

Cognitive Somnology RIKEN Hakubi Research Team (2023)

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(0) Research fields

CPR Subcommittee: Biology

Keywords: Sleep, Brain Plasticity, Learning, Memory

(1) Long-term goal of laboratory and research background

Sleep is crucial for the continuity and development of life. Sleep-related problems can alter brain function, and cause potentially severe psychological, behavioral, and economic consequences. However, the role of sleep in our mind and behavior is far from clear. Accumulating evidence has shown that remembering events and improving various skills are dependent on sleep, as are the abilities that shape who we are and allow us to adapt to changes in our environment without losing previous experiences. The ultimate goal of my research program is to elucidate how sleep contributes to learning and memory to shape our mind, behaviors, and health. To this end, my research employs neuroimaging, psychophysics and physiological measurements, which is a powerful combination of modalities to make advancements in the field of sleep research in humans.

(2) Current research activities (FY2023) and plan

1. Magnetic resonance spectroscopy using 7T MRI

Magnetic resonance spectroscopy (MRS) is a useful noninvasive neuroimaging method that would allow us to investigate the concentrations of neurotransmitters and brain plasticity in the human brain *in vivo*. However, spatial and temporal resolutions are still limited using a 3T MRI scanner, thus, improvements are required to better characterize human brain plasticity *in vivo*. For example, a temporal resolution of 2 minutes was the best we could achieve using 3T MRI (Tamaki et al., 2020, *Nature Neuroscience*; Tamaki et al., 2021, *STAR Protocols*). Additionally, subcortical regions, including the hippocampus, are known to be particularly difficult in 3T MRI. In this project, we aimed to develop an MRS technique to improve data quality by conducting simultaneous MRS and EEG measurements using a 7T MRI scanner. This fiscal year, we have developed a simultaneous MRS-EEG method at RIKEN 7T MRI. We have successfully measured from several regions (e.g. SMA, hippocampus), though the signal quality in the hippocampus is much lower than the SMA and instability in the signals was observed. In the SMA, the temporal resolution was ~10s, significantly improved from the 3T MRI (2-10min). By leveraging this technique, we plan to investigate how brain oscillations involved in learning and memory modulate the E/I balance during sleep.

2. Interactions of memories during sleep

Sleep plays a pivotal role in learning and memory. Although the current understanding has been based primarily on research in a single memory system, another line of research has suggested that different memory systems interact when there is a common rule between them. It remains unclear whether sleep facilitates learning interactions, and if so how. Here, we investigated the effects of sleep on interactions of different memories and the neural basis of the interactions. We have previously found that interactions of memories occur only after a sequence of NREM and REM sleep. We further found that segregation and integration of brain networks during sleep plays an essential role in memory interactions. We plan to investigate how the changes in the E/I balance during sleep are involved in the memory interactions by using a simultaneous MRS-EEG method in 7T MRI.

3. Sleep decoding

While it has been shown that sleep facilitates postsleep behaviors, the traditional correlational neuroimaging method is insufficient to show the causal relationship. Thus, in this research, we develop a unique sleep-induction technique based on functional magnetic resonance imaging (fMRI). This technique will allow a specific sleep-like state to be induced in a specific region in an awake human brain. This fiscal year, by employing an fMRI decoding technique on sleeping brain activation patterns, we first tested whether sleep spindles, a key oscillation for brain plasticity, are represented in cortical and subcortical brain regions known to be involved in learning and memory. Subjects took a 90-min nap during early afternoon in the MRI scanner. Simultaneous polysomnography and fMRI measurements were conducted during the nap session. Sleep stages were scored in accordance with

AASM criteria. Sleep spindles were detected from NREM sleep stages. Spindle-event decoder was created using SVM based on spindle and no-spindle events for each session. Leave-one-out cross validation was conducted within the same session. The generalization performance was examined between sessions within individual subjects. We found that brain activity patterns in hippocampus and calcarine fissure successfully decoded spindle activity. A label-shuffled decoder showed a chance-level performance.

4. Cerebrospinal fluid dynamics during sleep

While cerebrospinal fluid (CSF) dynamics during sleep have been implicated in reducing metabolic waste products in animals, how these are regulated in the human brains remains elusive. Arousal-related brain activities induced during light sleep have been proposed to be the core mechanisms for modulating CSF flows. Yet, a myriad of research has shown that crucial processing, such as learning and memory, is manifest in deep sleep, suggesting that the key in maintaining healthy brain functions lies in deep stable sleep. By leveraging a simultaneous sparse fMRI and polysomnography method developed for measuring sleep, our results thus far demonstrate that human deep sleep uniquely modulates faster and milder CSF dynamics. We found that the frequency of CSF signals becomes faster during deep sleep (slow wave sleep and REM sleep) than during wakefulness or light sleep. We are currently investigating how brain oscillations modulate CSF dynamics in the deep human sleep.

5. Contribution of sleep to functional recovery in stroke patients

Stroke is one of the major causes of disability. Thus, how stroke survivors can gain the skills that were once lost to adapt to daily life has been an important question. In chronic patients, it is now widely believed that good recovery of movement after stroke is dependent on rehabilitation, however, intense training during rehabilitation is not always followed by functional recovery. We have previously demonstrated that sleep plays an essential role in skill learning via the changes in the network reorganization and the E/I balance. In the present study, we investigate the role of sleep in motor skill learning in stroke patients. This fiscal year, we have developed a task that can be performed by stroke patients. We have also performed preliminary experiments and polysomnography experiments in several stroke patients.

(3) Members

(RIKEN Hakubi Team Leader)

Masako Tamaki

(Research Scientist)

Makoto Uji

(Postdoctoral Researcher)

Fumiaki Sato

(4) Representative research achievements

Uji M, Tamaki M. Sleep, learning, and memory in human research using noninvasive neuroimaging techniques. *Neuroscience Research*, 189, 66-74, 2023.

Nishimura Y, Ikeda H, Matsumoto S, Izawa S, Kawakami S, Tamaki M, Masuda S, Kubo T. Impaired self-monitoring ability on reaction times of psychomotor vigilance task of nurses after a night shift. *Chronobiology International*, 40(5), 603-611, 2023.

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Li X, Uji M, Tamaki M. Active learning consolidation hypothesis. *Japanese Journal of Sleep Medicine*, 17(1), 67-71, 2023.

Laboratory Homepage

<https://cbs.riken.jp/en/faculty/m.tamaki/>

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