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Activation of fast sleep spindles at the premotor cortex and parietal areas contributes to motor learning: A study using sLORETA

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ABSTRACT

Objective: The present study examined whether slow and/or fast sleep spindles are related to visuomotor learning, by examining the densities of current sleep spindle activities.
Methods: Participants completed a visuomotor task before and after sleep on the learning night. This task was not performed on the non-learning night. Standard polysomnographic recordings were made. After the amplitudes of slow and fast spindles were calculated, sLORETA was used to localize the source of slow and fast spindles and to investigate the relationship between spindle activity and motor learning.
Results: Fast spindle amplitude was significantly larger on the learning than on the non-learning nights, particularly at the left frontal area. sLORETA revealed that fast spindle activities in the left frontal and left parietal areas were enhanced when a new visuomotor skill was learned. There were no significant learning-dependent changes in slow spindle activity.
Conclusions: Fast spindle activity increases in cortical areas that are involved in learning a new visuomotor skill. The thalamocortical network that underlies the generation of fast spindles may contribute to the synaptic plasticity that occurs during sleep.
Significance: Activity of fast sleep spindles is a possible biomarker of memory deficits.

1. Introduction

Our daily lives constitute a series of highly sophisticated motor actions, the performance of which requires numerous skills. The acquisition of a new motor skill often requires careful training. This continuous and effective training ultimately enables automation of the movement. Presumably, this automation occurs as a result of consolidation and stabilization of the skill in procedural memory (Hikosaka et al., 2000). Recently, numerous reports have indicated that sleep plays an essential role in this memory consolidation process (Karni et al., 1998; Gais et al., 2000; Stickgold et al., 2001; Fischer et al., 2002; Walker et al., 2002, 2003; Tamaki et al., 2007, 2008). These studies demonstrate that one intervening night of sleep can increase motor skills to an appreciably high level. Therefore, it is possible that neuroplastic changes occur in the brain, not only during wakefulness but also during sleep. However, the actual mechanisms underlying this plasticity during sleep have yet to be fully investigated.

Recently, it has been suggested that sleep spindles contribute to the synaptic plasticity that facilitates both learning and memory. Sleep spindles are a major characteristic patterns of electroencephalograms (EEGs) observed during non-rapid eye movement (NREM) sleep. Their frequency ranges from 10 to 16 Hz, and they can continue for at least 0.5 s (Sleep Computing Committee of the Japanese Society of Sleep Research Society, 2001). Sleep spindles appear mainly during Stage 2 of NREM sleep. Some studies have suggested that sleep spindles are related to memory consolidation during sleep (Gais et al., 2002; Clemens et al., 2005; Fogel and Smith, 2006; Schmidt et al., 2006; Tamaki et al., 2008). For example, temporal correlations between hippocampal ripples (140–200 Hz) and cortical spindles (originating in the prefrontal and somatosensory cortices) have been demonstrated in both mice and rats (Siapas and Wilson, 1998; Sirota et al., 2003). In a study of humans, sleep spindle density was significantly higher following a paired association task, as compared to a control task that involved

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no significant memory component (Gais et al., 2002). Clemens et al. (2005) demonstrated that overnight verbal memory retention after a face-name association task was highly correlated with the number of observed sleep spindles. Finally, Fogel and Smith (2006) demonstrated that spindle (12–16 Hz) density (the number of spindles that occurred in 1 min) increased after participants learned four types of motor tasks.

Sleep spindles have been classified into two types. The first are the slow spindles, which have a frequency of approximately 12 Hz and are predominantly distributed in the frontocentral area of the scalp. The second are the fast spindles, which have a frequency of approximately 14 Hz and are predominantly distributed in the centroparietal area of the scalp (Jobert et al., 1992; Werth et al., 1997; De Gennaro et al., 2000). Although the broad topological distribution differs between fast and slow spindles, they can both be observed extensively throughout the surface of the head. The incidence of the two types of spindle differs over the course of a night's sleep. Slow spindles appear predominantly during the early part of sleep, whereas fast spindles generally appear later.

The two types of sleep spindle may play different roles in the memory consolidation process. Walker et al. (2002) used a finger-taping task, and demonstrated a significant relationship between improved task performance and amount of Stage 2 NREM sleep ($r = .66$). When the data were divided into distinct sleep cycles, a particularly strong relationship was found between performance and duration of the 4th cycle of Stage 2 NREM sleep ($r = .72$). Fast spindles were predominant in comparison to slow spindles during this period. Tamaki et al. (2008) used a visuomotor task to demonstrate that fast sleep spindle activity is correlated with improvements in motor skills. Fast spindles had greater amplitude and a longer duration on learning nights than on non-training control nights. Furthermore, significant relationships were found between skill improvement and fast spindle density, amplitude, and duration. In contrast to these findings, no significant relationships were observed between motor skill improvements and slow spindle activity. Fast spindles appear to be involved in motor-memory consolidation. However, the brain location where neural plasticity related to the activation of fast spindles can be observed remains to be clarified.

It should be possible to demonstrate the contribution of spindle activity to neural plasticity by analyzing current densities and localizing the source of the spindle generators. Standardized low-resolution brain electromagnetic tomography (sLORETA) could provide one useful approach to such a demonstration. sLORETA is a functional source imaging method based on certain electrophysiological and neuroanatomical constraints (Pascual-Marqui, 2002) and has been identified as an efficient functional mapping tool, as it is both consistent with physiology and capable of correct localization (Anderer et al., 2001). The sLORETA approach was developed to reduce the speculation error that is observed in low-resolution brain electromagnetic tomography (LORETA) (Pascual-Marqui et al., 1994; Pascual-Marqui, 2002) to zero, and that it does this has been mathematically confirmed (Greenblatt et al., 2005; Sekihara et al., 2005). Many basic and clinical EEG and ERP studies (see Anderer et al., 1998; Brandeis et al., 1998; Strik et al., 1998; Babiloni et al., 2006; Zumsteg et al., 2006; Gianotti et al., 2007; Rodriguez et al., 2007) have demonstrated functional sources using these efficient tools. With regard to EEG activity during sleep, Anderer et al. (2001) analyzed scalp-recorded sleep spindles via LORETA, showing that the two types of spindles are associated with activation in different cortical areas.

We generated the following hypotheses: (1) Fast spindle activity is enhanced after learning a skill, as compared to when no skill is learned, (2) The activation associated with fast spindle activity would be observed most strongly at the scalp sites that overlie brain regions involved in the consolidation of visuomotor skills, (3) Sleep spindle generators would be localized in neocortical areas, which are involved in the consolidation of visuomotor skills, and (4) No significant learning-associated activation would be observed as a function of slow spindle activity. Spindle activities were measured and compared across learning and non-learning nights. A visuomotor task was performed before and after nocturnal sleep on the learning night. The amplitudes of fast and slow spindles were measured, and the amplitudes during the non-learning night were subtracted from those during the learning night. In order to discriminate learning effects from the sleep-initiation process, subtracted amplitudes were used in sLORETA to detect learning-related spindle activation.

2. Methods

2.1. Participants

Ten healthy student volunteers (7 females and 3 males; mean 22.0 years) participated in the study. None of the volunteers had physical or psychiatric disorders that required concurrent medical treatment, and none were suspected of suffering from sleep disorders. After the purpose and the procedure of the study were explained to them, participants all provided their written informed consent to participate in the study. All the participants were told that they were free to discontinue the experiment at any time.

Prior to the experiment, participants completed a questionnaire that assessed their sleep–wake habits, including usual sleeping and waking times, phases of circadian activity cycles, regularity of sleep habits, napping, sleep complaints, and regularity of lifestyle (e.g., mealtimes). They also completed a Morningness–Eveningness questionnaire (Horne and Östberg, 1976), as well as questionnaires designed to measure physical and psychiatric health and sleep conditions.

All participants had regular sleep–wake cycles and slept for 6–9 h daily. None of them took regular naps, drank alcoholic beverages before going to sleep, smoked cigarettes, or were taking any prescription medications during the month prior to the experiment. Finally, all participants were right-handed, as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971), and possessed normal or corrected-to-normal vision.

2.2. Stimuli and apparatus

We used a five-pointed star and 6 irregular figures as the stimuli for our modified mirror-tracing task. The star was drawn using 2 lines that were 3 mm apart, forming a path. The perimeter of the star was 400 mm in total, with each of the 10 angles being 50 mm apart. Similarly, each of the 6 irregular figures was drawn using 2 lines that were 3 mm apart. Figure perimeters were all 600 mm, and each possessed 11 angles spaced at 50 mm intervals. These figures were made from basal plates. A test lead was used as a stylus to trace the paths, which made it possible for an electric current to pass when the stylus made contact. Each participant's right hand was placed out of view by covering it with an open-ended box (width, 300 mm; height, 280 mm; depth, 210 mm) that had an 85 mm closed-circuit camera (Akizuki Denshi Tsusho, Saitama, Japan) mounted on top. Stimuli were presented under the box, and images were projected onto a 14 in. display (KV-14AF1; Sony, Tokyo, Japan) that was placed in front of the participants. Turning the camera could rotate the view.

2.3. Task

We used a modified version of the classic mirror-tracing task. Stimuli were presented in front of the participants' hands, which were covered with a box. The participants kept their eyes closed