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Screening tools for clinical characteristics of probable REM sleep behavior disorder in patients with Parkinson's disease

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ABSTRACT

Introduction: The REM sleep behavior disorder (RBD) screening questionnaire (RBDSQ) has been used as a screening tool for RBD. We investigated the clinical characteristics of probable RBD (pRBD) using the RBDSQ in patients with Parkinson's disease (PD).

Methods: Seventy patients with PD (age: 69.2 ± 8.9 years old, 31 males and 49 females, length of PD morbidity: 7.4 ± 6.4 years, Hoehn and Yahr: 2.7 ± 0.8) underwent examination including the RBDSQ and Mini-Mental State Examination (MMSE) in both 2011 and 2013. We assessed the changes and characteristics of pRBD associated with PD during the two year interval.

Results: Nineteen patients (27.1%) in 2011 and 27 patients (38.6%) in 2013 were diagnosed as having pRBD because they scored 6 or higher on the RBDSQ. During the 2 year interval, twelve patients showed persistent pRBD, 15 developed pRBD, and 7 showed improved pRBD. In 2013, PD patients with pRBD took higher amounts of levodopa equivalents and scored lower on the MMSE than those without pRBD. Also, more PD patients with pRBD had dementia than those without pRBD. Similarly, more patients with persistent and developed pRBD had dementia than those without.

Conclusion: We found that RBD symptoms might fluctuate during the clinical course of PD, and RBD symptoms might temporarily affect cognitive impairment.

1. Introduction

REM sleep behavior disorder (RBD) is characterized by vigorous and injurious behaviors related to vivid, action-filled, and violent dreams during nocturnal REM sleep [1]. Recently, the existence of RBD has been suggested to be a risk factor for the development of dementia in Parkinson's disease (PD) [2]. According to the third edition of the International Classification of Sleep Disorders (ICSD 3rd), positive identification of REM sleep without atonia (RWA) on a polysomnogram (PSG) is used as an essential criterion for the diagnosis of RBD [1]. However, in the clinical setting, it is not possible to conduct a PSG for evaluation of RBD in all patients with PD. Thus, the RBD screening questionnaire (RBDSQ) was created as a diagnostic instrument [3]. The RBDSQ is also useful for detecting probable RBD (pRBD) in patients with PD.

In the present study, we evaluated changes in pRBD during the clinical course of PD. Furthermore, we investigated the clinical characteristics, including cognitive function, of pRBD in patients with PD.

2. Methods

The ethics committees of Tottori University approved this study, and all subjects gave their informed consent to take part in this investigation. This study investigated consecutive PD patients who visited the outpatient clinic of the Department of Neurology at Tottori University Hospital in 2011 and 2013. Diagnosis of PD was made based on standardized clinical criteria [4]. These patients included three cases taking clonazepam and two cases taking selective serotonergic receptor inhibitors. However, they kept taking these medicines. We analyzed only those patients who answered the RBDSQ in both 2011 and 2013. The exact intervals were 21.2 ± 2.9 months. Patients that scored 6 or more points on the RBDSQ-J were diagnosed as having pRBD [5]. We estimated the prevalence of pRBD at the two survey points. Patients were then divided into four groups based on the presence or absence of pRBD: patients with pRBD at both time points were categorized as the persistent pRBD group; patients in whom RBD symptoms had disappeared by the follow-up were categorized as the improved pRBD group; patients without pRBD at the initial evaluation who had developed pRBD by the follow-up were categorized as the newly developed pRBD group; and patients without pRBD at either time point were designated as the negative pRBD group.

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Table 1
Clinical comparison between PD with and without pRBD on the second survey.

	PD with pRBD (n = 27)	PD without pRBD (n = 43)	Significance
Age (years old)	68.8 ± 8.6	69.4 ± 9.2	n.s.
Gender (male/female)	15/12	16/27	n.s.
Length of PD morbidity (years)	9.1 ± 7.7	6.4 ± 5.2	n.s.
Hoehn &Yahr grade	2.8 ± 0.7	2.5 ± 0.9	n.s.
LDEs (mg/day)	500 ± 351	322 ± 243	0.009
MMSE	24.4 ± 5.2	26.8 ± 3.6	0.012
MoCA	21.0 ± 5.8	23.0 ± 5.0	n.s.
Cognition (dementia/normal)	8/19	3/40	0.011

Average ± SE and number, PD: Parkinson's disease, RBD: REM sleep behavior disorder. LDEs: levodopa dose equivalents, PSQI: Pittsburgh sleep quality index, ESS: Epworth sleepiness scale, MMSE: Mini-Mental State Examination, MoCA: Montreal cognitive assessment, n.s. = not significant.

Patients were also administered the Mini-Mental State Examination (MMSE) and Montreal cognitive assessment (MoCA) as a measure of cognitive function during the second evaluation period. PD patients were diagnosed with dementia if they scored; < 26 on the MMSE according to the specific criteria proposed by the Movement Disorder Society Task Force [6].

Descriptive variables including age at the time of first investigation, gender, length of PD morbidity, Hoehn & Yahr grade, dose of dopaminergic agents as levodopa dose equivalents (LDEs) [10], and MMSE scores were compared among the four groups. A chi-squared test followed by residual analysis was used to compare the categorical variables. Comparisons of continuous variables among the four groups were made using one way analysis of variance (ANOVA) followed by a post hoc Bonferroni correlation. A p-value of < 0.05 was considered to be statistically significant. The statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS, ver. 23.0J, 2015; SPSS, Tokyo, Japan).

3. Results

We evaluated 70 patients with PD (69.2 ± 8.9 years old, 31 males and 39 females, length of PD morbidity: 7.4 ± 6.4 years). At the initial evaluation, nineteen patients were diagnosed as having pRBD (27.1%). There were no significant differences in age, gender, length of PD morbidity, Hoehn and Yahr stage, LDEs, or MMSE scores between the PD groups with and without pRBD.

At the second evaluation, 27 patients were diagnosed as having pRBD (38.6%). PD patients with pRBD had significantly more LDEs and lower MMES scores. In addition, more PD patients with pRBD had dementia than those without pRBD. However, there were no significant differences in age, gender, length of PD morbidity, and Hoehn and Yahr stage between PD patients with and without pRBD. Regrettably, there was no significant difference of MoCA between the two groups ($p = 0.156$) (Table 1).

After comparing results from the two evaluation points, patients were divided into one of four groups. There were 12 patients in the persistent pRBD group, 15 patients in the newly developed pRBD group, 7 patients in the improved pRBD group, and 36 patients in the negative pRBD group. There were no significant differences in any of the parameters among the four groups. Interestingly, while not significant, there was a trend in the proportion of dementia among the four groups ($p = 0.072$). More patients with negative RBD tended to have normal cognition than the other groups (Table 2).

4. Discussion

This study suggests that pRBD fluctuates during the clinical course of PD based on results from the RBDSQ. The prevalence of RBD in patients with PD determined by the RBDSQ might be similar to that detected by standard methods of RBD diagnosis including PSG findings. Lavault et al. showed that the yearly appearance of RBD was 9% and yearly disappearance of RBD was 14% [7]. Another study showed probable RBD increased at 3 years follow up [8]. In our study, the yearly appearance of RBD was 10.7% and yearly disappearance of RBD was 3.6%. In their study, Lavault et al. showed a tendency toward motor aggravation during the early stages in PD patients with pRBD. However, in the present study, the existence of pRBD did not affect motor signs in patients with PD. In another study, PD patients with RBD had a longer length of PD morbidity, more severe motor symptoms, higher dosage of dopaminergic agents, and more frequent falls [9]. Lavault's data on PD patients with pRBD is inconsistent, similar with our data. These findings might indicate that the diagnosis of pRBD was inaccurate. However, the RBDSQ has the advantage of easily detecting RBD.

Previous reports indicated that the existence of RBD is one of the risk factors for developing dementia in patients with PD [2]. There were more PD patients with RBD with mild cognitive impairment than those without RBD [10]. Some reports indicated cognitive impairment, such as executive dysfunction and memory impairment [11], slowing of electroencephalograms [12], and decreased brain perfusion [13] in patients with idiopathic RBD. In the current study, PD patients with pRBD had lower MMSE scores than those without RBD at the second evaluation. In particular, the negative RBD group had more patients with normal cognition than the three other groups. In PD with dementia, MoCA is a better measure of cognitive status than MMSE [14]. Regrettably, the present study showed no significant difference on MoCA because of small sample. However, this finding suggests that the RBDSQ is useful in the clinical setting for easily detecting RBD as one of the risk factors for developing dementia in patients with PD.

The present study had three major limitations. First, we could not evaluate the presence/absence of RWA using PSGs. Our patients might include pseudo-positive and pseudo-negative cases. However, we could confirm that the RBDSQ was useful because of similar results in which RBD was confirmed using PSGs. The second limitation is that we could only use screening tools for dementia. However, screening tools for both RBD and dementia were shown to be useful in the clinical setting because this study utilized both easy screening tools. The last limitation is that the association between dementia and pRBD among the four groups did not reach statistical significance. This can be attributed to the small sample size of the groups. Larger studies should clarify

Table 2
Comparison of clinical backgrounds for the existence of pRBD in patients with PD.

	Persistent pRBD (n = 12)	Developed pRBD (n = 15)	Improved pRBD (n = 7)	Negative pRBD (n = 36)
Gender (M/F)	8/4	7/8	3/4	12/24
Age (years)	70.3 ± 6.9	67.6 ± 9.9	69.4 ± 10.4	69.4 ± 9.2
Periods of PD (years)	7.4 ± 6.2	10.5 ± 8.7	5.6 ± 2.8	6.5 ± 5.6
Hoehn & Yahr	2.8 ± 0.6	2.9 ± 0.8	2.1 ± 0.4	2.6 ± 0.9
LDEs (mg/day)	509 ± 286	492 ± 405	318 ± 98	323 ± 263
MMSE	24.6 ± 6.5	24.3 ± 4.2	27.6 ± 2.3	26.6 ± 3.8
MoCA	21.4 ± 4.4	20.6 ± 6.8	23.9 ± 3.4	22.8 ± 5.3
Dementia (yes/no)	4/8	4/11	1/6	2/34

Numbers and average ± SD. PD: Parkinson's disease, LED: Levodopa equivalents dose MMSE: Mini-mental state examination, MoCA: Montreal cognitive assessment.

the significance of the association between dementia and pRBD in the future.

5. Conclusion

Throughout the clinical course of PD, RBD might fluctuate and increase. Persistent RBD might be one of the risk factors for developing dementia in patients with PD. We further demonstrate that the RBDSQ and cognitive assessment such as MMSE and MoCA are useful for evaluating problems associated with PD in the clinical setting. We supported two step detection of RBD in PD patients. At first, RBDSQ found RBD symptoms in PD patients easily. Next, we made these patients defined RBD by PSG. Then, we should follow up PD patients with defined RBD carefully.

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