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Research on the contribution of REM sleep to procedural learning

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Abstract. Many studies have confirmed the contribution of sleep to memory consolidation. However, the benefit of rapid eye movement (REM) sleep on memory consolidation remains debatable due to discrepant findings. This paper reviewed the latest human studies that employed complex cognitive procedural learning tasks and new learning techniques, including metacognition stimulation and targeted memory reaction (TMR), to provide evidence on the correlation between REM sleep and memory consolidation of procedural learning. Next, the main hypotheses aiming to explain its underlying neurobiological mechanisms were summarized, with a discussion about the striatum's role, the cholinergic system's activity, and synaptic plasticity during REM sleep. Finally, the paper discussed potential reasons for data inconsistency and several aspects that should be considered in future sleep and memory research.

Keywords: rapid eye movement sleep, memory consolidation, implicit procedural memory, motor learning.

1. Introduction

One of the well-known functions of sleep is the processing and consolidation of new memories, which is necessary for efficient learning. Importantly, sleep is not a unitary process, and different sleep stages are likely to play roles in the consolidation of different types of memories [1-2]. Over the past few decades, non-rapid eye movement (non-REM) sleep has been extensively researched. The important involvement of slow-wave sleep (SWS) and N2 sleep spindles in hippocampal-dependent learning, which needed the consolidation of declarative memory, was strongly supported by consistent findings from a number of studies [3-5]. On the contrary, the benefit of rapid eye movement (REM) sleep on memory consolidation remains debatable due to inconsistent data results. Some of the previous studies provide evidence supporting the dual process hypothesis that REM sleep plays a main role in non-declarative, procedural memory consolidation [6-8]. However, there are several studies indicating unaffected procedural memory consolidation after selective REM sleep deprivation [9-10]. Furthermore, later studies have correlated the consolidation of procedural memories with SWS and N2 sleep spindles [11-12]. In order to clarify the function of REM sleep and the mechanism of procedural memory consolidation during sleep for the implications of efficient motor learning, it is important to explore the causes of the discrepant findings by performing a thorough reflection of previous and recent studies. Therefore, this paper first summarized previous findings about sleep and procedural memory consolidation from the perspective of different types of motor learning tasks; next it reviewed the most recent evidence supporting the function of REM sleep on procedural learning in humans; then it

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summarized theories to explain the neurobiological mechanisms underlying procedural memory consolidation during REM sleep; and finally it discussed potential explanations for data inconsistencies as well as pointed out aspects that should be considered in future sleep and memory research.

2. Consolidation of various types of procedural learning

Procedural memory, as a type of long-term memory, stores implicit knowledge of skill-learning, often described as “knowing how”. The performance of procedural learning can be greatly improved by repetition and practice. Early in the review by Smith, various types of tasks used in sleep studies were summarized (see Table 1) [13]. Simple motor procedural tasks are likely to include non-verbal, fine motor learning without cognitive factors. Those mostly used in the previous research included finger-sequence tapping and pursuit rotor. Another broad category of procedural motor tasks is considered “complex” due to the involvement of a complex cognitive adjustment. Common ones include mirror tracing and Tower of Hanoi. Discrepant findings existed in studies using simple motor tasks. Fischer et al. reported that improvement in the finger-sequence tapping task was positively correlated with the amount of time spent in REM sleep [8]. The same task, however, yielded conflicting findings according to Nishida and Walker: a strong link was identified between the quantity of stage 2 non-REM sleep and performance improvements [12]. With respect to the pursuit rotor task, early in 1994, Smith and NacNeill found that deprivation of stage 2 sleep, rather than REM sleep, significantly inhibited memory processing of the task [14]. Later, Peters et al. found a factor in participants’ initial task performance based on the findings that performance improvement was proportional to an increase in stage 2 spindle density in the high-skill group (i.e., participants who showed higher initial performance), while the low-skill group showed a significant correlation between REM density and performance enhancement [15]. The authors thus proposed a model that sleep stages impact memory consolidation of procedural learning depending on the novelty of the motor task and the initial skill level of the individual to explain the different roles of REM and N2 non-REM sleep on simple motor learning. Contrarily, studies using cognitive procedural tasks had more consistent results with regard to the contribution of REM sleep on memory consolidation. For instance, Plihal and Born discovered that following the late sleep retention interval as opposed to the early sleep retention interval, the amount of time needed to complete the mirror trace task was dramatically reduced [2]. Additionally, Smith et al. showed that after completing the Tower of Hanoi and mirror trace tasks, there was an upsurge in both the total number of REM and REM densities [16].. Interestingly, the study also found that participants with higher IQ scores showed a greater increase in the intensity of REM sleep after the training and more improvement in task performance in the retest. This finding, together with the result from Peters et al., provided important insights that the initial skill or intelligence level as an aspect of individual differences should be included in the consideration.

Table 1. Types of Common Procedural/Implicit Tasks in Memory and Sleep Studies.

Name of task	Task characteristics	Type of sleep necessary
Wff logic task	cognitive, non-verbal	REM
Word priming	visual, verbal	REM
Corsi block tapping task	cognitive, visuospatial, non-verbal	REM
Tover of Hanoi	cognitive, non-verbal	REM
Pursuit rotor	fine motor, non-verbal	Stage 2 (N2)

3. REM and procedural memory consolidation: recent evidence

In the past 10 years, scientists studying procedural memory consolidation during sleep have focused on the use of complex cognitive procedural tasks with the application of some of the latest learning techniques. Brand et al. examined REM sleep's role in transferring implicit procedural knowledge with metacognitive stimulation [17]. Metacognition refers to the ability to regulate one's own learning of procedural knowledge and understand how it can be applied. In order to reduce the influence of subjective factors, the experiment randomly assigned the participants. The Tower of Hanoi cognitive procedural task was taught to both groups, but only the experimental group received metacognitive stimulation. Sleep data were recorded, and re-assessment was conducted the next morning, including a harder version of the Tower of Hanoi task. Participants in the experimental metacognition group had a significant increase in time spent in REM sleep on the post-training night, and showed better performance in the task during re-assessment. The results of this investigation reveal that REM is crucial for the memory processing of procedural knowledge after metacognitive learning. Regrettably, there are no statistics available on sleep variables like REM density.

Suzuki et al. trained participants on a visual discrimination task, which requires implicit procedural knowledge to discriminate the orientation of letters and diagonal bars on the target screen [18]. Sleep variables were recorded on an experimental night, and a retest session was conducted the next morning. Improvement in performance on the task was found to have a positive correlation with EEG alpha power during REM sleep. However, it is worth mentioning that Crupi et al. came to a different conclusion using sleep deprivation [11]. After learning a similar visuomotor task, participants went to sleep. For those in the experimental group, acoustic stimuli were applied to suppress slow wave activities (SWA). As a result, visuomotor performance improved significantly under the control condition, whereas overnight improvement was inhibited under the experimental condition of slow-wave deprivation. The finding led to the conclusion that SWA plays a causal role in procedural memory consolidation using visual motor tasks.

Through the use of targeted memory reactivation (TMB), Picard-Deland et al. more recently examined the impact of various sleep stages on whole-body procedural learning [19]. In light of the previous discovery, it is possible to promote memory consolidation during the sleep by offline resetting memory traces with a conditioned cue. The participants had virtual reality (VR) flight training before going to sleep while being exposed to task-related tones during SWS or REM sleep. The control group did not receive TMR. Results indicate that learning performance was the best in the condition where TMR was applied in REM sleep compared to the other two conditions, leading to the hypothesis that complex skill learning is most benefited by memory reactivation coexisting with procedural memory processing during REM sleep.

4. Neurobiological mechanisms underlying procedural memory consolidation during sleep

Benefiting from the rapid development of neuroscience techniques, it becomes more plausible and easier for scientists to investigate the neural mechanisms underlying memory consolidation of procedural knowledge as well as the change in brain and neuronal activities during REM sleep. Even though a lot of debates and controversies still exist, several hypothetical models were widely studied as more and more evidence was reported. It is well known that the striatum plays an essential role in motor sequence memory consolidation, which induces the hypothesis that the striatum is also involved in sleep-dependent consolidation of motor sequence memory. Barakat et al. reported functional imaging results that demonstrated an increase in striatal activity during increased non-REM sleep spindle activity, which has been correlated with memory consolidation of simple motor procedural learning [20]. However, Albouy et al. found that the increase in striatal activation was also evident when sleep in the night after the training was restricted, and the behavioral data of the sleep deprivation group showed that task performance was maintained rather than improved [21]. Therefore, in the review by Albouy et al., the authors drew several important conclusions: sleep was not required for the striatum-dependent memory trace to be processed, and striatal activity does not seem to promote improvement in procedural learning but rather the maintenance of performance [22]. Striatum has a function to trigger performance

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stabilization during the early phases of consolidation of motor sequence memory via mechanisms that do not rely on sleep.

A study by Rasch et al. emphasized the importance of the cholinergic system in procedural memory consolidation during REM sleep [23]. Participants first slept for 3 hours during the early night, then completed a declarative word-pair learning task and a procedural finger sequence tapping task. Either a placebo or a combination of nicotinic and muscarinic acetylcholine (ACh) receptor antagonists was administered after learning. Participants then took 3 more hours of sleep to undergo late REM stage. A re-assessment was administered the next evening. It was found that both REM sleep time and REM density were significantly reduced by the blockage of combined cholinergic receptors compared to the placebo condition. Importantly, the results of the retest indicated an evident improvement in procedural task performance was made by the placebo group, while no enhancement was found in the treatment condition with cholinergic receptor blockade. However, no significant difference in performance on the declarative memory task was found between the two conditions. Furthermore, two additional pieces of information the authors provided from the supplemental experiments help elucidate the story. First, serotonergic or noradrenergic substances can inhibit REM sleep as well, but they do not impact memory consolidation for procedural learning. Second, impaired offline consolidation of procedural memory caused by the blockage of combined cholinergic receptors occurs specifically during the late retention sleep but not during a retention interval with wakefulness. These findings specify the involvement of high cholinergic activity during late REM sleep in the consolidation of motor learning.

By monitoring and manipulating neural circuits in rodent models, additional research has recently sought to elucidate the cellular and molecular principles underpinning the function of REM sleep. After learning a motor task, Li et al. discovered that pyramidal neurons' postsynaptic dendritic spines were eliminated during REM sleep in the rat motor cortex, which further facilitated the growth of new spines [24]. The authors additionally demonstrated that REM sleep regulates NMDA receptor-dependent dendritic calcium spikes, which prunes and strengthens newly generated spines. With the approach of sleep deprivation, Zhou et al. obtained the same result: REM sleep deprivation inhibited dendritic spine elimination [25]. It is known that synaptic refinement is involved in experience-dependent learning and development. These studies thus offer potential support for REM sleep's function in the consolidation of procedural learning.

5. Conclusion

In sum, there are several aspects that should be considered before drawing a general conclusion about the relationship between REM sleep and procedural memory consolidation. First, procedural tasks are essentially distinct from each other considering the skills required to complete the tasks. For example, one main characteristic used for categorization is whether the task requires a complex cognitive adjustment. Therefore, questions regarding whether implicit procedural memory can be further categorized into different types with different underlying mechanisms of consolidation occurring at different sleep stages remain unanswered. Second, a number of animal studies provided evidence for the existence of “REM windows”, suggesting that certain periods of REM sleep play a critical role in post-training memory consolidation while times outside of the windows are not necessary for consolidation to occur. It was also suggested that “REM windows” exist in human sleep as well, based on the finding that the fourth and fifth REM periods have a remarkable increase in REM density after learning. Thus, the microstructure of REM sleep should be considered, especially, for studies using sleep deprivation. Third, findings from studies using animal models advanced our knowledge about synaptic plasticity during REM sleep, but more research is needed to confirm its causal relationship with the contribution of REM sleep to procedural memory consolidation. Animal models allow scientists to manipulate neurons and brain circuits at the cellular level. However, limitations do exist. For example, previous studies have confirmed that, unlike in human sleep, SWS and N2 are not dissociable stages in animal sleep. Those aspects provide insights into explaining the inconsistent findings with regard to sleep stages and procedural memory, as well as point out some directions to be studied in the future.

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