Topographic Distribution of Sleep Spindles using 2DII

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Abstract

Sleep spindles are associated with the stage 2 sleep [1]. They are easily recognizable in EEG and MEG as distinctive bursts of waves with a frequency of 12-14 Hz lasting more than 0.5 sec. They are distinctive because of their comb-like waveform morphology. Previous MEG studies have identified a complex distribution of cortical sources that underlie spindle activity [2,3]. Pre-surgical mapping is performed in our laboratory utilizing simultaneous Electroencephalographic (EEG) monitoring and 148 MEG channels. Patients are monitored for up to 2 hours, during which time many enter stage 1 or stage 2 sleep. Numerous sleep spindles have been observed in several of these patients. In the present study, sources of the underlying spindle cortical activity were localized by means of Two Dimensional Inverse Imaging (2DII) [4] and MR-FOCUSS [5]. Source locations of the peaks of the sleep spindle pattern waveform were found in the parietal and frontal cortex with a unilateral hemispheric distribution. Since asymmetrical sleep spindles have been associated with brain lesions [6], further studies of abnormal spindle activity may help to determine underlying pathology.

1 Introduction

Although the neurophysiologic processes that produce spindle activity are still being elucidated, theories regarding the functional significance of these and other distinct sleep-related waveforms remain speculative. The study of specific brain oscillations during sleep can provide information regarding the dynamics of neuronal interconnections both within and across global states of arousal. Studies have revealed that sleep-related brain oscillations observed at the macroscopic EEG level are reflections of the complex synchronized interactivity of neurons within the thalamus and cortex as modulated by brain structures in the hypothalamus, basal forebrain, and brainstem [7].

One of these distinct oscillations, the sleep spindle, occurs during, and partially defines, stage 2 sleep [1]. Sleep Spindles are easily recognizable in electroencephalographic and magnetoencephalographic recordings as distinctive bursts of waves with a frequency of 12-14 Hz lasting more than 0.5 sec. They are distinctive because of their comb-like waveform morphology. As one falls asleep, afferent signal transmission through the thalamus is inhibited leading to deafferentiation of the cerebral cortex and sleep onset. Spindle activity reflects continued thalamocortical neuronal interactions. Specifically, spindles are generated by repetitive spike-bursts within GABAergic thalamic reticular neurons that produce rhythmic inhibitory postsynaptic potentials (IPSPs) in thalamocortical neurons. These IPSPs lead to postinhibitory rebound spike-bursts that produce excitation and occasional firing of cortical neurons and the characteristic comb-like waveform of the spindle [7].

Few studies of human spindle activity have attempted to map the spatial distribution of this waveform. In one EEG based study, Zygierewicz et al. [8], found that topographic spindle activity could be separated into frontal and parietal localizations associated with low and high temporal frequencies, respectively. Because the spatial resolution of the EEG signal is limited, MEG neuroimaging of sleep-related processes is increasingly being utilized. In a study by Hughes et. al. [9], cortical source modeling of spindle activity using MEG revealed two sources of spindle activity similar to results from EEG spindle studies [10]. However, due to the small number of MEG channels, specific source locations and topography could not be identified. More recent MEG studies using larger arrays for greater spatial resolution have identified parietal and frontal cortical source locations for sleep spindles [11,12]. Continued MEG investigation of the specific temporal and spatial characteristics that occur within a human spindle activity may help determine the function of sleep spindles.

In the present study we used MR-FOCUSS MEG imaging techniques [5] to determine the source localization and hemispheric stability (unilateral vs bilateral; left vs right) of cortical activity throughout the duration of a sleep spindle and between individuals.

2 Methods

2.1 Patient studies

Six patients (male = 2; female = 4) with histories of localization-related epilepsy (complex partial seizures) were monitored with 148-channel Neuromagnetometer (4-D Neuroimaging Magnes WH2500) and 32 channels of EEG (Neuroscan synamps using the 10-20 system).

Each subject changed into a hospital gown and removed all metal articles from his/her body, except for dental work, which was demagnetized with a commercial videotape eraser. Three small electrode coils, used to transmit subject location information to the neuromagnetometer probe, were taped to the subject's forehead with two-sided tape. Disposable ear molds of the correct size were placed in the ears and an additional localization coil was attached to each ear mold. Thirty-three EEG electrodes were glued to the subject's scalp using collodian glue. The subject then lay comfortably on the bed inside the magnetically shielded room, and automatic probe position routines were used to locate the head with respect to the neuromagnetometer detector coils. The neuromagnetometer helmet containing the detector array was then placed over the subject's head in close proximity to most of the cortical surface. The subject was asked to avoid both eye and body movements during data collection. Changes in the subject's position during the study were detected by changes in magnetic field locations from the coils on the forehead and ears. Runs during which the subject moved were repeated.

2.2 Data collection

MEG and EEG data were digitized at 508.63 samples per second from 0.1 Hz to 100 Hz. Three ten-minute continuous acquisitions were collected.

2.3 Analytical Technique

One distinct sleep spindle burst was analyzed for each subject. For each 0.5 second spindle burst, separate "spindle peaks" were identified within the 0.5 second MEG tracing (Figure 1). These MEG spindle peaks reflect the EEG wave peaks consistent with the 12-14 Hz of the spindle waveform. Each distinct peak within the waveform was analyzed according to the MR-FOCUSS modeling techniques outlined below.

2DII [4] is a current density source imaging technique that produces whole brain images of both focal and extended source structures that may be simultaneously active. The 2DII technique utilized approximately 3,000 cortical source locations derived from the MRI to model the continuum of cortical gray matter. Utilizing an iterative algorithm the 2DII technique transformed random initial amplitudes of the 3000-point cortical structure into a source structure corresponding to the magnetic field data. To ensure a robust result 20 solutions were used to create the images. MR-FOCUSS [5] utilizes the 2DII source structure and a least squares solution which replaces the minimum norm technique in the FOCUSS [9] iterative algorithm. The localization results are displayed on the volumetric MRI scan.

2.4 Data Analysis

Data were forward and backward filtered using a 3-100 Hz bandpass with a 60 Hz notch filter. Each recording was visually inspected by an experienced clinical polysomnographer who identified artifact free and distinct sleep spindles in each of the 6 subjects. A short interval of time encompassing the sleep spindle burst was selected and MR-FOCUSS analysis was performed. The waveforms were visual inspected for latency difference between the MEG and EEG vertex peaks.

MR-FOCUSS current density source solutions were generated for each sleep spindle bursts. The localizations were compared across subjects and within the same subject. The location of the epileptic activity was also localized for each subject. Amplitude of the underlying current source generating the peak of each sleep spindle burst was calculated and compared within each subject and across all subjects.

3 Results

All six subjects fell asleep and entered stage 2 sleep. Sleep spindles were easily identifiable in the EEG traces and these traces were used to verify spindles in the MEG channels. A typical sleep spindle is shown in Figure 1. The MEG, and EEG for one subject display the ease of identifying a spindle burst in the EEG and MEG recordings. Average duration of the sleep spindle burst was 500 ms.

MR-FOCUSS source localizations for all subjects found the generators of the underling source for each sleep spindle within a single hemisphere. This unilateral localization of each spindle was consistent for each "spindle peak" analyzed. However, different spindles localized to different hemispheres with an equal distribution (50% left; 50% right). Intrahemispherically, spindles localized to either parietal or frontal areas. Figure 2 displays the localization of the peak of a MEG spindle for one subject.

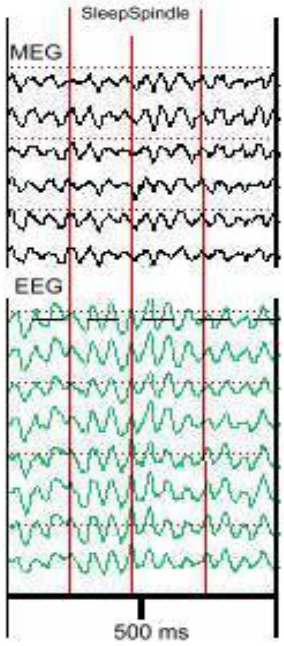

Figure 1: The MEG and EEG waveform of a sleep spindle. Lines are at peak MEG and EEG sleep spindle bursts.

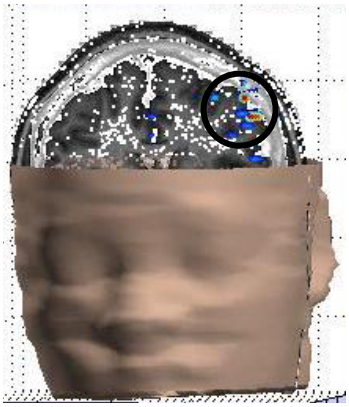

Figure 2. Sleep Spindle burst localization in one subject. Circle indicates most intense area of cortical activation.

4 Discussion

The present study demonstrates for the first time that sleep spindles occur unilaterally with an apparently equal hemispheric distribution. In addition, this study replicates previous findings in humans that used EEG as well as those using lower resolution MEG and demonstrates that the cortical sources of spindle activity are located predominately in the parietal and frontal areas of the cortex [10-12]. Although the functional significance of the unilateral distribution of sleep spindles and their parietal and frontal localization remains unclear, continued investigation using increasingly more sophisticated technological and analytical techniques may provide further insight into the cortical neurophysiology of these distinct sleep-related waveforms.

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