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Comparative study of nonmotor symptoms in progressive supranuclear palsy and Parkinson's disease

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Abstract

Background Nonmotor symptoms (NMSs) are under-recognized in progressive supranuclear palsy (PSP), despite their considerable impact on quality of life. The full spectrum and impact of NMSs in PSP remain insufficiently understood. This study is aimed to investigate NMSs in patients with PSP and compare the difference of NMSs between patients with PSP and patients with Parkinson's disease (PD).

Methods The study involved 44 patients diagnosed with PSP and 132 patients with PD. NMSs were assessed using a range of evaluation tools. Additionally, the relationship between NMSs and disease severity, as well as the impact on quality of life was analyzed.

Results The Non-Motor Symptom Scale (NMSS) and Movement Disorders Society-revised Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part I scores were significantly higher in patients with PSP than in patients with PD (42.52 ± 25.64 vs. 32.06 ± 21.45, $p = 0.007$; 11.89 ± 6.24 vs. 9.80 ± 5.61, $p = 0.049$). The severity of urinary symptoms was also greater in patients with PSP than in those with PD. Although clinically suspected rapid eye movement sleep behavior disorder (RBD), which was not assessed using polysomnography but rather through RBD Screening Questionnaire, was less common in patients with PSP compared with those with PD, cognitive impairment was more frequent and severe in patients with PSP. Hyposmia, cardiovascular symptoms, constipation, sleep disturbances, emotional symptoms, fatigue, and pain exhibited similar severity and frequency in both patient groups. Only emotional symptoms in patients with PSP were associated with the 39-item Parkinson's Disease Questionnaire scores, and none of the NMSs were associated with Hoehn & Yahr stage or MDS-UPDRS Part III scores.

Conclusion PSP is characterized by a higher burden of NMSs than PD, with some different and common symptom profiles. The impact of emotional symptoms on the quality of life in PSP underscores the importance of addressing these symptoms in clinical care to improve patient outcomes.

Keywords Progressive supranuclear palsy, Parkinson's disease, Nonmotor symptoms, Quality of life, Emotional symptoms, Urinary symptoms, Cognitive impairment, Rapid eye movement sleep behavior disorder, Hyposmia

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Background

Progressive supranuclear palsy (PSP) is a distinct parkinsonian disorder, primarily characterized by progressive postural instability, frequent falls, supranuclear vertical gaze palsy, levodopa-resistant parkinsonism, and frontal cognitive dysfunction [1]. Over the past decade, the understanding of symptomatology in parkinsonian disorders has evolved significantly, mainly due to the increasing recognition of nonmotor symptoms (NMSs) as key components of these conditions. However, the majority of research has focused on NMSs in Parkinson's disease (PD), with comparatively little attention given to NMSs in PSP. This has resulted in an under-recognition of these symptoms in PSP, despite their considerable impact on patients' quality of life [2, 3]. While some studies have identified various NMSs in PSP, including sleep disturbances, emotional symptoms, and cognitive impairment [4, 5], the full spectrum and impact of NMSs—particularly rapid eye movement sleep behavior disorder (RBD), hyposmia, autonomic dysfunction (such as cardiovascular symptoms, urinary disturbances, and constipation), fatigue, and pain—remain insufficiently understood. Previous studies suggest that PSP and PD may share certain NMSs [6]; however, the findings regarding the comparative frequency and severity of these symptoms between the two disorders have been inconsistent [7–9]. The aim of this study is to systematically evaluate and compare the frequency and severity of various NMSs domains in PSP and PD, utilizing multidimensional assessment scales. Furthermore, this study seeks to explore the relationship between NMSs and both disease severity and quality of life, providing a more comprehensive understanding of NMSs in PSP.

Materials and methods

Study participants

The study participants were selected between June 2021 and February 2024 from a cohort of Fujian Medical University Union Hospital-PD (FJMUUH-PD) aged 45–80 years. The patients with PD had a clinically established or probable diagnosis in accordance with the Movement Disorder Society (MDS) diagnostic criteria for PD (2015) [10]. The patients with PSP met the probable PSP diagnosis based on the International Parkinson's and MDS diagnostic criteria for PSP (2017) [1]. Patients were excluded if they presented with NMSs that could be attributed to other systemic conditions, such as cardiovascular disease, cerebrovascular disease, digestive disease, urinary disease, and endocrine disorders, etc.

This study was designed as a retrospective case–control study. The selected PSP/PD patients were matched for age, gender, and disease duration, and were in a 1:3 ratio. It adhered strictly to the ethics guidelines of medical research and was approved by the Medical Ethics Committee of the Fujian Medical University Union Hospital (approval number: 2023KJT075). All participants provided written informed consent, ensuring the protection of their rights and safety throughout the study.

Clinical assessment

For all patients, demographic data including age, sex, and education level, along with disease duration, were collected. Disease severity was assessed using the modified Hoehn and Yahr (H&Y) scale [11], as well as the Movement Disorder Society Unified Parkinson's Disease Rating Scale Part II (MDS-UPDRS-II) and Part III (MDS-UPDRS-III) [12]. These assessments were conducted during the off medication period, which was defined as more than 12 h after the last dose of dopaminergic therapy. Quality of life was evaluated using the 39-item Parkinson's Disease Questionnaire (PDQ-39) [13]. NMSs were assessed using several related clinical scales. The Non-Motor Symptom Scale (NMSS) was used for the assessment of the global NMSs and subdomains of NMSs [14]. The MDS Unified Parkinson's Disease Rating Scale Part I (MDS-UPDRS-I) [12] was utilized to assess the global NMSs as well. The Montreal Cognitive Assessment (MoCA) [15] were used to assess the global cognitive function. Additionally, the Hamilton Anxiety Rating Scale (HAM-A) [16] and the Hamilton Depression Rating Scale (HAM-D) [17] for measuring anxiety and depression symptoms, the Sniffin' Sticks Screening 12 (SS-12) [18] for measuring olfactory function, the Rapid Eye Movement Sleep Behavior Disorder Screening Questionnaire (RBDSQ) [19] for the assessment of RBD, and the Parkinson's Disease Sleep Scale 2 (PDSS-2) [20] for the assessment of sleep quality were conducted in all participants.

In the NMSS, nine item or subdomains of the NMSs—cardiovascular, fatigue, sleep, mood, attention/memory, constipation, urinary, hyposmia, and pain—were used to assess the frequency and severity of NMSs this study was concerned with. Each symptom is scored for severity (ranging from 0 to 3: 0 = none, 1 = mild, 2 = moderate, 3 = severe) and frequency (ranging from 1 to 4: 1 = rarely [< 1/week], 2 = often [1–2/week], 3 = frequent [3–6/week], 4 = very frequent [daily]). A patient scoring 1 or more on any item, calculated by multiplying the frequency (1–4) by the severity (0–3), was considered to have that NMSs. The frequency of subdomains of NMSS was determined by the percentage of patients scoring ≥ 1 in each NMSS item or subdomain. The severity of subdomains of NMSS was calculated by multiplying the frequency (1–4) by the severity (0–3).

Abnormal criteria for the assessment of other NMSs related scales were as follows: NMSS ≥ 1 [7]; MoCA < 26/30 (add 1 point if education ≤ 12 years) [15]; HAM-A ≥ 7 [16]; HAM-D ≥ 8 [17]; SS-12 ≤ 6 [18];

RBDSQ ≥ 1; and PDSS-2 ≥ 1. The frequency of NMSs was calculated based on the percentage of patients who scored abnormally on the NMSs related scales.

Statistical analysis

All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism 8.0 (GraphPad Software, La Jolla, CA, USA). Continuous data were presented as mean ± standard deviation, while categorical variables were expressed as numbers and percentages. Categorical variables were compared using the chi-square test. The Shapiro–Wilk test was used to assess the normality of the data distribution. For normally distributed data, a one-way analysis of variance or a *t*-test with Welch's correction (in cases of heterogeneity of variance) was used. For non-normally distributed data, the Kruskal–Wallis test or Mann–Whitney *U*-test was applied. Group comparisons of means and frequencies were conducted without adjustment for multiple comparisons due to the exploratory nature of these analyses and the relatively small sample size of the PSP cohort. Correlations between NMSs scales and other clinical characteristics were assessed using Pearson correlation analysis for normally distributed data or Spearman correlation analysis for non-normal distributions. Correlation analyses were adjusted for multiple comparisons using the Benjamini-Hochberg false discovery rate (FDR) procedure. Multivariate Linear Regression was conducted to determine the independent contributions of NMSs to PDQ-39, adjusting for sex, age, disease duration, and motor severity. All statistical analyses were performed with statistical significance set at a *p*-value of < 0.05 (two-tailed test).

Table 1 Clinical features and mean scores of NMSs related scales in PSP and PD

	PSP ($n=44$)	PD ($n=132$)	*p* value
Age	67.95 ± 6.93	66.46 ± 5.85	0.083
Sex, male, n%	21 (47.7)	84 (63.6)	0.062
Disease duration, months	38.75 ± 19.70	43.20 ± 24.44	0.325
Years of education	6.41 ± 5.02	8.03 ± 4.35	0.072
Modified H&Y stage	2.90 ± 0.70	2.38 ± 0.67	<0.001
PDQ-39	43.41 ± 21.55	25.36 ± 21.34	<0.001
MDS-UPDRS-I	11.89 ± 6.24	9.80 ± 5.61	0.049
MDS-UPDRS-II	20.51 ± 7.82	13.21 ± 7.47	<0.001
MDS-UPDRS-III	44.33 ± 15.86	35.05 ± 14.61	0.002
NMSS	42.52 ± 25.64	32.06 ± 21.45	0.007
MoCA	14.84 ± 6.43	18.48 ± 6.07	0.003
HAM-A	7.55 ± 4.28	6.78 ± 4.89	0.178
HAM-D	7.43 ± 5.45	6.19 ± 5.14	0.119
RBDSQ	0.80 ± 1.80	1.48 ± 2.21	0.014
PDSS-2	13.25 ± 8.05	14.84 ± 10.11	0.418
SS-12	3.61 ± 2.66	3.80 ± 2.44	0.651

NMSs, Non-Motor Symptoms; PSP, progressive supranuclear palsy; PD, Parkinson's disease; Modified H&Y stage, Modified Hoehn&Yahr stage; PDQ-39, 39-item Parkinson's Disease Questionnaire; NMSS, Non-Motor Symptom scale; MDS-UPDRS, Movement Disorder Society Unified Parkinson's Disease Rating Scale; MoCA, Montreal Cognitive Assessment Scale; HAM-A, Hamilton Anxiety Rating Scale; HAM-D, Hamilton Depression Rating Scale; RBDSQ, Rapid Eye Movement Sleep Behavior Disorder Screening Questionnaire; PDSS-2, Parkinson's Disease Sleep Scale 2; SS-12, Sniffin' Sticks Screening 12

Results

Sample characteristics and NMSs in PSP and PD

A total of 44 PSP and 132 PD cases were analyzed in this study. The demographic characteristics, disease duration, years of education and the mean scores of NMSs related scales in both groups are presented in Table 1. No significant differences were noted between the groups in terms of sex, age, disease duration, or years of education ($p > 0.05$). However, patients with PSP exhibited greater disease severity, as indicated by higher modified H&Y stage, MDS-UPDRS-II, MDS-UPDRS-III, and PDQ-39 scores compared to patients with PD. Additionally, the mean scores of the NMSS and MDS-UPDRS-I were significantly higher in patients with PSP than in patients with PD. In contrast, patients with PSP had lower mean scores of RBDSQ and MoCA than patients with PD. No significant differences were found between the groups in the mean scores of HAM-A, HAM-D, SS-12, or PDSS-2.

Frequency of abonormal assessment of NMSs related scales in PSP and PD

Patients with PSP and PD experienced at least one NMSs (NMSS ≥ 1, 100%). Among patients with PSP, the two most common related NMSs were "MoCA scores below the cutoff" (97.7%) and impaired sleep quality (95.5%). Anxiety and hyposmia were also frequently observed in patients with PSP and PD. The frequency of "MoCA scores below the cutoff" was significantly higher in patients with PSP than in patients with PD ($p < 0.05$). Conversely, the frequency of probable RBD was lower in patients with PSP than in patients with PD. There were no statistically significant differences between patients with PSP and PD in terms of impaired sleep quality, anxiety, depression, or hyposmia (all $p > 0.05$). A comparison of the concerned NMSs frequency between the two groups is provided in Table 2.

The severity and frequency of NMSs subdomains in NMSS evaluation in PSP and PD

In PSP, the most commonly affected NMSs subdomain was "sleep", followed by "attention/memory". Urinary and emotional symptoms were also prevalent in this group. The severity of urinary symptoms was significantly higher in patients with PSP than in those with PD. However, the severity of other NMSs subdomains, including cardiovascular symptoms, fatigue, sleep disturbances, mood, attention/memory, constipation, hyposmia, and pain, did not differ significantly between the two groups ($p > 0.05$).

Table 2 Frequency of the NMSs in PSP and PD

	PSP, *n* (%)	PD, *n* (%)	*p* Value
NMSS ≥ 1	44 (100)	132 (100)	1.000
MoCA under the cutoff value	43 (97.7)	109 (82.6)	0.011
HAM-A ≥ 7	29 (65.9)	65 (49.2)	0.055
HAM-D ≥ 8	19 (43.2)	41 (31.1)	0.142
RBDSQ ≥ 1	14 (31.8)	69 (52.3)	0.019
PDSS-2 ≥ 1	42 (95.5)	130 (98.5)	0.243
SS-12 < 6	31 (70.5)	97 (73.5)	0.696

NMSs, Non-Motor Symptoms; PSP, progressive supranuclear palsy; PD, Parkinson's disease; NMSS, Non-Motor Symptom scale; MoCA, Montreal Cognitive Assessment Scale; HAM-A, Hamilton Anxiety Rating Scale; HAM-D, Hamilton Depression Rating Scale; RBDSQ, Rapid Eye Movement Sleep Behavior Disorder Screening Questionnaire; PDSS-2, Parkinson's Disease Sleep Scale 2; SS-12, Sniffin' Sticks Screening 12

The frequencies of all NMSS subdomains were similar between patients with PSP and PD, with no statistically significant differences. A comparison of the mean scores and frequencies of NMSS subdomains in the two groups is presented in Table 3.

Correlation analysis between NMSs and clinical characteristics

In PSP, after FDR correction, only the HAM-D scores were significantly correlated with PDQ-39 scores, while other clinical variables showed no correlation with PDQ-39 scores. Notably, none of the assessed NMSs variables in PSP were correlated with MDS-UPDRS-III and the modified H&Y stage. In PD, after FDR correction, the total NMSS scores, MDS-UPDRS-I scores, nearly all mean scores of NMSs related scales, and most of the NMSS subdomains were correlated with PDQ-39 scores, modified H&Y stage and MDS-UPDRS-III scores. Detailed data can be found in Fig. 1 and Supplementary Table 1.

Multivariate linear regression analysis between NMSs, clinical characteristics and PDQ-39 scores

Multivariate linear regression analyses conducted on the above variables indicated that both the HAM-D scores ($\beta = 0.443$, $p = 0.030$) and the mood subdomain of NMSS ($\beta = 0.597$, $p = 0.002$) significantly predicted worse PDQ-39 in PSP. HAM-D scores and the mood subdomain of NMSS accounted for 35.3% and 34.1% of the variance in PDQ-39 scores, respectively. In PD, the modified H&Y stage ($\beta = 0.245$, $p = 0.016$) and the mood ($\beta = 0.274$, $p = 0.003$), memory ($\beta = 0.248$, $p = 0.001$), and pain ($\beta = 0.217$, $p = 0.005$) subdomains of NMSS predicted worse PDQ-39. Since the measurement of subdomains of NMSS exhibited multicollinearity with the total NMSS scores and other related NMSs scales, they were analyzed separately (Supplement Table 2 and Supplement Table 3).

Discussion

This study highlights some significant differences and overlap in the profile of NMSs between PSP and PD. The total NMSS scores and MDS-UPDRS-I scores were notably higher in PSP than in PD, indicating a heavier burden of NMSs in PSP. Additionally, urinary symptoms were more severe in patients with PSP than in patients with PD. Although patients with PSP exhibited a certain frequency of probable RBD, it was less common than in PD. As expected, cognitive impairment was more severe and common in PSP than in PD. The severity and frequency of hyposmia, cardiovascular symptoms, constipation, emotional disorders, impaired sleep quality, fatigue, and pain were similar between patients with PSP and PD. When examining the relationship between NMSs and clinical characteristics in PSP, emotional disorders showed a significant impact on PDQ-39 scores. Focusing on optimizing the treatment of emotional disturbance for patients with PSP is of great significance for improving their quality of life. However, NMSs in PSP did not exhibit significant correlations with MDS-UPDRS-III or modified H&Y stage, suggesting that the motor symptoms in PSP may be not directly tied to the burden of NMSs.

This study provides a more comprehensive assessment of NMSs using multidimensional scales, particularly

Table 3 The severity and frequency of NMSS subdomains in PSP and PD

Subdomain	PSP (*n* = 44)	PD (*n* = 132)	*p* 1[a] Value	PSP (*n* = 44)	PD (*n* = 132)	*p* 2[b] Value
	Score			Frequency, *n* (%)		
Cardiovascular	2.43 ± 3.77	1.79 ± 2.61	0.597	19 (43.2)	54 (40.9)	0.791
Fatigue	2.50 ± 3.06	2.15 ± 2.61	0.863	21 (47.7)	71 (53.8)	0.486
Sleep	6.36 ± 5.28	5.20 ± 4.62	0.186	37 (84.1)	102 (77.3)	0.336
Mood	5.30 ± 11.31	3.93 ± 5.95	0.358	28 (63.6)	73 (55.3)	0.333
Attention/Memory	5.23 ± 4.85	3.55 ± 3.43	0.099	32 (72.7)	96 (72.7)	1.000
Constipation	2.22 ± 2.82	2.56 ± 3.12	0.707	24 (54.5)	72 (54.5)	1.000
Urinary	9.27 ± 8.85	5.72 ± 7.25	0.015	30 (68.2)	77 (58.3)	0.247
Hyposmia	1.11 ± 2.03	1.39 ± 2.33	0.393	14 (31.8)	50 (38.2)	0.449
Pain	1.50 ± 2.66	1.55 ± 2.73	0.925	15 (34.1)	42 (31.8)	0.780

[a]: p1 value, compare mean scores of NMSS subdomains. [b]: p2 value, compare frequency of NMSS subdomains. NMSS, Non-Motor Symptom Scale; PSP, progressive supranuclear palsy; PD, Parkinson's disease

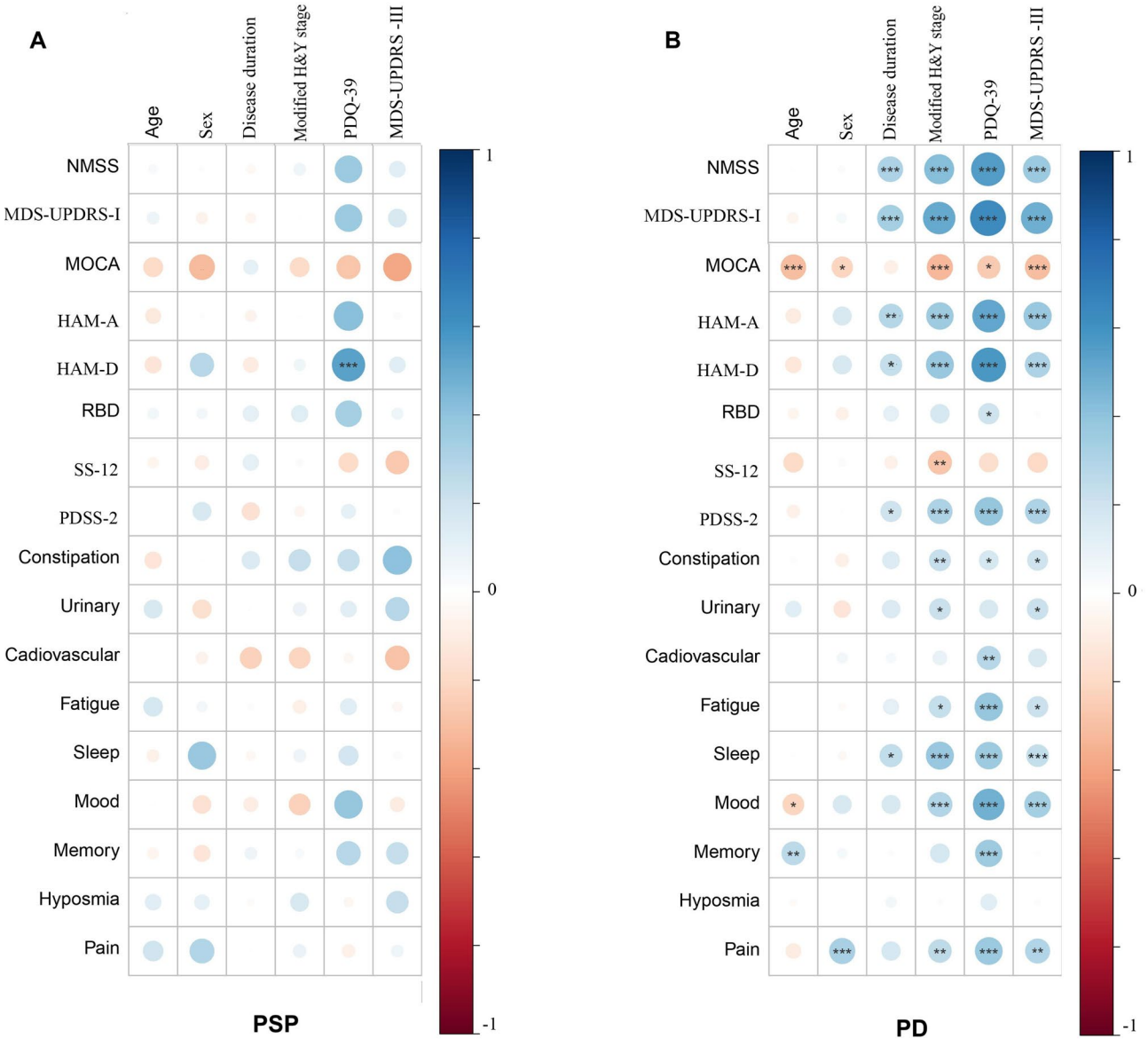

Fig. 1 The Correlation between NMSs and clinical characteristics. Significance: ***$p < 0.001$, **$p < 0.01$, *$p < 0.05$. Statistically significant correlations after Benjamini-Hochberg false discovery rate (FDR) correction (17 NMS parameters, 6 clinical features parameters). Sex is coded as 1 (male) and 2 (female). NMSs, Non-Motor Symptoms; PSP, progressive supranuclear palsy; PD, Parkinson's disease; modified H&Y stage, modified Hoehn&Yahr stage; PDQ-39, 39-item Parkinson's Disease Questionnaire; NMSS, Non-Motor Symptom scale; MDS-UPDRS, Movement Disorder Society Unified Parkinson's Disease Rating Scale; MoCA, Montreal Cognitive Assessment Scale; HAM-A, Hamilton Anxiety Rating Scale; HAM-D, Hamilton Depression Rating Scale; RBDSQ, Rapid Eye Movement Sleep Behavior Disorder Screening Questionnaire; PDSS-2, Parkinson's Disease Sleep Scale 2; SS-12, Sniffin' Sticks Screening 12

examining hyposmia, RBD, and autonomic dysfunction. Our results indicate that all patients with PSP and PD experienced at least one NMSs, which is consistent with findings from previous studies [5, 7, 8]. In addition to the well-established cognitive impairments, emotional disorders, sleep disturbances, and urinary symptoms were also prevalent in patients with PSP, corroborating earlier research [7, 9, 21]. Our analysis revealed that the total NMSS scores and MDS-UPDRS-I scores were significantly higher in PSP than in PD, which supports the findings of Radicati et al. [8]. This suggests that the burden of NMSs is greater in PSP than in PD. The primary pathological basis for NMSs in PSP involves regions beyond the basal ganglia, such as the cerebellar cortex, brainstem, spinal cord, limbic system, and neocortex [22]. These areas are affected more extensively and earlier in PSP than in PD, which may account for the more severe NMSs observed in PSP [4].

Interestingly, we found that urinary symptoms were common in PSP and more pronounced than in PD, which supports previous studies [23, 24]. This severity might be due to the involvement of different neuronal structures

in PSP, with evidence suggesting that neuronal and glial cytoskeletal pathology in the brainstem and basal ganglia plays a crucial role in regulating urinary function [25]. Additionally, frontal lobe involvement [26], detrusor sphincter dysfunction, and an overactive detrusor reflex may contribute to the more severe urinary symptoms observed in PSP than in PD [27, 28]. Furthermore, our study found that cardiovascular symptom in PSP was similar to that in PD, which is consistent with previous research [7, 8]. This suggests that PSP may also experience a certain incidence of cardiovascular autonomic dysfunction [29]. Another study reported similar frequencies of orthostatic hypotension (OH) in PD and PSP (18% vs. 19%) [30]. However, it is generally thought that OH occurs less frequently in PSP than in other alpha-synucleinopathies, such as multiple system atrophy and dementia with Lewy bodies [4].

It is believed that a wide range of sleep disorders that include insomnia, RBD, periodic limb movement disorder, excessive daytime sleepiness, and sleep apneas, may complicate the course in parkinsonian disorders [31]. Sleep quality impairment may be the results of motor sympotoms and all kinds of sleep disorders. Our study found a high incidence of sleep quality impairment (95.5%) in PSP, reflected by PDSS-2, and sleep disorders (84.1%), reflected by NMSS evaluation, in PSP, which supports previous findings [5, 7, 8]. Abnormal sleep architecture and insomnia are prevalent in PSP and have also been confirmed in polysomnography studies [32]. Moreover, this study found sleep disorders in PSP was comparable to PD, in line with the previous study [8]. RBD, a common manifestation of sleep disturbances in alpha-synucleinopathies, has been less studied in tauopathies, such as PSP. We found that the severity of probable RBD were less in PSP than in PD, and while patients with PSP did experience RBD, its frequency was significantly lower than in PD (31.8% vs. 52.3%, $p < 0.05$). Sleep disorders in PSP are thought to be associated with the degeneration of cholinergic neurons in the brainstem tegmental nucleus, particularly the pedunculopontine nucleus [33], which is crucial for regulating rapid eye movement sleep. It is believed that a downstream effect of the disease (either neurodegenerative or structural changes in the brainstem), rather than the direct consequence of the deposition of alpha-synuclein or tau, is the key factor in RBD [34]. Thus, while RBD is a hallmark of alpha-synucleinopathies, it can also occur in tauopathies, albeit less frequently [34–36].

Cognitive impairment is generally more severe in PSP than in PD [4, 7]. Our study found that patients with PSP not only had lower MoCA scores but also a higher frequency of "MoCA scores below the cutoff" than those with PD. Frontal executive dysfunction and language impairments are core clinical symptoms of PSP [1], alongside memory and visuospatial disorders [37, 38]. The more pronounced frontal deficits in PSP may account for the greater cognitive impairment than those in PD [39]. Cholinergic dysfunction is thought to underpin this cognitive decline [40]. Additional imaging studies have indicated that cerebellar atrophy and white matter damage—including the corpus callosum, upper right longitudinal fasciculus, lower longitudinal fasciculus, and left cingulate gyrus—may contribute to the cognitive impairments seen in PSP [41, 42]. Cognitive symptoms were neglected in patients reporting, as evaluated using the NMSS, but were detected using the MoCA assessment.

Hyposmia in PSP is generally considered rare [43, 44]. However, our study observed a significant frequency of hyposmia in PSP, slightly less than in patients with PD (70.5% vs. 73.5%), with no statistical difference ($p < 0.05$). This finding is in line with that of Hu et al.'s and Ebina et al.'s studies [45, 46]. However, Silveira et al. found that patients with PSP had more severe olfactory dysfunction than healthy controls but less severe olfactory dysfunction than patients with PD [47]. Autopsies of six patients with PSP revealed tau deposition and neurofibrillary tangles in the nasal brain area, suggesting that hyposmia is indeed present in PSP, and its presence cannot exclude PSP [47]. Our study also noted a higher frequency of abnormal SS-12 assessment compared with fewer subjective reports of hyposmia in patients with PSP and PD. Given the potential for subjective underreporting, it is advisable to combine objective tests with clinical evaluations of olfactory function.

Our study also found that emotional sympotoms were prevalent among patients with PSP, with 65.9% of patients meeting the criteria for anxiety (HAM-A ≥ 7) and 63.6% of patients reporting emotional disorders based on the NMSS, which aligns with previous findings [48, 49]. Although anxiety was more frequently observed than depression in this study, other research has reported depression as more common than anxiety [50]. No significant differences in emotional disorders were found between PSP and PD, which is consistent with some earlier studies [7]. However, some research using the NMSS has indicated that emotional disorders may be more pronounced in PSP than in PD [8]. This discrepancy could be attributed to cultural variations and differing research methodologies across populations. Interestingly, our study found that emotional disorders had a significant impact on the quality of life, independently. This result was consistent with previous research conducted by Schrag A et al. [2].

Nonetheless, our study has several limitations. First, the disease diagnoses were based on clinical evaluation rather than pathological results. However, diagnoses were made strictly in accordance with internationally recognized diagnostic criteria, and all patients were strictly verified.

Secondly, our PSP cohort was not subdivided into different subtypes and this study did not systematically adjust for the effects of dopaminergic or non-dopaminergic medications on NMSs, which might have influenced the NMSs findings. Third, there is potential for recall bias and subjectivity of patients when using some of the scales and questionnaires. Nonetheless, our study's assessments were conducted collaboratively by trained neurologists, patients, and their caregivers, and included objective tests such as SS-12. Future research could benefit from incorporating additional objective measures, such as polysomnography, tilt table testing, and urodynamics, to enhance the objectivity of NMSs evaluations. Fourth, this study was a retrospective study and limited the generalizability of findings due to potential selection bias. Patients with PSP or PD who were pathologically confirmed were not included in the present study. Lastly, the absence of multiple comparisons correction in group comparisons increased the risk of Type I errors. However, given the exploratory aims and limited statistical power, we prioritized sensitivity over specificity. Future replication in larger cohorts is warranted.

Conclusions

In summary, this study highlights the high prevalence of NMSs in PSP, demonstrating that the overall burden of NMSs in PSP is more substantial than in PD. Notably, cognitive impairment and urinary dysfunction were found to be significantly more severe in PSP than in PD. However, PSP and PD may share some common NMSs such as hyposmia, emotional disorders, sleep disturbance, constipation, cardiovascular symptom, fatigue, and pain. Furthermore, the study found that emotional disorders significantly impact patients' quality of life in PSP. Prioritizing the management of emotional disorders should be a key focus for clinicians to enhance the quality of life in individuals with PSP.

Abbreviations

NMSs	Non-motor symptoms
PSP	Progressive supranuclear palsy
PD	Parkinson's disease
Modified H&Y stage	Modified Hoehn&Yahr stage
PDQ-39	39-item Parkinson's disease questionnaire
NMSS	Non-motor symptom scale
MDS-UPDRS	Movement disorder society unified Parkinson's disease rating scale
MoCA	Montreal cognitive assessment scale
HAM-A	Hamilton anxiety rating scale
HAM-D	Hamilton depression rating scale
RBDSQ	Rapid eye movement sleep behavior disorder screening questionnaire
PDSS-2	Parkinson's disease sleep scale 2
SS-12	Sniffin' sticks screening 12
FDR	False discovery rate

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12883-025-04225-1.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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Author contributions

YC, XC and QY designed and conceived the experiment. YL, JH and YJC collected data. YJC, YL and JH analysed the data. YC and QY drafted the manuscript. All authors have read and approved the final manuscript to be published.

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Data availability

We can share our relevant raw data supporting our findings. If any scientist who wish to use them for non-commercial purposes, without breaching participant confidentiality, he/her can contact us directly, and we will share our raw data freely with he/her.

Declarations

Ethics approval and consent to participate

The protocol conformed to the principles of the declaration of Helsinki and was approved by by the Medical Ethics Committee of the Fujian Medical University Union Hospital (approval number: 2023KJT075). All participants and/or their legal guardian gave their written informed consent to participate in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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