-19 pandemic affected treatment in individuals with OSA?

PRESENTING AUTHOR: *Rizzo, D.*[4]

CO-AUTHORS: *Bailes, S.*[1,2]*; Huynh, N.*[3]*; Lavigne, G.*[3,4]*; Baltzan, M.*[6,7]*; Grad, R.*[2,4]*; Libman, E.*[1,2]*; Fichten, F.*[1,2]

AFFILIATIONS: *1 McGill University (Department of Psychiatry); 2 Jewish General Hospital; 3 Université de Montréal (Department of Dentistry); 4 McGill University (Department of Family Medicine); 5 Sacré-Coeur Hospital; 6 McGill University (Department of Epidemiology); 7 Mount-Sinai Hospital*

DESCRIPTION:

Introduction

The COVID-19 pandemic has rapidly spread across the globe, disrupting lives and undermining sleep, psychological and physical health. Social distancing, physical isolation and suspension of many clinical services may complicate the already prevalent underdiagnosis of OSA and potentially delay treatment for those who have been diagnosed. The healthcare and clinical outcome data generated from this research is designed to assess the impact of COVID-19 on sleep disorders diagnosis, treatment and mental health.

Methods

We administered the COVID-19 Impact on Sleep and Health interview to our existing longitudinal study cohort of 80 primary care patients who had been diagnosed with OSA eight years previously. We also evaluated sleep quality, physical and psychological health, lifestyle and quality of life (i.e. Sleep Questionnaire, Sleep Symptom Survey, SF-36, Insomnia Severity Index) at 3 previous testing times throughout the last 8 years.

Results

Our findings showed that individuals who were enrolled in a treatment program did not show significant differences on health outcomes, treatment trajectory or mental health. Individuals enrolled in the study who were not recommended treatment (e.g. mild positional OSA) showed more difficulty adjusting to the social changes due to the pandemic (i.e. anxiety, insomnia).

Conclusions

Since the COVID-19 pandemic, participants who were previously diagnosed with OSA did not experience a change in treatment trajectory. Accessibility to care through telehealth was expedient and convenient. Those who were not already undergoing treatment for OSA experienced more psychological maladjustment and insomnia-related symptoms. Accessibility to medical care for sleep disorders may be more difficult for those who are not already enrolled in a treatment plan.

PS2:S222

ABSTRACT TITLE:

Healthcare providers' perspective and experiences with insomnia management at primary healthcare centers in Qatar

PRESENTING AUTHOR: *Ali, Raja*[1]

CO-AUTHORS: *Awaisu, Ahmed*[1]*; Zolezzi, Monica*[1]

AFFILIATIONS: *1 Qatar University*

DESCRIPTION:

Introduction: Insomnia is a public health problem affecting one in every three adults and is the second most common complaint at primary healthcare settings. In Qatar, Primary Health Care Centers (PHCCs) are often patients' the first point of contact with the healthcare system.
Objective:This study aimed to explore Health Care Providers' (HCPs) perspective of insomnia and their role in its management.
Methods: This was a qualitative, semi-structured study in which interviews were conducted with pharmacists and physicians who have been working at PHCCs for a minimum of one year. Saturation was achieved after interviewing 19 HCPs. This study received approval from Institution review boards of Qatar University and Primary healthcare corporation. Consent forms were obtained from all participants. The interviews were thematically analysed.
Results: The interviews generated five themes, including general perspectives on insomnia, primary healthcare as the setting for insomnia management, current practices for insomnia management at PHCCs, HCPs' role perception, and challenges facing insomnia management. HCPs viewed Insomnia as a symptoms of an underlying health problem which should be managed at PHCCs if it was mild or referred to specialists if the case was complex. Participants reported the lack of insomnia specific treatments at PHCCs and indicated that other classes of medications (e.g., antihistamines and anxiolytics) are often used. HCPs opinions on the efficacy of non-pharmacological therapies differed, yet they were generally preferred over pharmacological treatments. Insomnia's assessment and management was viewed as being the role of physicians while pharmacist duties included providing drug related information and counselling. Time constraints, lack of insomnia guidelines and insufficient knowledge and training of HCPs were the main challenges highlighted by the participants.
Conclusion: HCPs at PHCCs in Qatar viewed insomnia as an important problem which requires management and indicated that PHCCs are suitable for the management of simple insomnia cases. Non-pharmacological treatments were the preferred options recommended by HCPs . The care provided at t at PHCCs is limited due to the lack of insomnia specific treatments and absence of insomnia management guidelines. Educating HCPs and training them on insomnia diagnosis and management is also needed.

PS2:S223

ABSTRACT TITLE:

The effect of sleep restriction on face-name association learning

PRESENTING AUTHOR: *Dimopoulos, Chris[1,3]*

CO-AUTHORS: *Delli Colli, Luca[2,3]; Mograss, Melodee[1,2,3,4]; Zvionow, Tehila[2,3]; Vacirca, Felicia[1,3]; Haiun, Jonathan[1,3]; Frimpong, Emmanuel[2,3] and Thanh Dang-Vu, Thien[1,2,3,4]*

AFFILIATIONS: *1. Dept of Psychology, Concordia University, Montreal, QC, CA; 2. Dept of Health, Kinesiology & Applied Physiology, Concordia University, Montreal, QC, CA; 3. Concordia University PERFORM Centre, Montreal, QC, CA; 4. Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal*

DESCRIPTION:

Background: Sleep loss is common in our modern society due to social, work and family commitments. Total sleep deprivation has shown to cause a wide variety of negative effects. There are a limited number of studies on individuals who sleep slightly less than the average 8hr of sleep/night on memory.

Objective: We aimed to assess the effects of sleep restriction on episodic memory using a face-name association learning task.

Methods: Participants completed on-line screening questionnaires for medical, psychological, sleep history, and physical activity status. A sleep diary was completed 4 days prior to and during the experimental night (Day 5) to determine consistency of sleep schedules. Included participants were randomized into two groups: Restricted sleep opportunity (s5, ~5-6 h/night) and Average sleep opportunity (s8, ~8-9 h/night). On Day 5, a three-part face-name recall task was performed. This task involved an encoding phase and immediate recall phase, separated by a 5-minute break, and a restricted or average nighttime sleep opportunity, inserted between immediate and delayed recall phases. All procedures were conducted remotely. Data for immediate and delayed retrievals were generated by the task, while differences between immediate and delayed retrieval performance metrics (accuracy, reaction time - RT) were also computed within each group. Normality was assessed using Kolmogorov-Smirnov and Shapiro Wilk tests. Participant demographics, screening questionnaire scores, and sleep diary entries were summarized as means and standard deviations. Groups were compared with unpaired t-test and Mann-Whitney U test.

Results: A total of 41 healthy, average sleepers (25.2±4.1 yrs), were included in this online pilot study. A significant difference in the experimental night (Day 5) was found between s5 vs. s8 for TST [(mean±SD, 5.35±0.3 vs. 8.07±0.3) hr, $p < 0.001$] and SOL [(8.2±6.0 vs 14.6±7.2) min, $p<0.05$] respectively. Recall performance showed no difference across the two groups for immediate retrieval of number of correct responses (accuracy) and reaction time (RT), delayed retrieval RT, and the mean difference between delayed and immediate retrieval accuracy, p's >0.05. During the delayed retrieval, there was a significant difference between s8 vs. s5 group in accuracy (72.00±9.27 vs. 67.15±9.65, Mann-Whitney U = 276.0, $p<0.05$) and in the Karolinska Sleepiness score, KSS (4.15±1.66 vs 6.30±1.63, Mann-Whitney U = 72.50, $p= 0.004$).

Conclusion: Sleep restriction appears to have detrimental effect on episodic memory recall. Seeing as this study was conducted online, future studies should aim to confirm these findings in a well-controlled lab environment, as well as determining if motivational or other factors influence sleep loss in individuals who are partially sleep deprived.

PS2:S224

ABSTRACT TITLE:

Predicting the Success of Maxillomandibular Advancement Surgery using Mandibular Advancement Therapy as a Diagnostic Tool

PRESENTING AUTHOR: *Makki, Armin*[1]

CO-AUTHORS: *Meisami, Tina*[2]

AFFILIATIONS: *1 University of Toronto, Faculty of Dentistry; 2 University Health Network, Toronto Rehabilitation Institute*

DESCRIPTION:

Maxillomandibular advancement surgery (MMA) is an alternative treatment for moderate to severe OSA in patients unable or unwilling to adhere to CPAP therapy. MMA in an extra-pharyngeal multi-focal surgery which increases the pharyngeal space and reduces pharyngeal collapsibility, helping to reduce AHI and sleep fragmentation. MMA is an effective and safe treatment in resolving OSA with reported success rates of 85-91%. Indeed the success and efficacy of MMA surgery in resolving OSA is well established. Furthermore there is evidence the MMA surgery provides significant further improvements beyond successful CPAP and Mandibular Advancement Therapy (MAD).

However there still remains the issue of success predictability in 9-15% of patients in whom MMA surgery may not prove to be effective, who will require further post-operative treatment with CPAP or MAD.

The purpose of this study was to increase success predictability by using two pre-operative diagnostic tools namely 1. Drug Induced Sleep Endoscopy (DISE) to determine the level of upper airway collapse and 2. Remote Controlled MAD with Home Sleep Study (HST) to determine the therapeutic position of mandibular advancement.

Traditionally a 10 mm advancement of the maxillomandibular complex has been recommended based on the work by Riley and Powel, which is adequate for some patients, excessive for others, and yet for some patients no degree of advancement is enough to prevent airway collapse. In certain patients with high loop gain, paradoxical increase in AHI, and conversion to Central Sleep Apnea (CSA) has also been observed. Indeed it has been shown that the magnitude of MMA is not an indicator of success.

There is a need for tailor made approach toward individualized OSA treatment as treatment success varies amongst patients. It remains unclear how much surgical advancement is needed in each individual patient.

Successful MAD treatment is a positive predictor of success for MMA surgery. In order to provide the patient with individualized care, we first determined the therapeutic point of mandibular advancement by using temporary MAD and home sleep test.

Secondly, patients underwent DISE to identify potential non-responders and identify patients who would do better with less MMA advancement. The patterns of collapse observed during DISE at the Palatal, Orophayrngeal, Tongue-base and Epiglottis, are able to predict success as well as treatment failure for MMA. DISE has been shown to be a positive treatment predictor in patients with lateral pharyngeal wall and tongue base collapsibility, and a negative predictor in patients with airway collapse at the level of the epiglottis. Concentric Collapse of the palate (CCCp) which was previously observed to be a negative treatment predictor has recently been shown to improve with maxillary advancement. This is important as CCCp is negative predictor

for MAD. In addition when CCCp is present, higher CPAP pressure is needed to alleviate the upper airway collapse.
Two preoperative validated diagnostic techniques namely MAD and DISE were used prior to MMA surgery to predict treatment success, increase efficacy of surgery, plan individualized magnitude of advancement, eliminate non-responders, and potentially reduce post operative morbidity

PS2:S225

ABSTRACT TITLE:

Predictors of Early Nap Cessation: Longitudinal Findings from a Large Nationally Representative Study of Young Children

PRESENTING AUTHOR: *Newton, Adam*[1]

CO-AUTHORS: *Reid, Graham*[1]

AFFILIATIONS: *1 The University of Western Ontario*

DESCRIPTION:

Objectives: Most children cease napping between 2-5-years-old. There is considerable variability in the duration and frequency of naps during this period. Earlier nap cessation has been linked to better receptive language and behavioral functioning. This may suggest nap cessation is a marker of development and may be linked to other outcomes in childhood. However, little is known about the predictors of this cessation. Children's developmental progression, psychosocial factors, and environmental factors were expected to predict cessation. These predictors were conceptualized using the Socioecological Model. This study evaluated these predictors of early nap cessation (i.e., children who stop napping before their third birthday). This was the first study to examine predictors of early nap cessation.

Methods: Data were used from three longitudinal cohorts from the Canadian National Longitudinal Study of Children and Youth (Statistics Canada; N = 5504). Persons Most Knowledgeable about the child (PMKs; 88.6% mothers) reported on demographic, perinatal, child growth, development, child and parent functioning, and child sleep variables. Children were 0-1-years-old at baseline and 2-3-years-old at follow-up; 51.1% were male, 89.8% were Caucasian. The outcome was children's nap status at follow-up: still napping vs. no longer napping at follow-up.

Results: Overall, 10.9% (95% CI ± 0.8%) of children had ceased napping at follow-up. Data analyses were conducted in Mplus and used a multiple groups logistic regression to account for nesting within cohorts and multiple imputation to account for missing data. Giving up naps early (before the child's third birthday) was predicted by: older child age, female sex, having at least one older sibling, having met more developmental milestones, and longer nighttime sleep duration. Children still napping at follow-up was predicted by: non-Caucasian race, birthweight < 2500 grams, PMK working or in school, mother consumed alcohol at least once during pregnancy, and typical sleep onset latency > 30 minutes. Notably, PMK educational attainment, income adequacy, child temperament, and parenting style were not related to children's nap cessation cross-sectionally or longitudinally.

Conclusions: Both socioecological and developmental predictors were observed, suggesting that developmental influence may be modified by a child's environment. Previous studies have supported non-Caucasian race, developmental status, and nighttime sleep duration as predictors of children's daytime sleep duration. This study demonstrates that these predictors are also related to early nap cessation. Future research should investigate attitudinal predictors of children's nap cessation (such as parental preferences), the predictors of nap cessation later in development, longitudinal differences in functioning by the timing at which children cease napping, and cultural differences in nap cessation prediction.

PS2:S226

ABSTRACT TITLE:

Environmental Correlates of Sleep Health Among Middle-Aged and Older Adults in the Canadian Longitudinal Study on Aging

PRESENTING AUTHOR: *Rodrigues, Rebecca[1]*

CO-AUTHORS: *Guaiana, Giuseppe[1]; Zou, Guangyong[1]; Gilliland, Jason[1]; Nicholson, Kathryn[1]; Anderson, Kelly[1]; Wilk, Piotr[1]; Alonzo, Rea[1]; Stranges, Saverio[1]*

AFFILIATIONS: *1 Western University*

DESCRIPTION:

Introduction: Emerging evidence emphasizes the importance of neighbourhood and environmental factors on sleep patterns. Neighbourhood and environmental effects may be opposing in terms of having a health enhancing versus a health threatening effect, therefore it is important to consider a range of factors together to determine the primary factors that influence sleep. Our objective was to explore the neighbourhood and environmental correlates of sleep health in a population-based Canadian sample.

Methods: We used cross-sectional baseline data from the Canadian Longitudinal Study on Aging (CLSA), a survey of 30,097 community-dwelling adults, aged 45-85. Self-reported sleep measures included sleep duration, sleep dissatisfaction (vs satisfied/neutral), and sleep disturbances (difficulty initiating or maintaining sleep). We used environmental data from the Canadian Urban Environmental Health Research Consortium (CANUE) linked to CLSA data at the postal code level. We explored built and social environment variables (greenness, intersection density, dwelling density, points of interest, material and social deprivation), ambient variables (proximity to roadways, nighttime light, air pollution), and weather and climate (temperature, humidity, pressure, precipitation). We used modified Poisson regression to estimate prevalence ratios (PR) for the associations between environmental variables and sleep dissatisfaction and disturbances, and linear regression for sleep duration. We estimated unadjusted associations, estimates adjusted for all environmental variables, and estimates additionally adjusted for individual-level sociodemographic and clinical variables.

Results: In our preliminary findings from our unadjusted analyses, we observed a higher prevalence of sleep dissatisfaction among people residing in the highest quintile of material deprivation relative to the lowest quintile (PR=1.11, 95%CI 1.02, 1.21), as well as sleep disturbances (PR=1.13, 95% CI 1.05, 1.22). Additionally, we observed shorter sleep duration within the highest quintile of material deprivation compared to the lowest (coefficient=-0.13, 95% CI -0.20, -0.06). Higher levels of neighbourhood greenness were significantly associated with a lower prevalence of sleep disturbances (PR=0.71, 95% CI 0.56, 0.90) and longer sleep duration (coefficient=0.34, 95% CI 0.10, 0.58). Full adjusted results will be available for presentation at the conference.

Conclusion: Our findings will provide needed evidence disentangling the relative importance of inter-related and competing environmental exposures on sleep health in a population-based Canadian sample of middle-aged and older adults.

AUTHOR INDEX