Anxiety Has Specific Syndromal Profiles in Parkinson Disease: A Data-Driven Approach

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Background: *Anxiety symptoms are common in Parkinson disease (PD). Recent evidence suggests that anxiety syndromes as encountered in clinical practice may not correspond to the DSM-IV classification of anxiety disorders.* **Objective:** *To examine the syndromal pattern of the anxiety spectrum in a large series of patients with PD, as determined with a data-driven approach using latent class analysis (LCA).* **Methods:** *342 patients with PD were recruited from referrals to movement disorders or psychiatry clinics at six tertiary centers. Participants were assessed with a structured psychiatric interview and specific scales rating the severity of anxiety, depression, cognition and parkinsonism. The main outcome measure was classes of patients with a specific syndromal profile of anxiety symptoms based on LCA.* **Results:** *LCA identified four classes that were interpreted as "no anxiety or depression", "episodic anxiety without depression", "persistent anxiety with depression", and "both persistent and episodic anxiety with depression". Symptoms of persistent anxiety were almost invariably associated with symptoms of depression. There were significant differences between classes in terms of history of depression and anxiety, use of psychoactive medication, and on the Mentation and Complications sections of the Unified Parkinson Disease Rating Scale.* **Conclusions:** *Patients with PD show different syndromic profiles of anxiety that do not align with the symptom profiles represented by DSM-IV anxiety disorders and major depression. Accordingly, DSM-IV criteria for anxiety disorders may not be clinically useful in PD. The different classes identified here provide empirically validated phenotypes for future research.* (Am J Geriatr Psychiatry 2013; ■:■–■)

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Anxiety is common in Parkinson disease (PD) and is associated with a negative impact on quality of life and activities of daily living, and more severe dyskinesias and motor fluctuations.[1] A major limitation to the study of anxiety disorders in PD is the lack of valid assessment instruments and valid diagnostic criteria for this patient group. The majority of studies on anxiety in PD have used DSM-IV criteria to classify the different anxiety disturbances.[2–6] Several studies, however, indicate that a significant proportion of PD patients have anxiety disturbances that are not captured by DSM-IV criteria.[1,7] Thus, it is not surprising that there are discrepancies in the reported prevalence of anxiety disorders in PD, ranging from 4%–30% for panic disorder,[3,6–8] 11%–21% for generalized anxiety disorder (GAD),[6,8] 8%–50% for social phobia,[3,4,7,8] and 11%–25% for anxiety disorder not otherwise specified.[1,7] Another important confounder is variability in the population studied (e.g., community versus tertiary care centers).

In a recent study, 34% of 342 patients with PD met DSM-IV criteria for at least one anxiety disorder, and 12% met criteria for multiple anxiety disorders.[1] GAD was the most frequently diagnosed condition (31%), but 18% of the sample that did not have a diagnosed anxiety disorder still reported clinically significant anxiety symptoms. An important confounder when assessing the frequency of anxiety in PD is the strong overlap between anxiety disorders and depression. In our study,[1] major depression was diagnosed in 26% of the patients and another 13% had dysthymia. Similar findings were reported in most studies on PD and anxiety[1,3] as well as in most studies of elderly individuals with or without neurodegenerative disorders.[9,10]

Converging evidence further supports that about one third of PD patients suffer from one or more type of anxiety disorder, but there is great variability in their relative frequency.[1] Early studies reported "episodic" anxiety (e.g., social phobia and agoraphobia in the context of non-motor fluctuations) as being more frequently reported than "persistent" anxiety (e.g., GAD),[3,7] but this has not been replicated in more recent studies.[1] Current data suggest that the present psychiatric nomenclature may lack validity to diagnose anxiety disorders in PD.[1] Therefore, the main aim of this study was to examine the validity of the most frequently diagnosed DSM-IV-based anxiety disorders in PD using a data-driven approach and latent class analysis. This technique assesses the symptom profile of individual patients and produces classes of patients as suggested by their respective pattern of symptoms. Given that the clusters thus obtained do not overlap, individual patients can only belong to one class. Similar analyses have been applied for depression in PD and Alzheimer disease.[11,12] For this study, we assessed 342 patients with PD using a structured psychiatric interview and specific scales to rate the severity of anxiety, depression, global cognitive deficits, and parkinsonism. Based on our previous findings, our hypotheses were that, first, anxiety disorders would not be present as discrete entities but would rather separate into "episodic" and "persistent" types; and second, that "persistent" anxiety would be significantly related to major depression.

METHODS

Settings and Inclusion Criteria

The PD group consisted of a series of 342 patients recruited from movement disorders, general neurology, and psychiatry clinics at six centers in the United States, Europe, and Australia. The inclusion criteria were: 1) meeting the Queen Square Brain bank criteria for idiopathic PD;[13] 2) providing written informed consent; and 3) scoring above 23 on the Mini Mental State Examination.[14] Patients with neurodegenerative or acute neurological disorders other than PD were excluded (additional information is provided in a recent publication).[1] The study was approved by the medical ethics committees at all participating centers.

Assessments

Demographic and disease-related variables were collected using an unstructured clinical interview. All patients were also assessed with the following instruments: 1) the Unified Parkinson's Disease Rating Scale (UPDRS) to assess motor function and complications of therapy;[15] 2) the Lawton Instrumental Activities of Daily Living scale to assess deficits on instrumental activities of daily living;[16] 3) the Mini International Neuropsychiatric Interview[17] (the MINI), a structured psychiatric interview that assesses the DSM-IV criteria for anxiety (and other) disorders (we used the

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