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Anxiety in Parkinson's disease: Symptom dimensions and overlap with depression and autonomic failure

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ABSTRACT

Introduction: Anxiety disorders are highly prevalent in patients with Parkinson's disease (PD) and have a major impact on wellbeing. They nevertheless receive limited scientific attention. This study aimed to establish the symptom dimensions of anxiety in PD, and their relationship with depression, autonomic failure and motor symptoms.

Methods: In this cross-sectional observational study, symptoms of anxiety were measured with the Beck Anxiety Inventory (BAI) in 294 PD patients. Symptom dimensions of anxiety in PD were explored through principal component analysis (PCA) of BAI items. The relationship between anxiety and depressive, autonomic and motor symptoms was assessed through PCA and regression analyses.

Results: Clinically relevant symptoms of anxiety were present in 45% of patients. PCA of the BAI resulted in five subscales, corresponding to a single affective and four somatic symptom dimensions (thermoregulation, hypotension, hyperventilation and trembling) of anxiety. Symptoms of anxiety and depression displayed a large overlap. All somatic BAI subscales were significantly influenced by motor and autonomic symptoms, while the affective subscale was not.

Conclusion: Anxiety in PD comprises affective and somatic symptom dimensions. The affective subscale of the BAI is not influenced by motor or autonomic symptoms, and may therefore prove useful for future research. Scores on the somatic subscales of the BAI were associated with autonomic failure and motor impairment, demonstrating a strong interplay between motor and non-motor symptoms in PD. These results stress the importance of a holistic approach of anxiety in PD.

1. Introduction

Despite a high prevalence and a major impact on daily functioning and quality of life in patients with Parkinson's disease (PD), anxiety has only recently attracted scientific attention. Estimates suggest that 40–50% of PD patients experience clinically relevant symptoms of anxiety [1,2], and approximately one third suffers from an anxiety disorder as specified by the Diagnostic and Statistic Manual of mental disorders (DSM) IV-TR criteria [1–4]. Generalized anxiety disorder, social phobia and anxiety disorder not otherwise specified (NOS) are most frequently diagnosed in this population [2,3,5]. Anxiety disorders are more common in PD patients than in the general population, in primary care clinics or in patients with other chronic medical conditions, where prevalence rates vary between 5 and 11% [4]. Anxiety in PD patients is associated with increased subjective motor symptoms [6], more severe gait problems [7], dyskinesias [7], freezing [8], motor response fluctuations [6], and a decrease in health-related quality of life [9].

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In clinical practice, anxiety disorders are often underdiagnosed in PD patients [10]. In a large proportion of patients with PD that report clinically relevant anxiety, the symptoms do not meet the criteria of a discrete DSM-IV disorder and are therefore classified as an anxiety disorder Not Otherwise Specified (NOS) [3]. This suggests that anxiety disorders may have an atypical presentation in this population. The poor recognition of anxiety might also be explained by the overlap and interaction with PD-related motor and non-motor symptoms, such as depression and autonomic failure.

An improvement of the diagnostics of anxiety in PD could be aided by an in-depth study of the symptom dimensions covered by self-report questionnaires such as the Beck Anxiety Inventory (BAI) [11] and their relatedness to other motor and non-motor symptoms. Factor analysis is a statistical technique that can help to explore the underlying factors or symptom dimensions covered by a questionnaire. In non-PD samples factor analysis has shown that the BAI comprises cognitive and somatic factors and that the BAI is able to differentiate between symptoms of anxiety and depression [12,13]. Dimensionality of the BAI in PD patients was only addressed in a single study [14], but no satisfactory factor solution was found, possibly due to the heterogeneity of the study sample.

In the present study, we analyzed the symptom dimensions of the BAI within a large sample of PD patients. Secondly, we assessed the overlap of symptoms of anxiety with depression, autonomic dysfunction and motor disability in PD.

2. Methods

2.1. Subjects

For this cross-sectional study, we used data collected during routine clinical assessments at the outpatient clinic for movement disorders of the VU University medical center (VUmc) in Amsterdam, the Netherlands, between May 2008 and January 2013. In this period, 383 PD patients were assessed. Patients were clinically diagnosed with idiopathic PD using the United Kingdom PD Society Brain Bank (UKPDSBB) criteria. The clinical diagnosis was supported by both magnetic resonance imaging (MRI) and dopamine transporter single-photon emission computed tomography (DAT-SPECT) scans in 244 patients, by MRI only in 37 patients and by DAT-SPECT scan only in 23 patients. In the remaining 79 patients, no brain imaging was performed. All included patients gave written informed consent to use their clinical data for scientific purposes. Patients with severe cognitive decline, defined as a Mini Mental State Examination (MMSE) score <24, were excluded.

2.2. Measurements

2.2.1. Anxiety

Symptoms of anxiety were measured with the BAI. The BAI is a 21-item self-report instrument asking for symptoms of anxiety over the past week [11]. Patients answer on a four-point Likert scale, ranging from 0 (not at all) to 3 (severely). In patients with PD, clinically relevant anxiety is defined as a BAI-score >12 [14]. This cut-off score is lower than in the general population, due to a lower construct validity of the BAI in PD patients [14].

2.2.2. Clinical and demographic factors

Age, gender and the use of dopaminergic medication (0 = no, 1 = yes) were registered for use in statistical analyses.

The independent variables of major interest were symptoms of depression, motor dysfunction and autonomic failure. We evaluated symptoms of depression with the Beck Depression Inventory (BDI) [15]. Severity of motor symptoms was assessed using section III and V (Hoehn and Yahr stage) of the Unified Parkinson Disease Rating Scale (UPDRS) [16].

We used the Scales for Outcomes in Parkinson's disease − Autonomic (SCOPA-AUT) [17] to assess autonomic failure. The SCOPA-AUT includes five questions on sexual function: item 22, 23 and 23a apply to men, and item 24 and 25 to women. The answers to these questions were unreliable on multiple occasions, e.g. patients choosing "not applicable" for all five items, or male patients answering question 24 or 25. Therefore, we decided to exclude the sexual items of the SCOPA-AUT from the analyses.

2.3. Statistical analyses

We performed all analyses using IBM SPSS Statistics 20 for Windows. The significance level was set at $p < 0.05$ with two-sided testing. Acceptability of missing values on the BAI, BDI and SCOPA-AUT was determined as less than 16.67% of items. In the event of more missing data, we excluded the patient for the analysis by pairwise exclusion. When less than 16.67% of data was missing, we filled in missing values by mean imputation. We performed no imputation of missing data on the UPDRS-III, since we considered this to be unreliable for this scale.

In the first analysis, we assessed dimensionality of the BAI with a principal component analysis (PCA). To determine the number of extracted factors we combined the Guttman–Kaiser Eigenvalue greater-than-one rule and the "scree plot" criterion. We used oblimin rotation because we expected the different factors to correlate with each other. The factors obtained in this analysis can be considered as subscales of the BAI or symptom dimensions of anxiety. Scores on the derived subscales of the BAI were used in further analyses.

Second, we studied the relationship between the BAI, BDI, SCOPA-AUT and UPDRS-III, by conducting multiple linear regression analyses. Assumptions for regression analyses (normality and homoscedasticity of residuals) were checked. Multicolinearity was evaluated with a correlation matrix and calculation of the variance inflation factor (VIF).

The total BAI score was the dependent variable in the first set of regression analyses. In the second set, it was the score on the subscale of the BAI, derived with PCA previously. The independent variables of interest were the total score on the BDI, SCOPA-AUT and UPDRS-III. We conducted all analyses first with only the independent variable of interest (unadjusted model). We then adjusted the model stepwise for age and gender (model 1), use of dopaminergic medication (model 2), and the other two independent variables of main interest, i.e. the BDI, SCOPA-AUT and/or UPDRS-III score (model 3). Finally, we examined confounding in all models.

3. Results

Of the original sample of 382 PD patients, 75 patients met exclusion criteria (MMSE <24). An additional 13 patients were excluded from the analyses for not meeting our standards of acceptability of missing values on the BAI. This resulted in a total sample size of 294 patients. Due to missing data on the BDI, UPDRS-III and/or SCOPA-AUT, 3 to 18 additional patients were excluded pair-wise during statistical analyses. The majority of patients was male. Mean age was 64.5 years. Patients had a mean UPDRS-III score of 25.8 and a median Hoehn and Yahr stage of 2. Demographic and clinical characteristics of the sample are given in Table 1.

3.1. Occurrence and symptom dimensions of anxiety in PD

The mean score on the BAI was 14.2 (SD 9.8, range 0–50). Forty-five percent of patients in our sample had a BAI score of 12 or more, which is considered to be a clinically relevant level of anxiety [14].

The Eigenvalue >1 criterium suggested that five factors should be extracted. This was confirmed by an inspection of the scree plot (see Fig. S1 in the supplementary material). Items 3 'wobbliness in legs', 7 'heart pounding/racing' and 18 'indigestion' had a loading of less than 0.4 on all factors and were therefore excluded from the factor solution.

The five obtained factors were interpreted as *anxiety*, *thermoregulation*, *hypotension*, *hyperventilation* and *trembling*. The factor solution explained 62.7% of variance. Fig. 1 demonstrates the distribution of the BAI items over the five factors, with corresponding factor loadings.

Table 1
Demographic and clinical characteristics of subjects ($n = 294$).

	Mean	SD	Range
% Female	39.5		
Age	64.5	10.3	27–89
Disease duration (yr)	5.1	5,6	0–40
MMSE score	28.0	1.7	24–30
BDI score	11.4	8.0	0–36
SCOPA-AUT score	35	10.0	0–64
UPDRS-III score	25.8	12.3	2–58
Hoehn &Yahr stage	2 (median)		1–5
% Use dopaminergic medication	48.6		

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