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Use of Latent Variable Modeling to Delineate Psychiatric and Cognitive Profiles in Parkinson's Disease

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Abstract

Objectives—A range of psychiatric symptoms and cognitive deficits occur in Parkinson's disease (PD), and symptom overlap and co-morbidity complicate the classification of non-motor symptoms. The objective of this study was to use analytic-based approaches to classify psychiatric and cognitive symptoms in PD.

Design—Cross-sectional evaluation of a convenience sample of patients in specialty care.

Setting—Two outpatient movement disorders centers at the University of Pennsylvania and Philadelphia Veterans Affairs Medical Center.

Participants—177 patients with mild-moderate idiopathic PD and without significant global cognitive impairment.

Measurements—Subjects were assessed with an extensive psychiatric, neuropsychological, and neurological battery. Latent class analysis (LCA) was used to statistically delineate group-level symptom profiles across measures of psychiatric and cognitive functioning. Predictors of class membership were also examined.

Results—Results from the LCA indicated that a four-class solution best fit the data. 32.3% of the sample had good psychiatric and normal cognitive functioning, 17.5% had significant psychiatric co-morbidity but normal cognition, 26.0% had few psychiatric symptoms but had poorer cognitive functioning across a range of cognitive domains, and 24.3% had both significant psychiatric co-morbidity and poorer cognitive functioning. Age, disease severity, and medication use predicted class membership.

Conclusions—LCA delineates four classes of patients in mild-moderate PD, three of which experience significant non-motor impairments and comprise over two-thirds of patients. Neuropsychiatric symptoms and cognitive deficits follow distinct patterns in PD, and further study

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is needed to determine if these classes are generalizable, stable, predict function, quality of life and long-term outcomes, and are amenable to treatment at a class level.

Keywords

Parkinson's disease; neuropsychology; psychiatry; cognition; depression

OBJECTIVES

A broad range of psychiatric disorders and cognitive deficits are common in Parkinson's disease (PD)(5,41). Prevalence estimates for some form of depression center around 30–40% (26). Anxiety and panic attacks(28), psychotic symptoms(4), fatigue(25), and disorders of sleep and wakefulness(9) all occur at frequencies of at least 30% in PD. In addition, many PD patients, even those without dementia, experience cognitive deficits, including executive, memory, attentional, and visuospatial impairments(23).

Given the high frequencies of different non-motor complications in PD, extensive co-morbidity is expected for PD patients among different psychiatric and cognitive conditions. Frequent concomitants of depression in PD are anxiety disorders(28) and cognitive deficits(37); apathy (36) and fatigue(25) are common among PD patients experiencing other psychiatric or cognitive conditions. In one study of psychiatric co-morbidity in PD, 59% of patients experienced at least 2 non-motor symptoms, while 25% experienced at least four symptoms (33).

There are several possible explanations for psychiatric and cognitive comorbidity in PD. For example, the overlap between symptoms may simply be due to chance. Alternatively, the expected frequency of comorbid symptoms may be higher than due to chance, suggesting that psychiatric and cognitive symptoms either share common etiologies (demographic, clinical, or pathophysiological) leading to their co-occurrence or are directly, or indirectly, related to one another through biological mechanisms.

Investigating these, and other, alternative explanations of the psychiatric and cognitive comorbidity in PD requires going beyond the typical comparison of PD and non-PD groups in the majority of research on PD. Heterogeneity among PD patients in the form of unidentified subgroups with different symptom profiles may help explain the psychiatric and cognitive overlap in PD. Such subgroups may vary by the different levels at which psychiatric and cognitive symptoms may appear together. Some subgroups may exhibit either psychiatric or cognitive symptoms, while others exhibit both to different degrees. A variety of statistical approaches are available for identifying such sub-groups based on observed symptoms.

Cluster analysis is one non-model-based methodology that has been used recently to identify groups of patients with dementia who present with similar neuropsychiatric symptom profiles (3,8,20). However, cluster analysis does not provide a rule for identifying clusters in a patient sample. Alternatively, latent class analyses (LCA) are model-based clustering approaches that characterize heterogeneity in symptom profiles at the patient level with discrete unobserved subgroups of patients experiencing similar patterns of co-morbidity across measures(30). In addition, demographic and clinical predictors of class membership can be explored, enriching the clinical utility of the information to be obtained from the latent classes. Thus, LCA has the potential to inform the assessment and management of patients in routine clinical care with information from the unobserved subgroups underlying the observed psychiatric-cognitive comorbidity relationship in PD patients. Accordingly, the current study employed LCA to identify subgroups based on symptom profiles across continuous and categorical measures of psychiatric and cognitive functioning in patients with mild to moderate PD and without

significant global cognitive impairment, and then to examine the association between identified subgroups and demographic and clinical characteristics commonly associated with non-motor complications in PD(40).

METHODS

Participants

Participants were a convenience sample of 177 outpatients receiving clinical care at the PD centers at the University of Pennsylvania (N=135) or the Philadelphia Veterans Affairs Medical Center (N=42). All participants had a diagnosis of possible or probable idiopathic PD(15), confirmed by a movement disorders specialist, and were participants in a study examining the frequency and correlates of psychiatric and cognitive complications in PD. Exclusion criteria included recent (within past 6 months) deep brain stimulation surgery, Mini-Mental State Examination(13) (MMSE) score <15, a current substance abuse diagnosis, and a self-reported history of bipolar disorder, schizophrenia, or schizoaffective disorder. Comparison of mean differences in patient characteristics across sites revealed that patients from the Philadelphia VAMC were significantly older ($t=5.01$, $M_{diff}=8.70$, $df=175$, $p<.001$) and had a higher average daily levodopa dosage ($t=2.73$, $M_{diff}=191.59$, $df=175$, $p=.007$) than patients recruited from the University of Pennsylvania. With regard to the latent class indicators (described in more detail below), while there were no site differences for any of the psychiatric measures, VA patients did score lower on attention ($t=-2.02$, $M_{diff}=-0.93$, $df=175$, $p=.05$), memory ($t=-2.47$, $M_{diff}=-2.66$, $df=175$, $p=.02$), and executive function ($t=-2.20$, $M_{diff}=-2.72$, $df=175$, $p=.03$) than patients recruited from Penn.

Procedures

The institutional review boards of both institutions approved all study procedures, and all subjects provided their own informed consent. Potential participants were screened with the 15-item Geriatric Depression Screen (GDS-15)(32) and the Mini-Mental State Examination (13) (MMSE) at a regularly scheduled clinic appointment, and patients who met basic study eligibility criteria were scheduled for a follow-up detailed neuropsychiatric, neuropsychological, and neurological assessment with trained research staff and one of the authors (DW).

Measures

Demographic and clinical characteristics—Patients provided the following information during the screening interview: age, sex, race, marital status, years of education, disease duration of PD, history of deep brain stimulation (DBS) surgery (yes/no), current levodopa (mg/day) and dopamine agonist (DA) use (yes/no).

Psychiatric assessments—The following psychiatric measures were used: Inventory for Depressive Symptomatology(31) (IDS; scores 0–84, higher scores indicating greater depression severity); Spielberger State Anxiety Inventory(34) (STAI; scores 20–80, higher scores indicating greater anxiety severity); Apathy Scale(36) (AS; scores 0 to 42, higher scores indicating greater apathy severity); and the Epworth Sleepiness Scale (ESS; scores 0 to 24, higher scores indicating greater severity of daytime sleepiness). Psychosis was assessed with a modified version of the Parkinson's Psychosis Rating Scale(14) (PPRS). In light of the fact that the distribution of PPRS scores was highly skewed (i.e., there were few scores in the high range) and nonspecificity of certain PPRS items for psychosis, a positive response to either the hallucination (modified to include auditory hallucinations) or paranoia item was considered a positive response for psychosis (entered as a dichotomous variable).

Cognitive assessments—The sum score for trials 1–3 on the free recall component of the Hopkins Verbal Learning Task(7) (HVLT; scores 0–36, higher scores indicating better performance) was used as the memory measure. Executive functioning was assessed with the Semantic Verbal Fluency Test (number of animals generated in one minute)(16). Attention was assessed with the backward score on the Digit Span test(1), which is thought to be more specific to attentional abilities and working memory compared with the forward Digit Span (24).

PD assessments—Severity of PD was assessed with the Unified Parkinson's Disease Rating Scale(12) (UPDRS) motor score and the Hoehn and Yahr Scale(17).

Other assessments—Olfaction was assessed with the University of Pennsylvania Smell Identification Test(11) (UPSIT; scores 0–40, lower scores indicating greater impairment).

Analyses

Descriptive statistics included means and standard deviations (SDs) for continuous variables, and frequencies and percentages for categorical variables. In addition, we conducted latent class analysis (LCA;(29،30)), a special case of finite mixture modeling whereby observed multiple dependent variables are used to obtain categorical latent (i.e., unobserved) variables, or classes. Specifically, we used LCA to estimate, 1) the number of classes that best captured subgroups of psychiatric and cognitive symptom profiles across patients' observed values, 2) the proportion of the sample that belonged to each class, and 3) each individual's class membership. We also used LCA to determine the extent to which various PD patient and disease characteristics predicted differential group membership across the identified latent symptom classes.

The first step in the LCA procedure involved determining the optimal number of categorical latent classes for the observed patterns of data across the 8 measures of psychiatric and cognitive functioning (i.e., latent class indicators). The continuous indicators included in this step of the procedure were daytime sleepiness, apathy, depression, state anxiety, memory, executive function, and attention. Psychosis was specified as a dichotomous indicator (yes/no) in the model. We compared a series of LCA models with increasing number of latent classes from two to six, using the Bayesian Information Criteria (BIC) as the model fit index (smaller values denote better model fit). Although the five (BIC=8050.23) and six (BIC=8050.23) class solutions yielded smaller BIC values than the four class solution (BIC=8068.12), the additional classes were parallel profiles of those identified in the four class solution and did not impart new clinically-relevant information. Thus, we selected the four class model as the best fitting model. The final LCA model produced separately for each of the four latent symptom classes means and standard deviations for the seven observed measures of psychiatric and cognitive functioning and thresholds for the categorical indicator psychosis. To test whether the means of the psychiatric and cognitive outcomes differed across the four identified classes, we ran a series of post-hoc ANOVA's. Pairwise comparisons between all class means were evaluated using a Bonferroni adjustment for the error rate. For indicators with unequal variances across classes (e.g., depression and anxiety), the Games-Howell multiple comparisons test was evaluated. The test of differences among the four classes with respect to the proportion of patients with psychosis was tested with the chi-square test.

Following identification of the optimal number of classes, we examined predictors of class membership by adding covariates to the LCA model. We estimated the probability of membership in each of the latent classes conditional on the following patient-level variables: age, PD duration, Hoehn and Yahr stage, UPDRS motor score, levodopa daily dosage, and DA use (yes/no). Specifically, this structural model was specified as a multinomial logistic

regression equation whereby the set of four categorical latent classes identified in the first step was regressed on the set of predictors.

All LCA analyses were conducted using Mplus version 5.0(30). The ANOVA and chi-square analyses were performed in SPSS(2).

RESULTS

Participant Characteristics

Participants on average were 64.5 (SD = 10.5) years old, and primarily male (73.4%) and Caucasian (93.8%) (Table 1). Overall, patients were representative of PD patients in specialty care settings, with a mean disease duration of 6.8 (SD = 5.4) years, PD of mild-moderate severity (mean Hoehn & Yahr Stage = 2.3 (SD = 0.7)), and a mean UPDRS motor score of 21.9 (SD = 10.6). Approximately half (53.1%) of the sample was taking a DA, and the mean levodopa dosage was 519.9 (SD = 404.3) mg/day.

Results from univariate analyses of the sample means and frequencies, standard deviations, and ranges for the 8 latent class indicators included in the LCA models are presented in Table 2. On average, patients reported mild-moderate symptom severity on measures of apathy, depression, anxiety, and daytime sleepiness, and 28% of the sample experienced psychotic symptoms. Mean performance on cognitive assessments suggested average global cognitive abilities overall, consistent with the mean (SD) MMSE score of 28.3 (2.0), with 97% of subjects having an MMSE score ≥24.

Determination of the Optimal Number of Psychiatric and Cognitive Symptom Classes

Comparing LCA models ranging from 2 to 6 classes, a 4-class solution best fit the data (BIC = 8258.13). The resulting proportion of the sample belonging to each of the four classes was: 32.0% in Class 4, 26.0% in Class 3, 24.3% in Class 2, and 17.5% in Class 1.

Figure 1 displays symptom profiles across the 7 continuous latent class indicators in each of the 4 classes, and Table 3 displays the corresponding estimated means and standard deviations for each of these classes. In order to facilitate comparison across measures, mean observed values for the latent class indicators presented in Figure 1 were transformed and scaled as the proportion of the maximum possible score for each measure. The distinctions among the four classes displayed in Figure 1 and Table 3 indicate that the four classes have the following interpretations: Class 1 is the Psychiatric Group (PsyG); Class 2 is the Psychiatric-Cognitive Group (Psy-CogG); Class 3 is the Cognitive Group (CogG); and finally Class 4 is the Intact Group (IntG). More specifically, the symptom profiles suggest that patients in both Classes 1 and 2 experienced moderate-severe symptoms of apathy ($F(3,173)=46.48$, $P<.001$), depression ($F(3,173)=143.95$, $P<.001$), and anxiety ($F(3,170)=117.03$, $P<.001$) relative to Classes 3 and 4 (please refer to Table 3 for results of post hoc, pairwise comparisons). However, compared to patients in Class 1 (PsyG), patients belonging to Class 2 (Psy-CogG) evidenced significantly worse performance across the 3 cognitive indicators (memory: $F(3,173)=33.31$, $P<.001$; executive function: $F(3,173)=35.26$, $P<.001$; attention: $F(3,173)=38.98$, $P<.001$; see Table 3 for post hoc pairwise comparisons) and were more likely to experience symptoms of psychosis (57.3% vs. 27.8%, x^2 (1, N=73) = 5.69, P =.02). Similarly, while patients in Classes 3 and 4 both reported absent-mild psychiatric symptoms, patients in Class 4 (IntG) performed significantly better on the three cognitive tasks than those in Class 3 (CogG). There were no significant between-class differences among the four classes in terms of severity of daytime sleepiness.

Patient-level Predictors of Class Membership

The extent to which patient-level characteristics predicted class membership is reflected in the parameter estimates and corresponding significance levels generated by the Mplus LCA procedure and reported in Table 4. Adjusting for all other variables in the model, increasing age was associated with a greater likelihood of belonging to Psy-CogG (Class 2) relative to the PsyG (Class 1) (OR=1.26, 95% CI=1.08–1.47, Wald χ^2=8.87, df=1, P=.003) and IntG (Class 4) (OR=1.21, 95% CI=1.04–1.41, Wald χ^2=5.83, df=1, P=.02). Increasing Hoehn & Yahr stage was associated with an increased likelihood of belonging to PsyG (OR=5.15, 95% CI=1.67–15.83, Wald χ^2=8.12, df=1, P=.004) and Psy-CogG (OR=21.55, 95% CI=1.67–277.59, Wald χ^2=5.55, df=1, P=.02) than IntG, and increasing UPDRS scores were associated with a greater likelihood of membership in Psy-CogG (OR=1.14, 95% CI=1.04–1.25, Wald χ^2=7.88, df=1, P=.005), CogG (OR=1.09, 95% CI=1.01–1.20, Wald χ^2=4.12, df=1, P=.04) and IntG (OR=1.09, 95% CI=1.01–1.19, Wald χ^2=4.35, df=1, P=.04) relative to PsyG.

With respect to medication use, higher daily levodopa dosages were associated with a greater likelihood of belonging to CogG than either of the groups with intact cognitive functioning (PsyG: OR (per 100-mg increase in dosage) =1.65, 95% CI=1.11–2.44, Wald χ^2=8.20, df=1, P=.004; IntG: OR =1.36, 95% CI=1.34–2.01, Wald χ^2=11.03, df=1, P=.001), as well as predicting membership in Psy-CogG as opposed to IntG (OR =1.35, 95% CI=0.91–2.00, Wald χ^2=4.33, df=1, P=.04). On the other hand, patients taking a DA were more likely to belong to the two classes with fewer psychiatric symptoms (i.e., CogG (OR=5.85, 95% CI=1.16–29.08, Wald χ^2=4.62, df=1, P=.03) and IntG (OR=13.07, 95% CI=1.40–146.45, Wald χ^2=4.35, df=1, P=.04)) than Psy-CogG.

CONCLUSION

Psychiatric and cognitive disorders are common and frequently co-occur in PD. In order to empirically delineate distinct classes of PD patients presenting with similar symptom profiles across both psychiatric and cognitive assessments, we utilized latent variable modeling to characterize profiles of non-motor symptoms among PD patients without significant global cognitive impairment. Overall, the findings lend support to the notion of multiple, distinct classes of PD patients, with each class characterized by a distinct psychiatric and cognitive profile. Furthermore, patient-level characteristics appeared to serve as significant predictors of PD patients' likelihood of membership in the various identified classes.

Results from the LCA models indicated that a 4-class model best captured group-level variability in PD patients' psychiatric and cognitive symptom profiles. Only one-third of the study sample could be considered intact from this standpoint (Class 4; IntG). Close to one-fifth of the sample (Class 1; PsyG) demonstrated a profile of numerous, significant psychiatric symptoms with intact cognition, and approximately one-quarter (Class 3; CogG) had worse cognitive abilities across a range of domains, without significant co-morbid psychiatric symptoms. The final quarter of the sample (Class 2; Psy-CogG) had both significant psychiatric symptoms and worse cognitive abilities across a range of domains. Our results are consistent with two recent cluster analyses of Neuropsychiatric Inventory(10) (NPI) scores in PD patients (3,8) that identified several clusters of patients, including one with minimal neuropsychiatric symptoms, one or more clusters with primarily affective symptoms, and another with primarily psychotic symptoms.

A number of notable associations emerged when examining the relationship between patient-level characteristics and latent class membership. Patients in Class 2 (Psy-CogG), the most impaired group overall, were older, had more advanced disease, and higher UPDRS motor scores on average than all the other groups, with many of these differences meeting statistical significance. This is consistent with previous research demonstrating that such factors are

associated with both cognitive impairment and some psychiatric symptoms in PD(22,41). Patients in Class 1, who had significant psychiatric symptoms but were intact cognitively, were the youngest group with the shortest disease duration and fewest motor symptoms on average, consistent with some research findings that younger PD patients may have an elevated risk of psychiatric disorders early in the disease course(35,38).

Class membership was also predicted by medication use. Specifically, higher levodopa dosages were associated with a greater likelihood of belonging to both classes with impaired cognitive functioning, and in the case of Class 2 (Psy-CogG), also a higher frequency of psychosis, as opposed to classes with relatively intact cognitive functioning. This is consistent with previous research demonstrating that higher levodopa dosages can be associated with cognitive impairment and psychosis, particularly in older patients and in those with more advanced disease(19,39,42). Conversely, patients taking a dopamine agonist were significantly more likely to belong to the groups characterized by low psychiatric symptom severity, consistent with preliminary evidence that this medication class may improve certain psychiatric symptoms (e.g., depression)(6), although the association between infrequent dopamine agonist use and high psychosis prevalence in Class 2 (Psy-CogG) suggests that some medication treatment decisions in PD are made *in response* to the presence of certain psychiatric symptoms.

There are several limitations to this study. First, our convenience sample, which was drawn from tertiary care clinics, was predominately male, white, college educated, and had mild to moderate severity of PD. Second, while there were significant site differences for age, levodopa dose, attention, and executive function, we chose not to include site as a predictor in the multinomial logistic regression portion of the LCA model due to the fact that the majority of patients were recruited from one of the two sites (i.e., the University of Pennsylvania). Had we included site as a predictor, we would have run the risk of small, or empty, cells when estimating the joint distribution of the four categorical latent variables and independent variables. Thus, additional studies in larger numbers of PD patients with greater demographic and clinical diversity are needed to verify and generalize our findings. Larger samples would also allow for more flexibility when modeling predictors and covariates. Third, although our study looked at a range of neuropsychiatric and cognitive variables, the ones included were those available from our assessment battery. Future studies should consider other non-motor symptoms or impairments for inclusion in symptom profiling. Finally, we were not able to assess the clinical impact of the psychiatric symptoms or worse cognitive performance in the affected groups, but the scores on the depression, anxiety, apathy and daytime sleepiness scales in the two psychiatric groups were above the cut-offs recommended to indicate clinically-significant symptoms(18,21,31,36), and in general neuropsychiatric symptoms in non-demented PD patients are associated with poorer quality of life(27).

Identifying discrete classes of patients with similar psychiatric and cognitive profiles and also certain demographic and clinical characteristics may shed light on the underlying etiology of different patterns of non-motor impairment. For instance, the group with psychiatric symptoms only (Class 1), younger on average with mild PD of short duration, may have psychosocially-mediated psychiatric symptoms, whereas the group with both psychiatric symptoms and worse cognitive functioning (Class 2), older and with longer disease duration, may have psychiatric and cognitive symptoms secondary to progressive disease-related neuropathological changes. As a result, more appropriate assessment and treatment plans may be developed that target discrete patient subgroups, addressing the shortcomings of traditional approaches that target individual symptoms (e.g., “target symptom” approach) or empirically derived clusters of highly correlated symptoms (e.g., factor analysis). Further research is needed to determine if identified classes are stable across time, and if the classes help predict function, quality of life, and long-term patient outcomes. Additionally, studies should also assess whether symptom profiles are amenable to treatment at a class level.

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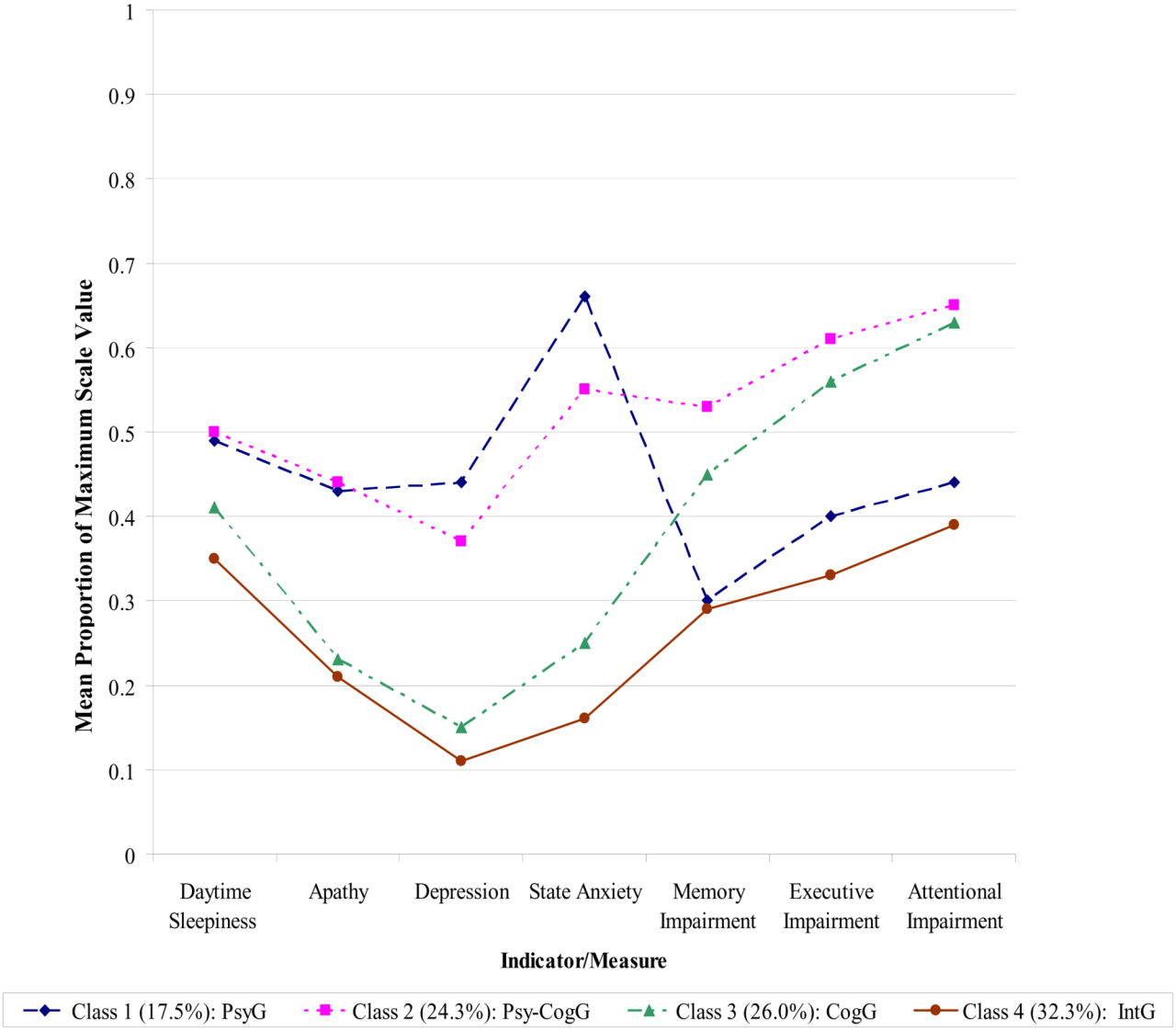

Figure 1. Latent class profiles of continuous psychiatric and cognitive measures

Note: Value (Y) axis represents mean observed values for LCA indicators scaled as the proportion of the maximum possible score for each measure. For free memory, executive function, and attention, proportions were transformed such that higher proportions indicate greater cognitive impairment.

Table 1

Demographic and clinical characteristics of study population

Variables	Mean (SD) or N (%)	Range
Sociodemographics		
Age (# years)	64.5 (10.5)	37–87
Education (# years formal education)	15.9 (3.1)	8–24
Sex (% male)	130 (73.4%)	-
Race (% white)	166 (93.8%)	-
Parkinson's disease and other clinical indices		
PD Duration (# years)	6.8 (5.4)	0–31
Hoehn & Yahr stage	2.3 (0.7)	1–5
UPDRS motor score	21.9 (10.6)	0–60
Levodopa dosage (mg/day)	519.9 (404.3)	0–2480
Dopamine agonist use (% yes)	94 (53.1%)	-
MMSE score	28.3 (2.0)	18–30[a]
UPSIT score[b]	19.3 (6.9)	7–38

[a] 96.6% of subjects had an MMSE score ≥24

[b] N=171

Table 2

Descriptive statistics for latent class analysis indicators

Variables	Mean (SD) or N (%)	Observed Range
Excessive daytime sleepiness severity score[a]	10.2 (5.0)	0–22
Apathy severity score	13.0 (6.9)	0–39
Depression severity score	20.1 (13.7)	0–60
Anxiety severity score[b]	41.7 (15.0)	20–76
Psychosis (percentage yes)	50 (28.4%)	-
Memory (# items free recall)	21.9 (6.2)	5–35
Executive function (# animals generated)	19.2 (7.1)	1–36
Attention (# items correct backward digit span)	6.6 (2.6)	2–13

[a] N=176

[b] N=174

Table 3

Latent class indicator mean values and significant differences across identified latent classes

Variables[a]	Class 1 (PsyG; n=31)	Class 2 (Psy-CogG; n=43)	Class 3 (CogG; n=46)	Class 4 (IntG; n=57)	Test (df), p-value
Excessive daytime sleepiness	11.66 (1.06)	11.89 (0.77)	9.74 (1.03)	8.51 (0.81)	F (3, 172)=4.93, p=.003
Apathy[b]	18.15 (1.19)	18.45 (1.09)	9.72 (0.88)	8.78 (0.76)	F (3, 173)=46.48, p<.001
Depression[c]	37.08 (2.69)	30.90 (1.62)	12.40 (1.86)	8.98 (0.88)	F (3, 173)=143.95, p<.001
Anxiety[d]	59.87 (2.60)	52.88 (1.53)	34.99 (2.25)	29.33 (1.43)	F (3, 170)=117.03, p<.001
Psychosis (n (%) yes)[e]	9 (27.8%)	25 (57.3%)	10 (21.6%)	7 (12.6%)	x^2 (3, N=176)=25.35, p<.001
Memory[f]	25.15 (0.85)	16.84 (1.10)	19.97 (1.03)	25.65 (0.99)	F (3, 173)=33.31, p<.001
Executive Function[g]	22.07 (1.52)	13.99 (0.81)	16.34 (1.24)	24.05 (1.07)	F (3, 173)=35.26, p<.001
Attention[h]	7.82 (0.46)	4.97 (0.45)	5.23 (0.32)	8.52 (0.42)	F (3, 173)=38.98, p<.001

[a] Cell values represent means (standard deviations) and frequencies (percentages) estimated by the LCA procedure for continuous and categorical indicators, respectively.

[b] Post hoc analyses revealed significant differences between Classes 1 & 3 (M_{diff} = 8.22, SE=1.20, P<.001), Classes 1 & 4 (M_{diff} =9.22, SE=1.15, P<.001), Classes 2 & 3 (M_{diff} = 9.00, SE=1.09, P<.001), and Classes 2 & 4 (M_{diff} = 10.00, SE=1.04, P<.001).

[c] Post hoc analyses revealed significant differences between Classes 1 & 2 (M_{diff} = 5.79, SE=2.11, P=.04), Classes 1 & 3 (M_{diff} =24.27, SE=2.01, P<.001), Classes 1 & 4 (M_{diff} = 27.94, SE=1.82, P<.001), Classes 2 & 3 (M_{diff} = 18.48, SE=1.67, P<.001), Classes 2 & 4 (M_{diff} = 22.15, SE=1.44, P<.001), and Classes 3 & 4 (M_{diff} = 3.67, SE=1.28, P=.03).

[d] Post hoc analyses revealed significant differences between Classes 1 & 2 (M_{diff} = 6.73, SE=2.26, P=.02), Classes 1 & 3 (M_{diff} =24.63, SE=2.32, P<.001), Classes 1 & 4 (M_{diff} = 30.70, SE=2.17, P<.001), Classes 2 & 3 (M_{diff} = 17.90, SE=1.79, P<.001), Classes 2 & 4 (M_{diff} = 23.97, SE=1.60, P<.001), and Classes 3 & 4 (M_{diff} = 6.07, SE=1.68, P=.003).

[e] Chi square analyses revealed significant differences between Classes 1 & 2 (x^2 (1, N=73)=5.69, p=.02), Classes 2 & 3 (x^2 (1, N=88)=11.61, p=.001), and Classes 2 & 4 (x^2 (1, N=99)=22.63, p<.001).

[f] Post hoc analyses revealed significant differences between Classes 1 & 2 (M_{diff} = 8.69, SE=1.17, P<.001), Classes 1 & 3 (M_{diff} =5.20, SE=1.16, P<.001), Classes 2 & 3 (M_{diff} = −3.48, SE=1.06, P=.007), Classes 2 & 4 (M_{diff} = −8.94, SE=1.00, P<.001), and Classes 3 & 4 (M_{diff} = −5.46, SE=0.99, P<.001).

[g] Post hoc analyses revealed significant differences between Classes 1 & 2 (M_{diff} = 8.38, SE=1.32, P<.001), Classes 1 & 3 (M_{diff} =6.02, SE=1.30, P<.001), Classes 2 & 4 (M_{diff} = −10.31, SE=1.13, P<.001), and Classes 3 & 4 (M_{diff} = −7.95, SE=1.11, P<.001).

[h] Post hoc analyses revealed significant differences between Classes 1 & 2 (M_{diff} = 2.80, SE=0.52, P<.001), Classes 1 & 3 (M_{diff} =2.69, SE=0.46, P<.001), Classes 2 & 4 (M_{diff} = −3.62, SE=0.44, P<.001), and Classes 3 & 4 (M_{diff} = −3.51, SE=0.37, P<.001).

Table 4

Membership in latent classes as a function of patient-level characteristics

Class[a]	Variable	OR	95% Confidence Interval	Wald χ^2 (df=1)	p-value
Class 1 (PsyG; n=31)	Age (# years)	0.96	(0.90, 1.02)	1.83	0.18
	PD duration (# years)	0.96	(0.78, 1.17)	0.20	0.65
	Hoehn & Yahr Stage	5.15	(1.67, 15.83)	8.12	0.004
	UPDRS motor score	0.92	(0.84, 0.99)	4.35	0.04
	Levadopa dosage (per 100 mg increase)	1.00	(0.82, 1.22)	0.04	0.85
	Dopamine agonist use (% yes)	0.83	(0.25, 2.80)	0.001	0.76
Class 2 (Psy-CogG; n=43)	Age (# years)	1.21	(1.04, 1.41)	5.83	0.02
	PD duration (# years)	1.18	(0.94, 1.49)	1.95	0.16
	Hoehn & Yahr Stage	21.55	(1.67, 277.59)	5.55	0.02
	UPDRS motor score	1.05	(0.98, 1.12)	1.56	0.21
	Levadopa dosage (per 100 mg increase)	1.35	(0.91, 2.00)	4.33	0.04
	Dopamine agonist use (% yes)	0.08	(0.01, 0.86)	4.35	0.04
Class 3 (CogG; n=46)	Age (# years)	1.17	(0.96, 1.43)	2.33	0.13
	PD duration (# years)	1.08	(0.85, 1.37)	0.41	0.52
	Hoehn & Yahr Stage	7.43	(0.69, 79.65)	2.75	0.10
	UPDRS motor score	1.00	(0.94, 1.08)	0.01	0.91
	Levadopa dosage (per 100 mg increase)	1.36	(1.34, 2.01)	11.03	0.001
	Dopamine agonist use (% yes)	0.45	(0.03, 5.83)	0.38	0.54

[a] Class 4 (IntG) is the reference category.

In addition to predicting membership in Class 2 relative to Class 4, increasing age was associated with a greater likelihood of belonging to Class 2 relative to Class 1 (OR=1.26, 95% CI= 1.08–1.47, Wald χ^2=8.87, df=1, P=.003). Increasing UPDRS scores were associated with a greater likelihood of membership in Class 2 (OR=1.14, 95% CI=1.04–1.25, Wald χ^2=7.88, df=1, P=.005) and Class 3 (OR=1.09, 95% CI= 1.01–1.20, Wald χ^2=4.12, df=1, P=.04) relative to Class 1. Higher levodopa dosages were associated with a greater likelihood of belonging to Class 3 relative to Class 1 (OR=1.65, 95% CI=1.11–2.44, Wald χ^2=8.20, df=1, P=.004). Patients taking a DA were more likely to belong to Class 3 than Class 2 (OR=5.85, 95% CI=1.16–29.08, Wald χ^2=4.62, df=1, p=.03).