

Relationships between disability, quality of life and prevalence of nonmotor symptoms in Parkinson's disease

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ABSTRACT

Patients with Parkinson's disease suffer from a variety of motor and nonmotor symptoms (NMS), report reduced quality of life and increased disability. Aims of this study are to assess the impact of Parkinson's disease on disability and quality of life, to evaluate the relationships between them and NMS prevalence.

In this cross-sectional study, adult patients were consecutively enrolled and administered the World Health Organization Disability Assessment Schedule (WHO-DAS II), the 36-Item Short-Form Health Survey (SF-36) and the Non Motor Symptoms Questionnaire (NMSQuest). One-sample *t*-test was used to compare WHO-DAS II and SF-36 scores with normative value. Pearson's correlation was performed between NMSQuest, WHO-DAS II and SF-36 summary scales. Independent-sample *t*-test was used to compare NMSQuest, WHO-DAS II and SF-36 scores in patients with Hoehn & Yahr stage <3 and ≥3. In total, 96 patients were enrolled. SF-36 and WHO-DAS II scores were significantly worse than the normative values. Correlation coefficients between NMSQuest, WHO-DAS II and SF-36's mental score were moderate, and were high between WHO-DAS II and SF-36's physical score. Patients with Hoehn & Yahr stage ≥ 3 reported reduced quality of life, higher disability and more NMS.

Parkinson's disease severity is strongly associated with reduced quality of life, increased disability and NMS prevalence. Disability and quality of life assessment tools measure psychosocial facets that are similar specifically with regard to physical health component of health-related quality of life, are sensitive enough to capture differences related to disease's progression and increased prevalence of NMS.

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1. Introduction

Parkinson's disease (PD) is a common progressive neurodegenerative disorder which generally affects persons over the age of 60 [1–3], and is characterized by a broad spectrum of motor (e.g. rest tremor and rigidity) and non-motor features (e.g. autonomic dysfunction, cognitive/neurobehavioral abnormalities). In later disease stages, the progressive symptomatic load often leads PD patients to require assistance for several activities, such as those connected to self-care [4].

PD is associated with increased disability and reduced health-related quality of life (HRQoL) [5,6]. The transition between Hoehn and Yahr (HY) [7] stage II and III, was reported as a pivotal stone in PD-related disability [8], and axial impairment is strongly associated with

disability and HRQoL decrement [5,9]. PD patients' HRQoL is affected in terms of physical, social and emotional functioning, and depression was found to be the most important determinant of reduced HRQoL [9,10]. In recent years presence and evaluation of nonmotor symptoms (NMS) captured the attention of clinicians and researchers [11,12]. NMS such as constipation, urgency, nocturia and feeling of sadness were reported by more than 50% of patients in a recent international study, were significantly more prevalent among PD patients than among age-matched controls, and correlated with duration of disease [13,14].

Despite the relevance of disability evaluation in PD, few studies measured it according to WHO's International Classification of Functioning, Disability and Health (ICF) model [15], which describes disability as the interaction between persons' health condition and the environment in which they live. Acknowledging the effect of environmental factors is relevant in long-term degenerative diseases like PD, as clinical worsening is accompanied by an increase in utilization of medical treatment, and by the need of relying on the

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help of other persons for daily needs [4]. In a previous paper, environmental factors relevant to PD patients' were identified through a direct application of ICF categories to a sample of PD patients [16]. Results showed that medications, support from family members, health services and device for communication (e.g. glasses) are the most widespread factors that contribute to improve patients' functioning.

The issue of the relationships between PD and self-report outcome measures such as HRQoL and disability have been previously evaluated, as well as the relationships between PD and NMS. On the contrary, little understanding exists on the relationships between NMS, HRQoL and disability in PD patients. Therefore, in addition to assessing the impact of PD on disability and HRQoL, and to evaluate the relationships between them using an ICF-based disability assessment tool, a secondary aim of this paper is to assess the relationships between NMS, disability and HRQoL, together with an analysis of the correspondence between PD severity and NMS prevalence.

2. Methods

2.1. Study design

The study was cross-sectional and observational, in which both inpatients and outpatients were consecutively enrolled at the division of Neurology I – Movement Disorders of the Neurological Institute C. Besta of Milan. Inclusion criteria were: diagnosis of PD according to the UK Parkinson's Disease Brain Bank criteria [17] and age >18. Patients were excluded if they were selected for technological PD treatment (e.g. surgical approaches such as deep brain stimulation, implantation of infusion pump for duodopa or apomorphine), were enrolled in clinical trials in the previous three years or had psychiatric comorbidities. All enrolled patients signed an informed consent form, and the study was approved by the institute's ethical committee.

2.2. Clinical evaluation

The stage of PD was defined by HY scale [7]. Nonmotor symptoms were evaluated using the Non Motor Symptoms Questionnaire (NMSQuest) [13,14]. The NMSQuest is composed of 30 items, which patients have to mark in case they have the described problem. Items can be summed to define nine subscales and a general score, which ranges between 0 and 30, with higher score reflecting more nonmotor symptoms.

2.3. Evaluation of disability and health-related quality of life

HRQoL was measured with the 36-Item Short-Form Health Survey (SF-36) [18], a widely used questionnaire which measures eight general health concepts regarding physical and mental status, and whose validity has been tested in a great amount of literature. Each scale is scored on a 0–100 scale, with higher scores reflecting better HRQoL. Two main scores are available to summarize these scales: Physical Composite Score (PCS) and Mental Composite Score (MCS), which are norm-based scores (mean 50, SD 10).

Disability was measured with the WHO-DAS II (World Health Organization Disability Assessment Schedule, second version) [19], a 36-items disability assessment tool that examines the difficulties experienced in the previous month due to a health condition. Patients have to answer questions regarding how much difficulty they had in the last thirty days: answers are rated on a five-point scale, from no problem to complete problem. WHO-DAS II is composed of a total score and of six subscores: Understanding and communicating; Getting around; Self care; Getting along with people; Life activities (divided into household and work); Participation in society. Scores range between 0 and 100, with higher scores reflecting greater disability. Its validity and reliability in populations of patients with chronic conditions – including PD – was recently confirmed [20], but a specific reliability analysis on PD patients only was never performed.

2.4. Statistical analysis

The relationship between SF-36 PCS and MCS, WHO-DAS II Summary score and NMSQuest total score scales was evaluated using Pearson's cross product correlation coefficient: the normal distribution for these scales was verified by One-sample Kolmogorov–Smirnov test. Correlations were considered weak for coefficient values <.29, moderate for values between .30 and .59 and strong for values >.60 [21]. The impact of PD on patients' daily lives, in terms of HRQoL and disability, was measured in two ways. First, by comparing WHO-DAS II and SF-36's scores against normative Italian scores referred to the general population [22,23] using One-sample *t*-test. Comparison

was not made with Life activities scale of the WHO-DAS II, because Federici and colleagues [22] made no distinction between household and work activities. Second, by evaluating the different disability and HRQoL profiles in patients HY stage <3 (patients without balance impairment) and those with HY stage ≥ 3 (patients with balance impairment). For this procedure, since dependent variables were normally distributed, the Independent-sample *t*-test and Levene's test for equality of variance were used. The same procedure was used to evaluate the impact of PD severity on nonmotor symptoms: NMSQuest was therefore tested comparing NMSQuest between patients with HY stage <3 and those with HY stage ≥ 3.

One-sample *t*-test was carried out also to compare the severity on nonmotor symptoms with the scores reported by the sub-sample of Italian PD patients (*N* = 132, mean age 65.01, SD 10.8; mean NMSQuest total score 9.28, SD 4.3) enrolled in a recent international study [13]. Comparison was made only with the total score, as data referred to the single sections were not available for the Italian sub-sample.

Cronbach's Alpha coefficient was used to test the internal consistency of WHO-DAS II in PD patients: an alpha-value higher than 0.70 [24] is considered to report a good internal consistency. Statistical significance was set with *P* < .05 and two-tailed testing for both Pearson's and Spearman's correlation, One-sample *t*-test and Independent-sample *t*-test. Data analysis was performed using SPSS 11.0.

3. Results

In total, 96 patients (64 males) were enrolled. Age ranged between 24 and 90 (mean 64.1, SD 11.3). Most of them were married (74%) and not employed (79.2%); 13 patients were in HY stage I, 55 in stage II, 22 in stage III and 6 in stage IV.

Table 1 reports means, standard deviation and comparison to Italian normative values referred to the general population for the SF-36 and WHO-DAS II. Significantly lower, therefore worse, values compared to normative scores were observed in all SF-36 scales, with the exclusion of Role Emotional and Mental Health, and wider differences are observed for PCS compared to MCS summary scores. With regard to the WHO-DAS II, values were significantly higher, therefore worse, than normative for all scales, excluding Understanding and communicating and Getting along with people. WHO-DAS II overall Cronbach's alpha coefficient was 0.84. Values observed to the NMSQuest are reported in Table 2. No difference was observed between total score reported in this study and total score for the Italian sample used for comparison (mean 9.28, SD 4.3; *t*-test 0.96, *P* = .34).

The analysis of correlation between SF-36 and WHO-DAS II is reported in Table 3. A strong correlation was observed between

Table 1
One-Sample *t*-test between study and normative data for SF-36 and WHO-DAS II.

	Mean score (SD)	Normative data	<i>t</i> -test	<i>P</i> -value
SF-36				
Physical Functioning	72.0 (22.6)	84.46	−5.04	<i>P</i> < .001
Role Physical	46.9 (38.9)	78.21	−7.88	<i>P</i> < .001
Bodily Pain	58.9 (29.9)	73.67	−4.83	<i>P</i> < .001
General Health	41.2 (20.5)	65.22	−11.44	<i>P</i> < .001
Vitality	56.7 (20.1)	61.89	−2.52	<i>P</i> = .013
Social Functioning	69.2 (27.6)	77.43	−2.93	<i>P</i> = .004
Role Emotional	68.4 (40.3)	76.16	−1.88	<i>P</i> = .063
Mental Health	64.6 (19.6)	66.50	−0.94	<i>P</i> = .350
PCS	40.0 (8.8)	50	−11.09	<i>P</i> < .001
MCS	46.7 (11.0)	50	−2.90	<i>P</i> = .005
WHO-DAS II				
Understanding and communicating	12.5 (14.4)	11.84	0.44	<i>P</i> = .659
Getting around	19.5 (17.9)	7.07	6.80	<i>P</i> < .001
Self-care	20.2 (24.2)	3.53	6.73	<i>P</i> < .001
Getting along with people	15.3 (18.9)	12.57	1.39	<i>P</i> = .167
Household activities	22.1 (24.7)	NA	NA	NA
Work activities	25.0 (26.4)	NA	NA	NA
Participation in society	27.6 (18.9)	12.12	8.03	<i>P</i> < .001
Summary score	19.3 (14.4)	12.95	4.10	<i>P</i> < .001

Note: *N* = 96 (d.f. = 95) for all scales, except WHO-DAS II Work Activities (*N* = 24, d.f. = 23), Household Activities and Summary Score (*N* = 86, d.f. = 85). NA, not applicable.

Table 2
Descriptive statistic for NMSQuest subscale.

	Mean score (SD)	Range
NMSQuest		
NMSQ Digestive	2.0 (1.5)	0–7
NMSQ Urinary	1.1 (0.8)	0–2
NMSQ Attention and Memory	1.1 (1.1)	0–3
NMSQ Hallucinations/Delusions	0.1 (0.4)	0–2
NMSQ Depression/Anxiety	1.1 (0.8)	0–2
NMSQ Sexual	0.9 (0.8)	0–2
NMSQ Cardiovascular	0.5 (0.7)	0–2
NMSQ Sleep	1.8 (1.3)	0–5
NMSQ Miscellany	1.3 (1.1)	0–4
NMSQ Total	9.8 (4.9)	0–29

Note: N = 96 for all scales.

WHO-DAS II Summary score and SF-36 PCS scale, while correlations with MCS and NMSQuest total score was moderate, and so were the correlations between NMSQuest total score and SF-36 scales.

In total, 68 subjects reported HY <3 (72.1% male; mean age 63.5, sd 11.6) and 28 HY ≥ 3 (53.6% male; mean age 65.4, sd 10.7). Independent-sample *t*-test showed that age was not significantly different, while significant differences were observed when SF-36 composite scores, WHO-DAS II summary score and NMSQuest total scores were compared between patients with HY <3 and HY ≥ 3 (Fig. 1). Compared to the group with lower HY stage, those with higher stage reported lower PCS and MCS scores (respectively, 16.8% and 18.1% reduction), higher WHO-DAS II and NMSQuest total scores (respectively, 79.5% and 51.8% increase).

4. Discussion

Three main results were derived from this study. First, PD has a strong effect on HRQoL and disability, as measured by the WHO-DAS II and by the SF-36. In fact, scores observed at majority of SF-36 scales were significantly worse compared to normative values, in particular with regard to the physical component of HRQoL; WHO-DAS II summary score too was worse than normative values, and areas connected to mobility, self-care and participation to social situation were the significantly higher than normative values, indicating that these areas were more impaired too among PD patients than among the general population. Second, increased disease severity is also connected to worsening in HRQoL and disability: in fact patients in higher HY stages reported higher disability and lower HRQoL than those in lower stages. In addition to these known issues, a third conclusion on the relationships between disability, HRQoL and prevalence of NMS can be drawn. Disability was strongly associated to physical issues of HRQoL, while the association with mental health issue was moderate, but still highly significant. Similarly, prevalence of NMS was moderately associated to increased disability and reduced HRQoL. Therefore, this study provides evidence on the association between presence of a high number of NMS, increased disability and reduced HRQoL.

Shulman et al. [8] reported that transition from HY stage II to III marks a pivotal stone in PD-related disability, measured as ability in self-care and other activities needed to function independently in

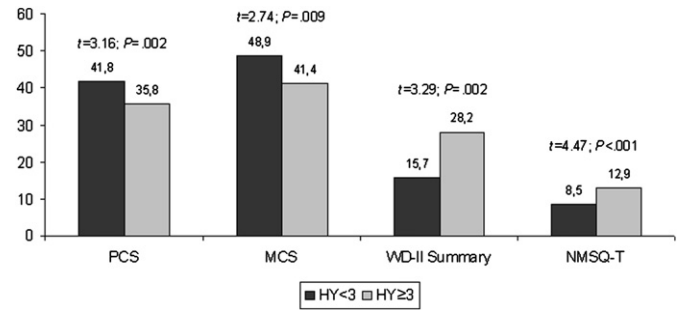


Fig. 1. SF-36 PCS and MCS, WHO-DAS II Summary Score and NMSQuest total score in patients with HY <3 and HY ≥ 3.

the environment. Our findings enlarge the value of Shulman's results by adding information HRQoL and NMS. We also found a similar pattern related to disability assessed with the WHO-DAS II. What is interesting to notice is that age was not significantly different between patients with HY <3 and HY ≥ 3, thus providing a preliminary evidence on the effect of disease progression on disability, HRQoL and prevalence of nonmotor symptoms, as also previously reported [14,15].

Prevalence of NMS in our sample was similar to that of the Italian sub-sample of a previous study by Martinez-Martin et al. [13]. Consistently with that study, we found that patients with HY <3 had significantly less NMS than those with HY ≥ 3. Scores observed at NMSQuest were similar too considering the group of patients with HY <3, but were not directly comparable in higher HY stages, since we grouped together all patients with HY ≥ 3, while in Martinez-Martin's study patients with HY = 3 were divided from those with HY >3. Moreover, we observed a significant correlations between the total scores of NMSQuest, WHO-DAS II and SF-36 summary measures: therefore results provide emerging input and evidence on the relationships between NMS prevalence, reduced HRQoL and increased disability.

The association between HRQoL and disability was previously evaluated in two studies that employed the same methodological approach in myasthenia gravis (MG) [25] and migraine [26]. The association between WHO-DAS II summary score and SF-36 MCS was similar, among PD patients the association with PCS was higher. This is likely to reflect the fact that physical health was more severely impaired in PD patients (PCS = 40.0), compared those with migraine and MG (PCS 42.1 and 44.7), as well as to the older age of PD sample (mean 64.1) compared to that of patients with migraine and MG (mean 43.5 and 47.2 respectively). The pattern of association was moderate to high, therefore suggesting that disability and HRQoL, specifically in its physical component, are not completely different.

Parallel to these differences, there is one issue reported in a similar way both in the papers on migraine and MG [25,26] and in the present one. PD patients reported more difficulties in activities connected to participation in social activities than in relational situations. Scores in WHO-DAS II "Participation in society" subscale were almost equal between the three groups of patients (25.2 for migraineurs, 25.6 for MG and 27.6 for PD patients, while normative Italian score was 12.1). The content of this scale reflects the difficulties persons encounter to take part in society, not only as a consequence of their inner health state, but also of the hindrances due to other persons. In our sample, difficulties in participation were even more pronounced than those referred to mobility. On the contrary, reported difficulties in the area of interpersonal relationships, which reflect the difficulties due to a health condition in dealing with other persons, were not different compared to normative values (15.5 for migraineurs, 8.3 for MG and 15.3 for PD patients, while normative Italian score was 12.6). This leads to the

Table 3
Pearson's correlations between WHO-DAS II, NMSQuest and SF-36 summary measures.

	SF-36's PCS	SF-36's MCS	NMSQuest
WHO-DAS II Summary score	-.70	-.52	.65
NMSQuest	-.54	-.40	NA

Notes: Pearson's correlations were all significant at $P < .0001$; NA, Not Applicable. SF-36 scales: PCS, physical composite score; MCS, mental composite score. N = 86 for all scales.

conclusion that the context in which difficulties are experienced is of primary relevance and should be considered when PD patients' disability profiles are investigated.

The impact of PD on patients' participation was also by Duncan and Earhart [27], that found strong correlation between PD severity, participation levels and overall quality of life. They measured participation evaluating the total amount of retained activities, i.e. instrumental activities of daily living (IADL), low and high demanding leisure activities and also social activities. With the exclusion of IADLs, their assessment measured involvement in social situations, which is quite similar to our ICF-based conceptualization of participation restriction. Our results are consistent with these findings and provide further inputs to the relevance of participation restrictions in PD patients, and their strong correlation with physical limitations.

The value added by the use of the WHO-DAS II to measure disability in PD is the possibility of getting both a general disability score as well as partial scores. In contrast to the paper of Federici and colleagues [22], data herein reported were derived from an item response theory-based (IRT) scoring, which allows for multiple levels of difficulty for each WHO-DAS II item [19], thus making it possible to use these data for comparative analysis across populations or subpopulations. Our results also show that the overall internal consistency of WHO-DAS II in PD patients ($\alpha = 0.84$) is good, even if lower compared to both Usun's [19] and Garin's study [20] that respectively found an $\alpha = 0.95$ and 0.96 . Although only a minor part of the sample completed the section on work-related difficulties, the information reported is relevant as PD is likely to increasingly affect people that are still employed, due to the trend towards increased retirement age. This should not be intended as an issue of secondary relevance, as PD is a costly disease that causes considerable strains on both patients and on society as a whole [28], which are directly connected to disease's progression.

Some limitations need to be taken into account in the interpretation of these results. First, sample was composed by a limited number of patients attending to a specialized centre, and majority enrolled patients were in HY stage I or II: therefore, these results should not be generalized to the whole PD patients population. Second, the cross-sectional design does not enable to define causal relationships. A third limitation lies in the utilization of generic instead of disease-specific HRQoL assessment tool. This choice was made to accommodate the need of relying on a widely used tool to support the utilization of the WHO-DAS II, which has been used in few papers. It should however be noted that a recent paper [29] concluded that the SF-36 had a superior responsiveness to change compared to PD-targeted measures. Finally, a comment should be made on the relationship between Italian and international data of SF-36 and WHO-DAS II. With regard to the SF-36, Italian version appears to be a valid and reliable multidimensional questionnaire, compared to the original U.S. data. With regard to the WHO-DAS II, the same cannot be said, as the available Italian validation study did not use the same scoring system used in the international validation study which, in turn, did not report precise normative values, but relied on a graphical representation. However, a visual comparison enables us to say that normative values reported in Federici's paper are higher than WHO's general population.

In conclusion, the findings of this study support the strong association between PD severity and patients' disability profiles and HRQoL status. The two dimensions revealed psychosocial facets that, in particular with regard to physical health component of HRQoL are similar. The assessment tools used are correlated and sensitive enough to capture differences related to PD progression, and demonstrated to be also positively related to the NMSQuest, a questionnaire for screening nonmotor symptoms in PD. Therefore, we recommend using them in public health and clinical research on PD.

Conflict of interest

None.

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