https://doi.org/10.36315/2024inpact158
Psychological Applications and Trends 2024

STUDY ON COGNITIVE PROFILES OF PARKINSON'S DISEASE PATIENTS WITH AND WITHOUT RAPID EYE MOVEMENT BEHAVIOR DISORDER

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Abstract

Research indicates that nearly all individuals diagnosed with Parkinson's Disease (PD) experience disruptions in sleep patterns, often emerging in the early stages of the disease. The etiology of sleep disorders is intricate, but the pathological degeneration of sleep-regulating centers in the brainstem and thalamocortical pathways appears to play a significant role. Rapid Eye Movement Behavior Disorder (RBD) is defined as a parasomnia marked by the absence of normal skeletal muscle atonia during REM sleep and has been observed in approximately one-third of PD patients. In this study, with a focus on the influence of REM sleep on cognitive processes, the aim is to compare the neurocognitive profiles of PD patients, distinguishing between those with and without RBD symptoms. Individuals meeting the diagnostic criteria of the "United Kingdom Parkinson's Disease Society Brain Bank" were included in the study. Subsequently, the patients were divided into two groups based on their scores from the Rapid Eye Movement Behavior Disorder Screening Questionnaire (RBDSQ) (cut-off point=5), with clinical assessments also being considered. Patients demonstrating a tendency toward RBD were allocated to the RBD+PD group (n = 30), while PD patients without RBD tendencies (n = 42) were assigned to the RBD-PD group. The groups were matched based on age, education level, disease duration, Hoehn and Yahr stages, Unified Parkinson's Disease Rating Scale scores, and Clinical Dementia Rating stages. Cognitive functions were assessed using various neuropsychological tests, and the neurocognitive assessment lasted an average of 2 hours. Statistical analyses were conducted using SPSS version 26, with the Independent Sample t-test employed for variables with a normal distribution, and the Mann-Whitney U test used for variables that did not exhibit a normal distribution. The results of the statistical analyses revealed that the RBD+PD group exhibited lower backward digit span scores compared to the RBD-PD group. Furthermore, phonemic and switching verbal fluencies were reduced, naming skills were impaired, and there was a decline in verbal immediate memory performance in the RBD+PD group compared to the RBD-PD group. Our results suggest that the presence of RBD is linked to decreased cognitive functions, with a notable emphasis on frontal dysfunction, in individuals diagnosed with PD.

Keywords: *Parkinson's disease, REM behavior disorder, frontal functions, neurocognitive assessment.*

1. Introduction

Understanding nonmotor symptoms in Parkinson's Disease is crucial due to their significant impact on patients' health and quality of life. While Parkinson's Disease has traditionally been viewed as a motor disorder, nonmotor symptoms are increasingly recognized as essential contributors to the overall disease burden (Kadastik-Eerme et al., 2016; Duncan et al., 2013). Non-motor symptoms are often underrecognized in clinical practice, which can result in missed opportunities for appropriate management and care (Chaudhuri et al., 2006). Research has shown that nonmotor symptoms can precede the onset of motor symptoms in Parkinson's Disease, highlighting their potential as early indicators of the condition (Hong et al., 2017; Pont-Sunyer et al., 2014).

Sleep and cognitive disorders are particularly important and prevalent in Parkinson's Disease due to their significant impact on patients' overall well-being and disease progression. Research has shown that cognitive impairment is common in Parkinson's Disease, with long-term studies indicating that most patients eventually develop dementia (Litvan et al., 2011). Cognitive dysfunction not only affects daily

functioning but also contributes to a decline in quality of life for individuals with Parkinson's Disease (Padovani et al., 2019). Additionally, cognitive impairment can be a predictor of dementia in Parkinson's disease, highlighting the importance of early recognition and management of cognitive symptoms (Hussain & Camicioli, 2017; Sommerauer et al., 2017).

The complex etiology of sleep disorders in PD is believed to involve the degeneration of sleep-regulating centers in the brainstem and thalamocortical pathways, playing a significant role in these disturbances. One prevalent sleep disorder in PD is Rapid Eye Movement Behavior Disorder (RBD), characterized by the absence of normal skeletal muscle atonia during REM sleep and observed in approximately one-third of PD patients.

Despite reports indicating a potential association between Rapid Eye Movement Sleep Behavior Disorder (RBD) in Parkinson's Disease and cognitive impairment, a consensus within the literature regarding this relationship has yet to be reached. Studies have demonstrated that the presence of RBD in Parkinson's Disease patients is associated with a higher risk of cognitive decline, particularly in attention and memory domains (Teng et al., 2023; Maggi et al., 2021). Furthermore, the relationship between RBD and cognitive dysfunction may be mediated by brainstem nuclei involved in RBD that also play a role in cognition (Yuan et al., 2022). Patients with RBD have been found to exhibit distinct patterns of cognitive impairment, affecting areas such as fronto-striatal and posterior cortex functions (Teng et al., 2023).

Moreover, RBD in Parkinson's disease has been identified as a predictor of faster deterioration in both motor and cognitive functions (Ye et al., 2022). The presence of RBD is associated with an increased frequency of cognitive impairment and a greater risk of developing dementia in individuals with Parkinson's disease (Rolinski et al., 2015). Additionally, RBD has been linked to a higher prevalence of mild cognitive impairment in Parkinson's disease patients (Oltra et al., 2022). Given the influence of REM sleep on cognitive processes, there is a growing interest in comparing the neurocognitive profiles of PD patients, with a specific focus on distinguishing between those with and without RBD symptoms. This study aims to shed light on the impact of REM sleep disturbances on cognitive functions in PD patients.

2. Methods

2.1. Participants

Following the criteria set by the United Kingdom Parkinson's Disease Society Brain Bank, a study encompassing 72 Parkinson's patients, aged 43 to 83, was conducted, consisting of 26 females and 46 males. Participants suspected of Parkinson-plus syndromes and those with a history of alcohol/substance abuse, stroke, head trauma, intoxication, and epileptic seizures were not included in the study. Participants were categorized into RBD+PD (n = 30), and RBD-PD (n = 42) groups based on clinical evaluation and scores obtained from the REM Sleep Behavior Disorders Screening Questionnaire (RBDSQ / with a cut-off point of 5). Clinical symptoms were evaluated using the Unified Parkinson's Disease Rating Scale (UPDRS) and the Hoehn Yahr Parkinson's Rating Scale (H&Y). The groups were matched in terms of age, education level, duration of disease, CDR stages, depression and apathy levels. All participants were predominantly right-handed.

2.2. Data collection

Data were gathered using a demographic information form and a neuropsychometric inventory. The neuropsychometric inventory comprised various assessments, including the personal and current information subtests of the Wechsler Memory Scale (WMS), orientation subtest of WMS, verbal fluency tests, abstraction skills tests, Stroop Test Çapa Version, Clock Drawing Test (CDT), visual memory subtest of WMS, logical memory subtest of WMS, Öktem Verbal Memory Processes Test (VMPT), Boston Naming Test (BNT), Benton Face Recognition Test (BFRT), Yesavage Geriatric Depression Scale (GDS), Neuropsychiatric Inventory (NPI), and Mini-Mental State Examination (MMSE). The neuropsychological evaluation took approximately 2 hours to complete.

2.3. Statistical analysis

The statistical analysis was performed using SPSS (Statistical Package for Social Science) version 26.0 for Windows. The normality of the variables was assessed using the Shapiro-Wilk Test, and their kurtosis and skewness values (+3/-3) were examined to determine the appropriate tests. Parametric tests were used for variables that met the normality criteria, while non-parametric tests were employed for those that did not. Descriptive statistics, including mean and standard deviation values, were reported for both the clinical and demographic characteristics of the participants. Specifically, the Independent Samples t-test was applied to variables with a normal distribution, whereas the Mann-Whitney U test was used for variables with a non-normal distribution. The significance level was set at $p < .05$ to indicate statistical significance.

3. Results

The demographic and clinical characteristics of the groups are shown in Table 1.

Table 1. Demographic and clinical characteristics of sample.

	RBD+PD n = 30	RBD-PD n = 42		
	Mean (SD)	Mean (SD)	*t/U/χ2*	*p*-value
Age (years)	69.73 (8.34)	68.24 (8.41)	-.747	.458
Gender (female/male)[a]	12/18	14/28	.337	.561
Education (years)	6.73 (4.40)	8.13 (4.59)	1.295	.200
Duration of disease (months)	79.21 (50.45)	81.73 (48.06)	.209	.835
UPDRS total score	45.54 (15.99)	38.05 (18.60)	-1.786	.079
Hoehn and Yahr Stages[b,c]	1.75	2.25	492	.239
GDS	10.24 (7.31)	8.59 (6.38)	-1.007	.318
AES	29.74 (12.50)	30.69 (11.49)	-.319	.750
CDR[b,c]	0.5	1	492	.071
NPI total score (frequency × severity)[b]	15.68 (2.44)	12.52 (1.93)	467.500	.148
NPI caregiver distress score[b]	9.14 (1.22)	8.45 (1.23)	-.887	.375
RBDSQ	6.03 (1.30)	2.71 (1.29)	-10.715	< 0.001***

Note. *p < .05; **p < .01; ***p < 0.001; AES = Apathy Evaluation Scale, CDR = Clinical Demanti Rating, GDS = Yesavage Geriatric Depression Scale, NPI = Neuropsychiatric Inventory, RBDSQ = REM Sleep Behavior Disorder Screening Questionnaire, SD = Standard Deviation, UPDRS = Unified Parkinson Disease Rating Scale.
[a] Chi-square test was used.
[b] Mann-Whitney U test was used.
[c] Median values are shown.

The a+PH group exhibited significantly lower scores compared to the RBD-PH group in the WMS reverse digit span ($t(68) = 3.187$, $p > .01$), VMPT immediate scores ($t(70) = 2.382$, $p > .05$), phonetic fluency scores ($t(61) = 2.095$, $p > .05$), alternating word fluency scores ($t(68) = 2.020$, $p > .05$), binary similarities test scores ($t(69) = 2.455$, $p > .05$), and BNT scores ($t(66) = 2.850$, $p > .01$). The neuropsychometric findings for both groups are summarized in Table 2.

Table 2. Neuropsychological characteristics of RBD+PD and RBD-PD groups.

		RBD+PD n = 30	RBD-PD n = 42		
		Mean (SD)	Mean (SD)	*t/U*	*p*-value
General Cognitive Function	MMSE	22.24 (4.21)	23.33 (2.83)	1.308	.195
Personal and Spatial Orientation	WMS personal and current information	4.53 (1.28)	4.95 (1.30)	1.336	.186
	WMS orientation	3.90 (1.47)	4.23 (1,29)	.982	.330
Digit Span	Forward digit span	2.43 (1.10)	3.18 (.84)	.613	.542
	Reverse digit span	4.67 (.92)	4.80 (.84)	3.187	.002**
Verbal Memory	VMPT learning	67.77 (22.68)	63.55 (19.70)	.953	.344
	VMPT total	10.77 (3.95)	11.88 (3.56)	1.252	.215
	VMPT immediate	2.37 (1.54)	3.14 (1,22)	2.382	.020*
Visual Memory	Visual memory immediate	4.26 (3.31)	5.45 (2.23)	1.369	.176
	Visual memory delayed	2.78 (2.33)	3.85 (3.23)	1.388	.170
Executive Functions	Phonetic fluency	15.54 (7.70)	20.69 (11.81)	2.095	.040*
	Semantic fluency	13.43 (4.60)	14.48 (5.87)	.811	.420
	Alternating word fluency	3.71 (2.40)	4.95 (2.67)	2.020	.048*
	Stroop interference score[a]	34.63	31.30	422.5	.493
	Proverb interpretation task	2.20 (1.22)	2.54 (1.03)	1.262	.211
	Binary similarities test	6.87 (2.01)	7.95 (1.70)	2.455	.017*
	CDT	2.36 (1.39)	2.71 (1.27)	1.107	.272
Language	BNT	20.86 (4.64)	24.10 (4.60)	2.850	.006**
Visuospatial function	BFRT	37.57 (6.48)	39.78 (5.07)	1.586	.118

Note. *p < .05; **p < .01; ***p < 0.001; BFRT = Benton Face Recognition Test, BNT = Boston Naming Test, CDT = Clock Drawing Test, MMSE = Mini Mental State Examination, VMPT = Öktem Verbal Memory Process Test
[a] Mann-Whitney U test was used and mean ranks are shown.

4. Discussion

The findings that the RBD+ PD group exhibited lower backward digit span scores, reduced phonemic and switching verbal fluencies, impaired naming skills, and a decline in verbal immediate memory performance compared to the RBD- PD group suggest a significant association between RBD and cognitive functions in PD. These results indicate that the presence of RBD in PD patients is linked to a range of cognitive impairments across various domains.

The lower backward digit span scores in the RBD+ PD group may reflect deficits in working memory and cognitive flexibility. Reduced phonemic and switching verbal fluencies suggest difficulties in word generation and information processing speed. Challenges in naming abilities may imply difficulties in retrieving and expressing language, while the decline in immediate verbal memory performance may indicate struggles in retaining and recalling information stored in working memory.

These findings align with existing research that highlights the impact of RBD on cognitive functions in PD. Studies have shown that RBD is associated with a higher risk of cognitive decline, including deficits in attention, memory, and executive functions (Maggi et al., 2021; Mahmood et al., 2020; Hong et al., 2017; Zhang et al., 2016; Delazer 2012; Huang et al., 2010; Gagnon et al., 2009).

Our results indicate that the existence of RBD is associated with reduced cognitive functions in PD patients. Additionally, our findings of decreased performance on neuropsychometric tests assessing frontal functions, along with prior research, suggest a potential link between RBD and cognitive dysfunction primarily focused on frontal lobe functions. Specifically, disruptions within frontal networks offer perspectives on the intricate nature of cognitive processing impairments observed in PD patients with RBD.

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