EXAMINING THE IMPACT OF EXPOSURE TO NATURAL & BUILT ENVIRONMENTS ON CHILDREN'S SLEEP DURATION

J. Gilliland [1,2]. [1] *Western University, Geography & Environment, Health Studies, Paediatrics, Epidemiology & Biostatistics, London, Canada;* [2] *Lawson Health Research Institute, Children's Health Research Institute, London, Canada*

Introduction: Inadequate sleep among school-aged children is a critical public health issue which has been linked to a variety of physical health problems. Lack of quality sleep can also negatively impact cognitive functioning and social behaviours. A growing body of research suggests that exposure to natural environments can have positive benefits for children's physical health, emotional well-being, and cognitive development. The purpose of this study is to examine the impacts of children's daily exposure to different environments (natural and built) on their sleep duration.
Materials and Methods: Data was collected for 614 children (aged 9-14 years) drawn from 22 elementary schools throughout London, Ontario. Participants completed the two-week STEAM (Spatial Temporal Environmental Activity Monitoring) protocol which involved completion of a survey, daily activity diary, and tracking the time they spent in different environments with a portable GPS for two weeks. Hierarchical multiple linear regressions were used to explore the relationship between children's sleep duration and exposure to neighbourhood level environmental features.
Results: In addition to a number of important individual level variables, analysis revealed that the amount of time spent in public parks and green spaces during the day had a positive impact on children's sleep duration. Implications for policy will be discussed.
Conclusions: This research fills gaps in our understanding of how natural and built environments may influence children's sleep. Implications for future research and policy will be discussed.
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FAVORIRE L'APPRENDIMENTO DI VOCABOLI DURANTE IL SONNO ATTRAVERSO UN SISTEMA DI CLOSED-LOOP TARGETED MEMORY REACTIVATION IN SETTING DOMESTICO: UNO STUDIO PILOTA

F. Salfi [1], A. D'Atri [1], B. Arnone [1], G. Amicucci [1,2], L. Viselli [1], D. Corigliano [1,2], D. Tempesta [1], M. Ferrara [1]. [1] *University of L'Aquila, Department of Biotechnological and Applied Clinical Sciences, L'Aquila, Italy;* [2] *"Sapienza" University of Rome, Department of Psychology, Rome, Italy*

Introduzione: Il sonno svolge un ruolo cruciale nel consolidamento delle memorie. La *Targeted Memory Reactivation* (TMR) è una tecnica in grado di manipolare il processamento notturno delle memorie, tipicamente utilizzata in *setting* laboratoriale. Stimoli sensoriali presenti nel contesto di apprendimento vengono usati per riattivare in maniera non invasiva tracce mnestiche durante il sonno profondo (N3). Considerando la vasta letteratura scientifica che supporta l'efficacia della TMR nel favorire il consolidamento delle memorie, il passo successivo consiste nella traslazione di questo paradigma alla vita di tutti i giorni. Pertanto, abbiamo sviluppato un sistema portatile per la presentazione automatica di stimoli uditivi durante la fase N3 (*closed-loop* TMR, CL-TMR) che si basa sulla registrazione dell'attività EEG di una *headband* EEG commerciale. Tale sistema è stato utilizzato per favorire il consolidamento di memorie dichiarative attraverso la presentazione di suoni durante il sonno in un *setting* domestico.
Metodologia: Dodici studenti universitari, (età media ± deviazione standard, 24.50 anni ± 2.32) hanno partecipato allo studio pilota. Nel tardo pomeriggio, i partecipanti hanno svolto un compito di apprendimento di vocaboli che richiedeva l'acquisizione della traduzione italiana di pseudo-parole (e.g., "tacipaca"), seguito da una sessione di test (T1) . Durante la notte, metà delle pseudo-parole è stata ripresentata acusticamente durante la fase ascendente delle oscillazioni lente attraverso il sistema di CL-TMR. Metà dei suoni consisteva nelle pseudo-parole tradotte correttamente nella sessione T1, mentre l'altra metà era composta da quelle pseudo-parole la cui traduzione non era stata appresa. I segnali EEG sono stati acquisiti utilizzando la *Dreem Headband* (*Rythm SAS*, Paris, France), il cui algoritmo di detezione delle oscillazioni lente è stato utilizzato per innescare la presentazione dei suoni. La rievocazione mnestica è stata misurata al mattino seguente (T2). È stata valutata la differenza tra T1 e T2 delle pseudo-parole tradotte correttamente, confrontando la *performance* per le pseudo-parole presentante durante la notte con quelle non presentate. A livello elettrofisiologico, sono stati valutati i potenziali evento-correlati (ERP) e la perturbazione spettrale evento-correlata alle stimolazioni nel range 5-18 Hz. Sono state confrontate le risposte corticali associate a una corretta traduzione al mattino con quelle associate a una mancata/errata traduzione.
Risultati: La riesposizione alle pseudo-parole durante il sonno migliorava la memoria per le rispettive traduzioni italiane (media ± deviazione standard, +13.20% ± 20.75) rispetto a quelle non presentate (-5.26% ±22.31; p=0.04). Le effettive riattivazioni erano associate a una maggiore positività e negatività frontale degli ERP. L'analisi tempo-frequenza ha evidenziato un incremento nella banda *spindle* a 1000–2000 msec dall'inizio della stimolazione (p<0.05) come correlato della riattivazione delle tracce mnestiche correttamente rievocate al mattino.
Conclusioni: Questo studio pilota dimostra la validità del sistema di CL-TMR nel favorire l'apprendimento di memorie durante il sonno in un *setting* domestico. Una stimolazione efficace determina un successivo aumento di attività *spindle*, confermando l'implicazione di specifiche dinamiche oscillatorie nell'effetto della TMR. L'utilizzo di un sistema portatile di CL-TMR potrebbe aprire la strada all'applicazione del paradigma di TMR alla vita quotidiana, promuovendo quei ritmi elettrofisiologici coinvolti nel consolidamento sonno-dipendente delle memorie.

FREQUENCY OF OBSTRUCTIVE SLEEP APNEA SYNDROME IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE PATIENTS

E. Atahan [1], S.F. Yalin [2]. [1] *Istanbul Cerrahpasa University, Chest Diseases, Istanbul, Turkey;* [2] *Sağlık Bilimleri University, Nephrology, Istanbul, Turkey*

Introduction: Autosomal dominant polycystic kidney disease (ADPKD), the most common inherited renal cystic disease, is characterized by progressive cyst growth in the kidney and other organs.Cyst expansion leads to focal areas of renal ischemia Increased activity of the renin-angiotensin system (RAS) secondary to ischemia seems to play an important role in the rise in blood pressure.On the other hand, obstructive sleep apnea (OSA) which is most seen sleep-disordered breathing, is characterized by apneas, hypopneas related to repeated upper airway obstruction during sleep, leading to intermittent hypoxaemia and sleep fragmentation(5). Hypoxia stimulates RAS activation. This activation leads to local inflammation in the carotid body which plays a pathogenic role in sleep apnea. Moreover, this activation leads to increase in blood pressure.In this study, we investigated the frequency of obstructive sleep apnea syndrome (OSAS) in ADPKD patients either with chronic kidney failure (CKF) or not. We also compared frequency of OSAS between ADPKD patients and a control group with normal kidney function and normal blood pressure. We also aimed to see effect of RAS blockage on obstructive sleep apnea.
Materials and Methods: We recruited 51 ADPKD patients for the study. Additionally, presence of sleep apnea syndrome symptoms, other comorbidities including hypertension, use of ACE-I or ARB were asked to all participants. Finally, 43 patients were enrolled into polysomnography (PSG) study. In-laboratory full night PSG which is gold-standard diagnostic test for OSA was performed to all participants. Patients with apnea hypopnea index (AHI) score higher than 5 were accepted as having OSAS.Patients with eGFR values below 60 ml/min were accepted as CKF patients. We matched the patients and controls with normal kidney function and normal blood pressure.
Results: 26 patients had OSAS in the study group. Regarding **severity of OSAS among 26 patients, 16 patients had mild OSAS, 7 patients had moderate OSAS and 3 patients had severe OSAS.** Frequency of OSAS in patients with eGFR levels below 60 ml/min were significantly higher than individuals with eGFR levels above 60 ml/min(14/17(82,3%); 12/23(52,1%), respectively, p:0,048). In terms of presence of OSAS, there was no significant difference between ADPKD and control groups (p=0,367). Subgroup

analysis of study group was conducted and subgroups were compared with control groups after adjusting age, gender and BMI. Regarding presence of OSAS, there was no significant difference between e-GFR>60 ml/min ADPKD patients and control group(p=0,759). However, there was significant difference between e-GFR<60 ml/min ADPKD patients and control group(p=0,018). Regarding effect of RAS blockage on frequency of OSAS in hypertensive ADPKD patients, there was no significant difference in terms of OSAS between patients using ACE-I/ARB compare to patients not using RAS blockers (18/27(66,6%), 3/5(60%), respectively; p=0,77)
Conclusions: It is well known that ESRD (e-GFR<15 ml/min) is associated with sleep disorders. In our study, we showed that ADPKD patients with CKF(e-GFR 15-60 ml/min) had higher rate of OSAS compare to non-CKF patients and healthy control group. As conclusion, uremia progression of rather than RAS activation seems to play a role for OSAS in ADPKD patients.
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HEARTBEAT-RELATED RESPONSES OF FRONTAL CORTICAL NEURONS IN THE SLEEP-WAKE CYCLE IN CATS

V. Lavrova [1]. [1] *Institute for Information Transmission Problems (Kharkevich Institute) RAS, Moscow, Russian Federation*

Introduction: The visceral theory of sleep (Pigarev, 2013) assumes that the cerebral cortex switch to the analysis of interoceptive information coming from visceral organs during sleep. This was first confirmed in gastrointestinal tract researches, when cortical responses related to its activity were actually detected in visual cortical areas during sleep. Moreover, we found some sleep-related responses for cardiac activity on iEEG and local field potentials (LFPs), which appeared in normal sleep in frontal and insular cortical region. This study aimed to explore heartbeat-related activitation of single neurons in frontal cortex regions during sleep-wake cycle.
Materials and Methods: In two adult cats, LFP and neuronal firing were recorded with transcranial intracerebral bipolar microelectrodes from frontal cortex. Electrodes' placement was selected according to pre-existing assumptions about the possible whereabouts of cortical areas related to heart activity. ECG was recorded with two electrodes located in the stomach and on the cat's head. We recorded iEEG, breath rhythm and eye movements as well, to identify the sleep phases. Our analysis included 2-5 hours records, with periods of wake, normal NREM and REM sleep. The processing and statistical analysis were made with Spike2 CED, including special self-made scripts.
Results: In 20 records, we marked out over 120 single neurons. Heartbeat-related responses as changes of neuronal firing were found in 32,4%, in frontal cortex of both hemispheres. This connection between neuronal firing and cardiac activity appeared during slow-wave sleep but was not observed in wakefulness.
Conclusions: Now we see that information related to cardiac activity reaches cerebral cortex during sleep indeed. Our results confirm that cerebral cortex becomes visceral-analyzing during sleep, and this special brain-heart axis develops information in sleep in order to restore the somatic functionality of all the body organ systems.
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HUMAN SERUM PROTEIN CHANGES AFTER 6 H OF SLEEP DEPRIVATION INVESTIGATED WITH NEWER PROTEOMIC METHODS

A.A. Bjørkum [1], J.T. Olsen [1], H. Hvesser [1], N. Omar [1], F. Berven [2,3], E. Birkeland [2,3]. [1] *Western Norway University of Applied Sciences, Department of Safety, Chemistry and Biomedical Laboratory Sciences, Bergen, Norway;* [2] *University of Bergen, The Department of Biomedicine, Bergen, Norway;* [3] *The Proteomics Unit at the University of Bergen (PROBE), Bergen, Norway*

Introduction: Sleep-wake associated studies using omic-methodology are increasing (O'Callaghan et al. 2019). Studying effects of partial sleep deprivation (SD) at night using proteomics- and systems biological approach has been sparse (Mauvoisin, 2019 and Noya et al. 2019). Earlier finding revealed changes in 34 proteins in human blood serum after 6 hour of sleep deprivation at night (Bjørkum et al. 2021). The aim of this study was to further identify differentially expressed proteins in human blood serum after loss of 6 h sleep at night using newer proteomic methods and exploring systems biological databases.
Materials and Methods: In a within subject-design-study a control night were the participants (n=6 females) slept from 10:00 pm to 07:00 am and the following night sleep deprivation (SD) was performed from 10.00 pm to 04:00 am. Sleep/wake data can be found in Bjørkum et al. 2021. Venous blood was sampled at 4:00 am. Proteins from blood serum was heat denatured at 95C° for 5min, prior to reduction (DiThioThreitol) and alkylation (Iodoacetamide). Denatured proteins were digested overnight (16h) at 37C° and desalted using Oasis (waters) spin columns. Desalted proteins were lyophilized and dissolved in HEPES buffer (pH 8.5). TMT-labels were added to each sample (16plex, ThermoFisher), and desalted and lyophilized prior to high-pH fraction using an offline HPLC (Waters, HPLC). The samples were run a Orbitrap Exploris masspectrometer (ThermoFisher) coupled to an Ultimate 3000 HPLC. Raw-files were search against the Swissprot database using Proteome Discoverer 2.5. Further analysis of the data was performed in Perseus. Gene ontology analysis were performed using Gene Set Enrichment Analysis, Omim, Webgestalt.
Results: We identified 590 proteins, 63 proteins were differentially expressed, 25 upregulated and 38 downregulated. The 63 proteins took part in 229 biological processes and 31 molecular functions.
The differentially expressed proteins after 6 hours of sleep deprivation at night could be linked to affected biological processes such as e.g., immune-, coagulation- and metabolic related cellular processes. Also, proteins associated with pathological conditions such as cardiovascular- and dementia related diseases and various types of cancer were affected.
Earlier published omic-studies after lack of sleep indicate cellular stress reflected in a distinctly changed serum proteome by identifying specific protein markers to reveal distinctly affected biological processes, molecular functions, cellular pathways, DNA damage and repair and disease related proteins after sleep deprivation (see refs. In Bjørkum et al. 2021). Impaired immune system and diseases associated with sleep deprivation have been reported (Bjørkum et al. 2021, Ma et al, 2018; O'Callaghan et al. 2019, Pellegrino et al., 2012 and Pinotti et al., 2010).
Conclusions: Acute sleep deprivation as little as 6h at night, at least in females, affects several differential expressed proteins taking part in several distinct biological processes- and molecular function categories. Also, the differentially expressed proteins are related to pathological associated conditions like impaired coagulation, oxidative stress, inflammation and immune suppression, neurodegenerative related disorders, and cancer. This is in line with earlier studies from our group (Bjørkum et al. 2021).
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HYPOCRETIN RELEASE AND PLASTICITY OF HYPOCRETINERGIC RECEPTORS IN A PHARMACOLOGICAL MODEL WITH NARCOLEPSY-LIKE FEATURES INDUCED BY SUVOREXANT IN RATS

C. Carrera-Cañas [1,2], M. Garzón [1], M. Callejo [1], I. De Andrés [1]. [1] *Universidad Autónoma de Madrid, Anatomy, Histology and Neuroscience, Madrid, Spain;* [2] *Tatiana Pérez de Guzmán el Bueno Foundation, Predoctoral Fellow, Madrid, Spain*

Introduction: The hypocretinergic (Hrct) system is a neuromodulatory network involved in many physiological processes among which is the control of the sleep-wake cycle. This system comprises two excitatory hypothalamic neuropeptides -Hrct1 and Hcrt2 (or orexins A/B)- and two G-protein-coupled receptors -HcrtR1 and HrctR2- widely distributed throughout the central nervous system. Malfunction of this system is related to narcolepsy. Low or undetectable levels of Hcrt1 in cerebrospinal fluid (CSF) constitutes a diagnostic criterion for Narcolepsy Type I. In the present study we have used Suvorexant, a dual Hrct receptor antagonist, to obtain a pharmacological experimental model with Narcolepsy-like features in rats by blocking the two Hrct receptors. In this model we have explored CSF Hcrt1 levels and HrctR1 and HcrtR2 expression within the hypothalamus.
Materials and Methods: In three groups of 8 rats daily i.p. injections of Suvorexant (10 or 30 mg/kg doses) or vehicle (DMSO) were done in the