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Prevalence of Psychotic Symptoms in a Community-Based Parkinson's Disease Sample

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Abstract

Objectives—To determine the prevalence of psychotic phenomena, including minor symptoms, in a Parkinson's disease (PD) sample and compare the clinical correlates associated with the various psychotic phenomena. To evaluate the extent to which cases met NINDS/NIMH proposed criteria for PD-associated psychosis.

Methods—250 patients with idiopathic PD and MMSE>23 from three community-based movement disorder clinics underwent comprehensive research diagnostic evaluations by a geriatric psychiatrist as part of a study on mood disorders in PD. Psychotic symptoms were categorized using a checklist, which included a breakdown of hallucinations, delusions and minor symptoms. Clinical characteristics of groups with minor and other psychotic symptoms were compared. The NINDS/NIMH criteria for PD-psychosis were retrospectively applied.

Results—Of the total sample, 26% of patients were found to have any current psychotic symptoms, with 47.7% of those having isolated minor symptoms, and 52.3% having hallucinations and/or delusions. Compared to those with no current psychiatric symptoms, minor symptoms were associated with more depressive symptoms and worse quality of life. 90.8% of those with psychotic symptoms fulfilled the NINDS/NIMH proposed criteria.

Conclusions—Psychotic symptoms are common in PD patients, with minor psychotic phenomena present in nearly half of affected patients in a community-based sample. Psychotic symptoms, including minor phenomena, were clinically significant. The NINDS/NIMH PD-

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psychosis criteria captured the clinical characteristics of psychosis as it relates to PD. Longitudinal studies are needed to determine whether minor psychotic symptoms represent a precursor to hallucinations and delusions, and to further validate diagnostic criteria.

Keywords

Psychosis; Parkinson's disease; Hallucinations; Delusions

Objectives

Patients with Parkinson's disease (PD) commonly experience neuropsychiatric symptoms [1,2]. Psychotic symptoms are especially prevalent, and are associated with greater physical disability, cognitive and affective dysfunction, caregiver distress, nursing home placement, and mortality [3–5]. However, the temporal and clinical profile of psychosis in PD is different from other psychotic disorders, such as schizophrenia or mood disorders with psychotic features. Therefore, definitions and schemas applied to other psychiatric illnesses have limited utility for describing and quantifying the scope of psychotic phenomena in PD.

Psychotic symptoms in PD include hallucinations and delusions, which define psychosis typically. There are also atypical symptoms, referred to as minor psychotic phenomena, which include sense of presence, passage hallucinations, and illusions (see Appendix). Furthermore, hallucinations are usually visual, although other sensory modalities can be involved. Cross-sectional prevalence estimates indicate that approximately one-third of patients experience psychosis, although published rates range from 16% to 75% [7–19]. The variability in reported prevalence of PD-psychosis is attributed to use of different criteria to define psychosis and inconsistencies in which psychotic phenomena were examined [6].

Minor phenomena, in particular, have been excluded from most studies on PD-psychosis. Reported prevalence for minor phenomena ranges from 17% to 72% [11,17,18,20]. The paucity of data on minor phenomena is likely due to the fact that these symptoms are not included in usual definitions of psychosis, e.g., the Diagnostic and Statistical Manual for Mental Disorders 4th Edition, Text Revision (DSM-IV-TR) [21]. Furthermore, no currently available rating scale adequately captures the phenomenology of PD-psychosis, including minor symptoms [22]. As a result, little is known about the clinical significance of minor phenomena. A National Institutes of Health (NIH) National Institute of Neurological Diseases and Stroke (NINDS)/National Institute of Mental Health (NIMH) workgroup proposed diagnostic criteria for PD-psychosis, including minor symptoms, to better define and standardize the unique features of PD-psychosis [23].

The present study determined the prevalence of hallucinations, delusions and minor psychotic symptoms in a PD sample from community-based movement disorders clinics, examined relationships between minor phenomena, hallucinations and delusions, and other clinical variables, and evaluated the extent to which cases met the NINDS/NIMH proposed criteria for PD-related psychosis.

Methods

Subjects

Subjects were a convenience sample recruited from a pool of 747 patients with idiopathic PD from three community-based movement disorder neurology practices. Patients were mailed letters by their neurologist asking them to participate in a study evaluating the psychometric performance of depression rating scales in patients with PD [the Methods of Optimal Depression Detection in PD (MOOD-PD) study]. Two hundred and eighty-seven

patients enrolled and completed initial screening. Eighteen subjects were excluded for Mini-Mental State Examination (MMSE) [24] score ≤ 23 , failure to meet United Kingdom Brain Bank (UKBB) criteria for idiopathic PD [25], inability to read or speak English fluently, or inability to complete study procedures. Two hundred and sixty-nine patients met screening criteria and completed questionnaires, which identified by self-report or informant those who (1) endorsed any degree of depression, apathy, anxiety, or irritability, (2) had been prescribed psychiatric medications, or (3) reported a history or a current diagnosis of a depressive disorder. Initially, subjects endorsing criteria 1, 2, or 3 and every fourth subject not meeting criteria 1, 2, or 3 were asked to take part in a diagnostic psychiatric interview. After only ten of the first 143 subjects failed to qualify for diagnostic interviews using these criteria, subsequent participants meeting initial screening criteria were considered eligible for diagnostic interviews. Of the 259 subjects referred for diagnostic evaluations, nine withdrew or were lost to follow-up. The 250 subjects completing diagnostic interviews are the focus of this analysis. The Johns Hopkins Institutional Review Board approved the study; participants and, when available, informants provided informed consent.

Assessment

The screening visit included the MMSE and the Unified Parkinson's Disease Rating Scale (UPDRS) [26] parts II and IV administered by the study coordinator, the UKBB criteria, UPDRS Part III, and Hoehn and Yahr stage (HY) [27] completed by the neurologist, and the 8-item Parkinson's Disease Quality of Life Questionnaire-8 (PDQ-8) [28] completed by the subject. The levodopa equivalent dose was calculated for each subject [29].

For 223 of 250 subjects completing diagnostic interviews, informants were interviewed by the study coordinator using the Composite International Diagnostic Interview-Short Form (CIDI-SF) [30] and the Informant Interview for the Diagnosis of Dementia and Depression in Older Adults (IDD-GMS) [31] to obtain collateral psychiatric and cognitive history.

The diagnostic interview was conducted by a geriatric psychiatrist using the DSM-IV Schedule for Clinical Interview and Diagnosis (SCID) [32] plus supplemental questions to obtain lifetime and current psychiatric history not included in the SCID and to evaluate current cognitive and motor status. In the context of the diagnostic interview, the psychiatrist also rated the Hamilton Depression Rating Scale-17 (HAM-D-17) [33] and a modified Neuropsychiatric Inventory (NPI) (completed as a direct interview with the subject instead of an informant interview) [34].

Psychotic symptoms, including minor phenomena, were further assessed during the diagnostic interview using a checklist developed by the study team (see Appendix). Psychotic symptoms were considered 'current' if they occurred within the past month or if they had been present but were controlled and in remission only as a result of ongoing antipsychotic medication treatment. Current and past hallucinations were assessed as to whether or not they were "benign", i.e., with retained insight and not affecting daily function. The NINDS/NIMH proposed diagnostic criteria for PD-psychosis, which were developed after the onset of the MOOD-PD study, were applied retrospectively to evaluate prevalence of cases that met criteria.

Final consensus current and lifetime best-estimate psychiatric diagnoses [35] were established by a panel of six psychiatrists with expertise in geriatrics or movement disorders that met monthly to review each subject's history and all collected data. Diagnoses were based on DSM-IV-TR criteria, but also included clinically significant disturbances irrespective of DSM-IV-TR, such as with PD-psychosis. The forty subjects found to have no current psychiatric symptoms functioned as the control group for further comparisons.

Analyses

χ^2 and t-tests were used to test group differences between patients with and without psychosis. Analysis of variance (ANOVA) and analysis of covariance (ANCOVA) with Sidak corrected post-hoc comparisons were used to test for group differences across psychosis subgroups. Statistical analyses were carried out using PASW Statistics 18 (SPSS, Inc., Chicago, IL). Statistical significance was set *a priori* at $p \leq 0.05$.

Results

The demographic and clinical features for the 250 subjects completing the diagnostic evaluation are shown in Table 1. The sample was two-thirds male and almost all individuals were living in their own home. Based on study criteria, no subject had a MMSE score below twenty-four.

Sixty-five subjects (26%) had current psychotic symptoms (PSY). The prevalence of specific psychotic symptoms is shown in Table 2. Twelve PSY subjects (18.5%) were taking antipsychotic medications, resulting in controlled (remitted) symptoms in eight subjects. Thus, fifty-seven subjects (22.8%) were symptomatic at the time of the diagnostic interview. The mean (SD) duration of psychotic symptoms was 132.5 (127.8) weeks (range 1 to 624 weeks, $n=61$). Duration of psychosis could not be determined in four subjects. Thirty-one PSY subjects (47.7%) had isolated minor symptoms (MIN), whereas the remaining thirty-four (52.3%) had hallucinations and/or delusions (H/D). Delusions were present in eight subjects, although symptoms were controlled (remitted) in six due to antipsychotic treatment. Only one subject had isolated delusions in the absence of concurrent hallucinations. Eight subjects in the MIN group reported more than one type of minor hallucination, whereas six patients in the H/D group reported multiple types of minor hallucinations. Eighty-two subjects (34.4%) reported a lifetime history of psychosis with fifty experiencing hallucinations, thirty-two minor symptoms, and ten delusions.

Fifty-nine PSY subjects (90.8%), or 23.6% of the total sample, met the NINDS/NIMH proposed criteria for PD-psychosis. For the six subjects not meeting criteria, three had duration of current psychotic symptoms less than one month and three had psychotic symptoms as a component of a mood disorder. Six subjects meeting NINDS/NIMH criteria were diagnosed with dementia due to PD by the consensus panel. Psychotic phenomena were reported as “benign” in all subjects in the MIN group and twenty out of thirty-two in the H/D group. All subjects meeting NINDS/NIMH criteria were being treated with antiparkinsonian medications.

Forty subjects (16%) reported no current psychiatric symptoms (NoP). The percentage of subjects with informant interviews was comparable for the NoP, MIN, and H/D groups (87.5% vs. 87.1% vs. 88.2%, respectively, $\chi^2=0.202$, $df=2$, $P=0.99$).

The demographic and clinical differences between PSY and NoP subjects are shown in Table 3. Compared to NoP, PSY subjects were younger and had a younger age of PD onset and longer duration of PD symptoms. While motor deficits were comparable across groups, PSY subjects reported greater activities of daily living (ADL) disability, based on the UPDRS Part II subscore. PSY subjects also experienced more depressive symptoms and reported worse quality of life (higher PDQ-8 scores). Significantly more PSY than NoP subjects met DSM-IV-TR criteria for diagnosis of Cognitive Disorder, Not Otherwise Specified (NOS) [43.1% ($n=28$) vs. 7.5% ($n=3$), $\chi^2=15.1$, $df=1$, $P<0.0001$] despite comparable MMSE scores across groups; however rates of dementia were comparable across the two groups [(10.8% ($n=7$) vs. 7.5% ($n=3$), $\chi^2=0.31$, $df=1$, $P=0.51$].

For the psychosis subgroups, the mean (SD) psychotic symptom duration was 85.2 (71.4) weeks for MIN (n=30) and 178.3 (152.7) weeks for H/D (n=31) [$t(59)=-3.04$, $p=0.004$]. Compared to MIN, H/D had an earlier age of PD onset [Mean(SD) 58.2(10.6) vs. 50.1(14.1), $F(2,102)=11.9$, $p=0.025$], and longer duration of PD symptoms [Years, Mean(SD) 7.7(4.7) vs. 12.45(9.2), $F(2,102)=9.5$, $p=0.012$]. Table 4 shows the demographic and clinical difference between NoP subjects and PSY subjects broken out as MIN and H/D groups, after adjustment for age, gender, years of education, duration of PD symptoms, and severity of depressive symptoms. Compared to NoP, MIN had lower quality of life and higher depressive symptom scores. Compared to MIN, H/D had greater depressive symptom scores. There were no significant differences between NoP, MIN and H/D in the levodopa equivalent dose.

Discussion

The present study reported the prevalence of all forms of psychotic phenomena, including minor phenomena, in a community-based, convenience sample of outpatients with idiopathic PD and MMSE>23. It also examined the validity of the NINDS/NIMH criteria for PD-psychosis against consensus diagnoses made by an expert panel. In this sample, the prevalence of any current psychotic symptom was 26% when based on consensus diagnoses from an expert panel, and 23.6% when based on the proposed NINDS/NIMH criteria. The presence of psychosis, in general, was associated with an earlier age onset of PD and a longer PD duration. Additionally, relative to NoP, PSY was younger with greater ADL disability, depressive symptoms, and cognitive dysfunction, as well as a worse quality of life. Minor psychotic phenomena alone were associated with significantly greater depressive symptoms and worse quality of life. Thus, regardless of the form of psychotic phenomena, psychotic symptoms in PD are associated with an increased disease burden and morbidity.

Greater ADL disability associated with H/D relative to NoP supports the persistent and progressive course of psychosis in PD, as demonstrated previously [36]. In our sample, PSY was associated with longer PD motor symptom duration, with H/D having significantly longer duration of psychosis compared to MIN. Interestingly, the PSY group had a younger age of PD symptom onset and PD diagnosis, and was significantly younger on average than NoP at the time of the study. This is in contrast to prior studies that found psychotic symptoms to be correlated with older age [10] or longer PD duration but not necessarily an earlier age of PD onset [7,8,11,17]. While any comments on disease course are speculative given the cross-sectional nature of this study, the results raise the possibility that younger age of PD onset may be a risk factor for a psychotic course in PD. Furthermore, the decreased frequency of “benign” symptoms in H/D compared to MIN speaks to the progressive loss of insight in PD-psychosis. Of note, our psychotic symptoms checklist used the term “benign,” a term Goetz et al. recognize as a misnomer [37]. As our checklist predates Goetz’s important proposal to drop the term “benign” from the PD-psychosis vocabulary, we would now replace this term with the more appropriate “with or without insight” set forth in the NINDS/NIMH criteria.

The present study supports the validity of the NINDS/NIMH criteria for diagnosis of PD-associated psychosis in that they capture all relevant psychotic phenomena, including minor symptoms, and exclude psychosis due to other illnesses. The NINDS/NIMH criteria provide an initial step toward a standardized, inclusive and categorical approach to the diagnosis of PD-psychosis, which is needed to evaluate potential treatments and enable valid comparisons across studies [20]. In a separate sample of 116 consecutive subjects from a movement disorders clinic, Fénelon et al. reported a 60% prevalence of PD-Psychosis using the NINDS/NIMH criteria versus 43% using a “usual” definition, which did not include minor phenomena [21]. Their higher prevalence rates compared to the current study may be

due to differences in the study populations, such as our exclusion based on MMSE < 24, or differences in questionnaire administration. We included passage hallucinations as ‘minor hallucinatory phenomena’ under the broader term “hallucinations” put forth in the NINDS/NIMH criteria. Given high prevalence of this phenomenon in our sample, it may be useful to specify passage hallucinations in the criteria. Further assessment of the validity and reliability of the criteria is needed, with expected refinement of the criteria as data become available.

Minor phenomena and visual hallucinations are the most common psychotic symptoms in PD psychosis [11], but less is known about minor phenomena. In this sample, 26% of those with psychosis experienced VH, and VH accounted for 53.1% of all hallucinations. In several studies, the proportion of subjects with psychosis who experienced VH approached or reached 100% [7,8,9,17], but these studies typically did not account for minor phenomena. The first systematic study including minor phenomenon found that 25.5% of 216 PD patients experienced minor phenomena, with 14.3% experiencing them in isolation [11]; later studies showed prevalence estimates as high as 72% [18]. Our results are consistent with previous reports. Minor phenomena in isolation were present in nearly half of those with psychosis (12.4% of the total sample) and accompanying H/D in 30.8% of psychosis cases. Hallucinations involving other sensory modalities and delusions also occur in PD, as in this sample, but they are less frequent and usually present only in those also experiencing VH [9,11,12,14,16]. Delusions are less common than hallucinations, but prevalence estimates have been as high as 14% (64% of those with psychosis) in a separate series [14]. Typically, delusions involve themes of persecution, abandonment, or jealousy, and are associated with greater morbidity.

Historically, psychotic symptoms in PD were considered a product of chronic dopaminergic therapy, but dopaminergic treatment alone is not sufficient to cause PD-psychosis. As in our study, an absence of difference in mean-daily levodopa or levodopa equivalent dose in hallucinators versus non-hallucinators has been shown repeatedly [7,8,15,36]. However, the current levodopa equivalent dose does not capture the previous prescribing behavior of treating clinicians, who may have adjusted dopaminergic medications in response to psychotic symptoms. Data on duration of dopaminergic therapy was not available for our sample, but others show longer dopaminergic therapy duration in those with formed hallucinations versus minor symptoms [17]. Early reports of levodopa-induced psychosis were often lumped into the category of “acute confusional states,” and Fénelon et al. presume that PD-related psychotic symptoms in the pre-levodopa era developed primarily in association with depression, dementia and confusional states [38,39,40]. Thus, these early reports are difficult to compare to PD-associated psychosis as defined by the NINDS/NIMH criteria. Psychotic symptoms in PD are typically associated with more depressive symptoms, an observation supported by our results and most previous studies [7,10,12,14,19,41]. However, Weintraub et al. found that co-occurrence of psychosis and depression, at a rate of 10%, was not higher than expected by chance [42]. We found that minor psychotic symptoms alone were associated with increased depressive symptoms, an association also supported in previous studies [11]. Of note, the high comorbidity of psychosis and depression in PD is not explained by presence of mood disorders with psychotic features [14,41]. The NINDS/NIMH criteria exclude cases of psychotic mood disorder, which we diagnosed in three subjects.

Dementia and cognitive impairment are the most consistently identified risk factors for PD-psychosis. Although our screening stage excluded enrollees with a MMSE score <24 and groups had similar mean MMSE scores, more subjects in PSY met DSM-IV-TR criteria for cognitive disorder, NOS compared to NoP. Others report that PD patients with psychosis (defined using the UPDRS thought disorder score) had significantly lower MMSE scores

and were more likely to meet criteria for dementia compared to non-psychotic PD patients [10]. The NINDS/NIMH criteria includes “with/without dementia,” as an associated qualification, which could be applied to six subjects in our sample.

This exploratory cross-sectional study has several limitations. First, our study was restricted to a community movement disorders practice population with MMSE>23. This approach excludes the most ill, but underestimates overall prevalence of PD-psychosis given strong correlations with cognitive impairment. Therefore, we cannot comment on the validity of the NINDS/NIMH criteria in a more cognitively impaired population and can only speculate about the role of psychosis in the course of PD. Second, asking participants, by mail, to enroll in a study related to depression possibly resulted in a group enriched for psychiatric morbidity, which could inflate the rate of psychosis. Furthermore, two-thirds of the subject pool elected not to participate and, therefore, cannot be compared. Third, while a comprehensive checklist was generated by the study team, this checklist has not been validated as a diagnostic instrument for PD-psychosis. Also, we combined subjects with “current” symptoms and those with “remitted” symptoms in the context of antipsychotic treatment; this may have affected other covariates in our analysis. Finally, we used the NPI to assess severity of psychosis and included information from subjects for scoring. The NPI was developed to involve interviews with informants about symptoms in patients with dementia; administered as such, it has limited utility in non-demented PD patients or for detection of the full range of psychotic symptoms in PD, including minor phenomena [23]. Consequently, our results are not directly comparable to other reports using the NPI. These latter points underscore the need for valid and reliable methods to diagnose PD-psychosis, assess severity, and track longitudinal progression of the range of psychotic phenomena.

In conclusion, psychosis is common in PD, and is associated with ADL disability, depressive symptoms, and lower quality of life. Minor psychotic symptoms are clinically significant and should be included in diagnostic criteria. The NINDS/NIMH proposed criteria for PD-associated psychosis provide an inclusive framework that captures the clinical, temporal, and associated characteristics of psychosis in PD. Minor refinements may be indicated along with further validation of the criteria and rating scales in other populations. While awareness of these issues is recognized by the Movement Disorder Society and those involved in the study of PD-psychosis, such standardized approaches will facilitate evaluation of therapeutics and dissemination of information to general psychiatrists, neurologists and internists. Additionally, our data suggest that longitudinal studies are needed to determine whether minor psychotic symptoms represent a precursor to hallucinations and delusions and if age of PD onset is indicative of a differing disease trajectory.

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Appendix

Psychotic Symptoms Checklist

1. Are psychotic symptoms present?	In Remission	Past History	Never Present
Active			
	No current symptoms	No current symptoms	
	Current treatment	No current treatment	
2. Is patient currently receiving antipsychotic treatment for psychosis (i.e., with neuroleptics)?	Yes No		
3. History of abnormal visual phenomena?	Yes No		
<i>If yes, please check the past or current type(s) and whether or not benign (i.e., insight and no functional impact).</i>			

	Current	Benign	Past	Benign
a. Sense of presence:	Yes No	Yes No	Yes No	Yes No
b. Passage hallucination:	Yes No	Yes No	Yes No	Yes No
c. Other illusions/functional hallucinations:	Yes No	Yes No	Yes No	Yes No
d. Unformed visual hallucinations:	Yes No	Yes No	Yes No	Yes No
e. Formed visual hallucinations:	Yes No	Yes No	Yes No	Yes No

4. History of other hallucinations? Yes No

If yes, please check the past or current type(s) and whether or not benign.

a. Unformed auditory:	Yes No	Yes No	Yes No	Yes No
b. Formed auditory:	Yes No	Yes No	Yes No	Yes No
c. Olfactory:	Yes No	Yes No	Yes No	Yes No
d. Tactile:	Yes No	Yes No	Yes No	Yes No
e. Gustatory:	Yes No	Yes No	Yes No	Yes No
f. Other: _____	Yes No	Yes No	Yes No	Yes No
g. Other: _____	Yes No	Yes No	Yes No	Yes No

5. History of delusions? Yes No

If yes, please check the type(s) present.

	Current	Past
a. General nonspecific paranoid:	Yes No	Yes No
b. Systematized paranoid:	Yes No	Yes No
c. Spousal infidelity:	Yes No	Yes No
d. First rank symptoms:	Yes No	Yes No
e. Other: _____	Yes No	Yes No
f. Other: _____	Yes No	Yes No

6. Is the psychosis a part of a mood disorder? Yes No

If so, are there also psychotic symptoms that are not part of a mood disorder? Yes No

Definitions of Terms

Hallucination- a perception in any of the five sensory

Delusion- a fixed, false, idiosyncratic belief

Minor Psychotic Phenomena [11]

Illusion- a distorted sensory perception of a real stimulus

Sense of Presence- Vivid sensation that someone is nearby, including behind the person, when no one is there and no one is seen

Passage Hallucination- a brief vision of a person, animal or other object that passes sideways in the peripheral visual fields

TABLE 1**Study Sample Characteristics (N=250)**

Age (years)	66.3 (10.3)
Gender n (%)	
Men	167 (66.8%)
Women	83 (33.2%)
Mini-Mental State Exam	28.3 (1.6)
Age PD onset (years)	59.8 (12.3)
Duration PD (years)	7.8 (6.4)
Hoehn and Yahr stage	2.2 (0.74)
<i>Unified Parkinson's Disease Rating Scale Subscores</i>	
II: Activities of Daily Living (n=243)	
on score	11.9 (6.1)
off score	13.5 (7.3)
III: Motor (n=242)	18.1 (11.0)
IV: Therapy Complications (n=237)	3.6 (3.2)

Notes: Mean (SD)

TABLE 2**Prevalence of Current Psychotic Phenomena (N=250)**

Any current psychotic symptom	65 (26.0%)
Minor psychotic phenomena	51 (20.4%)
In isolation	31 (12.4%)
Accompanying H/D	20 (8.0%)
Sense of Presence	9 (3.6%)
Passage hallucinations	45 (18.0%)
Illusions	15 (6.0%)
Hallucinations	32 (12.8%)
Visual	17 (6.8%)
Auditory	9 (3.6%)
Olfactory	5 (2.0%)
Tactile	3 (1.2%)
Delusions	8 (3.2%)

Notes: n (%); H/D: hallucinations and/or delusions

TABLE 3

Demographic and Clinical Characteristics: Any Current Psychotic Symptoms (PSY) vs. No Current Psychiatric Symptoms (NoP)

Variables	PSY (n=65)	NoP (n=40)	test statistic	p-value
<i>Univariate Analysis</i>				
Age (years)	64.2 (10.0)	69.9 (10.3)	$t(103)=2.80$	0.01
Gender (n)	40 M/25 F	27 M/13 F	$\chi^2=0.38$	0.54
Education (years)	15.6 (3.0)	16.6 (3.2)	$t(103)=1.67$	0.10
Symptom Duration (years)	10.2 (7.8)	6.0 (4.4)	$t(103)=-3.10$	0.003
Age Onset (years)	54.0 (13.1)	63.9 (11.3)	$t(103)=3.95$	0.0001
Dopamine Agonist Use [n (%)]	23 (35%)	16 (40%)	$\chi^2=0.23$	0.64
L-dopa Use [n (%)]	58 (89%)	33 (83%)	$\chi^2=0.97$	0.32
<i>Multivariate Analysis*</i>				
MMSE Total	28.3 (0.2)	28.6 (0.3)	$F(1,98)=0.78$	0.38
Cumulative L-dopa Equivalent (mg)	606.3 (51.4)	583.3 (68.3)	$F(1,98)=0.06$	0.81
Hoehn & Yahr Stage	2.1 (0.1)	2.3 (0.1)	$F(1,98)=1.5$	0.22
UPDRS Subscores				
II: Activities of Daily Living				
On score	12.2 (0.6) n=64	9.6 (0.9) n=38	$F(1,95)=5.1$	0.03
Off score	13.5 (0.7)	11.0 (0.9)	$F(1,98)=4.0$	0.05
III: Motor	16.2 (1.3) n=64	17.7 (1.7)	$F(1,97)=0.4$	0.51
IV: Therapy Complications	3.7 (0.3) n=63	2.8 (0.5) n=37	$F(1,93)=1.7$	0.20
Ham-D 17 Total	7.7 (0.6)	3.3 (0.8)	$F(1,99)=18.6$	<0.0001
PDQ-8 Total	6.8 (0.4)	3.8 (0.6)	$F(1,98)=15.7$	<0.0001

Notes: Univariate analysis: Mean (SD). Multivariate analysis: Mean (SE);

* All models adjusted for age, gender, education (years), and PD symptom duration (years). Except for Ham-D 17, all models were also adjusted for depressive symptom severity. MMSE: Mini-Mental State Exam, Ham-D 17: Hamilton Depression Scale 17, PDQ-8: Parkinson's Disease Questionnaire 8, UPDRS: Unified Parkinson's Disease Rating Scale.

TABLE 4

Demographic and Clinical Characteristics: No Current Psychiatric Symptoms (NoP) vs. Isolated Minor Symptoms (MIN) vs. Hallucinations/Delusions (H/D)

Variables	NoP (n=40)	MIN (n=31)	H/D (N=34)	Group-wise Test	Post-hoc Comparisons	
					p-value	
MMSE Total	28.6 (0.3)	28.4 (0.3)	28.1 (0.3)	F(2,97)=0.6	P=0.58	
Cumulative L-Dopa Equivalent (mg)	597.6 (69.3)	660.0 (69.6)	540.7 (77.1)	F(2,97)=0.7	P=0.51	
Hoehn & Yahr Score	2.3 (0.1)	2.0 (0.1)	2.3 (0.1)	F(2,97)=2.6	P=0.08	
UPDRS Subscores						
II: Activities of Daily Living						
On score	9.4 (0.9)	11.4 (0.9)	13.4 (1.0)	F(2,94)=3.7	P=0.03	NoP vs. MIN 0.27
Off score	10.8 (0.9)	12.7 (0.9)	14.4 (1.0)	F(2,97)=2.7	P=0.07	NoP vs. H/D 0.03
III: Motor	17.3 (1.7)	14.7 (1.7) n=31	18.1 (1.9) n=33	F(2,96)=1.0	P=0.36	MIN vs. H/D 0.36
IV: Therapy	2.7 (0.5) n=37	3.2 (0.5) n=30	4.2 (0.5) n=33	F(2,92)=2.0	P=0.14	
Complications						
NPI Delusions	0.00 (0.05)	0.01 (0.05)	0.11 (0.06)	F(2,97)=1.4	P=0.25	
Frequency*Severity						
NPI Hallucinations	0.00 (0.2)	2.4 (0.2)	2.1 (0.3)	F(2,97)=32.0	P<0.001	NoP vs. MIN <0.001
Frequency*Severity						NoP vs. H/D <0.001
Ham-D 17 Total	3.1 (0.8)	6.0 (0.8)	9.4 (0.8)	F(2,98)=14.5	P<0.001	MIN vs. H/D 0.78
						NoP vs. MIN 0.03
						NoP vs. H/D <0.001
						MIN vs. H/D 0.02
PDQ-8 Total	3.7 (0.6)	6.2 (0.6)	7.5 (0.6)	F(2,97)=9.0	P<0.001	NoP vs. MIN 0.005
						NoP vs. H/D <0.001
						MIN vs. H/D 0.393

Notes: Mean (SE). As appropriate, all models were adjusted for age, gender, education (years), and PD symptom duration. Except for Ham-D 17, all models were also adjusted for depressive symptom severity. Sidak's adjustment was used to correct for multiple comparisons. MMSE: Mini-Mental State Exam, Ham-D 17: Hamilton Depression Scale 17, PDQ-8: Parkinson's Disease Questionnaire 8, UPDRS: Unified Parkinson's Disease Rating Scale, NPI: Neuropsychiatric Inventory.