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Effect of sleep on interictal spikes and distribution of sleep spindles on electrocorticography in children with focal epilepsy

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Abstract

Objective: To determine how sleep with central spindles alters the spatial distribution of interictal spike frequency in children with intractable focal seizures, and whether such children have spindles arising from the medial temporal region in addition to the frontal–central region.
Methods: Seventeen children (age: 7 months–17 years) were studied using extraoperative electrocorticography (ECoG).
Results: Overall spike frequency across the subdural electrodes was greater during sleep with central spindles compared to wakefulness. In 13 children showing at least 1 spike/min in an electrode, the spatial distribution of spike frequency was similar during wakefulness and sleep; in addition, the spike frequency was greater in the seizure onset zones compared to the non-onset areas, regardless of wakefulness or sleep. Spindles were identified in the medial temporal region during sleep with central spindles in all 17 children.
Conclusion: Overall spike frequency may be increased by sleep with spindles, but the spatial distribution of spike frequency appears similar during wakefulness and sleep in children with intractable focal seizures.
Significance: Both awake and sleep ECoG may be useful to predict seizure onset zones in children with intractable focal epilepsy. Medial temporal spindles are present in some children with focal epilepsy.

Keywords: Clinical neurophysiology; Pediatric epilepsy surgery; Quantitative interictal intracranial EEG; Hippocampus; Tuberous sclerosis complex

1. Introduction

Interictal spike activity is considered as one of the hallmarks of epilepsy (Gibbs et al., 1936; Rosenow and Luders, 2001). Traditionally, induction of sleep state by sleep-deprivation has been routinely used to activate interictal spike activity on scalp EEG or magnetoencephalography in patients being evaluated for epilepsy surgery (Kellaway, 1950; Crespel et al., 1998; Xiao et al., 2006). Previous studies have shown that some types of seizures preferentially occur during sleep with spindles, and association between sleep and activation of epileptiform activity on EEG has been of interest to investigators for years (Caveness et al., 1950; Terzano et al., 1991; Nobili et al., 1999; Zucconi et al., 2000; Herman et al., 2001; Steriade and Amzica, 2003).

Sleep spindle is an oscillatory waveform ranging from 12 to 16 Hz on EEG, intermittently emerging during non-REM sleep. The frequency of spindles may be slower in patients with epilepsy treated with antiepileptic drugs (Drake et al., 1991; Steriade and Amzica, 2003). Extraoperative intracranial electrocorticography (ECoG) recording for presurgical evaluation in epilepsy surgery provides a unique opportunity to assess electrographic

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activity from deep brain structures in the human. Previous studies of adults with uncontrolled focal epilepsy demonstrated that sleep spindles can be recorded intracranially (Brazier, 1968; Montplaisir et al., 1981) and that the amplitude of sleep spindles is highest in the frontal–central region (Caderas et al., 1982). Several studies in adults have documented that sleep spindles are also present in the medial temporal region predominantly during non-REM sleep (Brazier, 1968; Montplaisir et al., 1981; Malow et al., 1999). The nature of such medial temporal spindles has not been clearly understood, and its possible association with epileptic or physiological phenomenon has been proposed (Montplaisir et al., 1981; Malow et al., 1999).

Does sleep with central spindles alter the spatial distribution of interictal spike frequency in children with focal seizures? For example, does sleep alter spike frequency differentially in a certain brain region? Are sleep spindles in the medial temporal region present also in children? None of the previous studies of intracranial ECoG recording have addressed these issues. In the present study, we determined how sleep with spindles altered the spatial distribution of interictal spike frequency in children with intractable focal epilepsy and also determined whether sleep spindles are present in the medial temporal region in these children.

2. Methods

2.1. Patients

The inclusion criteria of the present study included: (i) age ranging from 6 months to 17 years, (ii) epilepsy surgery using extraoperative ECoG monitoring in Children's Hospital of Michigan, Detroit, between March 2004 and March 2006, and (iii) subdural electrode placement involving the frontal–central region as well as the medial temporal region. The exclusion criteria included: (i) the absence of clear-cut sleep spindles in the frontal–central region on ECoG and (ii) the lack of interictal sleep ECoG segments due to very frequent seizures during sleep. Among a consecutive series of 22 children who met the inclusion criteria, three children with epileptic spasms were excluded due to the lack of clear-cut central spindles, and other two children were excluded because of the lack of interictal sleep ECoG segments due to very frequent seizures during sleep. Thus, we studied a total of 17 children with focal seizures (age: 7 months–17 years; 9 girls) who met the inclusion criteria and satisfied the exclusion criteria (Table 1).

All 17 subjects underwent scalp video-EEG monitoring, MRI, 2-deoxy-2-[^{18}F]fluoro-D-glucose (FDG) PET, and chronic intracranial ECoG monitoring with subdural electrodes as part of their presurgical evaluation. On MRI, six children showed the evidence of focal cortical dysplasia (Raymond et al., 1995); four children had multiple cortical tubers; three children had a brain tumor; one child each had a solitary tuber and focal ulegyria. In the remaining two children, MRI was normal but FDG PET scan showed cortical regions with glucose hypometabolism in the presumed epileptic hemisphere. The study has been approved by the Institutional Review Board at Wayne State University, and written informed consent was obtained from the parents or guardians of all subjects.

2.2. Subdural electrode placement

For extraoperative video-ECoG recording, platinum grid electrodes (10 mm intercontact distance; 4 mm diameter; Ad-tech, Racine, WI) were surgically implanted on the presumed epileptogenic hemisphere. As shown in our previous report (Asano et al., 2005), all electrode plates were stitched to adjacent plates and/or the edge of the dura mater, to avoid movement of subdural electrodes after placement. In addition, intraoperative pictures were taken with a digital camera before dural closure, to enhance spatial accuracy of electrode display on the three-dimensional brain surface reconstructed from MRI (Wellmer et al., 2002). The total number of electrode contacts in each subject ranged from 70 to 128.

2.3. Extraoperative video-ECoG recording

Extraoperative video-ECoG recordings were performed as shown in our previous report (Asano et al., 2003; Asano et al., 2004a). Antiepileptic medications were discontinued or reduced during ECoG monitoring until a sufficient number of habitual seizures (typically three seizures) were captured. A ground lead and a reference electrode were placed to the contralateral mastoid by a registered EEG technician. Surface EMG recordings from the left and right deltoid muscles were added as needed. ECoG data were obtained using a Stellate HARMONIE digital system (sampling rate: 200 Hz; Stellate Inc., Quebec, Canada) for 2–5 days. Clinical manifestations were assessed using synchronized digital videos with 30 frames/s.

2.4. Visual analysis of ECoG data

ECoG data were assessed mostly with a low frequency filter of 0.5–1.0 Hz and a high frequency filter of 35–100 Hz applied. A low frequency filter of 3.0 Hz or higher was occasionally used to assess a low-amplitude fast wave activity. While the subject quietly lay in a spine position with her/his eyes closed, minimal body movement and regular respiration noted in the video, sleep spindles in the frontal–central region (Sperling, 2003) were visually determined (Fig. 1). Subsequently, sleep spindles in the medial temporal region (Malow et al., 1999), while central spindles were present, were also visually determined by the consensus of two clinical neurophysiologists (E.A. and T.M.) (Fig. 1). 'Seizure onset zones' were defined as a single or multiple brain areas initially showing a sustained rhythmic change in the ECoG accompanied by subsequent clinically typical seizure activity, not explained by level of arousal,