## Cognitive Somnology RIKEN Hakubi Research Team（2021）
**RIKEN Hakubi Team Leader: Masako Tamaki (Ph.D.)**

**(0) Research field**

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 (Carskadon and Dement, 1981). However, the role of sleep in our mind and behavior is far from clear. Remarkably, 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. My research employs neuroimaging, psychophysics and physiological measureents, which is a powerful combination of modalities to make advancements in the field of sleep research in humans. Through my interdisciplinary approach, I am uniquely positioned to develop highly innovative and applicable research programs.

### (2) Current research activities (FY2021) and plan (until Mar. 2025)

The lab just started in April 2021. Setting up the new lab space went quite smoothly with only minor modifications. All the experimental rooms completed in November. Now we have two sleep chambers (sound-attenuated and electrically shielded, Fig. 1A, B) and three behavioral testing rooms (sound-attenuated, Fig. 1C).

**A** Control room for sleep experiments **B** Sleep chamber **C** Behavioral testing rooms

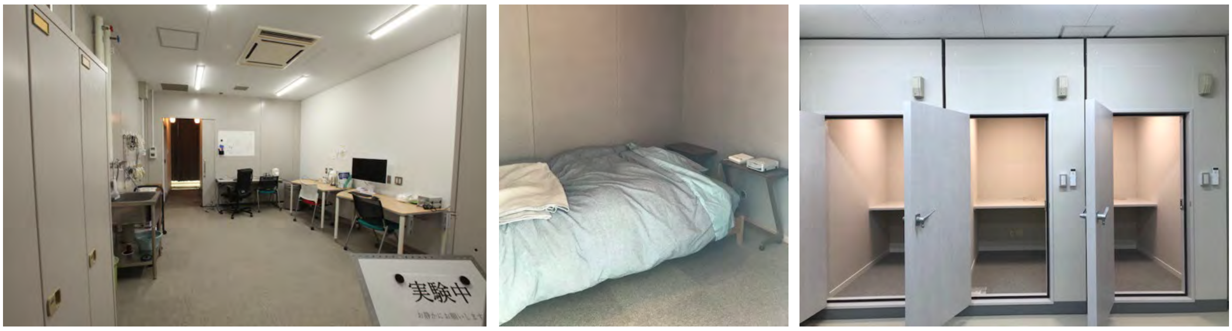


**Figure 1**: Experimental rooms in the Cognitive Somnology lab

1. **Learning-specific processing during sleep (2021)**

   How sleep leads to offline performance gains in learning, that is, significant improvements in performance after sleep, had remained controversial. A use-dependent model assumes that offline performance gains occur due to a general cortical usage during wakefulness, not specific to learning. A learning-dependent model assumes that this processing is specific to learning. In this project, we found evidence that supports a learning-dependent model in visual perceptual learning (VPL). We employed an interference paradigm to dissociate brain usage and learning. We measured the strength of brain oscillations during sleep. During sleep, slow-wave activity (SWA) and sigma activity during non-rapid eye movement (NREM) sleep and theta activity during REM sleep were source localized to the early visual areas, a brain region heavily involved in VPL, using retinotopic mapping. Inconsistent with a use-dependent model, only after learning, but not after brain usage, sigma and theta activity, increased in a trained region-specific manner and correlated with performance gains. There was no significant correlation between SWA, that reflects brain usage, and performance gains. These results demonstrate that sleep processing leading to performance gains is learning dependent in VPL and involves occipital sigma and theta activity during sleep. This research topic was published in the *Journal of Neuroscience*.

2. **Magnetic resonance spectroscopy using 3T and 7T MRI (2021-)**
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. As a first step, this year, we investigated the MRS data quality in the cortical (visual area) and subcortical (hippocampus) regions using ultra-short TE STEAM (TR=8s) and different types of shimming (standard shim, GRE shim, and fastestmap) were tested using 7T MRI (without EEG). MRS data were preprocessed using MRspa (www. cmrr.umn.edu/downloads/mrspa) and concentrations of Gamma-Aminobutyric Acid (GABA) and Glutamate were estimated using LCModel (Provencher, 1993). For the visual area, the temporal resolution was about 8-16 seconds (Fig.1). The Cramér-Rao lower bounds (or %SD), which indicates MRS data quality, were ~10% for GABA and 5-6% for Glutamate, with just an 8-second scan. As to the hippocampus, %SD was 8% for GABA and 3% for Glutamate with a 3-min scan (Fig. 2). By contrast, %SD was 16% for both GABA and Glutamate with a 10-minutes scan from the hippocampus, using a Siemens Prisma 3T MRI at RIKEN. Among the 3 types of shimming, the standard shim seemed to be the best at least for the hippocampus (standard, 8%; GRE, 9%; fastestmap, 35% for GABA).

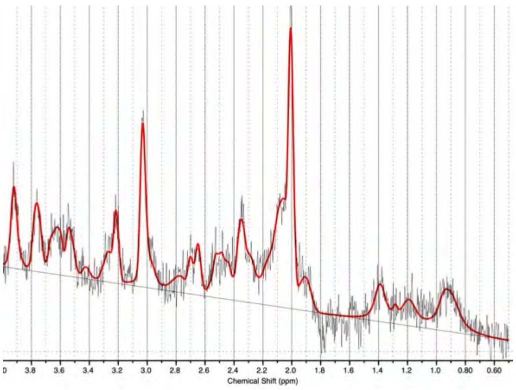


**Figure 2.** A representative spectrum (1TR data, no average) obtained from the visual area using 7T MRI.

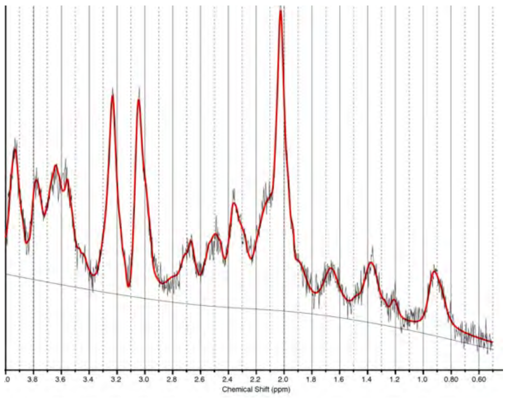


**Figure 3.** A representative spectrum (~3 minutes, 20 averages) obtained from the hippocampus using 7T MRI.

3. **Interactions of different types of memories during sleep (2021-)**
The roles of sleep in interactions of learning have remained elusive. One line of research has assumed that facilitatory effect of sleep is specific to a trained task and occurs locally in a brain region during nonrapid eye movement (NREM) sleep. However, another line of research has suggested that sleep involves plasticity changes in multiple brain regions over NREM and rapid eye movement (REM) sleep. How do such dynamic changes during sleep benefit learning? Interestingly, it has been shown that learning on a task can be transferred to a different type of learning if there is a common rule between them. This led us to ask whether sleep facilitates learning transfer via global reorganization of brain networks. This year, we mainly conducted behavioral experiments regarding this research theme. We used two tasks, a finger-tapping motor sequence task and a visual image memory task. On day 1, participants were trained and tested on the motor task. The visual task, which had the same sequence structure as the motor task, was introduced between the motor task sessions. On day 2, participants were retested on the same tasks. We found that performance on the motor task improved significantly from day 1 to day 2 intervening a night of sleep, only when the two tasks shared a common sequence. No significant improvement was found when the sequence structures were different. The results demonstrate that sleep indeed benefits learning interactions. These further suggest a possibility that sleep may play a role in reorganizing distinct memories that have been thought to depend on very different neural mechanisms. We are currently investigating the neural mechanisms of this facilitation of learning transfer during sleep.

**(3) Members**

**(RIKEN Hakubi Team Leader)**

Masako Tamaki

**(4) Representative research achievements**

Publications

1. **Tamaki M**. Role of NREM and REM sleep in visual perceptual learning. *Japanese Society for Physiological Psychology and Psychophysiology*, 39(1), 1-16, 2021. DOI: https://doi.org/10.5674/jjppp.2108si
2. **Tamaki M**, Watanabe T, Sasaki Y. Coregistration of magnetic resonance spectroscopy and polysomnography for sleep analysis in human subjects. *STAR Protocols.* 2, 100974, 2021. DOI: 10.1016/j.xpro.2021.100974
3. **Tamaki M**. Role of NREM and REM sleep in learning and memory. *Progress in Medicine.* 41(12), 1171-1175, 2021.
4. Wang Z, **Tamaki M**, Frank SM, Shibata K, Worden MS, Yamada T, Kawato M, Sasaki Y, Watanabe T. Visual perceptual learning of a primitive feature in human V1/V2 as a result of unconscious processing, revealed by Decoded fMRI Neurofeedback (DecNef). *Journal of Vision*. 21(24), 1-15, 2021. DOI: https://doi.org/10.1167/jov.21.8.24

Invited talks

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| 3/11/2022 | Consciousness Club Tokyo |
| 1/21/2022 | Vision Society of Japan, winter meeting |
| 12/24/2021 | CiNet, Friday Lunch Seminar |
| 12/11/2021 | Japan Society of Clinical Chemistry, Kanto meeting, Saitama |
| 9/23/2021 | The 46th Annual Meeting of Japanese Society of Sleep Research |
| 9/21/2021 | Japan Agency for Medical Research and Development |
| 9/16/2021 | The 21st NIPS meeting (memory meeting) |
| 7/30/2021 | The 44th Annual Meeting of the Japan Neuroscience Society, Toward understanding and breaking the limit of human minds and performance symposium |
| 6/27/2021 | Psychoneuroendocrinoimmunorogy meeting |

**Laboratory Homepage**

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

https://www.riken.jp/en/research/labs/hakubi/t_cogn_somno/index.html