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Cognitive Performance and Neuropsychiatric Symptoms in Early, Untreated Parkinson's Disease

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Abstract

This study was undertaken to determine the prevalence and correlates of cognitive impairment (CI) and neuropsychiatric symptoms (NPS) in early, untreated patients with Parkinson's disease (PD).

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Supporting Data

Additional Supporting Information may be found in the online version of this article at the publisher's web-site.

Background—Both CI and NPS are common in PD and impact disease course and quality of life. However, limited knowledge is available about cognitive abilities and NPS.

Methods—Parkinson's Progression Markers Initiative (PPMI) is a multi-site study of early, untreated PD patients and healthy controls (HCs), the latter with normal cognition. At baseline, participants were assessed with a neuropsychological battery and for symptoms of depression, anxiety, impulse control disorders (ICDs), psychosis, and apathy.

Results—Baseline data of 423 PD patients and 196 HCs yielded no between-group differences in demographic characteristics. Twenty-two percent of PD patients met the PD-recommended screening cutoff for CI on the Montral Cognitive Assessment (MoCA), but only 9% met detailed neuropsychological testing criteria for mild cognitive impairment (MCI)-level impairment. The PD patients were more depressed than HCs ($P < 0.001$), with twice as many (14% vs. 7%) meeting criteria for clinically significant depressive symptoms. The PD patients also experienced more anxiety ($P < 0.001$) and apathy ($P < 0.001$) than HCs. Psychosis was uncommon in PD (3%), and no between-group difference was seen in ICD symptoms ($P = 0.51$).

Conclusions—Approximately 10% of PD patients in the early, untreated disease state met traditional criteria of CI, which is a lower frequency compared with previous studies. Multiple dopaminergic-dependent NPS are also more common in these patients compared with the general population, but others associated with dopamine replacement therapy are not or are rare. Future analyses of this cohort will examine biological predictors and the course of CI and NPS.

Keywords

anxiety; apathy; cognition; depression; impulse control disorder; Parkinson's disease; psychosis

Cognitive impairment and neuropsychiatric symptoms (NPS) are frequent in patients with Parkinson disease (PD), negatively impacting patients' quality of life and increasing caregiver burden.[1] Approximately 25% of non-demented PD patients have mild cognitive impairment (MCI),[2] and up to 80% of all PD patients will eventually develop dementia.[3] Psychosis, depression, anxiety, apathy, and impulse control disorders (ICDs) are the most frequent and problematic NPS.[1]

To what extent cognitive impairment and NPS are attributable to the neurodegenerative process, psychosocial, demographic or clinical factors, or a complication of dopamine replacement therapy (DRT) is unclear. The contribution of each factor may differ by disease stage and other variables.

To better understand cognition and NPS in PD, patients need to be studied soon after diagnosis, before initiation of DRT. Preliminary studies have shown that a significant percentage (10%–30%) of new (sometimes treated) PD patients have cognitive deficits at rates higher than healthy controls (HCs).[4–8] Others have shown that a range of NPS are more common in early PD patients compared with HCs,[8–10] with non-motor symptoms predominating in 25% of newly diagnosed, untreated patients.[11]

The Parkinson's Progression Markers Initiative (PPMI) is the largest ongoing, prospective, longitudinal study of early untreated (at enrollment) PD patients and HCs.[12] Here we report the frequency and correlates of cognitive impairment (CI) and NPS at baseline.

Methods

Participants

Newly diagnosed, untreated PD patients (n = 423) and age- and sex-matched HCs (n = 196) were enrolled in PPMI. The PD participants were required to (1) have an asymmetric resting tremor or asymmetric bradykinesia, or two of bradykinesia, resting tremor, and rigidity; (2) have a recent PD diagnosis; (3) be untreated; (4) have a dopamine transporter (DAT) deficit on imaging; and (5) not have dementia as determined by the site investigator. Healthy controls were required to have: (1) no significant neurologic dysfunction; (2) no first-degree family member with PD; and (3) a Montreal Cognitive Assessment (MoCA) score greater than 26. The aims and methodology of the study have been published elsewhere[12] and are available at www.ppmi-info.org/study-design. The study was approved by the institutional review board at each site, and participants provided written informed consent.

Assessments

Cognitive Abilities—Global cognition was assessed with the MoCA[13]; no MoCA cutoff was applied for PD patients. The HCs were excluded for MoCA scores less than 27, resulting in the exclusion of approximately 10% of HC. The exclusion criterion for HCs precluded a direct comparison of PD patients and HCs on cognitive assessments, so the analyses for cognitive measures examined PD patients only.

The following cognitive tests were administered and categorized into these domains: memory: Hopkins Verbal Learning Test—Revised (HVLT-R)[14]; visuospatial function: Benton Judgment of Line Orientation[15] 15-item (split-half) version; processing speed-attention: Symbol-Digit Modalities Test[16]; and executive function and working memory: Letter-Number Sequencing[17] and semantic (animal) fluency.[18] Language abilities were not assessed. Published norms (referenced previously) were applied.

Cognitive impairment was defined at three levels: (1) at the screening level, the recommended MoCA cutoff was greater than 26[13,19]; (2) using psychometric tests, CI categorization was reached through a cognitive test–based classification, requiring impairment (>1.5 standard deviations below the standardized mean score, which is the halfway point of the recommend range [>1.0–2.0] of standard deviations below the mean to establish a cutoff point for MCI diagnosis[20]) on any *two* cognitive test scores (using immediate recall and recognition recall from the HVLT-R and single scores from each of the other tests); and (3) applying the MDS Task Force Level I (ie, based on abbreviated assessment) criteria for MCI,[20] which requires a report of cognitive decline and absence of significant functional impairment based on guidelines provided to each site investigator. This formal cognitive categorization process was instituted after study initiation; thus, results from the MDS Task Force Level I MCI criteria were available for only a subset of patients (n = 247).

Neuropsychiatric Symptoms—Depressive symptoms were assessed using the 15-item Geriatric Depression Scale (GDS-15),[21] with a cutoff score of 5 or more indicating clinically significant symptoms.[22] Anxiety symptoms were assessed with the State-Trait Anxiety Inventory[23]; cutoff scores greater than 39 on each subscale, based on the general population, were applied to indicate clinically significant symptoms,[24] because the State-Trait Anxiety Inventory has not been validated in PD patients specifically.[25] The short version of the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease screened for impulse control disorders (gambling, sexual, buying, and eating) and related behaviors (punding, hobbyism, and walkabout).[26] In addition, psychosis and apathy were assessed with single items from the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS)[27] Part I. Any nonzero score was considered presence of a given symptom for these two items.

Disease Severity—The MDS-UPDRS motor score assessed disease severity. Given previous associations between motor subtypes and cognitive impairment in PD,[28,29] patients were classified as having tremor-dominant (TD) versus non-TD subtypes (previously described as postural instability and gait disturbance; indeterminate motor subtypes were combined into one group because of concern regarding consistency of postural instability and gait disturbance classification in early PD[30]).

Statistical Analysis

T tests and chi-squared tests were used for comparisons of demographic, clinical, and neuropsychiatric variables between PD participants and controls. Raw cognitive test scores were converted to standardized scores based on available norms for each test (referenced previously). The effects of common demographic and clinical variables on specific NPS and cognitive variables were examined in univariate and multivariate logistic or linear regression models. Any variables that had univariate associations with *P*-values less than 0.20 were considered in a multivariate model. Variables were removed one at a time from the multivariate models in a backwards selection process until all variables were significant at the 0.10 level. Not significant (NS) variables listed in the results tables had a *P* value greater than 0.10 and were removed from the final model.

Results

Demographic and Clinical Characteristics

Baseline demographic and clinical characteristics for PD patients and HCs are listed in Table 1. No significant between-group differences were seen on any demographic characteristics.

Cognitive Performance in PD

The mean (standard deviation [SD]) MoCA score for PD patients at baseline was 27.1 (2.3). In individual cognitive tests, using a cutoff score of greater than 1.5 SD below the standardized mean to define impairment, the highest frequencies of impairment were seen on verbal memory (9%–17% impaired on the four HVLT-R subtests) and processing speed–attention (14%) (Table 2). Low levels of impairment were seen on executive abilities–working memory (semantic fluency [5%] and Letter-Number Sequencing [4%]) and

visuospatial abilities (3%). See Table 2 for number of participants meeting less (>1 SD) and more (>2 SD) stringent criteria for impairment.

Frequency of Cognitive Impairment in PD

Level 1—Using the prespecified MoCA cutoff score of less than 26, 22.0% of the subjects met criteria for cognitive impairment, including 1% who met criteria for dementia-level impairment (ie, MoCA score < 21)[19] (Table 2).

Level 2—Based on the detailed cognitive tests, 8.9% (37/415) of patients met threshold for CI. Of these, 51.4% (19/415) were impaired on two tests, 37.8% (14/415) on three tests, and 10.8% (4/415) on four tests. Nearly all (89.2%) CI patients had impairment on at least one memory test. Four patients (10.8%) were impaired on executive abilities/working memory and attention/processing speed tasks, without amnestic impairment. Given the limitations of the cognitive battery, the frequencies of amnestic versus non-amnestic or single- versus multiple-domain CI, according to MDS Task Force Level II criteria, were not calculated.[20]

The agreement between MoCA and cognitive test categorization of CI was low (kappa = 0.092). Of the 89 subjects who scored less than 26 on the MoCA and also had detailed cognitive test results, 14.6% had two or more abnormal cognitive test scores. Of the 37 participants who met cognitive test criteria for CI, 35.1% scored less than 26 on the MoCA.

Level 3—Investigators recorded cognitive decline in only 2.4% (6/247) participants. Using this variable and applying the more stringent MDS Task Force–recommended criteria yielded an MCI rate of only 0.4% (1/247). Subsequent to this finding of infrequent documentation of cognitive decline using the specific cognitive decline question, we substituted a nonzero score on the MDS-UPDRS Part I cognitive impairment item for the specific cognitive decline question to determine whether investigators were more likely to document cognitive impairment on this instrument, and this increased the frequency of MCI slightly, to 4.1% (17/415).

Predictors of Cognitive Impairment in PD Patients

On univariate analysis, predictors of worse MoCA performance in PD patients were older age, male sex, being nonwhite, and greater motor impairment (Table 3). On multivariate analysis, all four factors remained statistically significant, with the greatest effect for older age.

Using the MoCA screening cutoff, increasing age, being nonwhite, and higher MDS-UPDRS motor score predicted presence of CI (data not shown). In contrast, using the cognitive test–based diagnosis, CI was predicted by a higher MDS-UPDRS motor score and a trend effect for being non-white (Supplementary Table 1). Applying the MDS-UPDRS Task Force Level I MCI criteria using the MDS-UPDRS Part I cognitive impairment question to capture cognitive decline, in a multivariate model being nonwhite and lower education (trend effect) were associated with an MCI diagnosis (data not shown).

Psychiatric Symptoms

The PD patients had significantly higher depression scores compared with HCs; twice as many PD patients met criteria for clinically significant depressive symptoms (14% vs. 7%) (Table 4). No association was seen between depression and global cognition in PD patients (Supplementary Table 2).

The PD patients also had significantly more state and trait anxiety symptoms, and the frequency rates of clinically significant anxiety symptoms (PD patients vs. HCs) were 24.6% versus 7.7% ($P < 0.001$) for state anxiety and 20.1% versus 9.7% for trait anxiety ($P = 0.001$). There was no association between anxiety and global cognition in PD patients (Supplementary Table 3).

Regarding ICDs and related behaviors symptoms, no statistically significant between-group differences in symptoms were found for any of the four ICDs, hobbyism, or walkabout. A trend effect for punding was found to be more common in PD patients (5% vs. 2%). Apathy (17% vs. 5%) and psychosis (3% vs. 1%) were more common in PD patients per the MDS-UPDRS Part I items.

Predictors of Psychiatric Symptoms

The PD patients remained more likely to meet the GDS cutoff score for depression compared with HCs when controlling for demographic characteristics (odds ratio [95% confidence interval] = 2.30 [1.23, 4.33], $df = 1$, $P = 0.009$). Examining raw GDS scores in PD patients only, being non-white, higher MDS-UPDRS motor scores, and non-TD motor subtype were associated with increasing severity of depression (Supplementary Table 2). Using the GDS cutoff score in PD patients only, being non-white and having non-TD motor subtype was associated with depression, with a trend effect for higher MDS-UPDRS motor score (data not shown).

In a multivariate model, having PD was not associated with presence of ICD symptoms when controlling for demographic factors (odds ratio [95% confidence interval] = 0.87 [0.56, 1.33], $df = 1$, $P = 0.51$). Examining only PD patients, no demographic or clinical factors predicted a positive QUIP (data not shown).

Younger age, higher MDS-UPDRS motor scores, shorter duration of disease, and non-TD motor subtype were associated with more severe *state* anxiety in a multivariate model (Supplementary Table 3). *Trait* anxiety was associated with younger age, higher MDS-UPDRS motor scores, non-TD motor subtype, being non-white, and female sex (data not shown).

No demographic or clinical predictors of a positive psychosis score were seen on the MDS-UPDRS item in PD patients. Increasing disability (Hoehn & Yahr stage) (odds ratio [95% confidence interval] = 1.97 [1.13, 3.45], $df = 1$, $P = 0.02$) and non-TD motor subtype (odds ratio [95% confidence interval]) = 2.14 (1.26, 3.66), $df = 1$, $P = 0.005$) predicted a positive apathy score. The PD patients with apathy had higher depression scores than patients without apathy (3.89 vs. 2.01, t test = −6.17, $df = 421$, $P < 0.001$), but there was no association with global cognition (data not shown).

Discussion

The PPMI is the most comprehensive multicenter, international biomarker study to date in early, untreated PD patients and unaffected controls. Our primary findings were that, at the time of diagnosis, 20% of PD patients reach a screening threshold for CI, 10% meet cognitive test–based criteria for CI, and a very low rate of cognitive decline is reported by participants or site investigators. Multiple NPS (eg, depression, anxiety, and apathy) are more common in PD patients at the time of diagnosis compared with the general population; although these differences may have been impacted by the slight cognitive differences between the two groups, no association was found between either depression or anxiety symptoms and cognitive performance in the PD group. Rates of NPS associated with DRT (eg, psychosis and ICDs) are either low or similar to controls. The statistically significant findings were despite the potential for self-exclusion of patients with clinically significant cognitive impairment or NPS given the demands of this study.

The estimated rates of CI were higher when using a screening instrument versus a cognitive test battery (22% vs. 9%), because recommended cutoff scores for screening instruments prioritize sensitivity over specificity.[19] The rates of CI based on the cognitive battery were lower than the rates reported in previous studies of early, untreated PD patients.[4,7] Potential causes include a highly educated (82% of the PD patients reported having formal education beyond high school, and only two tests adjusted for education) and relatively young (mean age of PD patients at baseline was 61.7 years) PPMI cohort. To compare, a recent study examining nonmotor symptoms in early (mean disease duration = 4.4 mo) PD patients reported a mean MoCA score of 25.1,[31] 2 points below PPMI PD patients. Our interpretation of the cognitive data is limited by an inability to directly compare PD patients with HCs on cognitive performance because of the MoCA exclusion criterion.

When applying the recommended MDS MCI Task Force criteria for MCI,[20] 2% of PD patients met criteria for MCI, because of low recording of cognitive decline by the site investigators. The discrepancy between the reporting of cognitive decline and actual performance on cognitive tests may be attributable to lack of awareness of early, mild cognitive changes in PD, or that the chosen cutoff points on neuropsychological tests over-identify patients as having cognitive impairment. The low reporting rate of cognitive decline raises questions regarding the value of including this criterion when diagnosing PD-MCI, a concern that has been considered previously.[4,32] It also raises the question about how best to document significant cognitive functional impairment—an essential determinant between dementia and MCI. Finally, the low agreement between the MoCA and cognitive battery results demonstrates that the two methods of assessing cognition are not interchangeable. Perhaps a lower screen positive cutoff point on the MoCA may need to be applied in the PPMI and other early PD cohorts to better match the results of the detailed cognitive testing, and this can be explored in future analyses.

Our data are limited by the limited cognitive battery that lacked coverage of certain domains (ie, language) and unevenly covered the included domains. Memory was the most affected cognitive domain, with free recall being more affected than recognition recall, the typical pattern reported in PD, and supporting the idea that memory deficits in PD relate more to

retrieval rather than encoding deficits, although impairments in both can occur.[33] This is consistent with research showing that memory is affected in PD, even at the stage of MCI.[2] The next most affected domain was processing speed–attention, with sparing of the executive abilities–working memory and visuospatial skills. The difference between cognitive domains should be interpreted with caution, because the tests may have differential sensitivities and the number of tests varied across domains.

Predictors of worse cognitive performance included being older, male, and nonwhite, and having more severe motor symptoms. Most of these factors predict the development of dementia,[34] suggesting that clinical and demographic risk factors for cognitive decline manifest themselves at disease onset. The mean duration of illness was approximately 6 months, which precluded detecting an effect of disease duration. Future analyses can examine baseline predictors of long-term cognitive decline, because PPMI participants are assessed annually.

Increasing research on nonmotor symptoms can predict PD, including depression, anxiety, Rapid Eye Movement behavior disorder, impaired olfaction, and autonomic disturbances.[35] Our results support the notion that a range of NPS are already common at diagnosis. Formal diagnostic criteria were not used, and there are limitations in using single items from the MDS-UPDRS to document presence of symptoms (ie, for psychosis and apathy) or their correlates (eg, cognitive impairment), so these findings require replication. Depression, anxiety, and apathy were more common in PD patients compared with controls, with 15% to 25% meeting criteria for clinically significant symptoms. No association was found between cognitive performance and either depression, anxiety, or apathy severity in PD patients, suggesting that worse cognitive performance in PD patients did not play a role in elevated rates of NPS in PD patients compared with HCs. The elevated prevalence of these symptoms in early untreated PD and their inclusion as part of the premotor syndrome[36] suggests that early PD-related neuropathophysiological changes in key neurotransmitter systems (eg, norepinephrine, serotonin, and dopamine) and involvement of specific brain regions (eg, locus coeruleus) contribute to the development of depression, anxiety, and apathy, although psychological factors also likely contribute once a formal diagnosis is made.

The relatively high rates of NPS in early PD have clinical implications. First, NPS have a significant impact on function, quality of life, and caregiver burden,[1] and the initiation of DRT.[37] The NPS remain underrecognized and undertreated in PD.[38,39] Our findings highlight the importance of early, routine screening for a range of highly prevalent NPS to initiate optimal treatment. The most consistent predictors of NPS were non-TD motor subtype, increasing severity of motor symptoms, and being non-white. A clear relationship between motor subtype and NPS has not been reported previously, but our findings need to be verified through longitudinal analyses because of possible instability in motor subtyping in early PD. The association between race and NPS or cognition in PD has not been well explored, although some evidence exists that cognitive deficits[40] and dementia[41] are more common in nonwhite PD patients, and that non-whites receive lower quality of depression treatment compared with whites.[42] No difference was found between white and nonwhite PD patients for age, sex, education, MDS-UPDRS Part III score, TD versus non-TD

subtype, or PD duration that would have helped explain the differences in NPS (data not shown).

The NPS commonly associated with DRT treatment did not differ between PD patients and controls. Psychosis occurred in 3% of patients; follow-up of these patients will determine whether this group has increased risk of cognitive decline. The ICDs and related behavior symptoms were not more common in PD patients than in controls. This additional evidence supports the strong association between DRT use and development of ICDs in PD.[43,44] Seeing whether the approximately 20% of PD patients with a positive QUIP at baseline have an increased risk of developing an ICD after initiation of DRT will be important.

In conclusion, the PPMI baseline results confirm the high frequency of a range of NPS at disease onset, but significant cognitive impairment may not be common. They also support the hypothesis that some cognitive deficits and NPS are more likely related to the range of brainstem-midbrain monoamine deficiencies prominent in early PD, whereas others are associated with the initiation of DRT or more widely distributed neuropathology. As the PPMI cohort is followed longitudinally, future analyses can examine the long-term course, predictors, and association with biomarkers for these crucial nonmotor symptoms, which will inform future clinical research and be invaluable for patient education and treatment planning.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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The Corresponding Author had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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TABLE 1

Demographic and Clinical Characteristics in PD Patients and Controls

	Enrolled Subjects		
Variable	**PD Subjects (N = 423)**	**Healthy Controls (N = 196)**	***P* Value**
Age			0.33
Mean	61.7	60.8	
(Min, Max)	(33, 85)	(31, 84)	
Sex			0.77
Male	277 (65%)	126 (64%)	
Female	146 (35%)	70 (36%)	
Education			0.30
<13 y	77 (18%)	29 (15%)	
13 y or more	346 (82%)	167 (85%)	
Ethnicity			0.62
Hispanic/Latino	9 (2%)	3 (2%)	
Not Hispanic/Latino	414 (98%)	193 (98%)	
Race			0.85
White	391 (92%)	182 (93%)	
Non-white	32 (8%)	14 (7%)	
Family history			<.001
Positive PD	102 (24%)	10 (5%)[a]	
MDS-UPDRS Part III score			<.001
Mean	20.9	1.2	
(Min, Max)	(4, 51)	(0, 13)	
TD/Non-TD classification			NA
TD	299 (71%)	NA	
Non-TD	123 (29%)	NA	
Side most affected			NA
Left	180 (43%)	NA	
Right	233 (55%)	NA	
Symmetric	10 (2%)	NA	
PD duration			
Mean (SD) months	6.65 (6.50)	NA	NA

[a]Healthy controls were excluded for having 1st-degree relative with PD.

TABLE 2

Cognitive Performance in PD Subjects

Cognitive Domain	Variable	Mean (SD) or N (%)
Global	**MOCA score** (N = 423)	27.1 (2.3)
	30–26	330 (78%)
	21–25	89 (21%)
	<21	4 (1%)
Visuospatial	**Benton Judgment of Line Orientation Score** (N = 422)	12.8 (2.1)
	Mild impairment[a]	30 (7%)
	Moderate impairment[b]	**14 (3%)**
	Severe impairment[c]	2 (0%)
Memory	**HVLT Immediate Recall** (N = 422)	24.4 (5.0)
	Mild impairment	131 (31%)
	Moderate impairment	**73 (17%)**
	Severe impairment	29 (7%)
	HVLT Delayed Recall (N = 422)	8.4 (2.5)
	Mild impairment	139 (33%)
	Moderate impairment	**70 (17%)**
	Severe impairment	26 (6%)
	HVLT Retention (N = 422)	0.9 (0.2)
	Mild impairment	89 (21%)
	Moderate impairment	**47 (11%)**
	Severe impairment	21 (5%)
	HVLT Discrimination Recognition (N = 421)	9.6 (2.6)
	Mild impairment	102 (24%)
	Moderate impairment	**38 (9%)**
	Severe impairment	13 (3%)
Executive abilities—working memory	**Letter Number Sequencing Raw Score** (N = 422)	10.6 (2.7)
	Mild impairment	28 (7%)
	Moderate impairment	**19 (4%)**
	Severe impairment	4 (1%)
	Semantic Fluency Total Score (N = 422)	48.7 (11.6)
	Mild impairment	61 (14%)
	Moderate impairment	**22 (5%)**
	Severe impairment	9 (2%)
Processing speed—attention	**Symbol Digit Modalities Score** (N = 422)	41.2 (9.7)
	Mild impairment	110 (26%)
	Moderate impairment	**60 (14%)**
	Severe impairment	27 (6%)

[a] <1.0 SD below standardized mean score. The rows within a given test are cumulative from bottom up (e.g., mild impairment = severe impairment + moderate impairment + mild impairment).

[b] <1.5 SD below standardized mean score (used to classify patients as impaired for MCI categorization).

[c] <2.0 SD below standardized mean score.

TABLE 3

Demographic and Clinical Predictors of MoCA Score in PD Subjects

	Univariate Analysis[a]		Multivariate Analysis[b]	
Variable (Affected Group)	**Regression Coefficient**	***P* Value**	**Regression Coefficient**	***P* Value**
Age (older age)	−0.047	<.001	−0.043	<.001
Sex (male)	0.635	0.007	0.590	0.01
Education (>12 y)	−0.108	0.71	—	—
Ethnicity (Hispanic/Latino)	1.043	0.18	—	NS
Race (non–white)	−1.090	0.01	−1.327	0.001
Family history of PD (no)	−0.042	0.87	—	—
MDS–UPDRS Part III (greater motor impairment)	−0.033	0.01	−0.025	0.047
Hoehn & Yahr stage (stage 2 or above)	−0.263	0.24	—	—
Duration of disease (longer duration)	−0.026	0.13	—	NS
TD/Non–TD classification (TD)	0.133	0.59	—	—
Side most affected (left)	0.045	0.83	—	—

[a] Degrees of freedom = 1.

[b] Degrees of freedom = 422.

TABLE 4

Psychiatric Symptoms in PD Patients and Controls

	Enrolled Subjects		
Variable	**PD Subjects (N = 423)**	**Healthy Controls (N = 196)**	***P* Value**
GDS-15 score			<0.001
Mean	2.3	1.3	
(Min, Max)	(0.0, 14.0)	(0.0, 15.0)	
GDS-15 cutoff			0.008
Not depressed (<5)	364 (86%)	183 (93%)	
Depressed (≥5)	59 (14%)	13 (7%)	
STAI—State score			<.001
Mean	33.0	28.0	
(Min, Max)	(20.0, 76.0)	(20.0, 58.0)	
STAI—Trait score			<.001
Mean	32.4	29.1	
(Min, Max)	(20.0, 63.0)	(20.0, 53.0)	
QUIP disorders			
Any 1 or more disorders	87 (21%)	36 (18%)	0.51
Gambling	4 (1%)	1 (1%)	0.57
Sex	12 (3%)	5 (3%)	0.84
Buying	11 (3%)	4 (2%)	0.67
Eating	36 (9%)	18 (9%)	0.78
Hobbyism	31 (7%)	19 (10%)	0.31
Punding	21 (5%)	4 (2%)	0.09
MDS-UPDRS Part I Apathy item			<.001
Negative	352 (83%)	186 (95%)	
Any positive score	71 (17%)	9 (5%)	
MDS-UPDRS Part I Psychosis item			0.047
Negative	410 (97%)	194 (99%)	
Any positive score	13 (3%)	1 (1%)	