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Comprehensive identification of delusions and olfactory, tactile, gustatory, and minor hallucinations in Parkinson's disease psychosis

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ABSTRACT

Introduction: Psychotic symptoms are underdiagnosed in Parkinson's disease (PD), and there is a need for a comprehensive PD psychosis rating scale.
Methods: Cross-sectional analysis of 199 consecutive PD outpatients. After a routine clinical visit that included the Unified Parkinson's Disease Rating Scale (UPDRS) and Non-Motor Symptoms Questionnaire (NMS-Quest), subjects completed the enhanced Scale for the Assessment of Positive Symptoms in PD (eSAPS-PD), a structured clinical interview that included the standard SAPS-PD with additional prompts for delusions and olfactory, gustatory, and minor hallucinations. Based on the combined results of these assessments, subjects were categorized as having major psychotic symptoms (hallucinations or delusions; PDP-major), isolated minor psychotic symptoms (passage hallucinations, presence hallucinations, or illusions; PDP-minor), or no psychotic symptoms (PD-controls).
Results: We identified 58 subjects (29%) with psychotic symptoms, including 28 (14%) with major psychotic symptoms and 30 (15%) with isolated minor psychotic symptoms. Hallucinations were present in 56 subjects (28%); most commonly visual (24%, of which 21% were minor only), followed by olfactory (6%), tactile (4%), auditory (2%), and gustatory (1%). The eSAPS-PD detected psychotic symptoms in more subjects ($n = 55$, 28%) than all other assessments combined (clinical visit, UPDRS part 1, and NMS-Quest) ($n = 22$, 11%). Compared with PD-controls, PDP-minor subjects had a higher burden of other non-motor symptoms on the Non-Motor Symptoms Scale (37 [27–51] vs. 18 [9–36], $p < 0.001$) and lower quality of life scores on the PD Quality of Life Questionnaire (138 [125–151] vs. 149 [137–165], $p = 0.01$).
Conclusion: The eSAPS-PD can markedly improve detection of psychotic symptoms in PD.

1. Introduction

In addition to the classic motor features, Parkinson's disease (PD) encompasses a wide range of non-motor symptoms, including psychiatric, cognitive, and autonomic manifestations. Amongst these non-motor symptoms, PD psychosis (PDP) has been increasingly recognized as a common component of PD. PDP has been associated with multiple adverse outcomes, including increased caregiver burden [1], more frequent nursing home placement [2,3], and higher mortality [2,3]. Risk factors for PDP include advanced age, cognitive impairment, dementia, and medication use [4].

Auditory and visual hallucinations in PD have been heavily researched and thoroughly described in the literature. In contrast, hallucinations of other sensory modalities (including olfactory, gustatory, and tactile hallucinations), minor hallucinations (including illusions, passage hallucinations, and presence hallucinations), and many types of delusions remain understudied [4,5]. Minor hallucinations are now thought to be the most common type of hallucination in PD, potentially predating the onset of motor symptoms [6]. Most studies that have examined uncommon delusions or olfactory, gustatory, tactile, or minor hallucinations have focused on a specific type, but relatively few have attempted to look at all major and minor psychotic symptoms in PD simultaneously within a single cohort [7–9]. This is at least partially because of the lack of a validated scale that encompasses the full spectrum of PDP symptoms. Both the American Academy of Neurology Quality Standards Subcommittee (2006) [10] and the Movement Disorder Society (MDS) Task Force (2008) [11], as well as updated reviews (2009, 2016) [12,13], concluded that no existing scale comprehensively covers the entire phenomenology of PDP, and that a new PDP

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scale should be developed. The Psychosis and Hallucinations Questionnaire (PsycH-Q), which probes for delusions and minor, visual, auditory, olfactory, gustatory, and tactile hallucinations, was subsequently developed and validated in a cohort of non-demented PD patients in Australia [14]. The PsycH-Q is self-administered, however, and thus may be of limited utility in patients with loss of insight or advanced dementia.

While the MDS Task Force found no existing scale to be ideal, they recommended the Scale for the Assessment of Positive Symptoms (SAPS). This scale was originally developed to evaluate psychosis in patients with schizophrenia, and therefore contains many questions that are not pertinent to PD psychosis [11]. The SAPS-PD is a shortened version of the SAPS that excludes many of the questions that are not relevant to PD [15]. This SAPS-PD is administered in the form of a semi-structured clinical interview, and while it provides "suggested probes" to guide the interview, it is designed to be adapted at the discretion of the examiner to maximize detection of all potential psychotic symptoms. This format makes it highly amenable to modification in a way that preserves the integrity of the original scale and scoring system. The current template of the SAPS-PD, however, does not include probes for less common delusions, nor does it evaluate olfactory, gustatory, or minor hallucinations. In order to facilitate the systematic and comprehensive identification of the full spectrum of PDP symptoms, we have developed a structured clinical interview based on the SAPS-PD, to which we have added specific prompts for these less commonly studied psychotic symptoms.

2. Methods

2.1. Subjects

Consecutive outpatients with PD (n = 199) were recruited from the Marlene and Paolo Fresco Institute for Parkinson's and Movement Disorders at the NYU School of Medicine between June 2015 and April 2017. Subjects were eligible for inclusion if they met United Kingdom Parkinson's Disease Society Brain Bank criteria, were able to provide informed consent, and were able to complete the research questionnaires. Subjects were excluded from the study if they had atypical or drug-induced parkinsonism, prior neurosurgery, a life expectancy of <1 year, or an alternative cause for psychotic symptoms. The study was approved by and performed in accordance with the NYU School of Medicine Institutional Review Board. Written informed consent was obtained from all subjects prior to enrollment.

2.2. Data collection

All subjects completed a routine clinical appointment with a movement disorders specialist, including a full Unified Parkinson's Disease Rating Scale (UPDRS), Non-Motor Symptoms Questionnaire (NMS-Quest), modified Hoehn & Yahr staging (H&Y), and Schwab & England Activities of Daily Living Scale (S&E). Subjects were subsequently evaluated with a standardized battery of cognitive, psychiatric, and quality of life scales. These included the enhanced SAPS-PD (eSAPS-PD; Supplemental Fig. 1), a novel structured clinical interview that is based on the SAPS-PD, but has additional, specific questions about less common delusions and about olfactory, gustatory, and minor hallucinations. Administration of the eSAPS-PD took about 1–2 min in subjects who reported no psychotic symptoms, and up to 10 min in those with numerous or complex psychotic symptoms. Other questionnaires included the Montreal Cognitive Assessment (MoCA), Non-Motor Symptoms Scale (NMSS), Beck Depression Inventory-II (BDI-II), Beck Anxiety Inventory (BAI), and Parkinson's Disease Quality of Life Questionnaire (PDQL). Subjects who were unable to complete the entire battery of questionnaires on the day of the clinical appointment were given the option of completing them by telephone or returning to the office for a separate visit within 3 months of the initial office visit. Chart reviews of the EpicCare Ambulatory electronic medical record were used to obtain additional demographic and clinical data. Levodopa equivalent daily doses (LEDD) [16] and postural instability-gait disturbance (PIGD) scores [17] were calculated as previously described. All data were recorded on case report forms and entered into a secure electronic database (Research Electronic Data Capture; REDCap) [18].

2.3. Subject characteristics

Subjects were classified as having major psychotic symptoms (PDP-major) if hallucinations or delusions were detected by one or more of the following assessments: clinical impression (as determined by chart review), eSAPS-PD (score ≥1 on questions 2–13), UPDRS part 1 (score ≥2 on question 2), or NMS-Quest ("yes" to questions 14 or 30). Subjects were classified as having isolated minor psychotic symptoms (PDP-minor) if they had no major psychotic symptoms, but endorsed passage hallucinations, presence hallucinations, or illusions on any of these assessments. Subjects who had neither major nor minor psychotic symptoms were classified as PD-controls.

2.4. Statistical analysis

Descriptive statistics (including mean, median, standard deviation, and interquartile range for continuous variables, and frequency and percentage for categorical values) were calculated for demographic, motor, and non-motor characteristics of PD subjects in the PDP-major, PDP-minor, and PD-control groups. For the assessment of non-motor scores other than psychosis, the following questions about hallucinations and delusions were excluded from scoring: UPDRS part 1 (question 2), NMS-Quest (questions 14 and 30), and NMSS (questions 13 and 14). Univariate relationships between psychotic symptom group and these baseline characteristics were determined for the PDP-minor versus PD-control groups, as well as for the PDP-minor versus PDP-major groups. The Shapiro-Wilk test was used to determine the normality of continuous variables. The independent two-sample *t*-test or Mann-Whitney *U* test were used for continuous variables and the chi-square test or Fisher's exact test were used for categorical variables. All p-values are two-sided with statistical significance evaluated at the 0.05 alpha level. Due to the exploratory nature of the study, there was no correction for multiple comparisons. All analyses were performed using IBM SPSS Statistics Version 23.

3. Results

3.1. Prevalence and characteristics of psychotic symptoms in the cohort

Of the 199 subjects recruited for the study, 58 (29%) had psychotic symptoms identified by one or more clinical assessments. This included 28 subjects (14%) with major psychotic symptoms (PD-major) and 30 subjects (15%) with isolated minor psychotic symptoms (PD-minor). The remaining 141 subjects (71%) had no evidence of psychosis (PD-control).

As shown in Fig. 1, hallucinations (major and minor) were present in 56 subjects (28%). These were most commonly visual (47 subjects), followed by olfactory (11 subjects), tactile (7 subjects), auditory (3 subjects), and gustatory (2 subjects) hallucinations.

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