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Original Article

Association of rapid eye movement sleep behavior disorder with sleep-disordered breathing in Parkinson's disease

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ABSTRACT

Objective: Rapid eye movement (REM) sleep behavior disorder (RBD) and sleep-disordered breathing (SDB) are two major sleep disturbances observed in patients with Parkinson's disease (PD). However, prior studies exploring the clinical correlations between RBD and SDB in PD have been limited. We aimed to investigate the relationship between RBD and SDB in PD using a case–control study.
Methods: A total of 46 PD patients with Hoehn–Yahr stages ranging from 1 to 3 participated in the present study. Participants underwent polysomnography to diagnose the presence of RBD and SDB, and were classified into groups, accordingly. SDB was defined as an apnea–hypopnea index greater than 5. Comparison of clinical and sleep-respiratory parameters was performed among them.
Results: SDB was more frequent in the RBD group than in the non-RBD group (51.4% vs 9.1%, $p = 0.016$). PD patients with RBD had significantly reduced mean SaO_2 and more severe sleep apnea–related parameters during total sleep and non-REM sleep in comparison with non-RBD PD patients. However, there were no differences on the REM-related apnea/hypopnea variables between participants with and without RBD ($p > 0.05$). Both the frequency of RBD and RBD screening questionnaire (RBDSQ) scores were higher in the participants with SDB than in the participants without SDB ($p < 0.05$). Furthermore, a significant negative correlation was found between RBDSQ and mean SaO_2 in all participants.
Conclusions: In PD patients, SDB is more frequent and more severe in patients with RBD than in patients without, and RBD increases the risk of hypoxemia during sleep.

1. Introduction

Parkinson's disease (PD) is characterized by a progressive loss of dopaminergic neurons in the substantia nigra pars compacta that leads to the development of cardinal motor symptoms [1]. The clinical diagnosis of PD is based on motor features, including resting tremor, rigidity, bradykinesia, and postural instability [2]. However, sleep disturbances, which are one of the major nonmotor signs, have been recognized as prodromal or concomitant symptoms of PD and have a negative effect on sleep quality and quality of life among PD patients [3]. A number of sleep disturbances have been described in PD, including insomnia, sleep disordered breathing (SDB), rapid eye movement (REM) sleep behavior disorder (RBD), periodic leg movement syndrome (PLMS), and excessive daytime sleepiness (EDS) [4].

SDB and RBD are two common sleep disturbances in PD. SDB has been reported to be prevalent in PD patients, even though the frequency of SDB in PD patients is no more than that in matched controls [5,6]. RBD, which is characterized by abnormally increased muscle tone during REM stage, is another intriguing sleep disturbance in PD patients with a prevalence rate up to 58% [7,8]. Upper airway muscle atonia during REM sleep exacerbates obstructive apnea, but is notably absent during RBD and may contribute to preventing upper airway closure [9]. Therefore, it is of considerable clinical relevance to explore the association between these two conditions among patients with PD. Indeed, a thorough investigation may help to identify a common neurobiological process and to promote the development of interventions targeting sleep disturbance in PD patients.

Prior studies of the correlation between SDB and RBD in PD are limited. Furthermore, the results of some of these studies are inconsistent. Cochen De Cock et al. [6] reported that in PD patients the maintenance of chin muscle activity during RBD did not reduce

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the severity of sleep apnea during REM stage. Another study found that the severity of obstructive sleep apnea syndrome (OSAS) was alleviated in PD patients with RBD compared with non-RBD PD patients on several apnea-related parameters during REM sleep, suggesting that RBD may ameliorate the severity of OSAS [10]. To understand the relationship between SDB and RBD in PD further, we conducted a case–control study.

2. Methods

2.1. Participants

A total of 46 PD patients with Hoehn–Yahr (H-Y) stages ranging from 1 to 3 participated in the present study [11]. The age range was 50–80 years. All patients were diagnosed with PD by two senior neurologists according to the UK Brain Bank criteria for PD and had Mini-Mental State Examination (MMSE) scores greater than 21 [12,13]. All the participants gave written informed consent, and the study was approved by the ethics committee of Ruijin Hospital, which is affiliated with the Shanghai Jiao Tong University School of Medicine.

2.2. Clinical measures

The Unified Parkinson's Disease Rating Scale–III (UPDRS-III) was used to evaluate the severity of the participant's motor symptoms [14]. The Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS) were used to measure the quality of sleep and the severity of excessive daytime sleepiness (EDS), respectively [15,16]. In addition, RBD status in all patients was evaluated by the REM Sleep Behavior Disorder Screening Questionnaire (RBDSQ) [17]. PD medications were recorded and an L-dopa–equivalent dose (LED) was calculated for each patient [18]. Patients who took sedatives or hypnotics were excluded from the study.

The presence of RBD was defined according to the International Classification of Sleep Disorder (ICSD)–II criteria [7]. All participants had polysomnography (PSG) documentation and were divided into two groups: PD patients with RBD, and PD patients without RBD.

2.3. Procedure

2.3.1. PSG measures

All patients underwent an overnight video–PSG test with a Compumedics E-Series EEG/PSG Recording System (Compumedics Limited, Melbourne, Australia). A previous study demonstrated that single-night video–PSG is reliable and adequate for diagnosing RBD. The recordings included standard electroencephalography (C3-A2, C4-A1), electrooculography (LE-A2, RE-A1), chin EMG, bilateral leg EMG (anterior tibialis muscles), electrocardiography, nasal-oral pressure transducer airflow, thoracic and abdominal respiratory efforts, oxyhemoglobin saturation, breathing sounds, and body position. The sleep of RBD patients was simultaneously videotaped and closely observed by a technician for any movement or vocalization. All computerized sleep data were manually scored by experienced PSG technologists and clinicians according to standard criteria. Sleep stages were scored according to Rechtschaffen and Kales criteria using 30-second epochs, with modifications to allow the persistence of EMG tone during epochs that were otherwise clearly REM sleep (ie, epochs showing mixed-frequency low-amplitude EEG waveforms with the absence of sleep spindles or K complexes, accompanied by the presence of rapid eye movements) [19]. Arousal and periodic leg movements were scored according to standard criteria [20,21]. Chin EMG activity was assessed to quantify tonic and phasic muscle activities during REM sleep. Each 30-second epoch was scored as tonic when the amplitude of the submental EMG activity exceeded twice that of the background EMG activity for more than 50% of the epoch. The tonic chin EMG density during REM sleep was calculated by summing all epochs containing tonic muscle activity and dividing it by the total number of REM epochs. Phasic muscle activity was scored for a three-second mini-epoch during REM sleep. A phasic chin EMG event was defined as any burst of muscle activity that lasted 0.1–5 seconds with amplitude exceeding four times that of the background EMG activity. The phasic chin EMG density during REM sleep was derived from summing all of the mini-epochs containing phasic muscle activity and then dividing it by the total number of mini-epochs of REM sleep time [22].

2.3.2. Sleep apnea–related parameters

Apnea was defined as an absence of airflow lasting ≥10 seconds, irrespective of changes in oxygen saturation. Hypopnea was defined as a reduction of ≥50% in amplitude of the airflow signal and was quantified only if it lasted ≥10 seconds and was accompanied by oxygen desaturation ≥3% and/or arousal. Apnea and hypopnea were further categorized as obstructive, mixed, and central types, according to respiratory effort. The apnea–hypopnea index (AHI) was calculated as the total number of apnea–hypopnea episodes per hour of sleep [total sleep, REM sleep, and non-REM (NREM) sleep, respectively]. Similarly, an apnea index (AI) and a hypopnea index (HI) were also created and evaluated. In addition, the occurrence and severity of sleep-disordered breathing (SDB) were determined using the AHI (total sleep): (1) normal, <5/h; (2) mild, 5–15/h; (3) moderate, 15–30/h; or (4) severe, >30/h. The duration of apnea and hypopnea episodes (mean and maximum) was also measured. Oxygen desaturation episodes were defined as a dip in pulse oximeter oxygen saturation ≥3%. The oxygen desaturation index was calculated as the total number of desaturation episodes divided by total sleep time. Mean oxygen desaturation duration was the average period of all desaturation events during sleep. Minimum SaO_2 was defined as the lowest SaO_2 level during the sleep period [23].

2.4. Data analysis

Descriptive statistics are presented as mean (standard deviations), as well as frequency (percentage). SPSS version 17.0 software (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. The normality of data distributions was checked by the Kolmogorov–Smirnov test, and all data were normally distributed. Analysis of covariance (adjusted for age and sex) was used to compare the clinical variables between PD with RBD patients and their non-RBD controls. The rate differences in major medical diseases and gender between PD with RBD patients and the non-RBD PD patients were evaluated by the Fisher exact test. Pearson or Spearman correlations were performed to measure the relationships between sleep respiratory-related parameters and RBDSQ and chin EMG activity during REM sleep. A two-tailed p value of <0.05 was considered statistically significant.

3. Results

3.1. Comparisons of SDB between PD with and without RBD patients

A total of 46 patients with PD were recruited and underwent PSG, after which they were classified into two groups based on their RBD status: PD patients with RBD and the PD patients without RBD. No significant differences were found between the two groups with regard to age, body mass index, disease severity, or LED; the proportion of males was higher in the group of PD with RBD ($p = 0.043$). Furthermore, there were no significant differences between the two groups in regard to their PSQI or ESS scores, whereas RBDSQ scores were significantly higher in the PD patients with RBD than in the PD patients without RBD group ($p < 0.001$) (Table 1). No significant differences were found between the two groups in regard to