portable CL-TMR system could pave the way to the application of the TMR paradigm in everyday life, promoting the well-known electrophysiological rhythms involved in the sleep-dependent memory consolidation process.

BRAIN RESPIRATORY PULSATILITY OF FAST FMRI STABILIZES DURING NREM STAGE 2 SLEEP

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Introduction: Studies suggest that respiratory pulsatility is one phenomenon that drives the cerebrospinal fluid (CSF) flow[1,2], that is known to contribute in metabolic waste clearance during slow wave sleep[3,4]. Important physiological change in NREM sleep is, that ventilation becomes more regular than during awake[5]. It is not known whether this regularity of the respiratory pulsatility can be seen in the brain during different sleep stages.
Materials and Methods: 23 healthy subjects (27.0 ± 4.9 years, 12 females) were scanned with fast functional magnetic resonance imaging (fMRI) called magnetic-resonance-encephalography (MREG, repetition time 100 ms) during awake in the afternoon and during sleep in the evening (10 subjects) or in the morning after sleep deprivation (13 subjects). EEG and end-tidal carbon dioxide ($EtCO_2$) signals were measured in synchrony with MREG. Our trained EEG specialists made sleep scoring for the data based on standard AASM criteria. Physiological $EtCO_2$ signals were used to specify individual respiratory frequency range (varying between 0.08-0.49 Hz) for each subject, so that minimum and maximum values met the starting noise level. After standard preprocessing steps with FSL program, MREG data were bandpass filtered to individual respiratory frequency range. Then, spectral entropy, the measure of complexity or stability of the signal, was calculated for filtered MREG data. Awake data was compared with NREM stage 1 (21 subjects) and separately to NREM stage 2 (14 subjects) sleep data using two-sample paired T-test with FSL randomize (with Threshold-Free Cluster Enhancement and family-wise error).
Results: We found that spectral entropy decreased during NREM stage 2 sleep and, that no difference was found between awake and NREM stage 1 sleep. Decrease of spectral entropy in stage 2 sleep was brain wide ($p<0.05$) and the regions with smallest p-values were found in ventromedial prefrontal cortex and visual cortex ($p<0.015$).
Conclusions: Our results show that whole brain respiratory pulsatility stabilizes in NREM stage 2 sleep, which is in line with respiratory physiology[5]. Prefrontal cortex has been suggested to initiate slow waves with decreased blood flow[6], and visual cortex is known to produce increased very low frequency fluctuations in low vigilance levels and sleep[7,8]. These both could be further studied in relation to respiratory pulsations. We suggest that brain respiratory pulsatility change towards more regular pattern may contribute to CSF flow in NREM stage 2 sleep.
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CHARACTERIZATION OF ELECTROENCEPHALOGRAPHIC AND ELECTROMYOGRAPHIC AROUSALS DURING SLEEP

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Introduction: Though there are some studies dealing with the details of spontaneous arousal, they are mainly about micro-arousals (MAs) happening with K-complex during N2 phase of NREM sleep. The spontaneous arousals (with EEG and EMG signals) that happen throughout night have not been characterized in detail. It is also important to compare the final arousal that occurs in the morning with spontaneous arousals that take place during sleep. There are no studies on the sequence of appearance of physiological signals like EEG and EMG during spontaneous arousals and final arousal in the morning. The study of the time delay in the appearance of these two physiological signals may help in the better understanding of sleep-wake (SW) regulation. Spectral analysis of EEG power band and EMG activity, computed as the root mean square (RMS), will improve the quality of the findings
Materials and Methods: The research was approved by the Institutional Ethics Committee (No. IECPG/119/1/2019). Adult healthy non-smoker male participants (n=15), in the age group of 18 to 35 years with a normal SW cycle were included in the study. All the participants filled sleep diaries for a week followed by overnight Polysomnography as per standard AASM criteria
Results: Spontaneous arousals, with associated EEG and EMG changes, occurred almost uniformly throughout non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. EEG changes preceded EMG changes during a majority of the spontaneous arousals. While waking up finally in the morning, which mostly happened during the REM sleep, increased EMG activity preceded the EEG in the majority of the events. There was a delay of more than a second in between EEG and EMG changes, in both spontaneous arousals and early morning awakenings. There was a significant increase in the delta power and in all the frequency bands during spontaneous arousals, compared to the pre-arousal values. Though similar changes in EEG happened during the early morning awakenings also, there were significant differences in beta and sigma EEG powers and computed root mean square EMG during the early morning awakenings
Conclusions: The differences in the characteristic features of EEG and EMG changes during spontaneous arousal and early morning arousal indicated the probable role of these changes in facilitating the continuance of sleep in the former, and waking up from sleep in the case of the latter
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DETECTING OFF PERIODS IN MULTIUNIT ACTIVITY SIGNALS

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Introduction: OFF periods are times of neuronal silence associated with slow waves during NREM sleep, thus providing a link between fine-grain neuronal dynamics and whole brain EEG activity. Although there is general consensus on the concept of an OFF period, definitions and therefore methods of detecting OFF periods vary. Using a combination of clustering and thresholding informed by the behaviour of the data itself, we designed a pipeline for detecting OFF periods in multiunit activity signals (MUA) with the same dynamics as previously described but without the need for arbitrary thresholding.
Materials and Methods: Seven C57BL/6 mice were implanted with a laminar probe for recording local field potential (LFP) and multiunit activity (MUA) in motor cortex. Screws were implanted in the cranium and nuchal muscle to record electroencephalograms (EEG) and electromyograms (EMG) respectively. Mice were recorded over a 48 hour period; a baseline day (BL) with no intervention and a sleep deprivation day (SD) in which mice were prevented from sleeping from ZT0-ZT6. Four second epochs were scored as wake, NREM or REM based on electrophysiology. OFF periods were detected in a 3 stage pipeline. First, negative zero-crossings in a decimated variant of the MUA were detected. Second, we fit Gaussian Mixture Models (GMM) to a 2D dataset of NREM MUA signals smoothed at two different window lengths. Third, the intersection of negative zero-crossings and points clustered to the lowest amplitude

GMM component was calculated to find the final population of OFF periods.
Results: The majority of OFF periods were detected in NREM sleep (88.59%, CI=84.18 - 92.97) and REM sleep (6.87%, CI=3.46 - 10.29) with a small proportion detected in wake (1.15%, CI=0.39 - 1.91). Mean OFF period length across all animals and states was 114ms. The average LFP profile of all detected OFF periods shows a strong positive deflection that peaks ~45ms after OFF period initiation. There was a positive correlation between OFF period LFP amplitude and OFF period length with the regression of these variables significant (linear model, R^2=0.85, t=9.46, p<0.001). There was a significant fixed effect of prior experience on OFF period occupancy (linear mixed model, t=7.36,p<0.001), frequency (linear mixed model , t=7.39,p<0.001) and length (linear mixed model , t=13.42,p<0.001) during the second half of the dark phase (ZT6 - T12) with all three metrics higher for the sleep deprivation treatment. The temporal coincidence of OFF periods increased as laminar probe channel distance decreased.
Conclusions: OFF periods detected by our pipeline show similar properties to those previous described. OFF periods occur predominantly in NREM sleep and are associated with slow-wave like LFP profiles that increases in amplitude as a function of OFF period length. OFF periods show strong in homeostatic dynamics, increasing in frequency, length and overall occupancy time after sleep deprivation. Finally, OFF periods are shown to be both a global and a local phenomenon across layers of motor cortex.
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DISRUPTION OF SLEEP ARCHITECTURE AND RETICULAR THALAMIC (RT) NEURONAL FIRING ACTIVITY IN NEUROPATHIC PAIN

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Introduction: Neuropathic pain (NP) is an important public health problem with no effective treatments. It has been demonstrated that chronic pain condition produces changes in sleep pattern in about 80% of the patients (Finan et al., 2013). Indeed, poor sleep occurred in patients with a widely variety of pain disorders including musculoskeletal (Yu-Lin Wu et al 2017), post-herpetic trigeminal neuropathy (Roth et al. 2010), post-surgery neuropathic pain, HIV, multiple sclerosis, trigeminal neuralgia, cancer, trauma/accident and diabetes (Wafik Said Bahnasy et al, 2018). To date, the brain mechanisms linking pain and insomnia are yet to be clarified. In this work, we thus examined the effect of NP in the L5-L6 ligature rat model in sleep architecture and in the electrical activity of the neurons of the reticular thalamus (RT), which is an area related to both pain and sleep.
Material and Methods: We induced NP in Wistar rats. 14 days later, rats were evaluated for allodynia using von-Frey filament. Animals with NP were then separated in 2 groups: one group was implanted with six stainless-steel wire electrodes in the skull for the EEG/EMG 24h recording, while the second group underwent in vivo electrophysiological recordings in the reticular thalamus (RT) (for details in methods see Ochoa-Sanchez et al., 2011). Sham operated animals were used as a control for both groups.
Results: EEG/EMG analysis showed that NP animals displayed a reduced time in non-rapid eyes movement (NREM) sleep (-20%, $t_{(14)}$=3.94, p<0.001) and an increase in wakefulness (+19.13%, $t_{(14)}$=3.47, p<0.05). In addition, NP animals displayed a fragmented sleep architecture ($t_{(14)}$=4.3, p<0.0001) represented by transient EEG arousals. No changes in the latency to NREM sleep ($t_{(14)}$=4.3, p=0.15) were detected. Baseline firing rate as well as burst-firing activity of RT neurons in NP animals were significantly higher than in control rats (firing rate: +344 %, $t_{(10.3)}$=3.12, p<0.01; burst-firing activity:+843.1%, $t_{(8.6)}$=3.86, p<0.004).
Conclusions: These findings indicate that NP is associated with significant changes in the sleep-wake cycle, particularly a reduced duration of NREM sleep, and in the activity of the RT neurons.
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EFFECT OF HIV INFECTION ON SLEEP AND CHRONOTYPE IN AN AGEING RURAL SOUTH AFRICAN COHORT

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Introduction: Sleep disturbances are a well-established consequence of HIV infection. The pathophysiology of these disturbances have yet to be experimentally defined, but theories suggest that HIV infection may both impact the homeostatic and circadian systems of sleep-wake regulation. Studies to date have primarily explored sleep quality using the Pittsburgh Sleep Quality Index (PSQI), with limited objective data available to probe specific sleep characteristics in people living with HIV (PLWH). Those that have employed objective measures have utilised PSG, which describes aspects of sleep architecture, but does not allow for longer term monitoring of sleep habits in the home environment unlike actigraphy. Crucially, much of the research on HIV and sleep has been conducted in industrialised societies with greater access to HIV education and healthcare. Therefore, the aims of this study are to utilise actigraphy to explore sleep parameters in PLWH, and assess whether HIV infection impacts chronotype in a rural dwelling South African population.
Materials and Methods: Participants (N = 688; aged 45-100y, mean 66.4 ± 12.07y; 426 women, 166 HIV+) from the Agincourt Socio-demographic and Health Surveillance System (Mpumalanga, South Africa) were selected randomly for inclusion in this study. Participants were required to complete the Munich Chronotype Questionnaire (MCTQ), and a subset of these participants (N = 172; aged 45-93y, mean 67.06 ± 11.6y; 99 women, 31 HIV+) wore an accelerometer for a minimum of 5 nights of actigraphy (ActTrust, Condor Instruments). MCTQ data were processed in Rstudio using the 'mctq' package. ANOVA and subsequent multiple linear regressions were performed in RStudio to determine the relationship between HIV status and both actigraphy and MCTQ parameters, controlled for age and sex.
Results: Actigraphy analyses showed no significant relationship between HIV status and measures of sleep efficiency. However, there was a significant relationship between HIV status and total sleep time, with HIV+ individuals sleeping significantly less ($F_{(3,168)}$ = 2.69; P=.0482). Analysis of the MCTQ showed that the effects of HIV infection were most prominent on working days, with HIV+ individuals going to bed earlier ($F_{(3,599)}$ = 15.17; P≤.001) and spending more time in bed $F_{(3,599)}$ = 18.79; P≤.001). This effect was most pronounced in HIV+ men, and was not observed on free days. Analyses also revealed that HIV status had an interesting interaction with age on MCTQ derived chronotype (P=.002). In HIV+ individuals, chronotype was significantly later before the age of 60, but shifted earlier with age, whereas the opposite relationship was observed in HIV- individuals ($F_{(4,264)}$ = 3.24; P=.012).
Conclusions: Together, these data suggest that PLWH are more fatigued by work than HIV- individuals, and their earlier bedtimes may reflect an effort to combat . However, the reduced actigraphically derived total sleep time suggests that sleep needs may not be met, resulting in a cycle of sleep restriction and fatigue. Moreover, HIV may impact phase of the internal biological clock producing a shift in chronotype. Analysis of circadian phase markers will complement these data.
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EFFECTS OF AUDITORY SLEEP MODULATION APPROACHES ON SLOW WAVES AND AUTONOMIC RECOVERY FUNCTIONS

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