Fatigue correlates with sleep disturbances in Parkinson disease

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Abstract

Background: Many Parkinson disease (PD) patients complain about chronic fatigue and sleep disturbances during the night. The objective of this study is to determine the relationship between fatigue and sleep disturbances by using polysomnography (PSG) in PD patients.

Methods: Two hundred and thirty-two PD patients (152 with mild fatigue and 80 with severe fatigue) were recruited in this study. Demographic information and clinical symptoms were collected. Fatigue severity scale (FSS) was applied to evaluate the severity of fatigue, and PSG was conducted in all PD patients. FSS ≥4 was defined as severe fatigue, and FSS <4 was defined as mild fatigue. Multivariate logistic regression and linear regression models were used to investigate the associations between fatigue and sleep disturbances.

Results: Patients with severe fatigue tended to have a longer duration of disease, higher Unified Parkinson Disease Rating Scale score, more advanced Hoehn and Yahr stage, higher daily levodopa equivalent dose, worse depression, anxiety, and higher daytime sleepiness score. In addition, they had lower percentage of rapid eye movement (REM) sleep ($P = 0.009$) and were more likely to have REM sleep behavior disorder (RBD) ($P = 0.018$). Multivariate logistic regression analyses found that the presence of RBD and proportion of REM sleep were the independent predictors for fatigue. After the adjustment of age, sex, duration, body mass index, severity of disease, scores of Hamilton Rating Scale for Depression, Hamilton Anxiety Rating Scale, and other sleep disorders, proportion of REM sleep and degree of REM sleep without atonia in patients with PD were still associated with FSS score.

Conclusion: Considering the association between fatigue, RBD, and the altered sleep architecture, fatigue is a special subtype in PD and more studies should be focused on this debilitating symptom.

Keywords: Fatigue; Parkinson disease; Polysomnography; Sleep behavior disorder

Introduction

Fatigue is common in patients with Parkinson disease (PD). It is reported that the overall prevalence of fatigue in PD ranges from 33% to 58%, depending on the tools used for assessment and the selected study population.[1] Over 50% of the PD patients consider fatigue to be one of their three most debilitating symptoms.[2] Because fatigue may present in the early stage of PD, some studies found no significant associations between fatigue and motor severity.[1] However, results were not consistent in other studies.[3,4] Fatigue is commonly associated with sleepiness and depression.[1] It has a strong impact on the activities of daily life of PD patients and aggravates the burden of their caregivers.

The ignorance of fatigue in PD could be due to the reason that there was no item to evaluate the condition in the classic scales for PD, such as Unified Parkinson Disease Rating Scale (UPDRS). According to the self-report scales, 42% had significant fatigue (fatigue severity scale [FSS] ≥4),[5] 43% had sleep disturbances (Pittsburgh Sleep Quality Inventory [PSQI] >5),[6] 44% had depression (Beck Depression Inventory ≥10), and 39% had anxiety (Beck Anxiety Inventory ≥10).[7] However, the neurologist diagnosed these non-motor symptoms less frequency: 14% for fatigue, 39% for sleep disturbances, 21% for depression, and 19% for anxiety.

Many PD patients complain about chronic fatigue and sleep disturbances during the night. Sleep disturbances during the night are quite frequent.[8] Insomnia, rapid eye movement (REM), sleep behavior disorder (RBD), obstructive sleep apnea, excessive daytime sleepiness, and

periodic leg movement syndrome are the most prevalent sleep-related problem in PD. The prevalence of these disorders ranges from 60% to 98%.[9-11] It is common to sleep after exhaustion; however, PD patients are still tired after sleep. Little is known about the interaction of night-time sleep problem and fatigue in PD patients.

Fatigue may significantly overlap with various sleep disturbances. It is often associated with the feeling of tiredness physically and mentally. Some studies found that fatigue and daytime sleepiness were associated with cognitive impairment.[12] However, others suggested that fatigue might be an independent symptom, which was not related to the severity of sleepiness.[3] One major obstacle of the prior studies to investigate the relationship between sleep disturbances and fatigue is the absence of objective measurement to quantitively assess these sleep disorders.

As there were no reports on sleep patterns of fatigued PD patients, we thus performed overnight-polysomnography (PSG) to explore whether sleep disorders independently exacerbate fatigue or not in PD patients.

Methods

Ethical approval

This study was approved by the Ethics Committee of the Second Affiliated Hospital of Soochow University (clinical trial number: JD-LK-2018-061-01). All patients signed written informed consent.

Subjects

From February 2014 and January 2018, 261 PD patients were recruited from the Department of Neurology at the Second Affiliated Hospital of Soochow University. According to the United Kingdom PD Society Brain Bank clinical diagnosis criteria, all patients were diagnosed with PD.[13] Patients with severe anxiety and depression were excluded according to Diagnostic Statistical Manual-IV criteria. We also excluded patients with secondary parkinsonian syndrome, atypical Parkinsonian syndrome that may aggravate fatigue. Patients prescribed with selective serotonin reuptake inhibitors, beta-blockers, clonazepam, anti-cholinesterase inhibitors were excluded because of their effect on altered REM sleep without atonia (RWA). Twenty-nine patients were further excluded for failing to accomplish PSG. Two hundred and thirty-two patients were finally included in the analysis.

Clinical assessment

The following demographic information was collected from all patients: age at onset, sex, disease duration, medical history, and medications. Motor manifestations of PD patients including the UPDRS, and Hoehn and Yahr (H-Y) stage were evaluated in the "off" stage. Levodopa-equivalent daily dose (LEDD) was calculated according to Tomlinson *et al*.[14] We assessed fatigue by FSS, a nine-item scale that measures the severity of fatigue and its effect on patients' activities and lifestyle. Cognition was assessed by Mini-Mental State Examination (MMSE) and the

Montreal Cognitive Assessment (MoCA) in "on" stage. We evaluated daytime somnolence and quality of sleep using the Epworth Sleepiness Scale (ESS) and the PSQI, respectively. Depression and anxiety were assessed by the Hamilton Rating Scale for Depression (HRSD) and Hamilton Anxiety Rating Scale (HAMA), respectively. And non-motor symptoms were evaluated by non-motor symptoms questionnaire. Finally, we divided the PD patients into two categories: severe fatigue (defined as FSS ≥4) and mild fatigue (defined as FSS ≥4).[15]

Polysomnography

All patients underwent overnight video-PSG. Sleep stages, awakenings, arousal index, leg movements, and respiratory-related parameters, including apnea-hypopnea index (AHI) and oxygen desaturation index (ODI), were scored by experienced PSG technologists and clinicians according to the American Academy of Sleep Medicine guidelines.[16] Sleep technicians were blinded to the fatigue condition. Patients with AHI >15 were excluded because it might increase the muscle tone during REM sleep and make it difficult to differentiate behaviors emerging from REM sleep associated with apnea and true RBD behaviors. We also excluded patients with REM sleep that was less than 5 min as it would be insufficient for RWA surface electromyography activity assessment. PSG and its parameter were recorded by sleep technicians who were unknown to the fatigue status.

Tonic chin electromyography activity (tonic RWA%) and phasic chin electromyography density activity (phasic RWA %) were calculated according to a previously published method.[17] Tonic RWA was defined as chin EMG activity present for more than 50% of each 20 epoch and its amplitude was at least twice that of the background or greater than 10 μV. Phasic RWA was calculated as chin EMG activity lasting between 0.1 and 5 s and exceeding fourfold the amplitude of the background EMG as rated in each 2 s mini epoch. The cut-off values for the excessive tonic and phasic EMG activities during REM sleep were ≥30% and 15%, respectively, according to Montplaisir *et al*.[18] RBD was diagnosed according to the International Classification of Sleep Disorders 3rd edition criteria[17] using PSG and clinical evaluations. As dream-enacting behavior (DEB) could present in different nights and lack stability, we assessed DEB according to the video-PSG analyses and asked the patients their history of sleep-related shouting, gesturing, leaping out of bed, or punching bed partners.

Statistical analysis

SPSS software version 19.0 (IBM Corp., Chicago, IL, USA) was used for the statistical analysis. Continuous variables were represented as mean ± standard deviation or median (interquartile range) for continuous data. Comparisons were performed using independent Student's *t* test for continuous variables with normal distributions or Chi-square test for categorical variables, while Mann-Whitney *U* test was used for non-normal data. In addition, multivariate binary logistic regression analyses were used to assess the clinical and the sleep indices. Linear regression models were conducted to evaluate the trend between the severity of

fatigue and sleep parameters. In different models, the data were adjusted by age, sex, duration, BMI, UPDRS III score and LEDD, HRSD, HAMA, total sleep time, and index of periodic leg movements during sleep. *P* value less than 0.05 was considered statistically significant.

Results

A total of 232 patients were included in our study. The mean FSS score was 3.35 ± 1.24. Severe fatigue was reported in 80 patients with PD (34.38%). Similar age of onset and percentage of sex were found in different groups.

The demographics and clinical characteristics were reported in Table 1. Patients with severe fatigue, compared to those with mild fatigue, tended to have higher UPDRS scores, more advanced H-Y stage, and higher LEDD. They were also more likely to present as akinetic-rigid subtype and performed worse in depression, anxiety, and ESS scales. PD patients with severe fatigue had a higher frequency of hypersalivation and urinary urgency. However, there was no significant difference in scores of MMSE, MoCA, hyposmia, and constipation.

In terms of the PSG parameter, PD patients with severe fatigue had lower percentage of REM sleep (13.04 ± 9.27 *vs.* 16.23 ± 8.52, $P = 0.009$) and were more likely to have RBD, compared with mild fatigue PD patients. Figure 1 demonstrates that 90 (59.21%) PD with mild fatigue *vs.* 59 (73.75%) severe fatigue patients reported a history of DEB or screaming and/or vocalization, suggesting a possible clinical RBD ($P = 0.028$). The PSG results showed that 78 (51.31%) patients with mild fatigue and 54 (67.50%) patients with severe fatigue were diagnosed with RBD

($P = 0.018$). Furthermore, tonic and phasic RWA were significantly higher in patients with severe fatigue. No between-group difference was found in total sleep time, awakenings, sleep latency, or apnea-related parameters, such as AHI and ODI. Table 2 summarizes the sleep characteristics of PD patients with mild and severe fatigue.

The results of multivariate binary logistic regression analyses examining predictors of severe fatigue were given in Table 3. The multivariate analysis showed that after the adjustment for covariates, the significant risk factors for severe fatigue were higher LEDD (odds ratio [OR] = 1.004, $P < 0.001$, 95% confidence interval [CI] = 1.002–1.005), HRSD (OR = 1.099, $P < 0.001$, 95% CI = 1.051–1.149), RBD (OR = 2.256, $P = 0.015$, 95% CI = 1.167–4.359), and lower percentage of REM sleep (OR = 0.952, $P = 0.013$, 95% CI = 0.917–0.990). ESS was not significant (OR = 1.041, $P = 0.314$) after including the LEDD variance.

We further investigated the association between sleep characteristics and fatigue scores using different linear regression analyses for different adjustments [Table 4]. Multiple linear regression analysis revealed a significant association between the proportion of REM sleep and FSS (adjusted for RBD additionally in Model 3; $\beta = -0.037$, $P < 0.001$). To further characterize the relationship between RBD and severity of fatigue, we performed linear regression analyses to assess the association between tonic EMG activity and FSS score (adjusted for proportion of REM sleep additionally in Model 3; $\beta = 0.012$, $P = 0.015$) or phasic EMG activity (adjusted for proportion of REM sleep additionally in Model 3; $\beta = 0.013$, $P = 0.003$). The differences we found remained significant after adjustment for different confounders.

Table 1: Demographic and clinical information of PD patients with severe and mild fatigue.

Variables	Entire sample (*n* = 232)	Mild fatigue (*n* = 152)	Severe fatigue (*n* = 80)	Statistical values	*P*
Age of onset (years)	61.19 ± 8.78	61.27 ± 9.02	61.05 ± 8.36	0.181	0.857
Sex (M/F)	151/81	103/49	48/32	1.390	0.238
Duration (years)	3.93 ± 3.27	3.15 ± 2.49	5.40 ± 4.00	-5.257	<0.001
BMI (kg/m²)	23.96 ± 3.31	24.11 ± 3.24	23.69 ± 3.46	0.875	0.382
Education (years)	8.68 ± 3.49	8.76 ± 3.36	8.52 ± 3.72	0.491	0.624
UPDRS III	24.27 ± 10.77	19.87 ± 8.36	32.64 ± 9.87	-10.380	<0.001
UPDRS total	38.78 ± 15.61	31.88 ± 11.72	51.89 ± 13.58	-11.694	<0.001
AR/T	176 (75.86)	107 (70.39)	69 (86.25)	7.196	0.007
H-Y	2.16 ± 0.68	1.91 ± 0.55	2.63 ± 0.64	-8.935	<0.001
LEDD	300.0 (112.5–443.8)	262.5 (75.0–400.0)	400.0 (300.0–581.3)	-5.265	<0.001
MMSE	26.12 ± 2.65	26.31 ± 2.27	25.76 ± 3.24	1.499	0.135
MoCA	22.97 ± 2.97	23.08 ± 2.91	22.78 ± 3.09	0.741	0.460
HRSD	9.56 ± 7.19	7.89 ± 6.26	12.74 ± 7.77	-5.149	<0.001
HAMA	7.03 ± 5.83	5.85 ± 5.52	9.26 ± 5.77	-4.404	<0.001
ESS	6.60 ± 4.31	6.18 ± 3.93	7.34 ± 4.56	-2.010	0.046
PSQI	6.83 ± 4.46	5.83 ± 3.81	8.91 ± 4.99	-4.824	<0.001
Hypersalivation	72 (31.03)	32 (21.05)	40 (50.00)	20.520	<0.001
Hyposmia	157 (67.67)	102 (67.11)	55 (68.75)	0.065	0.799
Constipation	174 (75.00)	110 (72.37)	64 (80.00)	1.628	0.202
Urinary urgency	77 (33.19)	39 (25.66)	38 (47.50)	11.277	0.001

Values are shown as mean ± standard deviation, *n* (%), or median (interquartile range). PD: Parkinson disease; M/F: Male/female; BMI: Body mass index; UPDRS: Unified Parkinson Disease Rating Scale; H-Y: Hoehn and Yahr; MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment; HRSD: Hamilton Rating Scale for Depression; HAMA: Hamilton Anxiety Rating Scale; ESS: Epworth Sleepiness Scale; PSQI: Pittsburgh Sleep Quality Inventory.
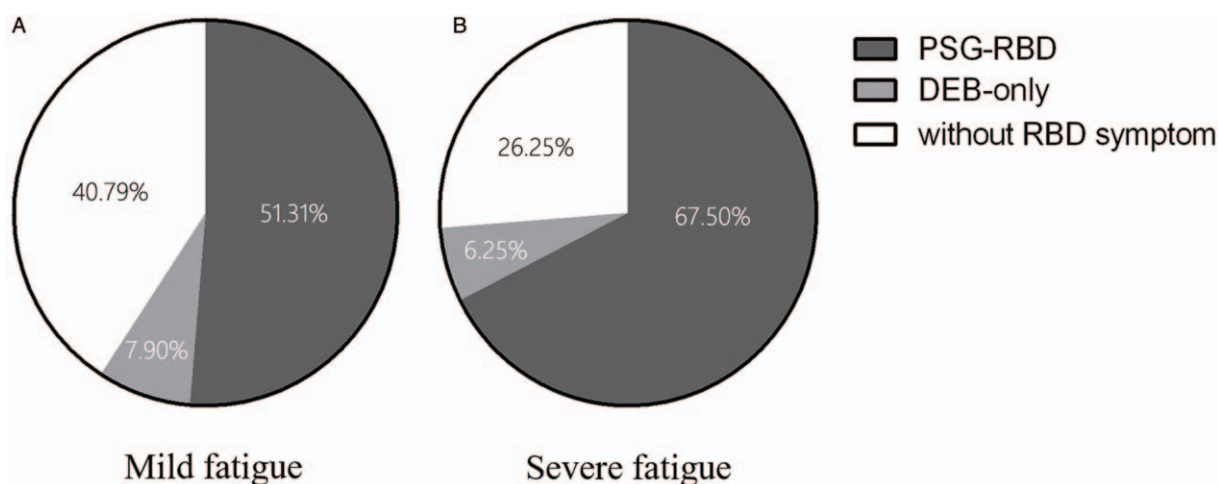
Figure 1: The distribution of RBD and DEB-only in PD patients with severe and mild fatigue. (A) Percentage of RBD and DEB-only in PD with mild fatigue; (B) percentage of RBD and DEB-only in PD with sever fatigue. DEB: Dream-enacting behavior; PD: Parkinson disease; RBD: Rapid eye movement sleep behavior disorder; PSG-RBD: Polysomnography confirmed RBD.

Table 2: Polysomnography parameters in PD with severe and mild fatigue.

Variables	Entire sample ($n = 232$)	Mild fatigue ($n = 152$)	Severe fatigue ($n = 80$)	Statistical values	P
TST	339.96 ± 99.69	344.23 ± 99.72	331.84 ± 99.77	0.899	0.369
SE	63.05 ± 17.39	63.73 ± 17.88	61.75 ± 16.44	0.828	0.409
SL (min)	13.00 (4.00–30.50)	14.25 (4.13–29.38)	10.00 (2.50–32.88)	−0.498	0.619
REML (min)	119.00 (65.50–215.50)	120.25 (67.13–208.13)	116.00 (52.50–221.75)	−0.194	0.846
Awakenings	23.10 ± 10.94	23.10 ± 10.41	23.09 ± 11.97	0.007	0.995
Arousal index	9.87 ± 10.87	9.37 ± 9.64	10.82 ± 12.91	−0.964	0.336
NREMS1	20.72 ± 15.71	19.18 ± 13.25	23.64 ± 19.32	−1.849	0.067
NREMS2	46.65 ± 15.73	46.21 ± 14.01	47.47 ± 18.65	−0.530	0.597
SWS	17.59 ± 12.62	18.21 ± 11.28	16.41 ± 14.83	1.035	0.302
REMS	15.13 ± 8.90	16.23 ± 8.52	13.04 ± 9.27	2.626	**0.009**
AHI	2.60 (0.00–7.90)	3.20 (0.00–7.80)	1.40 (0.00–9.35)	−0.118	0.906
ODI	2.05 (0.20–7.23)	2.15 (0.30–7.80)	1.90 (0.03–6.38)	−0.680	0.497
PLMSI (h)	6.50 (0.00–40.85)	9.85 (0.00–41.58)	4.10 (0.00–36.90)	−0.545	0.586
Tonic RWA%	15.32 (3.46–26.09)	13.25 (2.36–19.45)	20.77 (9.85–36.90)	−2.503	**0.012**
Phasic RWA%	12.12 (8.20–25.33)	11.11 (4.32–17.60)	22.76 (9.80–70.19)	−3.076	**0.002**
History of DEB (Yes/No)	149/83	90/62	59/21	4.822	**0.028**
PSG-RBD (Yes/No)	132/100 (56.89)	78/74 (51.32)	54/26 (67.50)	5.598	**0.018**

Values are shown as mean ± standard deviation, n/N, n/N (%), or median (interquartile range). PD: Parkinson disease; TST: Total sleep time; SE: Sleep efficiency; SL: Sleep latency; REML: Rapid eye movement sleep latency; NREMS: Non-rapid eye movement sleep; SWS: Slow wave sleep; REMS: Rapid eye movement sleep; AHI: Apnea-hypopnea index; ODI: Oxygen desaturation index; PLMSI: Index of periodic leg movements during sleep; RWA: Rapid eye movement sleep without atonia; DEB: Dream-enacting behavior; PSG-RBD: Polysomnography confirmed rapid eye movement sleep behavior disorder.

Table 3: Multivariate binary logistic regression analyses for predictors of severe fatigue in PD patients.

Variable	β	Standard error	Wald	P values	OR	95% CI
Age	0.015	0.020	0.550	0.458	1.015	0.976–1.055
Sex	−0.467	0.343	1.860	0.173	0.627	0.320–1.227
LEDD	0.004	0.001	21.153	**<0.001**	1.004	1.002–1.005
HRSD	0.094	0.023	16.909	**<0.001**	1.099	1.051–1.149
PSG-RBD	0.814	0.336	5.859	**0.015**	2.256	1.167–4.359
REMS	−0.049	0.020	6.219	**0.013**	0.952	0.917–0.990

PD: Parkinson disease; OR: Odds ratio; CI: Confidence interval; LEDD: L-dopa equivalent daily dose; HRSD: Hamilton rating scale for depression; PSG-RBD: Polysomnography confirmed rapid eye movement sleep behavior disorder; REMS: Rapid eye movement sleep.

Discussion

In this study, we found that PD patients with severe fatigue, compared with those with mild fatigue, had increased RWA and higher REM%. The association between RBD and fatigue remained significant after adjusting for variables that were different between the two groups on the basis of t-test analyses. Furthermore, five patients with fatigue who failed to show RWA at PSG reported DEBs. This condition was recently shown to represent prodromal

Table 4: Linear regression models for the association between FSS and sleep parameters.

Items	β	95% confidence interval	P
REMS (%)			
Unadjusted	−0.032	−0.049 to −0.014	<0.001
Model 1	−0.027	−0.043 to −0.010	0.002
Model 2	−0.021	−0.035 to −0.007	0.004
Model 3	−0.037	−0.054 to −0.019	<0.001
Tonic RWA%			
Unadjusted	0.022	0.010–0.033	<0.001
Model 1	0.017	0.005–0.028	0.005
Model 2	0.015	−0.104–0.081	0.002
Model 3	0.012	0.002–0.022	0.015
Phasic RWA%			
Unadjusted	0.022	0.012–0.032	<0.001
Model 1	0.019	0.009–0.029	<0.001
Model 2	0.014	0.006–0.022	0.001
Model 3	0.013	0.005–0.022	0.003

Model 1: Adjusted for age, sex, duration, and BMI. Model 2: Adjusted for age, sex, duration, BMI, UPDRS III score and levodopa equivalent daily dosage, HRSD, and HAMA. Model 3: Adjusted for age, sex, duration, BMI, UPDRS III score and levodopa equivalent daily dosage, HRSD, HAMA, TST, AHI, ODI, and PLMSI. For REM%, adjusted for RBD, and for RWA%, adjusted for REM% additionally. FSS: Fatigue severity scale; REMS: Rapid eye movement sleep; RWA: REM sleep without atonia; BMI: Body mass index; UPDRS: Parkinson disease rating scale; HRSD: Hamilton rating scale for depression; HAMA: Hamilton anxiety rating scale; TST: Total sleep time; AHI: Apnea-hypopnea index; ODI: Oxygen desaturation index; PLMSI: Periodic leg movements during sleep; REM: Rapid eye movement; RBD: REM sleep behavior disorder.

RBD.[19,20] These results appeared to be robust since we performed additional multivariate binary logistic regression, linear regression analyses, and adjusted for potential confounding variables.

In our present study, patients with fatigue showed higher UPDRS, LEDD, HRSD, HAMA, ESS, and PSQI scores and higher percentage of hypersalivation and urinary urgency, demonstrating that fatigue may be associated with higher burden of motor and non-motor symptoms. The logistic regression analysis, however, demonstrated that only the severity of motor symptoms, depression, RBD, and the proportion of REM sleep were the independent factors contributing to the presence of fatigue in PD patients.

The concepts of primary and secondary fatigue are relevant in PD patients as a result of depression, sleepiness, pain, and other comorbidities. Fatigue appears to have both emotional and physiological components. Although there were data on muscle fatigue, little is known about the pathophysiology of central fatigue in PD. Certain areas of the brain, including frontal lobe dysfunction, brainstem, and dopaminergic dysfunction in limbic structures, are thought to be related to fatigue in PD.[21] Covington[22] described a feedback loop in which fatigue, pain, depression, and bradykinesia act synergistically to increase disability. The presence of high concurrence of non-motor symptoms in PD may be illustrative of this cycle. In our results, we demonstrated that fatigue was correlated with depression, sleep disturbances, and motor severity, which were consistent with previous studies.[23]

The relationship between sleep disorders and fatigue in PD was complex. Our results indicated that RBD (higher tonic RWA% and phasic tonic RWA%) was a significant predictor of fatigue in PD patients. Zuo et al[24] evaluated 102 PD patients and found that fatigue patients had significantly increased α-synuclein oligomer level in cerebrospinal fluid (CSF). Their previous work also demonstrated that the increased CSF α-synuclein oligomer level was associated with RBD.[25] The oligomer was the most neurotoxic form of α-synuclein in Lewy bodies and might be released from degenerative or dead neurons.[26] Furthermore, the increased CSF α-synuclein level might be a marker for more severe synaptic degeneration in PD,[27] which implied that RBD and fatigue might be predictors for rapid progression.[28]

To the best of our knowledge, the current study was the only one to evaluate the association between fatigue and sleep disorders in PD patients via PSG. Some studies assessed fatigue in PD by using several question-naires.[29,30] The association between RBD, REM%, and fatigue was a novel finding. PD patients always felt constant exhaustion, which was a characteristic of central fatigue. Disturbed sleep pattern aggravated the severity of fatigue in PD patients. We found that the reduction of REM sleep was one of the culprits for fatigue in PD patients. More importantly, we speculated that there might be a compensatory decrease in REM sleep in fatigue patients and a relatively higher proportion of non-REM sleep (NREMS). The slow wave sleep in NREMS contributes to memory and energy recovery. We believed that sleep disturbances and fatigue were worth to be investigated since the PD-related neuronal loss and Lewy body accumulation involved brain regions, such as basal forebrain, brainstem, thalamus, and hypothalamus, which were thought to be associated with both sleep-wake regulation and fatigue.[31] More attention should be paid to the pathological mechanisms of altered sleep architecture and fatigue.

Few studies in the literature had specifically examined the interaction between fatigue and sleep disorders. Previous studies only investigated this relationship on daytime sleepiness scales, such as ESS. But they ignored the sleep disturbances during the night. Recently, a study of 81 PD patients using ESS and detailed neuropsychological evaluations suggested that fatigue was associated with sleepiness and anxiety.[32] Another study demonstrated that fatigue and excessive daytime sleepiness were related to cognitive impairment reported on UPDRS,[12] even though some researchers insisted that there was no correlation between fatigue and degree of sleepiness.[3] Our negative association between fatigue and daytime sleepiness was also consistent with previous studies,[33] which were conducted in early PD patients.[34-36] These discrepancies could also be explained by the adjustment of disease severity in the non-correlated studies. We believed that the relationship between daytime sleepiness and fatigue may not be meaningful as the correlation became insignificant after adjustment for disease severity.

Interestingly, in terms of total sleep time, awakenings, sleep latency, AHI, or ODI, we did not find any difference

between patients with severe or mild level of fatigue in our study. This was quite surprising because, in healthy population, these factors could promote exhaustion. However, these factors clearly did not dominant in PD with fatigue according to our results and previous finding.[3] Further replications with larger sample size were needed to explain these phenomena.

This study had several limitations. First of all, we had a relatively small sample size and only from one hospital. Secondly, more objective measures and complex scales should be used to assess fatigue in PD patients in future studies since FSS was a self-reported questionnaire with relatively low sensitivity and specificity. Lastly, to conduct the PSG successfully, most of the PD patients in our study were in the mild to moderate stage.

To sum up, our findings of fatigue associated with RBD and altered sleep architecture suggested that fatigue could be a special subtype in PD and more studies should focus on this easily neglected symptom.

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Conflicts of interest

None.

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