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.
Acknowledgements: We thank Dr. Sinan Trabulus.

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.
Acknowledgements: This study was supported by RFBR grant No 16-04-00413.

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).
Acknowledgements: Beate Kluge, Tiril Knutsen, Kristina Lærdal, Siri Bildøy

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

dark period for 7 days. Body weight was monitored throughout the treatment. After treatments, CSF Hcrt1 concentration was determined by competitive enzyme immunoassay (EK-003-30, Phoenix Pharmaceuticals Inc). HcrtR1 and HcrtR2 levels within the hypothalamus were analyzed by western blotting (HcrtR1 antibody - ab68718; HcrtR2 antibody - ab183072). Paired t-tests, ANOVAs for repeated measures and independent samples, and post-hoc Fisher PLSD test were used for statistical comparisons.

Results: Systemic blockade of the hypocretinergic transmission with the high dose of Suvorexant produced a statistical significant increase in body weight by the end of the treatment. In control conditions hypothalamic HcrtR1 expression was significantly higher than that of HcrtR2. The high dose of Suvorexant also produced statistical significant changes in both, Hrct1 levels in CSF and HrctR1 expression in the hypothalamus, while, not significant changes occurred with the low dose. That is, daily i.p. administration of 30mg/kg of Suvorexant produced a significant decrease in Hcrt1 concentration in CSF together with a significant overexpression of HcrtR1 in the hypothalamus with respect to the control group. HcrtR2 hypothalamic levels did not change significantly.

Conclusions: The pharmacological model with narcolepsy-like features induced by chronic administration of high doses of suvorexant showed a significant increase in body weight and a significant decrease in CSF Hcrt1 levels as observed in narcoleptic type1 patients. These effects were accompanied by a compensatory overexpression of HcrtR1 in the hypothalamus while HcrtR2 expression remained almost unchanged. Altogether, they indicate an autoregulatory role of HcrtR1 within the hypothalamus for the synthesis and/or release of hypocretins.

Acknowledgements: This study was supported by FI19058 FEDER grant

INVESTIGATING THE RELATIONSHIP BETWEEN SLEEP AND FASTING-INDUCED TORPOR IN THE LABORATORY MOUSE

S. Wilcox [1], V. Munday [1], S. Peirson [2], D. Bannerman [3], V. Vyazovskiy [1]. [1] *Univerisity of Oxford, Physiology, Anatomy and Genetics, Oxford, United Kingdom;* [2] *Univerisity of Oxford, Nuffield Department of Clinical Neurosciences, Oxford, United Kingdom;* [3] *Univerisity of Oxford, Experimental Psychology, Oxford, United Kingdom*

Introduction: Torpor is a controlled state of hypometabolism that many species utilise to conserve energy. It is thought that there is a relationship between torpor and sleep. For example, torpor is entered via non-rapid eye movement sleep (NREMS), and a rebound in slow wave activity (SWA, EEG power density between 0.5-4 Hz) is observed in sleep immediately following arousal from torpor in Djungarian hamsters. Laboratory mice are known to readily enter bouts of torpor when undergoing food restriction protocols, which are commonly used in sleep and circadian studies, and behavioural neuroscience. However, the relationship between euthermic sleep and torpor in laboratory mice has not been well characterised, as such torpor induction may be confounding data generated in these fields when food restriction (FR) is used. The aim of this study was to further investigate how torpor and euthermic sleep processes interact.

Materials and Methods: Chronic EEG/EMG implants were performed in adult male C57Bl/6J mice (n=4). Mice subsequently underwent a 6-hour sleep deprivation (ZT 21-3) under ad libitum feeing conditions. Following a recovery period, mice were fed once daily and maintained at ~85% of their free feeding weight to induce torpor. Peripheral body temperature (Tskin) was continuously monitored using non-invasive thermal imaging cameras, to detect hypothermia bouts associated with torpor. Torpor bouts were operationally defined as a Tskin of >2 standard deviations below baseline for at least 1 hour. Once the animals were reliably entering torpor, another 6-hour sleep deprivation was conducted, followed by feeding. As a control, mice were also fed following a ~6-hour torpor bout occurring between ZT 21-3. Vigilance states were scored offline by visual inspection of EEG/EMG signals in 4s epochs.

Results: On days where no manipulations where performed, mice spent a greater percentage of time in NREMS during FR compared to during ad libitum (56% vs 38%, P<0.05). In the 6 hours following sleep deprivation, mice spent significantly less time in NREMS when food restricted compared to when fed ad lib (52.1 ± 2.5% vs 62.9 ± 4.9%; p=0.04). Mice fed after a torpor bout also spent less time in NREMS compared to post-sleep deprivation in ad libitum conditions (48.6 ± 3.8% vs 62.9 ± 4.9%; p<0.05). In the 24 hours following sleep deprivation/torpor, mice spent more time in NREMS (Ad lib: 42.6 ± 5.1%; FR: 50.8 ± 2.1%; Torpor: 53.1 ±2.9%), but less time in REMS (Ad lib: 7.0 ± 1.4%; FR: 6.0± 1.3%; Torpor: 6.2 ± 1.3%), when undergoing food restriction although these differences were not significant (P>0.05). In all conditions, initial sleep after sleep deprivation or torpor was characterised by increased levels of SWA. However, peak SWA in the FR and post-torpor condition was delayed and lower than during ad libitum conditions (Ad lib peak: 153 ± 1.3%; FR peak: 118 ± 2.1%; Torpor peak: 98 ± 4.6%).

Conclusions: Our preliminary results support the notion that daily sleep architecture is altered in association with fasting-induced torpor in mice, but provide limited evidence for that fasting-induced torpor is a sleep-depriving state.

Acknowledgements: NC3Rs (NC/S001689/1)

MACHINE LEARNING APPROACH FOR DETECTION OF INTRACRANIAL INTERICTAL DISCHARGES IN THE MEDIAL TEMPORAL LOBE DURING SLEEP

R. Falach [1], L. Goldstein [2], F. Fahoum [2,3], Y. Nir [1,4,5]. [1] *Sagol School of Neuroscience, Tel Aviv University, Tel Aviv, Israel;* [2] *EEG and Epilepsy Unit, Department of Neurology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel;* [3] *Department of Neurology and Neurosurgery, Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel;* [4] *Department of Physiology and Pharmacology, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel;* [5] *The Sieratzki-Sagol Center for Sleep Medicine, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel*

Introduction: Interictal epileptiform discharges (IEDs) are brief paroxysmal electrographic events observed between spontaneous recurrent seizures in epilepsy patients. IEDs (i) have a duration of 70–200 ms (for a sharp wave) or 20–70 ms (for a spike), (ii) entail an abrupt change in polarity, (iii) have a restricted physiological spatial field, and (iv) are most prevalent in non-rapid eye movement (NREM) sleep. IEDs occurring in the medial temporal lobe (MTL) during sleep may impair memory by affecting hippocampal-cortical coupling, and their reliable detection has clinical value in epilepsy and other neurological conditions. Here we set out to develop and validate automatic detection of IEDs with a machine learning approach in intracranial EEG (iEEG) and in scalp EEG.

Methods: Six drug-resistant mesial temporal lobe epilepsy (MTLE) patients underwent clinical pre-surgical evaluation and were implanted with intracranial depth electrodes in the MTL. Overnight iEEG recorded with Blackrock system, referenced to a central scalp electrode sampled at 2KHz and bandpass- filtered between 0.1-500Hz. Sleep was scored using established guidelines of the American Academy of Sleep Medicine. We focused on three channels per hemisphere: the anterior hippocampus referenced to Cz, the anterior hippocampus referenced to adjacent electrode (5mm more laterally), and the amygdala referenced to Cz. Preprocessing included segmentation of the signal to 250ms intervals and extraction of signal features for the current and the previous interval, such as spectral power in specific frequency bands and statistical features such as variance and skewness. Then, we split intervals randomly into train (75%) and test (25%) subsets and trained two algorithms- Random forest and LightGBM. The first task aimed at detecting IEDs in iEEG. To this end, we used a dataset that contained 337 IEDs in NREM sleep (overall: 30 minutes, n=6) tagged by an expert neurologist. The second task aimed at detecting IEDs in a limited number of scalp EEG (Fz, Cz, Pz) and EOG electrodes. To this end, we used the results from the first model on the entire overnight dataset. This dataset contained 3466 IEDs (overall: 40 hours, n=6) as tagged by the random forest classifier. For each task and algorithm, we assessed the test results using standard metrics of precision (number of positive class predictions that indeed belong to the positive class) and recall (also known as sensitivity; number of positive class predictions out of all positive examples in the dataset).

Results: Results of the first task (automatic detection in intracranial data) were assessed by comparing model outputs to manual annotation by expert neurologists. We obtained with random forest classifier: precision=92% and recall=66%, and with LightGBM classifier: precision=88% and recall=74%. Results of the second task (automatic detection in scalp