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Short communication

Impact of anxiety, apathy and reduced functional autonomy on perceived quality of life in Parkinson's disease

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ABSTRACT

Introduction: Parkinson's disease (PD) is characterized by a wide spectrum of non-motor symptoms that may impact negatively on the activities of the patient's daily life and reduce Health-related quality of life (HRQoL). The present study explored the impact of specific non-motor symptoms on the HRQoL in PD.
Methods: Eighty-four outpatients underwent the Montreal Cognitive Assessment (MoCA) assessing global functioning and several questionnaires to assess depression, apathy, impulse control disorders (ICD), anxiety, anhedonia and functional impact of cognitive impairment. The perceived QoL was assessed by Parkinson's Disease Questionnaire (PDQ-8).
The PD sample was divided into patients with high and low HRQoL around the median of PDQ-8 and compared on clinical features, cognitive and neuropsychiatric variables. A linear regression analysis, in which the global functioning, apathy, depression, anxiety, anhedonia, ICD and the functional autonomy scores were entered as independent variables and PDQ-8 score as dependent variable, was applied.
Results: Patients with lower HRQoL were more depressed, apathetic, anxious and showed more severe reduction of functional autonomy and global functioning than patients with high HRQoL. The regression analysis revealed that higher level of anxiety, executive apathy and more reduced functional autonomy were significantly associated with higher score on PDQ-8.
Conclusions: The finding indicated that anxiety, apathy associated with impaired planning, attention and organization (i.e., executive apathy evaluated by the Dimensional Apathy Scale) and reduced functional autonomy contribute significantly to reduce the HRQoL in PD. Therefore, early identification and management of these neuropsychiatric symptoms should be relevant to preserve HRQoL in PD.

1. Introduction

The Health-related quality of life (HRQoL) is defined as "the perception and evaluation by patients themselves of the impact caused on their life by the disease and its consequences" [1]. In Parkinson's Disease (PD), the HRQoL can be reduced by motor and non-motor symptoms [2], in particular, neuropsychiatric symptoms [3]. These symptoms can profoundly impact on the patient's daily activities and quality of life, causing severe disabilities [3].

Suzukamo and his colleagues [4] affirmed that the effect of the psychological burden on the quality of life in PD patients was even greater than the severity of the disease itself. As a consequence, PD patients need psychological intervention in addition to pharmacological efforts in order to improve the perception of their QoL.

A recent review [2] investigated which neuropsychiatric symptoms were potential determinants of HRQoL in PD and the authors underlined that until now depression and anxiety were the most neuropsychiatric manifestations investigated. The impact of depression on HRQoL has been consistently found in all studies which investigated only the depression as potential determinant; however, when depression was investigated in association with

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other neuropsychiatric symptoms (e.g apathy and anxiety), the results were mixed: some studies found that depression impacted negatively HRQoL whereas others did not. Moreover, the studies investigating the role of apathy in HRQoL also provided discordant results; the divergence could depend on different methodological procedures used to measure the apathy: some studies used global tools for non-motor symptoms whereas others employed specific questionnaires (i.e. Lille Apathy Rating Scale, Apathy Scale) which do not consider the possible effect of motor dysfunctions of PD [2].

It is also necessary to underline that anhedonia and functional impact of cognitive impairment have never been investigated as possible contributors to HRQoL, whereas the influence of impulse control disorders (ICDs) were investigated in association with other non-motor symptoms only in three studies which provided discordant results [2]. Taking into account the abovementioned reports and their limitations we better explored which non-motor symptoms contribute to poor HRQoL in PD, by means of symptom-specific scales [2].

2. Materials and methods

We enrolled consecutive 84 PD outpatients referred to our centre. To be included in the study each patient had to meet the following criteria: 1) a diagnosis of idiopathic PD according to clinical criteria; 2) free from dementia and other neurodegenerative disorders other than PD. Demographic and clinical features (i.e., disease duration, Levodopa Equivalent Daily Dose, and severity of motor symptoms assessed by part III of Unified Parkinson's Disease Rating Scale (UPDRS-III) and Hoehn & Yahr (H&Y)) were recorded.

All PD patients underwent the Montreal Cognitive Assessment (MoCA) for the evaluation of global cognitive functioning. Moreover, they completed the following self-report questionnaires: the Parkinson's Disease Questionnaire (PDQ-8) to evaluate the HRQoL; the Beck Depression Inventory-II (BDI-II) to evaluate depression; the Italian version of the Dimensional Apathy Scale (DAS; developed with the purpose to minimize the effect of motor disability), to evaluate apathy; the Italian Observer-rated version of the Parkinson Anxiety Scale (OR-PAS: A, B, C) to evaluate persistent (OR-PAS-A), episodic anxiety (OR-PAS-B) and avoidance behaviour anxiety (OR-PAS-C); the Temporal Experience of Pleasure Scale (TEPS) and the Parkinson's Disease Cognitive Functional Rating Scale (PD-CFRS) to evaluate anhedonia and the functional impact of cognitive impairment in PD, respectively. The Minnesota Impulsive Disorders Interview (MIDI) was administered to evaluate ICDs. The references of the neurological, behavioural and cognitive tools are reported in Supplemental Material 1.

2.1. Statistical analysis

Descriptive statistics were reported as mean and standard deviation. To identify PD patients with high and low HRQoL, we refer to the median of the PDQ-8 total score, as cut-off value has never been provided in literature before.

Demographic and clinical comparisons between patients with high and low HRQoL were performed by the *t*-test or Mann-Whitney *U* test (for H&Y stages). To compare the two groups on cognitive and neuropsychiatric variables, multivariate analysis of variance (MANOVA) was applied.

The association between PDQ-8 score and clinical, cognitive or neuropsychiatric scores was explored using Pearson correlation coefficient or Spearman correlation coefficient (for H&Y stages). Finally, non-motor parameters attaining a significant correlation with PDQ-8 were included as independent variables in a linear regression analysis where PDQ-8 was entered as a dependent variable.

All analyses were performed using SPSS-20 (SPSS Inc., Chicago, IL) with p value < 0.05 considered statistically significant.

3. Results

The sample included 84 PD patients: 42 patients (50%) had a PDQ-8 score < 8.50 (i.e., median of PDQ-8; H-HRQ group) whereas the remaining 42 patients had a score > 8.50 (L-HRQ group). H-HRQ and L-HRQ groups did not differ on demographic and clinical features, but they showed a significant difference in the following measures: MoCA, BDI-II, DAS, OR-PAS, and PD-CFRS (Table 1). In detail, the L-HRQ subgroup showed a lower MoCA score and a higher score on questionnaires assessing depression, apathy, anxiety and functional impact of cognitive impairment.

Correlational analysis revealed a moderate correlation between the total MoCA score and PDQ-8 total score ($r = -0.358$, $p = 0.001$). Moreover, PDQ-8 was strongly correlated with PD-CFRS ($r = 0.657$, $p < 0.001$), BDI-II ($r = 0.595$, $p < 0.001$), OR-PAS ($r = 0.737$, $p < 0.001$) and all three subscales (OR-PAS-A, $r = 0.622$, $p < 0.001$; OR-PAS-B, $r = 0.672$, $p < 0.001$; OR-PAS-C, $r = 0.621$, $p < 0.001$), total DAS ($r = 0.501$, $p = <0.001$) and Executive ($r = 0.665$, $p < 0.001$) and Cognitive/Behavioural Initiation subscales scores ($r = 0.394$, $p = 0.001$). No correlation between PDQ-8 and clinical features was found.

Linear regression analysis (with corrected $R^2 = 0.617$, $F(3, 52) = 30.476$, $p < 0.001$) showed that high OR-PAS (A, B, C) (Beta = 0.389, t = 3.510, p = 0.001, 95% Confidence Intervals: 0.113–0.414) and PD-CFRS (Beta = 0.283, t = 2.381, p = 0.021, 95% Confidence Intervals: 0.079–0.924) total score and Executive subscale score of the DAS (Beta = 0.251, t = 2.132, p = 0.038, 95% Confidence Intervals: 0.019–0.633) were significantly related to high PDQ-8 total score (Table 2). Moreover, we found that 22% of the variance of the outcome was explained by independent effect of the significant predictors, whereas 42% of the variance was explained by overlapping effects of the independent variables. However, our results from regression did not seem to be influenced by problems with multicollinearity as evidenced by collinearity indexes (i.e. VIF and tolerance).

4. Discussion

The present study revealed that patients with a reduced HRQoL showed a poorer cognitive performance and more severe neuropsychiatric symptoms (i.e., depression, apathy, anxiety) than patients with a high level of HRQoL. Moreover, we found that a higher level of anxiety and apathy, a more reduced functional autonomy contributed significantly to reduce HRQoL in PD patients. Finally, no significant correlation between HRQoL and patient's clinical features was found, indicating that the HRQoL might be independent by the severity of PD.

Our results of an association between more severe cognitive impairment and poorer HRQoL are consistent with previous studies where the cognition was evaluated by global cognitive battery [5] or neuropsychological tests [6].

As for the neuropsychiatric symptoms assessment, we found that patients with low HRQoL were more depressed than patients with high HRQoL as previously reported [2]. Previous studies reported that a poor HRQoL in PD patients was associated with a higher level of anxiety, measured by symptom-specific scales not specifically developed for PD population (e.g. Hospital Anxiety and Depression Scale) [7]. In the present study, we demonstrated that a poor HRQoL is negatively influenced by a higher level of anxiety measured by the Observed-rated version of the PAS, developed and

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