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Non-rapid eye movement sleep characteristics in idiopathic REM sleep behavior disorder☆

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ABSTRACT

This study investigated slow waves (SW; >75 μV and <4 Hz) characteristics in patients with idiopathic rapid eye movement (REM) sleep behavior disorder (iRBD). Thirty patients with iRBD and 30 age- and sex-matched healthy subjects underwent one polysomnographic (PSG) nocturnal sleep recording. SW automatic detection was performed on F3, C3, P3, and O1 leads and SW characteristics were derived (SW density, amplitude, frequency, slope, and duration of negative and positive phases). We also compared iRBD patients and control subjects on PSG variables and delta (0.25–4.0 Hz) spectral power. No between-group differences were found on PSG variables, delta spectral power, or SW characteristics. Results show no SW abnormalities in iRBD patients compared to healthy participants, which suggests similar level of synchronization of thalamo-cortical neurons during N-REM sleep.

1. Introduction

Rapid eye movement (REM) sleep behavior disorder (RBD) is a parasomnia characterized by a loss of muscular atonia normally observed during REM sleep which ensues in undesirable motor manifestations associated with dream mentation [1]. Idiopathic RBD (iRBD) is a risk factor for the development of Parkinson's disease or Lewy body dementia [2]. Several markers of neurodegeneration have been identified in iRBD, such as mild cognitive impairment (MCI) [3]. Electroencephalogram (EEG) anomalies have also been found in these patients, notably a slowing of waking and REM sleep EEG activity [4,5]. It is unclear whether these EEG abnormalities may also be generalized to non-rapid eye movement (N-REM) sleep or are specific to REM sleep and wakefulness. Some studies reported a higher percentage of slow-wave sleep (SWS) in some patients with iRBD [6–8], whereas others found no differences [5,9].

The EEG during N-REM sleep in humans is characterized by low-frequency, high-amplitude waves (slow waves; SW>75 μV and<4 Hz). SW are thought to play an important role in memory consolidation, brain plasticity [10], synaptic strength [11], and sleep homeostasis [11,12]. A study previously conducted in our laboratory found that iRBD patients show more SWS and higher delta spectral power than controls, with a greater difference in women [6]. These results suggest that iRBD is associated with both slowing of wakefulness and N-REM sleep, which may reflect abnormal EEG patterns rather than increased physiological N-REM sleep.

The aim of this study was twofold: to reproduce previous results showing higher delta spectral power in N-REM sleep using an independent sample of iRBD patients and controls; and to evaluate SW density and other SW characteristics as indices of cortical neural synchronization during N-REM sleep [10,13] in order to better understand the mechanisms underlying iRBD.

2. Methods

2.1. Subjects

Thirty patients with iRBD (21 men; mean age, 61.4 ± 10.7 years; mean RBD duration, 11.1 ± 7.3 years) and 30 age- and sex-matched

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controls (20 men; mean age, 59.6 ± 10.9 years) were studied. iRBD patients were recruited at the Sleep Centre of the Hôpital du Sacré-Coeur de Montréal. Control subjects were recruited through newspaper advertisements and by word of mouth. None of the iRBD patients or control subjects had participated in previous EEG spectral analysis studies on RBD in our laboratory. Patients with iRBD were diagnosed by a sleep specialist according to standard clinical and PSG criteria for RBD [1,14]. All participants underwent a neurological evaluation to exclude the presence of other neurodegenerative or neurologic disorders. No subjects had dementia, according to the DSM-IV-R [15], or scored lower than 26 on the Mini-Mental State Examination [16], and subjects underwent a neuropsychological evaluation when possible. Nineteen iRBD patients underwent a complete neuropsychological assessment, and nine of these (47%) met the criteria for MCI. In addition, subjects were excluded from the study if they had a history of head injury, seizure, brain tumor, or stroke. Moreover, patients with drug-induced RBD, narcolepsy or with an apnea index greater than 10 or a respiratory event index greater than 20 were excluded. All subjects were required to be withdrawn from any medication known to influence sleep architecture, EEG or motor activity for at least 2 weeks before PSG recordings. The hospital's ethical committee approved the study and all subjects signed an informed written consent before their participation.

2.2. Procedures

2.2.1. Polysomnographic recordings

All participants were recorded for one night in the sleep laboratory. The montage included frontal (F3, F4), central (C3, C4), parietal (P3, P4), and occipital (O1, O2) EEG leads in reference to linked ears with 10 kΩ resistance, bilateral electro-oculogram, and chin EMG recordings. Respiration was monitored using a nasal canula or a nasal/oral thermistor, with thoracic and abdominal strain gages. PSG was recorded with a Grass polygraph (amplifier gain 10,000; bandpass 0.3–100 Hz) and signals were digitized at a sampling rate of 256 Hz, except for nine iRBD patients, whose PSG recordings were digitized at 128 Hz using Harmonie software (Stellate Systems, Montreal, Canada). N-REM sleep stages were visually scored on 20-second epochs according to a modified version of Rechtschaffen and Kales's method [17]. REM sleep in iRBD patients and controls was scored according to Montplaisir et al.'s method [14]. EMG artifacts were automatically detected and eliminated before analysis. Further artifacts were rejected by visual detection. PSG variables included sleep latency and efficiency, sleep duration, REM sleep latency and efficiency, number of awakenings, and sleep stage proportions.

2.2.2. Quantitative EEG analysis and SW algorithm detection

Spectral analyses of N-REM sleep (stages 2, 3, and 4) were computed using Harmonie software (Stellate Systems, Montreal, Canada) on left derivations F3, C3, P3, and O1. Fast Fourier Transformation (FFT) (cosine tapering) on 4-s artifact-free sections yielded a spectral resolution of 0.25 Hz. EMG artifacts were automatically and visually detected and then rejected before spectral analysis. Epochs containing artifacts were considered missing data to maintain sleep continuity. Five 4-s spectral epochs were averaged to preserve correspondence with the 20-s sleep scoring windows. Spectral power in the delta range (0.25–4.0 Hz) was averaged for all-night N-REM sleep.

SW were automatically detected on left parasagittal derivations F3, C3, P3, and O1. EEG data were bandpass filtered between 0.1 and 4.0 Hz using a linear phase finite impulse response (FIR) filter (−3 dB at 0.1 and 4.0 Hz). SW detections were performed on artifact-free epochs using the following criteria: 1) negative peak < −40 μV; 2) peak-to-peak amplitude >75 μV; 3) duration of negative phase >125 ms and <1500 ms; and 4) duration of positive phase <1000 ms. For each SW, a number of characteristics were derived (see Fig. 1): SW density (number of SW per minute), SW amplitude (difference in μV between negative peak *b* and positive peak *d*), SW frequency (number of SW per second), SW slope (negative peak *b* to positive peak *d* slope, expressed in μV/s), duration of SW negative phase (number of seconds between peaks *a* and *c*), and duration of SW positive phase (number of seconds between peaks *c* and *e*). SW characteristics were averaged over all-night N-REM sleep.

2.3. Statistical analyses

To assess changes in sleep architecture, analyses of variance (ANOVAs) with two independent factors (group and sex) were performed on all PSG parameters. Abnormally distributed sleep variables were log- or square-root-transformed before analyses to bring distributions closer to normal. Three-way ANOVAs (2 groups * 2 sex groups) and one repeated measure (4 derivations) were performed to compare all-night delta spectral power and SW characteristics. P levels were adjusted for sphericity with Huynh–Feldt corrections for repeated measures with more than two levels, but original degrees of freedom are reported. Mean comparison analyses were performed with post hoc Tukey HSD for significant main effects, and simple effect analyses were used to decompose significant interactions. Statistical power analyses were performed to evaluate the effect size (f) and number of subjects needed to reach significant difference with a power of 0.80 (alpha = 0.05) for variables that showed no between-group differences.

3. Results

3.1. Polysomnographic parameters

No significant between-group differences or significant interactions between group and sex were found for any of the PSG variables (Table 1). Main sex differences were found for SWS percentage (stages 3 and 4) ($F(1,56) = 5.2$; $p < 0.03$), indicating that women showed a greater percentage of SWS than men.

3.2. Spectral analysis for all-night N-REM sleep

No significant group differences (effect size, f = 0.11) or significant interactions between group and sex or between group and derivation

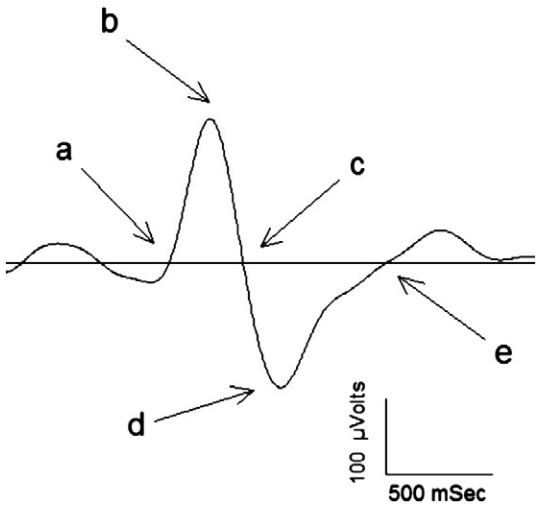

Fig. 1. Slow wave characteristics: SW density (number of SW per minute), SW amplitude (difference in μV between negative peak *b* and positive peak *d*), SW frequency (number of SW per second), SW slope (negative peak *b* to positive peak *d* slope, expressed in μV/s), duration of SW negative phase (number of seconds between peaks *a* and *c*), and duration of SW positive phase (number of seconds between peaks *c* and *e*).