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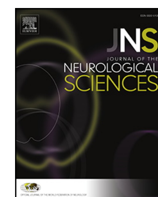

Review Article

Reprint of “Neuropsychiatric symptoms, behavioural disorders, and quality of life in Parkinson's disease”☆

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ABSTRACT

Parkinson's disease is a complex neurodegenerative disorder characterized by motor and non-motor symptoms, with neuropsychiatric manifestations among the most frequent non-motor symptoms. Health-related quality of life is a patient-reported outcome that reflects the impact of the disease on physical, mental, and social wellbeing, and on other aspects of patient' life. Although older studies on health-related quality of life in Parkinson's disease mainly investigated the role of the motor impairment, recent research focused on non-motor symptoms has highlighted the critical role that behavioural disturbances due to neuropsychiatric symptoms play in determining health related quality of life. A considerable number of studies have demonstrated the importance of depression as a determinant of health-related quality of life in this population, but less evidence is available regarding the role of other neuropsychiatric symptoms such as anxiety, apathy, psychosis, and impulse control disorders. This narrative review analyses recent literature on this topic, focusing on studies in which neuropsychiatric symptoms were investigated as potential determinants of quality of life using regression techniques, including discussion of the assessment tools used.

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1. Introduction

Parkinson's disease (PD) is a complex neurodegenerative disorder causing motor and non-motor symptoms (NMS). Even though motor symptoms have historically been identified as the most relevant aspect of the disease [1], recent research has highlighted the relevance of NMS in the clinical spectrum. NMS occurring in PD cover a wide variety of manifestations, including autonomic, sensorial, cognitive, and neuropsychiatric symptoms [2]. Neuropsychiatric features (NPS) are among the most frequently reported NMS in PD [3,4] (Table 1) and accompany other features of the disease in both early and late stages, or might even precede the diagnosis of PD [11].

Neuropsychiatric symptoms severely affect patients' global health, and their behavioural manifestations have disruptive effects on familial and social dynamics, may result in nursing home placement [12] and,

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Table 1
Prevalence of neuropsychiatric features in Parkinson's disease.

NPS	Prevalence in PD	Reference
Major depressive disorder	17%	Reijnders et al. [5]
Minor depression	22%	
Dysthymia	13%	
Anxiety	31% (24.5%–46.7%)	Broen et al. [6]
Apathy	39.8% (34.6–45%)	Den Broek et al. [7]
Impulse control disorders	6–18.4%	Zhang et al. [8]
Dopamine dysregulation syndrome	3–4%	
Psychotic symptoms	16%–75%	Chang et al. [9]
Visual hallucinations	22–38%	Fénelon et al. [10]
Auditory hallucinations	0–22%	
Minor psychotic symptoms	17–72%	
Delusions	5%	

finally, cause a severe negative impact on patient quality of life and caregivers' burden [13,14].

Health-related quality of life (HRQoL) is a fraction of the global quality of life and can be defined as “the perception and evaluation by patients themselves of the impact caused on their life by the disease and its consequences” [15]. HRQoL assessment is relevant to obtain a complete evaluation of the patient's condition, addressing priorities in care, and allowing more global monitoring that goes beyond the clinical evaluation. Although past studies on HRQoL in PD focused mainly on motor symptoms, more recent and inclusive studies demonstrated that non-motor symptoms, especially NPS, are relevant to patients' quality of life [16].

The aim of the present review is to summarize the results of studies exploring the impact of behavioural disturbances due to NPS on the HRQoL of patients with PD.

2. Methods

This is a narrative review on NPS-related behavioural changes as predictors of patients' HRQoL. Depression, anxiety, apathy, impulse control disorders (ICDs), dopamine dysregulation syndrome (DDS) and psychotic symptoms have been considered for the present review. The authors carried out an independent literature search from January 2006 to August 2016 in PubMed. In addition, peer-reviewed publications from personal archives and references of other publications were considered. Only studies that performed regression techniques to identify determinant factors of HRQoL and included NPS as independent variables were considered. The literature search was not exhaustive and used the following terms: Parkinson's/Parkinson's disease [AND] quality of life [AND] neuropsychiatric symptoms/behaviour* [OR] behavior*/depression/anxiety/apathy/hallucinations/delusions/psychosis/impulse control disorders/dopamine dysregulation syndrome. The articles included in the review were selected on the basis of their contribution to the global knowledge on the topic or specific findings that made the publication relevant (e.g., discrepancy with previous studies). Discrepancies and doubts about inclusion of particular data were discussed between the authors until reaching agreement.

3. Results

Fifty-two studies were initially considered for inclusion. Fourteen studies were excluded due to incomplete information, lack of regression analysis, etc. Therefore, thirty-eight articles were examined in detail for the present review [17–54]. All studies were clinic-based, except three population-based studies [17–19], and all were cross-sectional with exception of three longitudinal studies [17,18,20] and one retrospective cohort study [21].

3.1. Assessments

The studies included in this review used at least one specific tool to evaluate HRQoL in PD patients [Table 2]. The questionnaires used were the PD Questionnaire 39 Items (PDQ-39) [55]; its short form, the PD Questionnaire 8 Items (PDQ-8) [56]; the Parkinson's Disease Quality of Life Questionnaire (PDQL) [57]; and the Scales for Outcomes in Parkinson's Disease-Psychosocial questionnaire (SCOPA-PS) [58]. Other instruments not specific to PD were also used, such as the Short Form Health Survey (SF-36) [59], EQ-5D [60], Nottingham Health Profile (NHP) [61], and Subjective Rating of Perceived QoL (PQ10) [43]. To be highlighted, the majority of these studies used specific or generic HRQoL assessments that have been recommended by the Movement Disorders Society (MDS) [62].

The instruments used to assess NPS for each study are shown in Table 2. These measures were used as independent variables (predictors) in the multiple regression models built to investigate the influence of the respective NPS on the HRQoL of patients. To assess anxiety and depression simultaneously, the most used scale was the Hospital Depression and Anxiety Scale (HADS) [63]. To specifically assess depression, the majority of the studies reviewed used rating scales for depression recommended by the MDS [64], and the most used was the Beck Depression Inventory (BDI) [65]. Regarding anxiety, none of the scales reviewed by the MDS Task force in 2008 met the criteria to be recommended [66]. In the present review, besides the studies that used the HADS, the most used scale for anxiety was the Beck Anxiety Inventory (BAI) [67].

To assess apathy, the Apathy Scale (AS) [68] is the only MDS recommended tool [69]. Two studies used the Lille Apathy Rating Scale (LARS) [70]. This scale reached a recommendation of “suggested” in the MDS review as it still had not been used by other researchers apart from the developers [69]. Nonetheless, since it has been recently used by independent groups [71,72] at present, it would be considered “recommended”.

No MDS recommendation on instruments to assess ICDs in PD is currently available. However, the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP) [73] is considered a valid instrument for screening of ICDs in PD patients [74]; one of the studies considered in the present review used this tool for this purpose.

Currently, no scale has been recommended by the MDS for testing psychotic symptoms in PD patients [75]. To this purpose and for simultaneously assessing other neuropsychiatric symptoms, some studies used comprehensive tools such as the Neuropsychiatric Inventory (NPI) [76], UPDRS Part I [77], MDS-UPDRS part I [78], Non-Motor Symptoms Questionnaire [79], the Non-Motor Symptoms Scale [80], the Ardouin Scale of Behaviour in PD (ABSP) [81], the Scale for Evaluation of Neuropsychiatric Disorders in PD (SEND-PD) [82].

Table 2 shows authors and references of the considered studies with their respective assessments of HRQoL and NPS.

3.2. NPS as predictors of quality of life

Table 3 shows details of each study included in the review.

Depression was the most frequently explored NPS as determinant of HRQoL. Accordingly with previous findings [83], several studies considered in this review identified depression as the most important neuropsychiatric symptom influencing HRQoL [18,27,31,37,39,43–45,48,52], and the wide majority of them identified depression as an independent determinant factor of HRQoL [17–19,21–28,30–32,37,38–41,43–46,48,51,52,54]. However, it should be noted that the wide heterogeneity across studies (in design, objectives, number and type of considered NPS, and factors used as independent variables) precludes direct comparisons. For example, some studies evaluated the impact of depression on HRQoL together with motor and non-motor symptoms, but without including other NPS in their analysis [19,21,22,24,28,30,32,33,38,43]. Nevertheless, these studies consistently found that depression was a

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