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Relationship Between Self-reported Apathy and Executive Dysfunction in Nondemented Patients With Parkinson Disease

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Abstract

Objective—The prevalence of apathy was assessed across select cognitive and psychiatric variables in 32 nondemented patients with Parkinson disease (PD) and 29 demographically matched healthy control participants.

Background—Apathy is common in PD, although differentiating apathy from motor, cognitive, and/or other neuropsychiatric symptoms can be challenging. Previous studies have reported a positive relationship between apathy and cognitive impairment, particularly executive dysfunction.

Method—Patients were categorized according to apathy symptom severity. Stringent criteria were used to exclude patients with dementia.

Results—Approximately 44% of patients endorsed significant levels of apathy. Those patients performed worse than patients with nonsignificant levels of apathy on select measures of verbal fluency and on a measure of verbal and nonverbal conceptualization. Further, they reported a greater number of symptoms related to depression and behavioral disturbance than did those patients with nonsignificant levels of apathy. Apathy was significantly related to self-report of depression and executive dysfunction. Performance on cognitive tasks assessing verbal fluency,

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working memory, and verbal abstraction and also on a self-report measure of executive dysfunction was shown to significantly predict increasing levels of apathy.

Conclusions—Our findings suggest that apathy in nondemented patients with PD seems to be strongly associated with executive dysfunction.

Keywords

Parkinson disease; apathy; executive dysfunction; neuropsychologic assessment

Apathy is characterized as having indifference to one's surroundings, loss of interest or motivation in goaldirected behaviors, and/or flattening of affect that is not attributed to a decline in levels of arousal or intellect.[1–6] Reported prevalence rates of apathy in patients with Parkinson disease (PD) have been estimated to range from 16% to 51%, which is greater than rates reported for demographically matched healthy individuals.[1,7–10] The anatomic correlates of apathy in PD have not been fully elucidated; however, research has suggested that disruption to select frontostriatal circuits and the mesolimbic system may play a significant role in its clinical demonstration.[6–8,11–16]

Apathy is common in many neurologic, medical, and psychiatric disorders, although it is often ascribed to symptoms related to depression, especially in patients with PD.[1,17] Depression occurs in approximately 40% of patients with PD, although this rate varies considerably across studies.[3,18–22] Symptoms related to apathy and depression can overlap considerably in any given individual with PD, and the relationship between symptom expression and severity across the 2 is an inconsistent one.[1,9,10,23–25] In assessing neuropsychiatric symptomatology in patients with Alzheimer disease, frontotemporal dementia, PD, Huntington disease, and progressive supranuclear palsy, Levy et al[26] discovered that, in their combined patient sample, apathy symptoms did not correlate significantly with depression. In fact, a diagnosis of apathy was disproportionately higher than depression in individuals with progressive supranuclear palsy, Alzheimer disease, and frontotemporal dementia, whereas the severity of symptoms related to apathy and depression in patients with PD was similar. Kirsch-Darrow et al[9] reported that the frequency and severity of apathy [assessed with a self-report measure from the Modified version of the Apathy Evaluation Scale (AES)][24] was greater in patients with PD compared with a younger sample of individuals with dystonia. Moreover, 23.8% of their PD sample and none of their dystonia sample reported significant apathy without depression. This finding may suggest that the dissociation between depression and apathy may be more complex for PD compared to that for individuals with neurodegenerative disorders other than PD because of the potential overlap in neuropsychiatric symptomatology in PD.[3,9,26,27]

An issue that has not been extensively addressed is the relationship between cognitive impairment and apathy in patients with PD. Previous studies have reported that executive dysfunction is positively related to apathy symptom severity in this patient population. [8,10,24] Pluck and Brown[10] studied nondemented PD patients with and without significant levels of symptoms related to apathy using the clinician report version of the AES (AES-C)[28] and demonstrated that those patients with significant levels ("high") of apathy (37.8% of their PD sample) completed fewer categories and made more errors on the

Wisconsin Card Sorting Test than those patients without clinically significant levels of apathy. In addition, PD patients with significant levels of apathy, performed worse on the Controlled Oral Word Association Test, the memory and language subtests of the Cambridge Examination of Cognition in the Elderly (CAMCOG), and the Stroop Test when compared with patients with nonsignificant ("low") levels of apathy. In a separate, although similar, investigation, Isella et al[8] categorized their sample of nondemented PD patients into 3 subgroups, based on the frequency distribution of scores, using a self-report measure of apathy (modified version of the AES). Their 3 PD subgroups included the following: n = 10 (AES ≤14), n = 10 (AES = 15–18), and n = 10 (AES ≥19). Isella et al[8] reported that 45% of their PD sample endorsed significant levels of apathy. PD patients with clinically elevated levels of apathy (AES≥15) performed significantly worse on executive measures, particularly on a test of semantic verbal fluency, compared with normal control (NC) participants and PD patients with nonclinical levels of apathy (AES≤14). Further, they did not report any significant PD group differences on tests of memory or global intellectual functioning.

Lastly, there is an inherent concern when rating neuropsychiatric symptoms via self-report in a given patient population. However, apathy, like other neuropsychiatric syndromes, is an internal experience, not just an external manifestation of behavior. As such, self-report may be a meaningful measure for addressing this important construct in PD, especially in those individuals who are not demented. When rated by others (ie, caregivers or clinicians), symptoms related to apathy can be misinterpreted.[8] By virtue of being apathetic, one could assume that an individual could not perform such ratings. However, like other self-report ratings of neuropsychiatric symptoms [eg, Beck Depression Inventory (BDI)], insight into a patient's perception of their dysfunction is important for treatment and caregivers, alike.

The overall aims of the present study were to (a) determine whether increasing executive dysfunction may be a marker for the possible emergence of apathy in patients with PD not suffering from dementia, and (b) to provide further evidence for the feasibility of the use of a self-report measure in gauging neuropsychiatric symptoms related to apathy in a nondemented neurologic population. Specific hypotheses that will be addressed include (1) the prevalence of apathy in our sample of nondemented individuals with PD will be consistent with previous reports; (2) in line with previous findings, we expect to discover PD subgroup differences (defined by clinically significant versus nonclinical levels of apathy) across select executive and psychiatric variables; and (3) we expect a less heterogeneous PD sample with regards to global intellectual functioning with the use of stringent exclusionary criteria in characterizing dementia.

METHODS

Participants

Participants were 61 right-handed adults, including 32 nondemented patients with PD (59% men) and 29 demographically equated healthy NC individuals (48% men). The majority of patients with PD were recruited from the Movement Disorders Center at North Shore University Hospital and Long Island Jewish Medical Center in New York. The remaining patients with PD were recruited from a monthly PD support group that met at North Shore

University Hospital. The majority of NC participants were spouses and/or caregivers of our patients. Patients were recruited over a 1-year period of time in this metropolitan clinic, and selection for participation was nonrandom, but was determined by the willingness of participants and family members.

Men and women were similarly represented, χ^2 (1) = 0.76, P = 0.385. Handedness was determined by self-report and confirmed by the Coren et al[29] lateral preference inventory. All participants were native speakers of English; were between the ages of 50 and 79 (overall M = 66.8, SD = 7.0); had an overall mean education level of 15.8 years (SD = 2.5); and had an overall mean occupational level of 7.4 (SD = 1.5) on the Hollingshead Scale,[30] ranging from "1" (unskilled service worker) to "9" (major professional). See Table 1 for group means and standard deviations for demographic and screening variables.

All relevant medical history and demographic information were obtained via medical record review and a structured clinical interview. All patients were receiving pharmacologic therapy for parkinsonian motor symptoms at the time of testing. A diagnosis of PD and a disease severity rating [modified Hoehn and Yahr Staging (0–5)][31] were verified by a neurologist (A.F., D.E., or M.F.G.) as part of the patient's clinical visit. For study inclusion, clinical severity of PD was limited to mild-to-moderate levels to minimize confounding factors (eg, incoherent speech or immobility). The sample included 5 stage 1.5 patients, 15 stage 2 patients, 1 stage 2.5 patient, and 11 stage 3 patients (M = 1.92, SD = 0.99). Laterality of motor symptoms was not considered in light of previous work that revealed nonsignificant differences between PD patients with either left-sided or right-sided motor symptoms on numerous measures of cognitive functioning.[32]

Participants were excluded from the study if they (a) displayed impaired global intellectual functioning [total score on the Mattis Dementia Rating Scale (MDRS)][33]; cutoff <*133*),[34] (b) had undergone a surgical procedure for the treatment of PD, (c) had a history of any other neurologic disorder and/or acquired brain injury, (d) presented with Parkinson-plus symptomatology (eg, myoclonus, apraxia, oculomotor abnormalities, ataxia, and/or sensory loss), (e) were on anticholinergic therapy (eg, trihexyphenidyl or benztropine), (f) were taking medications that could directly or indirectly impact cognitive functioning (eg, sedatives, anticonvulsants, and/or neuroleptics), (g) indicated prior history of polysubstance abuse, and/or (h) indicated prior history of psychiatric disorder (eg, depression) with or without medical treatment or hospitalization. Informed consent was obtained, and all procedures were approved by the institutional review board.

Procedures

The test battery, consisting of standardized screening tests, behavioral/psychiatric inventories, and cognitive executive measures, was administered to all participants in counterbalanced order. The current study was part of a larger protocol (ie, an observational, cross-sectional study design comparing PD and NC groups) that assessed the relationship between executive dysfunction and frontostriatal circuitry in patients with PD.[16] The standardized neuropsychologic tasks in our battery were exclusively selected to compensate for PD motor symptomatology,[35] thereby minimizing motor involvement and fatigue. The single testing session lasted approximately 2 hours. The current test battery should not be

viewed as a comprehensive assessment of executive functions, as we only used a select number of neuropsychologic measures.

Materials

Screening tasks included the following: *global intellectual functioning*—MDRS[33]; *estimate of premorbid level of intellectual functioning*—method of Barona et al[36]; *visual perception*—Visual Form Discrimination Test[37]; and *auditory divided attention*—Brief Test of Attention.[38]

The Frontal Systems Behavioral Scale (FrSBe)[39] is a self-report rating scale consisting of 46 items designed to assess behavioral traits typically associated with frontal lobe damage. The FrSBe incorporates 3 subscales: Apathy Scale (14 items), Disinhibition Scale (15 items), and Executive Dysfunction Scale (17 items). Each patient was asked to rate their pre-PD affective status (before illness or injury) to the best of their recollection, and also their current (after illness or injury) affective status. NC participants were only required to rate their current affective status. Each item is rated on a scale ranging from 1 to 5 (1 = almost never, 2 = seldom, 3 = sometimes, 4 = frequently, and 5 = almost always). The Apathy Scale of the FrSBe addresses behavioral characteristics involving decreases in initiation, spontaneity, drive, and task persistence, with a noted lack of concern for self-care and blunted affective expression. An example of an item on the Apathy Scale of the FrSBe is "Sit around doing nothing." The Executive Dysfunction Scale of the FrSBe addresses behavioral traits such as sustained attention, working memory, organization, planning, sequencing, and problem-solving. An example of an item from this scale is "Cannot do two things at once (eg, talk and prepare a meal)." The Disinhibition Scale of the FrSBe addresses traits unique to behavioral disturbances, such as impulsivity, hyperactivity, socially inappropriate behavior, lack of conformity to social conventions, and irritability. An example of an item from this scale is "I do things impulsively." Raw scores that are greater than or equivalent to a T-score of 65 on the FrSBe are indicative of clinically significant symptom severity. On the FrSBe, higher raw scores indicate greater endorsement of clinical symptomatology. The reliability and construct validity of the FrSBe have been previously demonstrated using individuals with frontal brain injury and neurodegenerative disorder.[39]

Depressive symptomatology was assessed using the Beck Depression Inventory.[40] The BDI contains 21 individual statements reflecting depressive symptoms (eg, mood, sense of failure, indecisiveness, work inhibition, and appetite) based on the participant's experiences and feelings over the past week, including the day of test administration. Each item on the BDI has 4 choices indicating the level of severity with which one agrees with the presenting statement. For example, the range of statements under self-hate is "0 = I don't feel disappointed in myself," "1 = I am disappointed in myself," "2 = I am disgusted in myself," and "3 = I hate myself." Classification of depression severity by BDI scores has been previously defined: 0–9 = normal, 10–15 = minimal, 16–19 = mild/moderate, 20–29 = moderate/severe, and 30+ = severe.[41]

For cognitive tests, we used measures that assess a variety of cognitive executive functions. This test battery included: *set-shifting*—Odd Man Out Test[42]; *verbal working memory*—the backwards trial from the Digit Span subtest from the Wechsler Memory Scale III[43];

nonverbal working memory—the backwards trial of the Spatial Span subtest from the Wechsler Memory Scale III[43]; *letter fluency*, *category fluency*, *category switching*, *switching accuracy*, *and first interval fluency*—verbal fluency subtest from the Delis-Kaplan Executive Function System (D-KEFS)[44]; *error monitoring/cognitive flexibility*—Stroop Color-Word Test[45]; and *feedback monitoring/verbal abstraction*—Twenty Questions subtest from the D-KEFS.[44] See Appendix for the possible score ranges and description of each cognitive variable.

RESULTS

Statistical Analyses

Data were analyzed using SPSS v. 11.0 (SPSS, Chicago, IL). Between-group comparisons were performed using a Multivariate Hotelling's T^2 Test.[46] This test is a special case of multivariate analysis of variance (MANOVA) for only 2 independent samples to prevent the inflation of Type I error when comparing multiple dependent variables. Correlation analyses were performed using the Pearson product-moment correlation coefficient, with the Bonferroni correction for multiple comparisons, $P = 0.002$. Lastly, a multiple regression analysis of apathy symptoms in combination with other cognitive and psychiatric variables was performed using stepwise linear regression.

Group Comparisons of Clinical, Demographic, Screening, and Experimental Variables

The prevalence of significant levels of apathy symptoms in our PD cohort was 43.8% based on patients' endorsement of current affective status (ie, after injury or illness) on the Apathy Scale of the FrSBe. Moreover, 15.6% of the patients reported significant levels of apathy in the absence of depression, 3.1% of the patients reported mild-to-severe symptoms related to depression in the absence of apathy, and 12.5% of the patients reported a combination of significant levels of apathy and mildto- severe symptoms of depression. None of our NC participants exceeded the clinical cutoff for apathy on the FrSBe or reported mild-to-severe symptoms related to depression on the BDI. The overall *F*-test for the MANOVA was statistically significant [F (1, 59) = 1.90, $P = 0.04$]. PD and NC groups did not differ significantly on any of the demographic or screening variables (Table 1).

The PD group performed significantly worse than the NC group for all cognitive and psychiatric measures ($P<0.05$) with the exception of the total score of the BDI ($P = 0.112$) and the Disinhibition Scale of the FrSBe ($P = 0.954$). See Table 2 for group means and standard deviations for all cognitive variables.

For PDs only, a paired sample *t* test revealed that the endorsement of apathy symptoms was significantly greater, $t(31) = -5.20$, $P<0.0001$, when rating apathy symptoms *after illness or injury* ($M = 29.50$, SD = 9.5) compared with their recollection of apathy symptoms *before illness or injury* ($M = 21.88$, SD = 6.81). Next, we compared the apathy scores for the NC participants ($M = 23.41$, SD = 5.19) with the *before illness or injury* apathy scores for our PD sample ($M = 21.88$, SD = 6.81). No significant differences were found [t (59) = 0.99, $P = 0.329$]. These findings suggest a lack of significant premorbid (ie, pre-PD onset) apathy in our patient group.

Correlation and Regression Analyses

For the PD group as a whole, correlation analyses revealed that self-report behavioral inventories assessing depression (BDI; $r = 0.68$) and executive dysfunction (FrSBe; $r = 0.79$) were significantly ($P<0.001$) related to apathy. A stepwise multiple linear regression analysis [F (4, 31) = 15.70, $P<0.001$; $r = 0.89$] was significant. Further examination of individual cognitive and psychiatric variables in this model indicated that measures shown to significantly predict increasing levels of apathy in our patient sample included a self-report measure of executive dysfunction (FrSBe; $t = 8.00$, $P<0.0001$) and cognitive executive tasks that assess verbal working memory (digits backward trial from the WMS-III; $t = 4.10$, $P<0.0001$), category fluency (D-KEFS; $t = -2.180$, $P = 0.038$), and verbal abstraction [the initial abstraction score from the Twenty Questions Test (D-KEFS); $t = -2.10$, $P = 0.041$].

PD Subgroup Comparisons of Demographic and Clinical Variables

The PD group was divided into 2 subgroups using *after illness or injury* ratings on the Apathy Scale of the FrSBe [clinical cutoff (T-score≥65)]: those with clinically significant apathy symptoms (PD-apathetic; n = 14) and those with nonsignificant apathy symptoms (PD-non-apathetic; n = 18). The PD-apathetic subgroup endorsed more depressive symptoms than the PD-nonapathetic subgroup ($P = 0.001$, Table 5). As a result of this finding, 2 separate MANOVAs were conducted—with and without BDI scores. The overall F tests were both statistically significant [F (1, 30) = 8.50, $P = 0.05$ and F (1, 30) = 11.30, $P = 0.015$, respectively]. These 2 subgroups did not differ significantly on age, education, occupational level, estimated premorbid intelligence, or clinical motor severity. See Table 3 for means and standard deviations for PD subgroup comparisons on demographic and clinical variables.

For performance on cognitive measures, the PD-apathetic subgroup performed significantly worse than the PD-nonapathetic subgroup on tasks of category ($P = 0.04$) and letter ($P = 0.049$) verbal fluency from the D-KEFS, and on the conceptualization subtest from the MDRS ($P = 0.034$). Performance on the Brief Test of Attention ($P = 0.055$) and the WMS-III Spatial Span subtest (backwards trial; $P = 0.063$) revealed statistical trends, with PD-apathetic patients performing worse than PD-nonapathetic patients. Of note, the 2 subgroups did not differ statistically on the total score of the MDRS. See Table 4 for PD subgroup comparisons on all cognitive variables. For self-report psychiatric inventories, PD-apathetic patients reported a significantly greater number of symptoms related to apathy (FrSBe), behavioral disinhibition (FrSBe), executive dysfunction (FrSBe), and depression (BDI) than did PD-nonapathetic patients ($P≤0.002$). See Table 5 for group means and standard deviations.

DISCUSSION

In the current study, scores on a self-report measure of apathy were compared with cognitive and other psychiatric variables in nondemented patients with PD and demographically matched, healthy control participants. The prevalence of clinically significant levels of apathy in our PD group was 43.8%. The PD and NC groups were well matched on

demographic and screening variables; however, the NC group outperformed the PD group on all cognitive variables. Of note, the majority of the cognitive tasks administered were untimed, suggesting that motor symptoms associated with PD did not likely confound cognitive task performance. As for psychiatric variables, between-group comparisons revealed that patients with PD had a significantly greater number of apathy symptoms, but not depressive symptoms, compared with NC participants.

Apathy symptoms for all patients with PD revealed a significant relationship to self-report endorsements of depression (BDI) and executive dysfunction (FrSBe). Moreover, increasing levels of apathy in our patient sample were best predicted by cognitive measures assessing verbal fluency, verbal working memory, and verbal abstraction. Of the psychiatric variables, the total score from the Executive Dysfunction Scale of the FrSBe was a significant predictor of increasing apathy symptoms, whereas the total score from the BDI was not. This finding lends support to recent work suggesting that apathy, not depression, may be a "core" feature of PD.[9]

Our 2 PD subgroups, categorized by apathy symptom severity, did not differ on demographic or clinical variables although significant performance differences were noted on select cognitive executive and psychiatric variables. Of mention, one might argue that significant symptoms related to apathy might preclude adequate effort on tasks, but this did not appear to be the case in the current study, as subgroup differences only applied to select tests and did not extend across all tests of executive functions. For cognitive executive variables, the PD-nonapathetic subgroup performed significantly better than the PD-apathetic subgroup on 2 versions of a word generation task (phonemic and semantic verbal fluency) and on the conceptualization subtest from the MDRS. For psychiatric variables, the PD-apathetic group endorsed significantly higher scores on self-report inventories of apathy, disinhibition, executive dysfunction, and depression.

The prevalence of apathy in our PD group (43.8%) is relatively consistent with previous findings.[7–10] Nonetheless the fairly wide range of apathy prevalence rates in patients with PD reported in the literature (ie, 16% to 51%) may be explained by the following factors: (a) differing levels of cognitive impairment (eg, demented or not) across study participants; (b) the type and/or manner with which a particular diagnostic assessment tool (eg, structured interview or questionnaire) is constructed, validated, used, and/or interpreted; and (c) overlapping symptoms between various mood disorders (eg, apathy and depression).

First, unlike previous studies, the current study implemented a stringent cutoff for dementia as an exclusionary criterion. Similar studies performed by Pluck and Brown[10] and Isella et al,[8] although elegantly designed, employed PD samples with more heterogeneous levels of global intellectual functioning that may have included patients with dementia. Pluck and Brown[10] used the CAMCOG total cutoff score of <80 as an exclusionary criterion for dementia. They reported that 3 of their PD patients with high levels of apathy scored below 80. A fourth patient was not administered the CAMCOG, but based on his/her performance on experimental cognitive measures, it was determined that the patient had clinically significant cognitive impairment indicative of dementia. In another investigation, Isella et al[8] used the total score of the MDRS as a measure of global intellectual functioning. The

mean MDRS total scores and standard deviations for their 3 derived PD subgroups (based on the frequency distribution of scores from the AES) were 130.4 (SD = 6.7), 130.8 (SD = 5.6), and 127.3 (SD = 6.7), respectively. Differences among PD subgroups for the MDRS were not significant, although all 3 subgroups performed significantly worse than a group of demographically matched healthy individuals (M = 137.3, SD = 4.2). According to published criteria using the MDRS in classifying dementia using a highly educated Alzheimer disease cohort (cutoff <133; sensitivity = 0.96; specificity = 0.92),[34] Isella et al's[8] subgroup means (ie, 130.4, 130.8, and 127.3) were below this cutoff. In the current study, we used a more stringent exclusionary criterion for classification of dementia; with mean total MDRS subgroup scores considerably higher than the Isella et al's cutoff. The NC and PD subgroup scores in the current study (NC: M = 141.8, SD = 2.3; PD-apathetic:M = 140.1, SD = 2.8; and PD-nonapathetic: M = 141.6; SD = 2.0) revealed no significant betweengroup differences for the total MDRS scores [F (2, 58) = 2.63, P = 0.08]. The possibility of dementia is critical, since the relationship between executive function and apathy could be confounded by concurrent dementia. Therefore, stringent screening criteria are indicated.

Next, in assessing apathy in patients with PD, previous studies have used various sources (ie, clinician, caregiver, and self-report). The assessment of apathy using "external" sources (ie, clinicians or caregivers) might result in biased reports.[8] For example, a caregiver of a patient with PD might misattribute a decrease in the frequency of previously performed behaviors or activities as a sign of being intentionally languid, rather than as a symptom of apathy despite the patient having preserved knowledge and/ or ability to perform these behaviors or activities independently. Further, poor initiation and/or decreased motivation to perform activities of daily living might be misinterpreted as resulting from clinical/motor severity (eg, bradykinesia) or emotional processing deficits (eg, masked facial expression) associated with the disease process instead of apathy.[15] Thus, apathy may be less apparent to caregivers or clinicians when parkinsonian symptoms become more severe.[17,47]

In the current study, a significant statistical difference was not found between apathy scores for NC participants (M = 23.4, SD = 5.2) compared with *before illness or injury* apathy scores for PD participants (M = 21.9, SD = 6.8) (t = 0.985, P = 0.329). Moreover, a paired sample t test revealed that the endorsement of apathy symptoms was significantly greater (P<0.001) when patients with PD were asked to reflect on their current (*after illness or injury*) status (M = 29.5, SD = 9.5) compared with their recollection of pre-PD onset (*before illness or injury*) behavioral characteristics (M = 21.9, SD = 6.8). These findings suggest that considerable changes had occurred in PD patients' affective status since disease onset. Further, we can posit that our nondemented PD patients appeared to have demonstrated good insight into these changes. Thus, it seems feasible to use self-report as a means to assess symptoms related to apathy in a nondemented sample. A possible avenue for future work would be to assess and compare apathy symptomatology from all sources (ie, selfreport, clinician-report, and family-report), as each source may report affective symptoms differently.

Lastly, when confronted with a differential diagnosis of either apathy or depression, there tends to be a bias favoring a diagnosis of depression. This phenomenon may be best

explained by an interesting finding by Shulman,[17] who reported that during a same period in the previous decade, there were 500 papers published about apathy and 50,000 papers about depression. This relationship may result from similarities in symptom presentation as apathy is traditionally viewed as being a feature of depression.[17,27] In an attempt to assess the overlap between apathy and depressive symptoms on self-report inventories (using elderly participants), Marin et al[48] removed 4 items from the Hamilton Depression Rating Scale that appeared to specifically address apathy. The authors discovered that these 4 items actually correlated significantly with items from the AES, but not with the remaining "depressive" items from the Hamilton Depression Rating Scale. In the current study, we investigated the relationship between depression and apathy in PD. In the PD group, as a whole, there was a positive and significant relationship between depression and apathy. Moreover, the PD-apathetic subgroup endorsed more depressive symptoms than did the PD-nonapathetic subgroup. These findings provide continued support for the notion of a unique relationship between these 2 psychiatric syndromes in PD.[26] Thus, a statistical analysis that would attempt to control (ie, covary) for apathy or depression levels, particularly in this patient population, could potentially be misleading. Miller and Chapman[49] do not recommend the use of such statistical approaches when variables such as apathy and depression share considerable amounts of variance. We believe that the close relationship between symptoms of apathy and depression in our PD sample may reflect the existence of a common mechanism in the expression of symptoms for both neuropsychiatric syndromes. Some potential shared mechanisms may be reduced speed, low motivation, anergia, and/or avolition, *or* underlying frontostriatal circuitry.

The findings from the current study have implications for the use of neuropsychologic assessment, with an emphasis on the evaluation of executive functions, in assessing apathy in PD patients and providing appropriate treatment recommendations. The quality of life for individuals with PD, particularly those who are not demented, may be stabilized or potentially enhanced with early detection of apathy and subsequent intervention. To date, pharmacologic and surgical management for symptoms related to apathy have been investigated in patients with PD with varying results.[7,50–52] Clinical trials assessing the efficacy of non-pharmacologic interventions for apathy have not, to our knowledge, been conducted for nondemented patients with PD. However, a preliminary randomized, controlled, clinical trial[53] assessing a nonpharmacologic intervention for non-PD demented patients with apathy did not seem to be effective in the long term. Here, the authors did not find a discernable treatment effect when comparing task performances between patients in a control and an experimental condition. Nonpharmacologic, behavioral interventions with appropriate education may be the treatment of choice for apathy in nondemented patients with PD, as these patients can most likely continue to be active participants in their respective communities if given appropriate resources, support, and/or guidance. Similar interventions, along with appropriate family education (eg, support groups or seminars), may also be beneficial to caregivers, who may endure significant amounts of distress in caring for their loved ones who are presenting with apathy symptoms.[17]

Some methodologic and statistical limitations were present in the current study. First, unlike the PD patient sample, our sample of NC participants was relatively healthy and did not

present with motor impairment. This is a limitation, as self-reported apathy in patients with PD can arguably be associated with exogenous factors related to motor impairment rather than endogenous factors related to the disease process. To control this, previous research has used patient groups with or without cortically based motor deficits as a comparison group instead of healthy volunteers. [9,10] Second, our PD sample appeared to be more highly educated compared with samples recruited in previous related studies.[8,10] This is an important factor to consider and further emphasizes the need to use high cutoff points to determine severity of potential cognitive impairment. However, although the education levels for both the PD and NC groups do not represent the general population, their respective group means were equated. Third, as discussed above, self-report measures of depression may be nonspecific and reflect other symptoms than depression such as anxiety, general distress, or even apathy. Thus, this places the construct validity of these scales into question. Fourth, the current test battery was not exhaustive in its assessment of executive functions. This may have clearly limited the range of potential interrelationships between cognitive and neuropsychiatric constructs, particularly apathy and executive functions. Lastly, our findings seem to reflect one particular point on the disease timeline in our sample, as PD patients were only included if they demonstrated mild-to-moderate clinical severity. Thus, we did not assess patients at the more impaired end of the clinical spectrum. We can only speculate that patients in the later stages of PD might have exhibited greater executive dysfunction and, hence, greater frequency and severity of apathy.

CONCLUSIONS

The current findings support previous work suggesting the existence of a distinct subgroup of nondemented patients with PD with clinically significant levels of apathy and associated executive dysfunction. A comprehensive neuropsychologic evaluation, with an emphasis on executive task performance, may be beneficial in detecting the presence of apathy in patients with PD. Future research may consider implementing more stringent exclusionary criteria for levels of global intellectual functioning to reduce the possible confounding of underlying cognitive impairment. Depressive symptomatology was not discovered to be a significant predictor of increasing apathy in patients with PD in the current study, although the relationship between these 2 affective states, and their respective assessment instruments, still requires further investigation.

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APPENDIX

Principal Cognitive Dependent Variables

Test	Dependent Variables	Variable Description	Possible Score Range
Odd Man Out Test	Total raw score	Set-shifting	0-40+
Spatial Span (WMS-III)	Total raw score—backwards trial	Nonverbal working memory	0-15+
Digit Span (WMS-III)	Total raw score—backwards trial	Verbal working memory	0-15+
Verbal Fluency (D-KEFS)	Total raw score (letter fluency)	Phonemic fluency	—+
	Total raw score (category fluency)	Semantic fluency	—+
	Total raw score (category switching)	Set-shifting	—+
	Total raw score (switching accuracy)	Set-shifting accuracy	—+
	Total raw score (initial fluency)	Number of words generated in first 15 seconds	—+
Stroop Test	Total raw score (Color/Word trial)	Error monitoring	0-100+
	Interference score	Cognitive flexibility	− 30-+30+
Twenty Questions Test (D-KEFS)	Total questions asked	Feedback monitoring	0-84*
	Initial abstraction score	Verbal abstraction	0-60+
	Total weighted achievement score	Concreteness	0-20+

"+" higher scores indicate "good" performance; "*" lower scores indicate "good" performance.

TABLE 1

Between-group Comparisons for Demographic and Screening Variables

	PD (Mean/SD) N = 32	NC (Mean/SD) N = 29	*t* Value	*P*
Age	66.9/8.1	66.7/5.7	− 0.1	0.919
Education	15.4/2.7	16.2/2.2	1.2	0.220
Hollingshead	7.3/1.7	7.5/1.4	0.6	0.560
Estimate Premorbid IQ	113.6/7.4	115.4/5.0	1.1	0.270
Mattis Dementia Rating Scale (total score)	140.9/2.5	141.8/2.3	1.3	0.185
Brief Test of Attention	17.1/1.9	17.8/1.3	1.9	0.066
Visual Form Discrimination Test	30.6/1.6	30.5/1.4	− 0.3	0.578

TABLE 2

Group Means and Standard Deviations for Cognitive and Psychiatric Variables

	PD (N = 32) (Mean/SD)	NC (N = 29) (Mean/SD)	*P*
Cognitive Variables			
Stroop Color/Word Trial	43.1/8.2	49.2/7.5	0.004
Stroop Interference Index	2.6/6.1	5.8/6.2	0.045
Category Fluency (D-KEFS)	33.8/10.2	41.8/12.6	0.008
Initial Fluency (D-KEFS)	34.9/8.0	41.9/8.4	0.002
Letter Fluency (D-KEFS)	37.0/13.1	45.9/15.7	0.018
Category Switching (D-KEFS)	12.4/4.2	14.6/2.9	0.026
Switching Accuracy (D-KEFS)	11.1/4.2	14.0/3.3	0.005
Odd Man Out Test	30.6/6.4	37.2/5.3	0.001
Spatial Span (WMS-III)	5.1/1.9	7.1/1.5	0.001
Digit Span (WMS-III)	5.7/1.8	7.0/2.4	0.020
Twenty Questions Test (D-KEFS)—Initial Abstraction Score	23.2/11.7	33.5/13.9	0.003
Twenty Questions Test (D-KEFS)—Total Questions	33.8/11.6	26.2/5.9	0.003
Twenty Questions Test (D-KEFS)—Weighted Achievement Score	13.7/4.1	15.7/3.0	0.034
Psychiatric Variables			
Apathy Scale (FrSBe)	29.5/9.5	23.4/5.2	0.003
Executive Dysfunction Scale (FrSBe)	34.7/10.4	29.2/7.5	0.021
Disinhibition Scale (FrSBe)	23.5/5.4	23.4/6.2	0.954
BDI	7.7/6.0	5.5/4.5	0.112

TABLE 3

PD Subgroup Comparisons for Demographic and Clinical Variables

	PD-apathetic (Mean/SD) N = 14	PD-nonapathetic (Mean/SD) N = 18	*P*
Age	68.6/5.2	65.5/9.8	0.285
Education	14.7/3.1	15.9/2.3	0.234
Hollingshead	6.6/1.9	7.7/1.3	0.071
Estimate Premorbid IQ	111.6/8.4	115.1/6.4	0.200
Hoehn and Yahr Stages	2.4/0.5	2.1/0.5	0.063

TABLE 4

PD Subgroup Comparisons for Screening and Cognitive Task Performances

	PD-apathetic (Mean/SD) N = 14	PD-nonapathetic (Mean/SD) N = 18	*P*
Mattis Dementia			
Rating Scale Attention	36.8/0.6	36.7/0.5	0.532
Initiation/ Perseveration	36.1/1.6	36.7/1.4	0.336
Construction	6.0/0.0	6.0/0.0	1.000
Conceptualization	36.5/1.7	37.7/1.3	0.034
Memory	24.6/1.1	24.6/0.9	0.926
Total MDRS Score	140.1/2.8	141.6/2.0	0.077
Visual Form Discrimination Test	30.3/1.8	31.0/1.0	0.163
Brief Test of Attention	16.4/1.8	17.6/1.7	0.055
Wechsler Memory Scale-III			
Spatial Span (backwards trial)	4.4/1.7	5.7/1.9	0.063
Digit Span (backwards trial)	5.5/1.5	5.9/2.1	0.553
Verbal Fluency Test (D-KEFS)			
Letter Fluency	31.8/13.0	40.9/11.9	0.049
Category Fluency	29.6/9.4	37.0/9.8	0.040
Category Switching	12.0/4.0	12.7/4.5	0.638
Switching Accuracy	10.0/4.4	11.9/4.0	0.201
Initial Fluency	32.3/8.6	36.9/7.0	0.105
Stroop Task			
Incongruent (Color/Word)	41.1/9.4	44.7/7.1	0.225
Interference Index	0.8/6.9	3.9/5.2	0.150
Twenty Questions Test (D-KEFS)			
Initial Abstraction Score	20.1/9.2	25.6/13.0	0.192
Total Questions	34.1/14.9	33.5/8.8	0.893
Weighted Achievement Score	13.8/5.4	13.6/2.9	0.908
Odd Man Out Test	29.8/5.6	31.2/7.0	0.537

TABLE 5

PD Subgroup Comparisons for Psychiatric Variables

	PD-apathetic (Mean/SD) N = 14	PD-nonapathetic (Mean/SD) N = 18	*P*
Apathy Scale (FrSBe)	38.7/3.6	22.4/5.9	0.001
Disinhibition Scale (FrSBe)	26.6/5.5	21.1/3.9	0.002
Executive Dysfunction (FrSBe)	44.0/6.6	27.5/6.3	0.001
BDI	12.1/4.9	4.3/4.3	0.001