



Parkinson's disease-subjective cognitive decline and health-related quality of life

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Abstract

Background Parkinson's disease-subjective cognitive decline (PD-SCD) is defined by subjective cognitive complaints (SCC) in the absence of objective cognitive impairment and has been associated with an increased risk of future cognitive decline. However, its impact on health-related quality of life (HRQoL) remains unclear. This is particularly relevant in early PD, when patients often maintain high levels of social-occupational functioning and subtle cognitive concerns may interfere with daily life. This study aimed to explore the association between SCC and HRQoL in cognitively unimpaired PD patients (PD-SCD).

Methods Cross-sectional data from the COPPADIS cohort were analyzed. Patients with normal cognition according to PD-MCI level I criteria (Parkinson's Disease-Cognitive Rating Scale > 81) were included. HRQoL was assessed using the 39-item Parkinson's Disease Questionnaire (PDQ-39). SCC were defined as a Non-Motor Symptoms Scale (NMSS) domain ≥ 1 .

Results A total of 497 patients with median age 62 years, disease duration 4 years, and 61% of PD-SCD were included. HRQoL was significantly worse in PD-SCD patients across all PDQ-39 domains. In adjusted linear regression models, PD-SCD was independently associated with higher PDQ-39 total score as well as with worse scores in activities of daily living, social support, cognition, and communication domains.

Conclusions PD-SCD is independently associated with poorer HRQoL across multiple domains. These findings highlight the clinical relevance of SCC within a patient-centered approach to PD management.

Keywords Parkinson's disease · Subjective cognitive decline · Subjective cognitive impairment · PD-SCD · Cognitive complaints · Quality of life

The members of the 'COPPADIS Study Group' are mentioned in Acknowledgements section.

Extended author information available on the last page of the article

Introduction

Parkinson's disease (PD) is the second most prevalent neurodegenerative condition and produces a substantial impact on patients' health-related quality of life (HRQoL) (Tosin et al. 2024). Even in the early stages of the disease, non-motor symptoms, especially depression, sleep disturbances, cognitive impairment, or apathy, emerge as the main determinants of impaired HRQoL, often exerting a greater impact than motor manifestations (Marras et al. 2008; Barone et al. 2009; Santos García et al. 2021; Tosin et al. 2024).

Cognitive impairment is one of the most disabling non-motor symptoms in PD (Martinez-Horta and Kulisevsky 2019). Although it represents a continuum, it is usually categorized according to its impact on functional independence into PD-mild cognitive impairment (PD-MCI) or PD-dementia (PDD) (Martinez-Horta and Kulisevsky 2019). PD-MCI is relatively common with a prevalence of 40%, and affecting more than 30% of patients at the time of diagnosis (Yarnall et al. 2014; Baiano et al. 2020). While functional impairment related to cognitive decline is inherently associated with PDD in the advanced stages, cognitive deficits at the PD-MCI stage can represent a substantial burden for patients, possibly due to preserved insight that allows them to recognize emerging cognitive difficulties (Marras et al. 2008; Barone et al. 2009; Kulisevsky et al. 2013). Accordingly, an increasing number of studies are focusing on the development of pharmacological and non-pharmacological interventions aimed at improving cognitive symptoms already at the PD-MCI stage (Rodríguez-Antigüedad et al. 2025b).

Over the past decade, the presence of subjective cognitive complaints (SCC) in the absence of objective cognitive impairment has been recognized as the prodromal stage of cognitive impairment, and has been associated with an increased risk of developing PD-MCI or PDD (Siciliano et al. 2024). There is substantial variability in the terminology used to describe this construct. In line with the broader framework of subjective cognitive decline (SCD) in Alzheimer's disease (AD), PD-SCD has been more widely used in the literature, although recent reviews have favored the term PD-subjective cognitive impairment (Oikonomou et al. 2025). In addition to these terminological variability, PD-SCD is a heterogeneous condition that may not only reflect early neurodegenerative changes, but also mood disturbances, sleep disorders, medication effects, or psychosocial factors (Jessen et al. 2020).

Beyond its potential prognostic value, the immediate clinical relevance of PD-SCD remains insufficiently understood. Some studies have reported that SCC are associated with worse HRQoL in PD patients with cognitive impairment; however, it is unclear whether SCC have a meaningful

impact on patients' HRQoL in the absence of objective cognitive impairment (Barone et al. 2009; Jaramillo-Jimenez et al. 2021). This question is particularly relevant in the early stages of PD, when patients often maintain high levels of professional, social, and functional engagement, and even subtle cognitive concerns may interfere with daily functioning and overall well-being (Mehanna and Jankovic 2019). Therefore, the objective of the present observational study is to explore the association between SCC and HRQoL in cognitively unimpaired PD patients (PD-SCD).

Methods

Study design and participants

Participants were enrolled between January 2016 and November 2017 from 35 centers across Spain as part of the COPPADIS study (COhort of Patients with Parkinson's Disease in Spain, 2015), a prospective study designed to investigate the natural progression of PD. Eligible participants were individuals between 35 and 75 years, diagnosed with PD according to the UK PD Brain Bank criteria, free of dementia, and not receiving advanced PD therapies. This project received approval from the ethics committee in Galicia, Spain (2014/534; 02/DEC/2014). All participants voluntarily provided a written informed consent to participate. Further details on the study design have been previously reported (Santos-García et al. 2016). For the present analysis, we included patients with normal cognitive performance according to PD-MCI diagnostic criteria level I, defined as Parkinson's Disease-Cognitive Rating Scale (PD-CRS) total score > 81 (Litvan et al. 2012; Fernández de Bobadilla et al. 2013).

Clinical assessments

Motor symptoms were assessed using the Unified Parkinson's Disease Rating Scale part III (UPDRS III) and the Hoehn & Yahr (H&Y) scale. Cognitive performance was assessed using the PD-CRS, depression using the Beck Depression Inventory II (BDI-II), sleep using the Parkinson's Disease Sleep Scale (PDSS), and additional non-motor symptoms using the Non-Motor Symptoms Scale for Parkinson's Disease (NMSS) (Chaudhuri et al. 2007). HRQoL was assessed with the 39-item Parkinson's Disease Questionnaire (PDQ-39).

SCCs were defined as NMSS domain 5 score ≥ 1 (Chaudhuri et al. 2007). This instrument includes three rater-administered items assessing concentration, attention and memory: item 16 "Does the patient have problems sustaining concentration during activities?", item 17 "Does the

patient forget things that he/she has been told a short time ago or events that happened in the last few days?" and item 18 "Does the patient forget to do things?"

Statistical analysis

Descriptive statistics were used to summarize demographic and clinical variables. Normality of all continuous variables was formally assessed using the Shapiro-Wilk test, and none fulfilled criteria for a normal distribution. Accordingly, continuous variables are reported as median and interquartile range (IQR), and between-group comparisons were performed using the Mann-Whitney U test. Effect sizes were estimated using the rank-biserial correlation coefficient (r). Categorical variables are presented as counts and percentages, and group differences were assessed using the χ^2 test.

Linear regression analyses were performed to evaluate the independent association between baseline PD-SCD and HRQoL. The PDQ-39 total score, excluding items from the cognitive domain to avoid overestimation of associations, was used as the primary dependent variable. Additional models were fitted using each of the eight PDQ-39 domain scores as separate dependent variables. SCC was considered as the main independent variable of interest and was analyzed both as a global measure (presence of PD-SCD) and as three distinct cognitive complaint domains in separate models. All models were adjusted for clinically relevant covariates known to influence HRQoL in PD, as established in prior literature. All predictors were standardized to Z-scores to improve the interpretability and comparability of the estimated coefficients. Model assumptions, including linearity, normality and homoscedasticity of residuals, and absence of multicollinearity, were assessed and confirmed.

The analyses were conducted using R (version 4.4.2). A two-tailed p value of <0.05 was considered significant for all tests. P -values of the main results were corrected for

multiple comparisons using the Benjamini-Hochberg false discovery rate (FDR) method.

Results

We identified 497 PD patients with normal cognition at baseline and a median age of 62 years (IQR 55–68). Patients were in the early stages of PD, with a median disease duration of 4 years (IQR 2–7), a median UPDRS III of 20 (IQR 13–28), and a median PD-CRS total score of 97 (IQR 90–106), well above the established cutoff for PD-MCI (≤ 81). Additional demographic and baseline characteristics are summarized in Table 1.

A total of 303 patients (61%) reported SCC at baseline and were classified as PD-SCD. No significant differences were observed in demographics, disease duration or motor symptom severity between patients with and without PD-SCD, whereas the burden of non-motor symptoms was significantly higher across all domains in the PD-SCD group (Table 2). HRQoL was significantly worse in patients with PD-SCD across all PDQ-39 domains.

Adjusted linear regression analyses revealed that PD-SCD (any SCC) was independently associated with higher PDQ-39 total score (excluding the cognitive domain items) after FDR correction ($p=0.012$) (Table 3). This association remained significant for the specific NMSS domains of concentration ($p=0.001$) and memory ($p=0.003$), but not for attention ($p=0.178$) (Table 4).

We finally explored the impact of PD-SCD (any SCC) on each PDQ-39 domain. In the adjusted linear regression models, PD-SCD was independently associated with higher PDQ-39 scores in the activities of daily living (ADL) ($p=0.048$), social support ($p=0.004$), cognition ($p<0.001$), and communication domains ($p=0.001$), whereas no significant associations were observed for the mobility, emotional well-being, stigma, or bodily discomfort domains (Table 5).

Table 1 Baseline characteristics of the cohort

<i>n</i>	497
Age	62 (55–68)
Biological sex, women	200 (40.2%)
Disease duration, years	4 (2–7)
LEDD	460 (250–780)
H&Y	2 (2–2)
UPDRS III	20 (13–28)
NMSS Total	33 (18–56)
PD-CRS	97 (90–106)

Continuous variables are presented as median (interquartile range) and categorical variables as number (percentage)

H&Y Hoehn & Yahr scale; *LEDD* levodopa-equivalent daily dose; *UPDRS III* Unified Parkinson's Disease Rating Scale part III; *NMSS* Non-Motor Symptom Scale for Parkinson's Disease; *PD-CRS* Parkinson's Disease-Cognitive Rating Scale

Discussion

In this cross-sectional observational study, we found that SCC in the absence of objective cognitive impairment (PD-SCD) are independently associated with a reduction in HRQoL in patients with early PD. This association was particularly evident in the ADL, social support, cognitive functioning, and communication domains. These findings indicate that, although it is well established that cognitive impairment negatively impacts HRQoL even at early PD-MCI stages, perceived cognitive difficulties may also affect patients' HRQoL before these deficits are detectable on standard neuropsychological assessments.

Table 2 Baseline characteristics according to PD-SCD status

	No PD-SCD (<i>n</i> =194)	PD-SCD (<i>n</i> =303)	<i>p</i>	Effect size, <i>r</i>
Age	62 (54.2–68)	62 (55.5–68.5)	0.807	
Biological sex, women	80 (41.2%)	120 (39.6%)	0.779	
Disease duration, years	4 (2–7)	5 (2–7)	0.164	
LEDD	410 (220–745)	480 (260–800)	0.103	
H&Y	2 (2–2)	2 (2–2)	0.253	
UPDRS III	19 (13–27)	21 (14–29)	0.073	
NMSS				
Cardiovascular	0 (0–1)	1 (0–2)	<0.001	0.260
Sleep/fatigue	2.5 (0–7)	8 (3–13)	<0.001	0.400
Mood/Cognition	0.5 (0–4)	5 (1–12)	<0.001	0.425
Perceptual/hallucinations	0 (0–0)	0 (0–1)	<0.001	0.196
Attention/Memory	0 (0–0)	3 (2–7)	<0.001	1.000
Gastrointestinal	1 [0–2)	2 [0–6)	<0.001	0.288
Urinary	2 (0–8)	6 (2–12)	<0.001	0.280
Sexual	0 (0–4)	2 (0–8)	<0.001	0.223
Miscellaneous	3 (0–8)	7 (2–12)	<0.001	0.324
Total	19 (8–34)	42 (25–69.5)	<0.001	0.547
PD-CRS	98.5 (90–107)	96 (90–105.5)	0.208	
BDI-II	4 (1–7.8)	9 (4–14)	<0.001	0.425
PDSS	129 (117–140)	118 (98.2–131)	<0.001	-0.336
PDQ-39				
Mobility	2.5 (0–12.5)	10 (2.5–25)	<0.001	0.319
ADL	8.3 (0–16.6)	16.6 (4.2–29.1)	<0.001	0.274
Emotional well-being	8.3 (0–20.8)	20.8 (8.3–35.4)	<0.001	0.359
Stigma	0 (0–17.1)	6.2 (0–25)	0.008	0.133
Social support	0 (0–0)	0 (0–16.6)	<0.001	0.277
Cognition	0 (0–12.5)	18.7 (12.5–31.2)	<0.001	0.665
Communication	0 (0–8.3)	8.3 (0–16.6)	<0.001	0.290
Bodily discomfort	16.6 (0–33.3)	25 (8.3–41.6)	<0.001	0.253
Total	7.7 (4.5–13.9)	16 (9.6–25)	<0.001	0.467

Continuous variables are presented as median (interquartile range) and categorical variables as number (percentage). Bold values indicate statistical significance

ADL activities of daily living; *BDI-II* Beck Depression Inventory-II; *H&Y* Hoehn & Yahr scale; *LEDD* levodopa-equivalent daily dose; *UPDRS III* Unified Parkinson's Disease Rating Scale part III; *NMSS* Non-Motor Symptom Scale for Parkinson's Disease; *PD-CRS* Parkinson's Disease-Cognitive Rating Scale; *PDQ-39* 39-item Parkinson's Disease Questionnaire; *PD-SCD* Parkinson's disease-subjective cognitive decline; *PDSS* Parkinson's Disease Sleep Scale

SCC are a highly prevalent symptom, affecting up to 25% of individuals older than 60 years and 50–80% above 75 years (for Cohort Studies of Memory in an International Consortium (COSMIC) et al. 2020; Cappa et al. 2024). Although these complaints may represent an early stage preceding neurodegenerative cognitive decline, they constitute a nonspecific symptom that can also be associated with a wide range of other conditions, including normal aging, depression, sleep disturbances, medication use, substance exposure, or cultural factors (Jessen et al. 2020). For this reason, in 2014 the SCD-initiative working group undertook a major effort to standardize terminology and diagnostic criteria, defining SCD as a self-experienced persistent decline in cognitive capacity in the presence of normal performance on standardized cognitive testing adjusted for age and sex (Jessen et al. 2014). Although these criteria were originally

developed in the context of AD, they are conceptually applicable to other neurodegenerative conditions, including PD. However, the study of SCD in PD remains less well established, with heterogeneous terminology and substantial limitations arising from the wide variability of instruments used to assess SCC (Huang et al. 2023). Accordingly, although a recent meta-analysis reported an pooled prevalence of SCC of 36%, prevalence estimates varied widely across studies, ranging from 6.3% to 82.9% (Hong and Lee 2023; Siciliano et al. 2024). In our study, consistent with a previous report from the same cohort, we observed a PD-SCD prevalence of 61%, which lies in the upper range of reported values (Rodríguez-Antigüedad et al. 2025a). However, this is not unexpected in an age-related neurodegenerative disorder associated with a high risk of cognitive impairment.

Table 3 Unadjusted and adjusted linear regression models assessing the association between PD-SCD (any SCC) and PDQ-39 total score (excluding cognitive domain)

	Any cognitive complaint	
	β (95% CI)	<i>p</i>
PD-SCD (any, unadjusted)	0.7 (0.5, 0.9)	<0.001
PD-SCD (any)	0.2 (0.04, 0.3)	0.012
Age	-0.1 (-0.1, 0)	0.058
Biological sex	0.1 (0, 0.27)	0.058
UPDRS III	0.2 (0.15, 0.29)	<0.001
BDI-II	0.2 (0.1, 0.27)	<0.001
PDSS	0 (0, 0)	0.171
NMSS total*	0.5 (0.4, 0.5)	<0.001

Bold values indicate statistical significance

BDI-II Beck Depression Inventory-II; *CI* confidence interval; *UPDRS III* Unified Parkinson's Disease Rating Scale part III; *NMSS* Non-Motor Symptom Scale for Parkinson's Disease; *PD-SCD* Parkinson's disease-subjective cognitive decline; *PDSS* Parkinson's Disease Sleep Scale

NMSS total*: NMSS total score excluding the cognitive domain (domain 5)

The clinical significance of PD-SCD remains uncertain. Several studies have associated this clinical marker with an increased risk of future cognitive decline, although the progression is highly heterogeneous, as many SCC may reflect mood or sleep disturbances rather than a primary cognitive deficit (Siciliano et al. 2024; Rodríguez-Antigüedad et al. 2025a). In line with this view, anxiety and depression have been shown to modulate SCC, highlighting the role of metacognitive processes and self-awareness in shaping subjective symptom reporting (Ball et al. 2023). Nevertheless, PD-SCD may also represent a prodromal stage of PD-MCI. Similar to AD-related cognitive impairment, recent studies have shown that AD-biomarkers in CSF (reduced β -amyloid₁₋₄₂ and elevated phosphorylated-tau) are predictors of cognitive decline in PD-SCD (Rostamzadeh et al. 2022; Rodríguez-Antigüedad et al. 2025c). This association

may reflect well-established links between cognitive impairment in PD and increased amyloid deposition in the cerebral cortex or hippocampus, as well as genetic susceptibility factors such as APOE ϵ 4 (Halliday et al. 2014).

Beyond the potential of PD-SCD to predict future cognitive impairment, the main finding of this study is that SCC may have a significant impact on current HRQoL. After adjustment for motor severity, depressive symptoms, sleep quality, and overall non-motor symptom burden (excluding the cognitive domain), PD-SCD remained independently associated with poorer HRQoL. This is consistent with previous studies showing that the presence of any type of SCC is associated with impairments in cognitive-related functioning (Weintraub et al. 2024). Although this concept does not strictly correspond to HRQoL, it reflects a closely related construct. In our study, concentration and memory SCC were associated with worse global HRQoL. Importantly, the impact of PD-SCD was not confined to the cognitive domain of the PDQ-39, where conceptual overlap is expected with the NMSS, but extended to other domains including ADL, social support, and communication. This suggests that PD-SCD may interfere with patients' daily lives and interpersonal functioning in ways that are not fully captured by objective cognitive testing.

In the absence of curative treatment, current management strategies in PD are primarily directed to optimize symptoms and improve HRQoL. To date, therapeutic efforts addressing cognitive impairment in PD have largely focused on PDD, for which only one drug has been classified as *clinically useful* according to the Movement Disorder Society-Evidence-Based Medicine (MDS-EBM) recommendations (Seppi et al. 2019). Although the negative impact of PD-MCI on HRQoL is now well established and an increasing number of clinical trials have targeted this condition, no pharmacological intervention has so far demonstrated efficacy or been classified as *clinically useful* according to

Table 4 Unadjusted and adjusted linear regression models assessing the association between specific cognitive complaints and PDQ-39 total score (excluding cognitive domain)

	Concentration		Attention		Memory	
	β (95% CI)	<i>p</i>	β (95% CI)	<i>p</i>	β (95% CI)	<i>p</i>
PD-SCD (specific, unadjusted)	0.7 (0.6, 0.9)	<0.001	0.6 (0.4, 0.8)	<0.001	0.5 (0.4, 0.7)	<0.001
PD-SCD (specific)	0.2 (0.1, 0.4)	0.001	0.1 (-0.1, 0.3)	0.178	0.2 (0.1, 0.4)	0.003
Age	-0.1 (-0.1, 0.01)	0.092	-0.1 (-0.1, 0)	0.049	-0.1 (-0.1, 0)	0.058
Biological sex	0.1 (0.01, 0.3)	0.042	0.1 (-0.01, 0.3)	0.067	0.1 (-0.01, 0.3)	0.079
UPDRS III	0.2 (0.14, 0.3)	0.000	0.2 (0.2, 0.3)	<0.001	0.22 (0.2, 0.3)	<0.001
BDI-II	0.2 (0.1, 0.3)	<0.001	0.2 (0.1, 0.3)	<0.001	0.2 (0.1, 0.3)	<0.001
PDSS	0 (0, 0)	0.160	0 (-0.01, 0)	0.136	0 (-0.01, 0)	0.119
NMSS total*	0.4 (0.4, 0.5)	<0.001	0.5 (0.4, 0.6)	<0.001	0.5 (0.4, 0.5)	<0.001

Bold values indicate statistical significance

BDI-II Beck Depression Inventory-II; *CI* confidence interval; *UPDRS III* Unified Parkinson's Disease Rating Scale part III; *NMSS* Non-Motor Symptom Scale for Parkinson's Disease; *PD-SCD* Parkinson's disease-subjective cognitive decline; *PDSS* Parkinson's Disease Sleep Scale

NMSS total*: NMSS total score excluding the cognitive domain (domain 5)

Table 5 Unadjusted and adjusted linear regression models assessing the association between PD-SCD (any SCC) and PDQ-39 domains

	Mobility		ADL		Emotional well-being	
	β (95% CI)	<i>p</i>	β (95% CI)	<i>p</i>	β (95% CI)	<i>p</i>
PD-SCD (any, unadjusted)	0.5 (0.3, 0.6)	<0.001	0.5 (0.3, 0.6)	<0.001	0.6 (0.4, 0.8)	<0.001
PD-SCD (any)	0.1 (-0.1, 0.3)	0.159	0.2 (0.01, 0.3)	0.048	0.03 (-0.1, 0.2)	0.706
Age	0.02 (-0.1, 0.1)	0.696	-0.1 (-0.2, 0)	0.056	-0.1 (-0.2, -0.02)	0.014
Biological Sex	0.3 (0.1, 0.4)	0.001	-0.2 (-0.4, -0.1)	0.011	0.2 (0.04, 0.3)	0.011
UPDRS III	0.3 (0.2, 0.4)	<0.001	0.3 (0.2, 0.4)	<0.001	0.1 (-0.01, 0.1)	0.115
BDI-II	0.1 (-0.04, 0.2)	0.207	0.03 (-0.1, 0.1)	0.623	0.5 (0.5, 0.6)	<0.001
PDSS	0 (0, 0)	0.699	0 (-0.01, 0)	0.204	0 (0, 0)	0.205
NMSS total*	0.4 (0.2, 0.5)	<0.001	0.3 (0.2, 0.4)	<0.001	0.3 (0.2, 0.4)	<0.001
	Stigma		Social support		Cognition	
	β (95% CI)	<i>p</i>	β (95% CI)	<i>p</i>	β (95% CI)	<i>p</i>
PD-SCD (any, unadjusted)	0.2 (0.04, 0.4)	0.016	0.5 (0.3, 0.7)	<0.001	1 (0.9, 1.2)	<0.001
PD-SCD (any)	0.03 (-0.2, 0.2)	0.766	0.3 (0.1, 0.5)	0.004	0.7 (0.5, 0.8)	<0.001
Age	-0.1 (-0.2, -0.04)	0.004	-0.02 (-0.1, 0.1)	0.635	0.01 (-0.1, 0.1)	0.868
Biological sex	-0.02 (-0.2, 0.2)	0.856	0.1 (-0.1, 0.3)	0.211	-0.1 (-0.2, 0.1)	0.279
UPDRS III	0.1 (0.01, 0.2)	0.035	0.1 (0.03, 0.2)	0.010	0.1 (-0.03, 0.1)	0.230
BDI-II	0.03 (-0.1, 0.2)	0.672	0 (-0.1, 0.1)	0.939	0.2 (0.1, 0.3)	0.001
PDSS	0 (-0.01, 0)	0.575	0 (0, 0)	<0.001	-0.01 (-0.01, 0)	<0.001
NMSS total*	0.2 (0.1, 0.3)	0.001	0.3 (0.2, 0.4)	<0.001	0.2 (0.1, 0.3)	<0.001
	Communication		Bodily discomfort			
	β (95% CI)	<i>p</i>	β (95% CI)	<i>p</i>		
PD-SCD (any, unadjusted)	0.5 (0.4, 0.7)	<0.001	0.4 (0.3, 0.6)	<0.001		
PD-SCD (any)	0.3 (0.1, 0.5)	0.001	0.02 (-0.2, 0.2)	0.790		
Age	-0.04 (-0.1, 0.04)	0.306	0.03 (-0.1, 0.1)	0.501		
Biological sex	-0.2 (-0.4, -0.1)	0.007	0.4 (0.2, 0.6)	<0.001		
UPDRS III	0.2 (0.1, 0.2)	<0.001	0.03 (-0.1, 0.1)	0.526		
BDI-II	-0.02 (-0.1, 0.1)	0.785	0.2 (0.1, 0.3)	0.003		
PDSS	0 (-0.01, 0)	0.392	0 (-0.01, 0)	0.019		
NMSS total*	0.3 (0.1, 0.4)	<0.001	0.4 (0.2, 0.5)	<0.001		

Bold values indicate statistical significance

ADL activities of daily living; *BDI-II* Beck Depression Inventory-II; *CI* confidence interval; *UPDRS III* Unified Parkinson's Disease Rating Scale part III; *NMSS*:Non-Motor Symptom Scale for Parkinson's Disease; *PD-SCD* Parkinson's disease-subjective cognitive decline; *PDSS* Parkinson's Disease Sleep Scale

NMSS total*: NMSS total score excluding the cognitive domain (domain 5)

the MDS-EBM recommendations (Seppi et al. 2019; Rodríguez-Antigüedad et al. 2025b). The present findings extend the clinical relevance of cognitive symptoms to even earlier stages of the disease, suggesting that SCC warrant attention when the primary therapeutic goal is to optimize HRQoL. While earlier intervention is generally expected to confer greater benefit for strategies aiming to modify disease progression, symptomatic treatments have not traditionally been considered at this level. The demonstration of a measurable impact of PD-SCD on HRQoL supports the rationale for exploring patient-centered therapeutic approaches targeting SCC already at these early stages of the disease. To date, the few interventional studies aimed at improving SCD have largely been conducted outside the context of PD and have primarily focused on non-pharmacological approaches (Canevelli et al. 2013). In PD, such approaches should explicitly include the evaluation and treatment of potentially modifiable contributors to SCC, such as mood

disturbances, sleep disorders, other non-motor symptoms, and medication effects.

Finally, we underscore the importance of conceptualizing cognition in PD as a dynamic process rather than relying exclusively on fixed cross-sectional cutoffs from global cognitive scales (Litvan et al. 2012; Puig-Davi et al. 2024). PD-SCD may reflect clinically meaningful cognitive change that is not fully captured by Level I diagnostic approaches. For example, a patient exhibiting a substantial longitudinal decline in PD-CRS total score while remaining above conventional PD-MCI thresholds may nonetheless experience subjective cognitive difficulties with functional consequences. This highlights the need for future studies integrating longitudinal cognitive trajectories, detailed neuropsychological profiling, and measures of insight and affective state to refine the clinical interpretation of PD-SCD.

Several limitations should be acknowledged. The NMSS does not capture complaints across all cognitive domains;

however, within the heterogeneity of tools currently used to assess SCC, it represents one of the more comprehensive instruments available. Moreover, although commonly applied in previous studies, defining SCC as a score ≥ 1 on the NMSS cognitive domain may overestimate the proportion of patients classified as PD-SCD (Santos-García et al. 2023). There is also partial overlap between the cognitive items of the NMSS and the cognition domain of the PDQ-39, which may introduce redundancy and potentially inflate the strength of their association. Nevertheless, the impact of SCC extended beyond the cognition domain of the PDQ-39, supporting their broader relevance to HRQoL. In addition, classification of patients as cognitively unimpaired was based on the PD-CRS, corresponding to a Level I diagnostic approach for PD-MCI, which is less sensitive than Level II comprehensive neuropsychological assessments and may fail to detect subtle domain-specific deficits. Finally, the cross-sectional design precludes causal inferences regarding the relationship between SCC and HRQoL.

In conclusion, this study demonstrates that PD-SCD, both when considered as a global construct and at the level of individual SCC, is associated with worse HRQoL. Importantly, this association extends beyond the cognitive domain of HRQoL and affects other key areas, including ADL, social support, and communication. While PD-SCD represents a heterogeneous and multifactorial construct, its presence identifies patients experiencing a clinically meaningful burden. These findings support the relevance of SCC as part of a comprehensive, patient-centered approach to HRQoL in PD, and provide a rationale for further research into targeted interventions at these early stages of the disease.

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Data availability The protocol and the statistical analysis plan are available on request. Deidentified participant data are not available for legal and ethical reasons.

Declarations

Conflict of interest The authors declare no competing interests.

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