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Quality of life and non-motor symptoms in Parkinson's disease patients with subthreshold depression

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Abbreviations: BDI-II, Beck Depression Inventory-II; FOG-Q, Freezing Of Gait Questionnaire; NMSS, Non-Motor Symptoms Scale; NPI, Neuropsychiatric Inventory; PD, Parkinson's disease; PD-CRS, Parkinson's Disease Cognitive Rating Scale; PDQ-39SI, 39-item Parkinson's Disease Quality of Life Questionnaire Summary Index; PDSS, Parkinson's Disease Sleep Scale; QUIP-RS, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale; S&E, Schwab & England Activities of Daily Living Scale; UPDRS, Unified Parkinson's Disease Rating Scale; VAFS, Visual Analog Fatigue Scale; VAS-Pain, Visual Analog Scale-Pain.

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ABSTRACT

Background: The role of subthreshold depression (subD) in Parkinson's Disease (PD) is not clear. The present study aimed to compare the quality of life (QoL) in PD patients with subD vs patients with no depressive disorder (nonD). Factors related to subD were identified.

Material and methods: PD patients and controls recruited from the COPPADIS cohort were included. SubD was defined as Judd criteria. The 39-item Parkinson's disease Questionnaire (PDQ-39) and the EUROHIS-QOL 8-item index (EUROHIS-QOL8) were used to assess QoL.

Results: The frequency of depressive symptoms was higher in PD patients (n = 694) than in controls (n = 207) (p < 0.0001): major depression, 16.1% vs 7.8%; minor depression, 16.7% vs 7.3%; subD, 17.4% vs 5.8%. Both health-related QoL (PDQ-39; 18.1 ± 12.8 vs 11.6 ± 10; p < 0.0001) and global QoL (EUROHIS-QOL8; 3.7 ± 0.5 vs 4 ± 0.5; p < 0.0001) were significantly worse in subD (n = 120) than nonD (n = 348) PD patients. Non-motor Symptoms Scale (NMSS) total score was higher in subD patients (45.9 ± 32 vs 29.1 ± 25.8;p < 0.0001). Non-motor symptoms burden (NMSS;OR = 1.019;95%CI 1.011–1.028; p < 0.0001), neuropsychiatric symptoms (NPI; OR = 1.091; 95%CI 1.045–1.139; p < 0.0001), impulse control behaviors (QUIP-RS; OR = 1.035; 95%CI 1.007–1063; p = 0.013), quality of sleep (PDSS; OR = 0.991; 95%CI 0.983–0.999; p = 0.042), and fatigue (VAFS-physical; OR = 1.185; 95%CI 1.086–1.293; p < 0.0001; VAFS-mental; OR = 1.164; 95%CI 1.058–1.280; p = 0.0001) were related to subD after adjustment to age, disease duration, daily equivalent levodopa dose, motor status (UPDRS-III), and living alone.

Conclusions: SubD is a frequent problem in patients with PD and is more prevalent in these patients than in controls. QoL is worse and non-motor symptoms burden is greater in subD PD patients.

1. Introduction

Depression has been strongly associated with Parkinson's disease (PD) as previous studies estimate the prevalence rate to be between 2.7% to 90% [1]. A systematic review found the weighted prevalence of major depressive disorder to be 17% of PD patients, that of minor depression to be 22%, and dysthymia 13% [2]. Patients considered to have subsyndromal or subthreshold depression (subD) are those who do not meet criteria for major depression, minor depression, or dysthymic disorder but present at least 2 current depressive symptoms daily for at least 2 weeks continuously or for most hours of the day [3]. The prevalence of subD in PD patients ranges from 8% to 28.8% [4]. However, few studies have addressed subD in PD [4–8], and these have inconsistent results with regard to demographic and clinical correlation. Although depression is a key determinant of a reduced quality of life (QoL) in PD [9] and has also been associated with sleep disturbances, fatigue, decreased functional ability, and impairment of activities of daily living [10], the impact of subD in PD patients is unclear.

The present study aimed to compare QoL in PD patients with subD to PD patients without subD or other depressive disorders (nonD). Moreover, we compared subD prevalence in the PD group to prevalence in a control group and analyzed factors associated with subD in PD patients.

2. Methods

PD patients and controls recruited from 35 centers of Spain from the COPPADIS cohort [11] were included in this study. Methodology about COPPADIS-2015 study can be consulted in https://bmcneurol.biomedcentral.com/articles/10.1186/s12883-016-0548-9 [12].

Beck Depression Inventory II (BDI-II) [13] was used to assess mood. With regard to mood status, participants from the COPPADIS-2015 study were classified to have major depression, minor depression, subD, or nonD [12]. Specifically, regarding to items 1, 4, 5, 9, 13, 15, 16, 17, and 18 of the BDI-II, depression was defined: major depression, ≥ 5 symptoms with the presence of item 1 (feeling of sadness) and/or item 4 (anhedonia) (DSM-IV criteria); minor depression, from 2 to 4 symptoms with the presence of item 1 and/or item 4 (DSM-IV criteria); subthreshold depression, from 2 to 4 symptoms without the presence of item 1 and item 4 (Judd criteria) [14,15] (Table 1.SM). Non-depression was considered when no criteria for major, minor, or subthreshold depression were observed.

Three different instruments were used to assess QoL: 1) the 39-item Parkinson's disease Questionnaire (PDQ-39) [16]; 2) a rating of global perceived QoL (PQ-10) on a scale from 0 (worst) to 10 (best) [17]; and 3) the EUROHIS-QOL 8-item index (EUROHIS-QOL8) [18]. The PDQ-39 is a PD-specific questionnaire that assesses the patient's health-related quality of life (HRQoL). There are 39 items grouped into 8 domains: (1) Mobility (items 1 to 10); (2) Activities of daily living (items 11 to 16); (3) Emotional well-being (items 17 to 22); (4) Stigma (items 23 to 26); (5) Social support (items 27 to 29); (6) Cognition (items 30 to 33); (7) Communication (items 34 to 36); and (8) Pain and discomfort (items 37 to 39). For each item, the score ranges from 0 (never) to 4 (always). The symptoms refer to the 4 weeks before assessment. Domain total scores are expressed as a percentage of the corresponding maximum possible score. A Summary Index is obtained as an average of the domain scores (PDQ-39SI). The EUROHIS-QOL8 is an 8-item global QoL questionnaire (quality of life, health status, energy, autonomy for activities of daily living, self-esteem, social relationships, economic capacity, and habitat) derived from the WHOQOL-BREF. For each item, the score ranges from 0 (not at all) to 5 (completely). The total score is expressed as the mean of the individual scores. A higher score indicates a better QoL.

2.1. Data analysis

Data were processed using SPSS 20.0 for Windows. Patients and controls with major and minor depression were excluded for comparing the impact of subD on QoL vs nonD. For comparisons between patients and/or controls with subD and nonD, the Student's t-test, Mann-Whitney U test, Chi-square test, or Fisher test, as appropriate, were used (distribution of values and scores was verified by one-sample Kolmogorov-Smirnov test). A NMSS total score > 40 and > 70 was defined as severe and very severe non-motor symptoms burden, respectively [19]. Binary regression model was used for determining in what grade different variables were related to subD (subD as dependent variable). The p-value was considered significant when it was < 0.05.

2.2. Standard protocol approvals, registrations, and patient consents

For this study, we received approval from the appropriate local and national ethical standards committee. Written informed consents from all participants in this study were obtained before the start of the study. COPPADIS-2015 was classified by the AEMPS (*Agencia Española del Medicamento y Productos Sanitarios*) as a Post-authorization Prospective Follow-up study with the code COH-PAK-2014-01.

2.3. Data availability

The protocol and the statistical analysis plan are available on request. De-identified participant data are not available for legal and ethical reasons.

3. Results

The frequency of depressive symptoms was higher in PD patients ($n = 694$) from the COPPADIS cohort than in controls ($n = 207$) ($p < 0.0001$): major depression, 16.1% vs 7.8%; minor depression, 16.7% vs 7.3%; subD, 17.4% vs 5.8% [11]. After excluding participants with major and minor depression, 120 out of 468 patients (25.6%) presented subD vs 348 patients (74.4%) with nonD.

Table 1 shows the clinical characteristics of subD PD patients compared to nonD PD patients. The score on UPDRS-IV (Unified Parkinson's Disease Rating Scale – part IV), NMSS (Non-Motor Symptoms Scale), BDI-II, NPI (Neuropsychiatric Inventory), QUIP-RS (Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale), and VAFS (Visual Analogue Fatigue Scale) was significantly higher in PD patients with subD whereas on PDSS (Parkinson's Disease Sleep Scale) and ADLS (Schwab and England Activities of daily living Scale) was significantly lower. NMSS total score was also higher in patients with subD compared to those with nonD even after excluding domain 3 (emotional well-being) (Table 1). When subD PD patients, nonD PD patients, subD controls, and nonD controls were compared regarding non-motor symptoms burden, sleep, and cognition, PD patients with subD presented a greater non-motor symptoms burden and worse quality of sleep and cognitive function (Table 2.SM and Fig. 1). Non-motor symptoms burden was greater and quality of sleep was worse not only in subD PD patients vs controls but also in nonD PD patients vs controls (Table 2.SM). However, when specific items from the PDSS were analyzed, significant differences were observed in many of them between PD patients and controls but not between PD patients with subD and without.

With regard to QoL, both HRQoL and global QoL were significantly worse in subD PD patients than in nonD PD patients (Table 2 and Fig. 2). Scores on all domains of PDQ-39SI except domains 4 (stigma) and 5 (social support) were significantly higher in PD patients with subD. Similarly, scores across all domains of EUROHIS-QOL8 were lower in PD patients with subD except domains 1 (quality of life), 7 (economic capacity), and 8 (habitat) (Table 2). When controls were considered, both HRQoL and global QoL was not only worse in subD PD patients compared to controls but also in nonD PD patients compared to controls (Fig. 2). Even when all controls of the COPPADIS cohort ($n = 207$; major depression, $n = 16$; minor depression, $n = 15$; subD, $n = 22$; nonD, $n = 154$) were considered, QoL was not only significantly worse in PD patients with subD (PDQ-39SI, PQ-10 and EUROHIS-QOL8, $p < 0.0001$) but also in PD patients with nonD (PDQ-39SI and EUROHIS-QOL8, $p < 0.0001$; PQ-10, $p = 0.004$) compared to the control group as well.

Non-motor symptoms burden (NMSS; OR = 1.019; 95%CI 1.011–1.028; p < 0.0001), neuropsychiatric symptoms (NPI; OR = 1.091; 95%CI 1.045–1.139; p < 0.0001), impulse control behaviors (QUIP-RS; OR = 1.035; 95%CI 1.007–1063; $p = 0.013$), quality of sleep (PDSS; OR = 0.991; 95%CI 0.983–0.999; $p = 0.042$), and fatigue (VAFS-physical; OR = 1.185; 95%CI 1.086–1.293; p < 0.0001; VAFS-mental; OR = 1.164; 95%CI 1.058–1.280; $p = 0.0001$) were associated with subD after adjustment to age, disease duration, daily equivalent levodopa dose, motor status (UPDRS-III), and living alone (Table 3.SM). The relationship between subD and non-motor symptoms burden remained consistent even after excluding domain 3 (emotional well-being) from the NMSS total score (OR = 1.022; 95%CI 1.012–1.032; p < 0.0001). Specifically, to have a severe or very severe non-motor symptoms burden (NMSS > 40) multiplied by 2.5 the probability of presenting subD, after adjustment to previously commented covariates. Finally, a worse HRQoL and global QoL were associated with subD as well (Table 3.SM), even after adjustment to non-motor symptoms burden (NMSS) added to the other covariates: PDQ-

Table 1
Clinical characteristics in PD patients with subD vs those with nonD (n = 468).

	nonD (n = 348)	subD (n = 120)	p
Age	62.2 ± 9.2	62.5 ± 8.8	0.812
Males	65.5	62.5	0.312
Disease duration (years)	5.7 ± 4.4	5 ± 4.4	0.169
Motor phenotype	49.1	47.1	0.204
Tremoric dominant	33.2	42	0.171
PIGD	17.7	10.9	0.512
Indeterminate	1.9 ± 0.5	2 ± 0.6	0.948
Hoehn & Yahr	26.2	24.4	0.005
Stage 1	68.4	66.1	0.116
Stage 2	4.4	7.8	0.384
Stage 3	1	1.7	0.154
Stages 4–5	21.7 ± 10.5	21.9 ± 11.1	0.112
UPDRS-III	1.6 ± 2.1	2.1 ± 2.3	0.266
UPDRS-IV	29.4	35.8	0.126
Motor fluctuations	15	16.7	< 0.0001
Dyskinesia	3 ± 4.3	3.5 ± 3.1	< 0.0001
FOG-Q	7	11.1	< 0.0001
Falls	94.1 ± 15.5	91.8 ± 16.7	< 0.0001
PD-CRS	22.4	28.2	0.002
Cognitive impairment	29.1 ± 25.8	45.9 ± 32	< 0.0001
(PD-CRS ≤ 84)	25.9 ± 21.5	40 ± 27.6	0.288
NMSS	4.6 ± 4.2	8.8 ± 5.1	0.093
NMSS without domain 3	2.9 ± 5.1	5.6 ± 6.5	< 0.0001
(emotional well-being)	3.2 ± 7	5.8 ± 9.2	< 0.0001
BDI-II	121 ± 26.2	114.3 ± 23	0.015
NPI	2.1 ± 2.8	2.3 ± 2.7	0.126
QUIP-RS	48.3	55.8	0.142
PDSS	2.1 ± 2.4	3.3 ± 2.6	0.444
VAS-PAIN	1.4 ± 2.1	2.2 ± 2.5	0.016
Patients with pain	91 ± 9.3	88.9 ± 9	0.018
VASF − physical	22.4	28.2	0.124
VASF – mental	533 ± 404.4	577 ± 570.8	
ADLS	6.9 ± 4	7.3 ± 4	
Patients with functional	2.2 ± 2.2	2.7 ± 2.3	
dependency	14.9	24.2	
L-dopa eq. daily dose (mg)	74.4	68.3	
Total number of pills/day			
Total number of non-antiparkinsonian drugs/day			
Use of antidepresive agent			
Use of dopamine agonist			

Chi-squared, Mann-Whitney-Wilcoxon and/or t-Student test were applied (only PD-CRS Total Score and Fronto-Subcortical had normal distribution). The results represent percentages or mean ± SD. Data about H&Y and UPDRS-III are during the OFF state (first thing in the morning without taking medication in the previous 12 h).

ADLS, Schwab and England Activities of daily living Scale); BDI, Beck Depression Inventory-II; NMSS, Non-Motor Symptoms Scale; NPI, Neuropsychiatric Inventory; PD, Parkinson's disease; PD-CRS, Parkinson's Disease Cognitive Rating Scale; PDSS, Parkinson's Disease Sleep Scale; PIGD, Postural Inestability Gait Dificulty; QUIP-RS, Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale; UPDRS, Unified Parkinson's Disease Rating Scale; VAFS, Visual Analog Fatigue Scale; VAS-Pain, Visual Analog Scale-Pain.

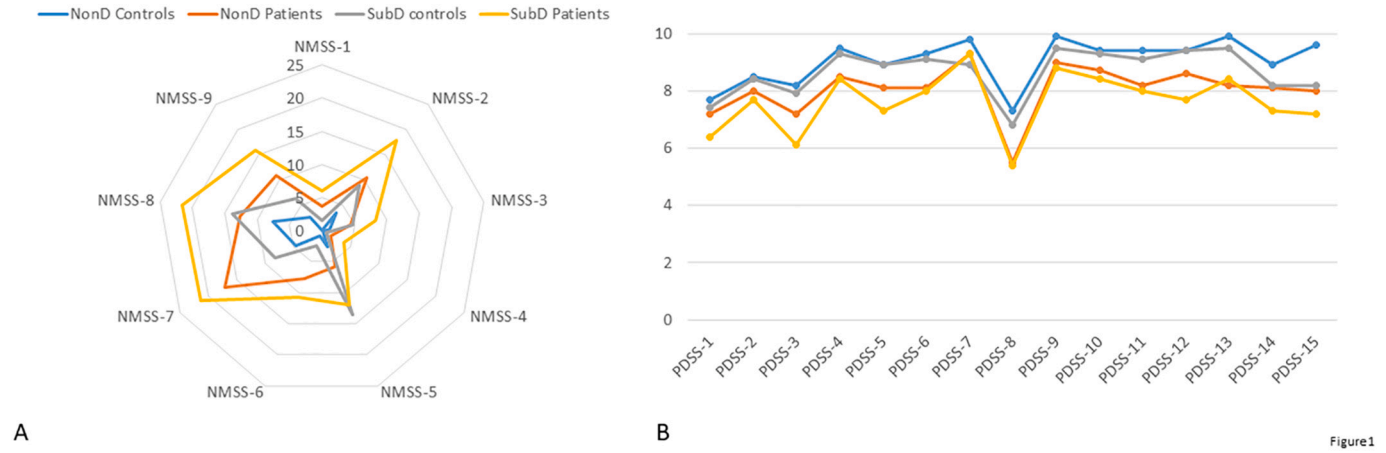

Fig. 1. Mean value of different NMSS domains in nonD controls (n = 154), in nonD PD patients (n = 348), in subD controls (n = 22) and in subD PD patients (n = 120). B. Mean value of different items from the PDSS in the same four groups as A. NMSS, Non-Motor Symptoms Scale; PDSS, Parkinson's disease Sleep Scale.

Table 2
HRQoL and global perceived QoL in PD patients with subD vs those with nonD (n = 468).

	nonD (n = 348)	subD (n = 120)	p
PDQ-39SI	11.6 ± 10	18.1 ± 12.8	< 0.0001
Mobility	10.8 ± 15.3	17.2 ± 18.4	< 0.0001
Activities of daily living	13.7 ± 16.3	20.5 ± 19.5	< 0.0001
Emotional well-being	12.2 ± 13.4	20.6 ± 16.8	< 0.0001
Stigma	10.4 ± 16.1	14 ± 19	0.150
Social support	5.3 ± 13.4	7.6 ± 15.6	0.066
Cognition	13.4 ± 14.2	21.8 ± 19	< 0.0001
Communication	7.4 ± 11.7	11.7 ± 16.2	0.04
Pain and discomfort	18.9 ± 18.9	28.7 ± 23.4	< 0.0001
PQ-10	7.8 ± 1.3	7.5 ± 1.4	0.051
EUROHIS-QOL8	4 ± 0.5	3.7 ± 0.5	< 0.0001
Quality of life	4 ± 3.9	3.9 ± 4	0.098
Health status	3.4 ± 0.8	3.1 ± 0.8	0.001
Energy	4 ± 0.7	3.7 ± 0.7	< 0.0001
Autonomy for activities of daily	3.9 ± 0.8	3.5 ± 0.8	< 0.0001
Living	4.1 ± 0.6	3.8 ± 0.8	< 0.0001
Self-esteem	4.3 ± 0.6	4 ± 0.7	< 0.0001
Social relationships	4 ± 0.7	3.9 ± 0.7	0.115
Economic capacity	4.4 ± 0.6	4.2 ± 0.7	0.014
Habitat			

Mann-Whitney-Wilcoxon test were applied. The results represent mean ± SD. EUROHIS-QOL8, EUROHIS-QOL 8-item index; PDQ-39SI, 39-item Parkinson's disease Questionnaire Summary Index.

39SI, OR = 1.028; 95%CI 1.003–1.054; p = 0.029; EUROHIS-QOL8, OR = 0.457; 95%CI 0.269–0.777; p = 0.004.

4. Discussion

This study found that subD is a frequent problem in patients with PD and is more prevalent in these patients than in controls. Also, both HRQoL and global QoL is significantly worse in PD patients with subD compared to PD patients with nonD. Moreover, different non-motor symptoms such as sleep problems, neuropsychiatric symptoms, and fatigue as well as a greater non-motor symptoms burden as a whole were associated with subD in PD patients. All this suggests that detection of subD in PD could be an important factor in clinical practice.

The prevalence of subD in our cohort (17%) is slightly lower than observed in previous studies. Ehrt et al. [7] identified subD in 116 of 538 PD patients (21%), Reiff et al. [5] in 28 of 110 (25%), Santagelo et al. [4] in 30 of 115 (26%), and Nation et al. [6] in 32 of 107 (29%). However, Starkstein et al. [8] only identified subD in 8% of a consecutive series of 173 PD patients. Heterogeneity between the studies could explain the differences since some studies included patients with dementia [7], nondemented patients but with moderate to severe PD [6], or even different criteria for defining subD [6]. Our study is along with Starkstein study [8] in which patients with less disease duration were included and the prevalence of other types of depressive symptoms were in line with previous reports [1,20]. Importantly, this study is not only the largest study analyzing subD in PD but also the only study in which a control group was included. SubD was three times more frequent in patients than in controls.

Regarding the principal aim of this study, QoL was observed to be worse in PD patients with subD compared to PD patients with nonD. Only one study (n = 81) compared QoL in PD patients with subD vs those with nonD [5] in which a worse HRQoL was observed in subD patients. As in our study, PDQ-39 was used and similar results in total PDQ-39SI score were observed in both groups. The subD PD patients scored significantly higher on the PDQ-39 subscores "mobility," "emotional well-being," stigma," "cognition," and "communication" [5]. However, in our study (n = 468), the score was significantly higher in all subscores except "stigma" and "social support." Moreover, for the first time, we investigated the relationship between subD and global QoL as HRQoL, which was worse in subD patients after adjustment to other covariates. On the other hand, Reiff et al. [5] observed that HRQoL was better in subD PD patients than PD patients with depression. Previously, we described in the COPPADIS cohort a relationship between the severity of mood disorder (major depression vs minor depression vs subD vs nonD) and the perception of QoL. We found that greater severity of symptoms correlated to a poorer QoL [21]. Although it is known that mood is an important factor affecting QoL in PD patients, explaining between the 28% (PDQ-39) and 44% (EUROHIS-QOL8) of the variance in the COPPADIS cohort [21], other factors, such as non-motor symptoms burden and gait problems, are important too, [21–23]. This could explain why HRQoL and global QoL were worse in PD patients with nonD vs controls in the present study, even when subD controls were considered.

In this study, we compared subD to nonD PD patients not only concerning QoL but also to several other motor and non-motor symptoms. Again, there is a lack of knowledge about this topic and our study is the most complete and largest concerning this association. Santangelo et el. [4] did not find differences in objective cognitive measures (MOCA [Montreal Cognitive Assessment] and PD-CQ [Parkinson's Disease Cognitive Questionnaire]) in 30 subD patients compared to 36 with nonD whereas subD patients did report more cognitive complaints than nonD patients. We observed the same for objective overall cognition, fronto-subcortical, and posterior cortical functions (PD-CRS). However, as in Santangelo study, cognitive complaints were more frequent in subD patients (NMSS – attention/memory and PDQ-39 –

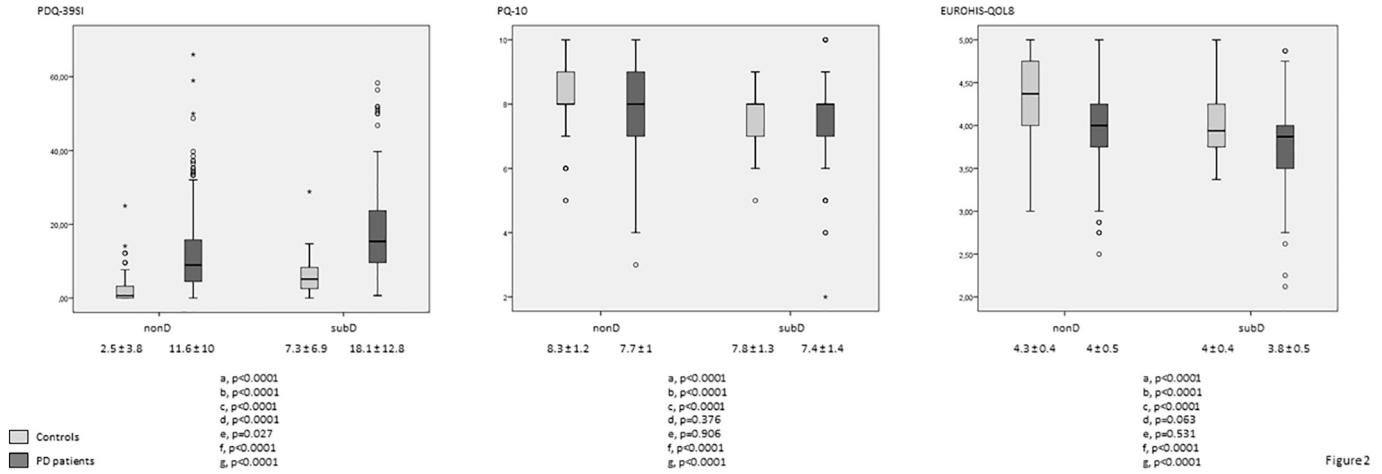

Fig. 2. PDQ-39SI, PQ-10 and EUROHIS-QOL8 in nonD controls (n = 154), in nonD PD patients (n = 348), in subD controls (n = 22) and in subD PD patients (n = 120); a, comparison between all groups; b, comparison between PD patients and controls; c, comparison between nonD patients and nonD controls; d, comparison between subD PD patients and subD controls; e, comparison between nonD PD patients and subD controls; f, comparison between subD PD patients and controls (with and without subD); g, comparison between nonD PD patients and controls (with and without subD). Extreme outliers (*) are data points that are more extreme than Q1–3 * IQR or Q3 + 3 * IQR. Mild outliers (O) are data points that are more extreme than than Q1–1.5 * IQR or Q3 + 1.5 * IQR, but are not extreme outliers.

cognition). Other studies observed similar results when Mattis Dementia Rating Scale [5] and MMSE [6,8] were used. These findings suggest that cognitive complaints reflect the effect that negative mood has on the subjective perception of cognitive impairment in PD, but these complaints do not necessarily associate with actual cognitive disorders. The five year follow-up of the COPPADIS cohort [12] will analyze if subD patients could develop cognitive impairment because cognitive complaints might predict a future cognitive deterioration [24,25]. As in previous studies, we did not find motor status differences between subD and nonD patients [4–8]; however, the difference between both groups in non-motor symptoms is very interesting. Fatigue, sleep problems, neuropsychiatric symptoms, and non-motor symptoms burden as a whole, were significantly related to subD. All domains score of NMSS, except gastrointestinal and urinary symptoms, were significantly higher in subD patients compared to nonD patients. Also, more than the double the number of subD patients presented a severe or very severe non-motor symptoms burden compared to nonD patients. This has not been previously investigated in subD PD patients. An important question is if this is a cause or a consequence of bad mood. Experiencing more non-motor symptoms could affect mood but also be related to mood disturbance due to specific brain areas affected. This point of view has been further supported by evidence that depression is associated with more extensive neuropathology within the substantia nigra itself [26], more severe motor and non-motor symptoms [27], and a more malignant course [28]. This suggests that somatic symptoms may continue to be important features of depressive mood in PD, although they are a direct result of the same underlying pathophysiological process. However, it has previously been suggested that mood can influence the patient's perception of the symptoms analyzed, in turn causing the results assessed in subjective questionnaires could not reflect the real status of the patient [29], as seen through cognition complaints. In the COPPADIS cohort, in line with this, a higher NMSS total score to higher degree of depression was observed in PD patients [30]. However, scores observed in non-motor symptoms scales indicating a greater affectation in subD controls supports the hypothesis that mood could influence, at least in part, the perception of non-motor symptoms, since presumably there would not be pathological brain involvement that explain them in this group. In previous studies, age and sex influence non-motor symptoms in controls [31], but the influence of mood is unclear. Clinical-pathological studies which evaluate the correlation between scores on different scales to assess non-motor symptoms and pathological findings are required.

It has been argued that the subtle mood symptoms thought to characterize subD represent prodromal manifestations of an imminent mood disorder or residual symptoms of a waning depressive episode [32]. In contrast with a previous study, the fact that our data show differences in the use of antidepressants between groups could suggest that subD is merely major depression partially resolved with pharmacotherapy, but longitudinal follow-up is necessary.

The present study has some limitations. For some variables, the information was not collected in all cases. All scales or questionnaires used to assess motor and NMS are validated except PQ-10. This is a very simple question about GQoL from 0 to 10 used in previous studies that takes very little time and provides information similar to the EUROHIS-QOL8 total score [17,21]. As it has been commented, the influence of mood on the patient's perception of the symptoms affecting the results of the questionnaires can't be ruled out. On the other hand, although mood is included in NMSS (NMSS-domain 3), when mood was excluded from the NMS burden ([NMSS total score] – [NMSS-domain 3]), results were similar. Dysthymic disorder (Table.1.SM) and mood fluctuations were not considered. Our sample is not fully representative of the PD population due to inclusion and exclusion criteria (i.e., age limit, no dementia, no severe comorbidities, no second line therapies, etc.) which subsequently entails a bias toward early PD. Finally, this is a cross-sectional study, but the aim of the COPPADIS-2015 study [17] is to follow-up the cohort for 5 years and to analyze predictors of changes in QoL and mood.

In conclusion, the present study shows that subD is frequent in PD patients. Also, this study demonstrates that subD patients present a worse QoL and are more affected by different non-motor symptoms than patients with no depressive symptoms. The origin of this relationship should be analyzed with specific studies.

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Declaration of Competing Interest

None.

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Appendix A. Supplementary data

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Appendix B. Appendix 1

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