Aspects of tree shrew consolidated sleep structure resemble human sleep

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Abstract:
Understanding human sleep requires appropriate animal models. Sleep has been extensively studied in rodents, despite substantial differences from human sleep like, for example, sleep fragmentation and number of discernible stages. This lead researcher to study sleep in a variety of animal models. Here we investigate sleep in tree shrews, small diurnal mammals phylogenetically close to primates and humans. We provide detailed information about tree shrew sleep structure, cycles, transitions and spindle occurrence. Tree shrews exhibited a consolidated sleep structure, with few interruptions by wake episodes, unlike the fragmented sleep structure in rodents that is often punctuated by extended wakefulness. The sleep bout duration parameter, which we estimated for tree shrews, was uncharacteristically high for a small mammal, and was similar to the parameter describing human sleep. We observed two distinct NREM sleep stages in tree shrews: a mixed NREM2 and NREM3 stage characterized by high delta waves and sleep spindles as well as a transitory NREM1 stage that occurred on NREM2/3 to REM transitions and consisted of intermediate delta waves with concomitant pronounced transient theta-alpha activity. Transition analyses confirmed that NREM1 to REM transitions reliably occurred in tree shrews, were undetectable in rats and interestingly appeared to occur also in humans, albeit on only a minority of stage transitions. Finally, coupling events between sleep spindles and slow waves tended to cluster near the beginning of the sleep period, paralleling findings in humans. Our results suggest a close homology of sleep structure between humans and tree shrews in spite of the large difference in body mass between these species.

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The Effect of a Mindfulness-Based Stress Reduction Program in FND – Design and Preliminary Results

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Abstract:
Background: Functional neurological disorder (FND) is a disorder in which patients present with a variety of neurological symptoms involving the motor system (e.g., weakness, tremor, seizures) and the sensory system (e.g., numbness, pain). However, in contrast to known disorders associated to those symptoms (e.g., stroke, epilepsy, movement disorders), no underlying organic brain damage can be identified. The pathogenesis of FND is partially unknown, but some studies suggested a role of stress and abnormal emotional awareness/regulation as predisposing factors. Detailed understanding of the interaction between stress and FND is however still missing.

Objective: The aim of this study is to investigate the effect of a mindfulness-based stress reduction (MBSR) program on stress and emotional awareness in FND.

Methods: In a longitudinal randomized controlled trial, 12 FND patients were recruited. During an 8-week interventional phase, 6 patients participated in a standardized MBSR program (active group), while another 6 patients followed their therapy as usual (control group). Before and after the interventional phase, both groups were tested for quality of life, perceived stress, symptom severity, interoceptive awareness and abilities in mindful cognition using self-reported questionnaires.

Results: At baseline, no significant differences were detected between the two groups. Comparing post-intervention to pre-intervention, patients participating in the MBSR program reported higher emotional awareness and enhanced abilities in mindful observing of internal and external phenomena compared to the control group. Furthermore, physical health improved over time in the active group compared to the control group. No changes in perceived stress or symptom severity were reported.

Conclusion: A mindfulness-based stress reduction program led to enhanced abilities in mindfulness and emotional awareness and improved physical health in FND patients. Overall, these preliminary results may suggest that the improvement of subjective physical health is due to changes in interoception. In order to elaborate the potential of MBSR as treatment in patients with FND, still more research is needed.

Keywords: *Functional neurological disorders, Mindfulness Based Stress Reduction (MBSR), Stress*

Face perception and pareidolia production in patients with Parkinson's disease.

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In Parkinson's disease (PD) patients, visual misperceptions are a major problem within the non-motor symptoms. Pareidolia, i.e., the tendency to perceive a specific, meaningful image in an ambiguous visual pattern, is a phenomenon that occurs also in healthy subjects. Literature suggests that the perception of face pareidolia may be increased in patients with neurodegenerative diseases. We aimed to examine, within the same experiment, face perception and the production of face pareidolia in PD patients and healthy controls.

Thirty participants (15 PD patients and 15 controls) were presented with 47 naturalistic photographs in which faces were embedded or not. The likelihood to perceive the embedded faces was modified by manipulating their transparency. Participants were asked to decide for each photograph whether a face was embedded or not.

We found that PD patients were significantly less likely to recognize embedded faces than controls. However, PD patients also perceived faces significantly more often in locations where none were actually present than controls. Linear regression analyses showed that gender, age, hallucinations, and Multiple-Choice Vocabulary Intelligence Test (MWT) score were significant predictors of face pareidolia production in PD patients. Montreal Cognitive Assessment (MoCa) was a significant predictor for pareidolia production in trials in which no face was embedded.

We conclude that our new embedded faces paradigm is a useful tool to distinguish face perception performance between healthy controls and PD patients. Furthermore, we speculate that our results observed in PD patients rely on disturbed interactions between the Dorsal (DAN) and Ventral Attention Networks (VAN).

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Dissociation of neglect in writing and painting: A case study

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Intro. Hemispatial neglect is a common neurological syndrome following a right hemispheric stroke (e.g., Di Monaco et al., 2011) that is commonly manifested in an inability to attend to the left, contralesional space (Heilman et al., 1993). This inability seem to arise from attentional deficits rather than deficiencies in the visual cortex (e.g. Kaufmann et al., 2020). It has been observed that painters exhibiting a hemispatial neglect concentrate on the right side of their paintings, while the left side of the painting is either completely lacking or strongly minimalized and simplified (Bäzner & Hennerici, 2006). At the same time, writing is also often affected by neglect resulting in some form of dysgraphia (Cubelli et al., 2000; Hartman et al., 1985). However, to our knowledge, no study to date investigated the differential expression of neglect in painting and writing within the same subject.

Methods. Here, we report a patient (M.) who exhibited a hemi syndrome on the left and a multimodal left hemispatial neglect after having suffered from a right temporal infarct. During his stay at the neurorehabilitation unit, he developed a strong wish to paint. His favorite subject was trees, which he painted in all sizes and colors, producing several watercolor paintings per day. Already prior to stroke, he had expressed an interest in painting but this urge to paint became amplified after the occurrence of stroke, resulting in a production of 41 watercolor paintings within 19 days. In order to analyze his output, an independent rater was instructed to score all the 41 paintings considering the relative location of every painting as well as location of the text within the painting. Furthermore, M.'s performance in two standardized creativity tasks such as the divergent pareidolias task (DPT) (Diana et al., 2020) and the Alternative Uses Task (AUT) (Guilford et al., 1978) was measured. Fisher's exact test was applied to determine an eventual nonrandom association between two categorical variables, i.e., "relative location of painting" (right vs. left) and "location of text within the painting" (right vs. left). Also, the modified *t*-test (Crawford & Howell, 1998) was run to compare M.'s performance in the two standardized creativity tasks to the performances of an age-matched (> 50 years, < 70 years) healthy control group (DPT: N=22, AUT: N=23).

Results. Fisher's exact test indicated that the relative location of the painting has an influence on the location of the text (p=.02), i.e., while paintings were most often located on the right side and while left side was very often neglected, the text was very often located on the left side. That is, out of the 41 pictures, 33 also contained text and of these 33 pictures, in 14 pictures the text was located on the left side while the painting was located on the right side, in 10 pictures both text and painting were located on the right side, in 8 pictures the painting was located on the left side while the text was located on the right side and in just one picture both text and painting were located on the left side. Furthermore, M's performance in the two administered creativity tasks was significantly higher as compared to the performance of an age-matched, healthy control group (DPT: p=.037 and AUT: p=.004).

Discussion and conclusions. The case of M. hints that there might be a different influence of spatial neglect with respect to painting or writing. Given that the vast majority of his paintings were located to the right side while the left side remained neglected (in agreement with Bänzer and Hennerici, 2006), the text was located on the neglected, left side in almost fifty percent of the pictures. While exhibiting this dissociation with respect to expression of spatial neglect when painting or writing, compared to a healthy, age-matched control group, he produced significantly more valid answers in two different creativity tasks.

Electroencephalographic biomarkers of attention observed among healthy participants performing a motor task.

Joaquin Penalver-Andres, Karin A. Buetler, Thomas König, René M. Müri, Laura Marchal-Crespo

Motor learning is a complex cognitive and motor process underlying neurorehabilitation. Cognitive (e.g., attentional) engagement is important for motor learning, especially early in the learning process. Training parameters supporting the cognitive engagement of participants – e.g., visual cues or task instructions – may be used to improve motor learning. In this study, we investigated if task instructions enforcing the underlying task rule of a virtual sailing task modulate motor learning and attentional networks engaged (reflected in alpha-band cortical activity) using Electroencephalography. Healthy participants (n = 36) were trained to surf waves as fast as possible in a virtual environment using a joystick. The explicitness of instructions was manipulated across implicit (I: participants sailed freely), explicit (E: verbally instructing them how to correctly align the boat), and explicit-implicit (EI: implicitly instructing them to move correctly using visual cues) conditions.
Our findings show superior motor learning linked to training with explicit knowledge about the task rules (E) and with visual cues enforcing these rules (EI) compared with training without any enforcement of the task rules (I). In a period of -50 ms to 350 ms relative to wave onset, we observed that EI participants significantly enhanced alpha strength over parieto-occipital and frontal areas compared with participants training with the other task instruction conditions.
Even though participants in the E and EI conditions improved their motor performance, training with visual cues (EI) may be associated with cognitive facilitation – namely, a lower engagement of selective visual (parieto-occipital) and executive (frontal) attentional brain networks after training. Together, our results suggest that training parameters such as task instructions indeed modulate the attentional engagement during motor learning and may be an important factor to consider in fields where instructions are commonly used to improve motor (re)learning (e.g., sports, rehabilitation, etc.).

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Neural, cognitive and metabolic characteristics of early-treated adult patients with Phenylketonuria

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Background
Phenylketonuria (PKU) is a rare genetic disease affecting the conversion of Phenylalanine (Phe) to Tyrosine (Tyr). This forces patients to adhere to a very strict low-protein diet to prevent severe neurological and cognitive impairments during development. However, even with a rigorous treatment, patients are often affected by mild cognitive impairments in comparison to their healthy peers and display abnormalities in the white matter of the brain. The present study aims to investigate white matter of the brain, cognitive functioning and metabolic parameters in adult patients with PKU. A preliminary analysis was performed on the data, which has been acquired so far.

Methods
As of yet, 19 early-treated patients with PKU (median age: 29.34, 8 female) and 22 healthy controls (median age: 27.01 years, 12 female) have been recruited for the study. All patients and controls underwent an MRI examination (diffusion tensor imaging, DTI) as well as a neuropsychological assessment including measurements of IQ and executive functioninig (shifting, working memory). In patients only, blood was drawn on the day of the examination to evaluate concurrent Phe- and Tyr-levels. The Phe:Tyr ratio was then calculated to evaluate the substrate:product ratio.

Results
IQ scores in patients (median = 97, IQR = 12) were significantly lower compared to controls (median = 108, IQR = 22; z = -2.29, p = .022). Additionally, patients showed worse performance in executive functioning (switching, z = -3.39, p = .001; working memory, z = -2.35, p = .019). DTI revealed abnormalities in the white matter integrity of the corpus callosum in patients compared to controls. The median metabolic scores were Phe = 715 µmol/L (IQR 338), Tyr = 40 µmol/L (IQR 13) and Phe:Tyr ratio =18 (IQR 7). Cognitive functions did not correlate with Phe- or Tyr-levels nor with the Phe:Tyr ratio.

Conclusion
Similar to the literature, we found cognitive impairments and abnormalities in the white matter integrity in early-treated patients with PKU compared to healthy controls. The current European guidelines for PKU suggest a Phe-level < 600 µmol/L. Despite the fact that most of our patients have surpassed this target level, we did not find a relationship between metabolic parameters and cognitive performance. Our results nicely follow up on some recent studies that call into question the traditional usage of concurrent Phe-levels as a predictor for cognitive impairments. Instead, it is suggested to use the long-term course of individual Phe-levels, which seems to better reflect the impact on cognitive functioning.

The role of sleep in the evolution of cognitive functioning after stroke

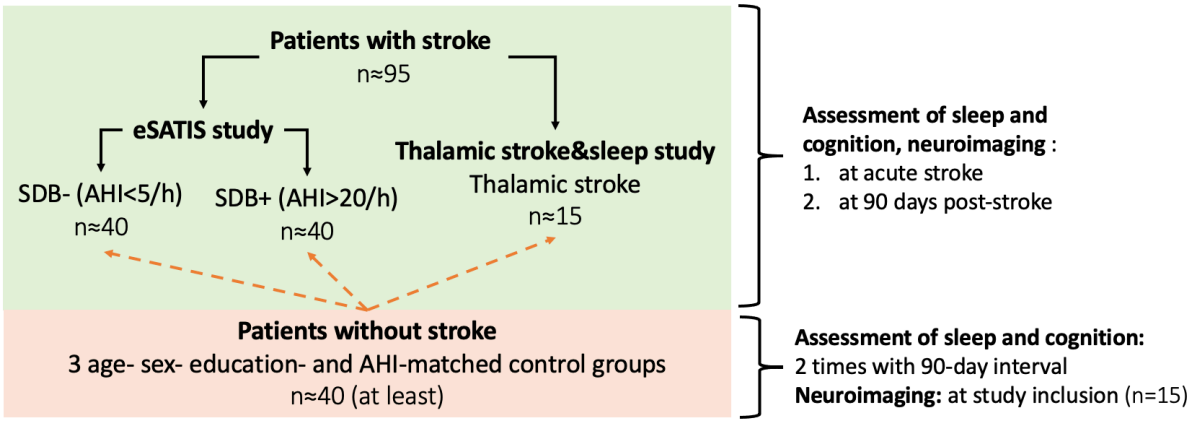
Irina Filchenko, Claudio Bassetti, Markus Schmidt, Simone Duss

Background
Cognitive dysfunction is common after stroke and has a tendency to recover over time. We hypothesized that sleep-wake-disturbances (SWD) may predict its evolution. The aim of this project is to assess the evolution of cognitive functioning from acute to subacute ischemic stroke and to investigate how sleep-disordered breathing (SDB) and the changes in sleep macro- and microarchitecture following a thalamic lesion affect this evolution.

Methods
We plan to perform two observational cohort studies in acute stroke patients ("Early sleep apnea treatment in stroke" (eSATIS) study, Thalamic stroke&sleep study) and to establish a matched non-stroke cohort to control for the effect of stroke and SDB on cognitive functioning (Figure 1). The stroke and non-stroke participants will undergo the assessment of sleep and cognitive functions and neuroimaging at study inclusion and at 90 days after study inclusion (Table 1).

Significance of results
The results of this project would allow to estimate how sleep characteristics and SWD relate to the post-stroke evolution of cognitive functioning. This knowledge would provide the basis for the future studies to clarify whether poor sleep could be regarded as a modifiable risk factor for cognitive dysfunction after stroke and to propose targeted therapeutic strategies in affected individuals.

Figures and tables
Figure 1. The structure of patient population and study procedures.



Abbreviations: SDB – sleep-disordered breathing, AHI – apnea-hypopnea index.

Table 1. The data acquired within eSATIS study, the study in non-stroke participants and Thalamic stroke&sleep study.

	eSATIS	**Control group**	**Thalamic stroke&sleep**
Cognitive parameters	Memory (HVLT, BVMT, number span and Corsi-Block tapping test), language (Bern Word Finding Test), neglect (Bells Test)		
	Attention (Psychomotor Vigilance Task), executive functions (Go/No-Go Task, TMT, Victoria Stroop)[3]		-
Sleep parameters	Objective (RPG) Subjective (ESS, FSS)	Objective (RPG/HD-EEG; actigraphy) Subjective (PSQI, ESS, FSS, SSS)	
Neuroimaging	Structural and functional 3T MRI	Structural and functional 3T/7T MRI[3]	Structural and functional 3T/7T MRI

Abbreviations: HVLT – Hopkins Verbal Learning Test, TMT - Trail Making Test, BVMT - Brief Visuospatial Memory Test, PSQI - Pittsburg Sleep Quality Index, ESS - Epworth Sleepiness Scale, FSS - Fatigue severity scale, SSS- Stanford Sleepiness Scale.

The Relationship between Perceived- and Biological Stress and distinct Neuroimaging Endophenotypes in Functional Neurological Disorder

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Abstract

Functional neurological disorder (FND) is a neuropsychiatric condition in which patients experience neurological symptoms in the absence of an organic neurological disease. Functional imaging studies linked abnormal motor control to an impaired emotional- and stress regulation. Current psychoneurobiological models aim at integrating both the neuroimaging findings underlying symptoms production and the role of psychosocial stressors as a risk factor for developing FND. However, little is known on the biological stress regulation in FND and only few studies have investigated brain network-stress relationships in FND.

In this study, we examined potential alterations in the biological stress regulation of 15 FND patients and 15 healthy controls assessed by the cortisol awakening response (CAR), basal diurnal cortisol levels and perceived subjective stress levels. Furthermore, we used a graph theory approach to elucidate perceived and biological stress effects on resting state functional connectivity architecture. Thereafter, we compared perceived- and biological stress in FND with regional differences in weighted functional connectivity.

FND patients had a significantly lower CAR and higher perceived subjective stress compared to healthy controls. Furthermore, diurnal baseline cortisol levels correlated with weighted-degree functional connectivity in the right frontal regions, bilateral anterior cingulate cortex, bilateral precuneus, bilateral temporal pole and the bilateral caudate. In summary, these preliminary results point towards an altered activity of the HPA axis in FND patients, which has neural correlates in terms of altered functional connectivity. This might represent an endophenotype of the disorder. Further longitudinal studies of these endophenotypes will advance the understanding of the pathophysiology of FND.