Anxiety and Depression Are Better Correlates of Parkinson's Disease Quality of Life Than Apathy

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Due to controversy regarding the influence of apathy on quality of life (QoL), the authors examined the independent influence of apathy, depression, and trait anxiety in a nondemented sample of patients with Parkinson disease (PD). Participants (N=107) completed standard self-report measures of QoL and mood/motivation. Analyses investigated the contribution of these measures and empirically derived factor scores on QoL. QoL was predicted by trait anxiety, dysphoria, and decreased interest, with no independent contribution of apathy. Different patterns emerged with respect to domain-specific QoL, with trait anxiety being the strongest predictor across most domains. Anxiety was most widely related to QoL in PD, with minimal contribution of apathy. Future studies should examine different roles of PD mood/motivation symptoms on caregiver QoL.

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Quality of life (QoL) refers to the general well-being of individuals and is affected by multiple factors including health-related conditions. In Parkinson disease (PD), it is well known that motor symptoms dramatically influence QoL.[1,2] However, nonmotor features also impact QoL, even more so than motor dysfunction in many patients.[2,3] Particularly detrimental to QoL are depression and anxiety.[4–6]

What remains unclear is whether apathy, a disorder of motivation/goal directed behavior that is distinct from depression and linked to disease progression, also exerts detrimental effects on QoL.[7,8] This is important because treatments for apathy and depression may differ, and the use of selective serotonin reuptake inhibitors may actually worsen apathy.[9] On one hand, some have argued that apathy is not associated with QoL, although it is associated with worsened cognition and functional abilities.[10] Others, however, have found that newly diagnosed patients with PD with heightened levels of apathy reported worse QoL across multiple life domains (i.e., mobility, self-care, pain/discomfort, mood).[11]

One possibility accounting for these divergent views is that, although depression and apathy may reflect distinct syndromes, they share overlapping features and components. Recently, Kirsch-Darrow et al.[12] examined overlapping features of depression and apathy in PD and identified four factor-based constructs: 1) dysphoria or sadness (pure depression), 2) decreased interest (mixed depression and apathy), 3) pure apathy, and 4) somatic symptoms.

The goal of the present study was twofold: 1) to systematically examine the unique contributions of apathy, depression, and anxiety symptoms on QoL in a sample of cognitively intact individuals with PD; and 2) to determine whether parsing of symptoms that are unique to each mood/motivation construct might offer a clearer understanding of unique and shared influences of mood on QoL. The latter was examined using the previously reported factor structures of Kirsch-Darrow et al.[12]

METHODS

Participants and Procedures

Participants included a convenience sample of 107 individuals with idiopathic PD who were seen through the University of Florida Center for Movement Disorders and Neurorestoration. All participants met UK Brain Bank diagnostic criteria for a diagnosis of PD.[13] Exclusion criteria included comorbid neurological illnesses, previous neurosurgical treatment (i.e., deep brain stimulator placement or pallidotomy), or evidence of cognitive impairment based on scaled scores less than 7 on the Dementia Rating Scale II.[14] Participants completed mood, psychosocial, and cognitive measures as part of a comprehensive neuropsychological evaluation. Informed consent was obtained according to university and federal guidelines. Demographic and disease characteristics of this sample are shown in Table 1.

Measures

Quality of life: parkinson's disease questionnaire-39. Quality of life was assessed using the Parkinson's Disease Questionnaire-39 (PDQ-39), a 39-item self-report survey of common problems

TABLE 1. Sample Characteristics

	Range	Mean (standard deviation)
Age (years)	42–86	64 (8.6)
Years of education	7–22	15 (2.8)
Disease duration (years)	1–20	9 (4.5)
UPDRS motor score (on levodopa)	9–46	24.1 (7.9)
Global cognitive status (DRS-II total)	127–144	138.6 (3.6)
	N	%
Gender		
Male	74	69%
Female	33	31%
Hoehn andYahr stage of disease		
1.5	1	0.9%
2.0	65	60.7%
2.5	17	15.9%
3.0	14	13.1%
4.0	1	0.9%
Data not obtained	9	8.4%
Disease subtype		
Tremor predominant	73	68.2%
Akinetic/rigid	22	20.6%
Gait/instability	3	2.8%
Unspecified	9	8.4%

DRS: Dementia Rating Scale; UPDRS: Unified Parkinson's Disease Rating Scale.

experienced by patients with PD.[15] Participants report how often in the last month they have encountered each problem using a five-point Likert-type scale ranging from Never to Always or Cannot Do. The PDQ-39 contains eight discrete domains: mobility, activities of daily living, emotional well-being, stigma, social support, cognition, communication, and bodily discomfort. Scores from each domain are computed into a scale ranging from 0 to 100, with lower scores indicating fewer problems and better QoL. The PDQ-39 summary index score (PDQ-SI) is an index of overall QoL and is computed by summing the eight domain scores and standardizing the score on a 0–100 scale.[15] The PDQ-39 has been extensively studied and shown to be appropriately reliable, valid, and sensitive to change.[16]

Mood measures: beck depression inventory-II. The Beck Depression Inventory II (BDI-II) consists of 21 items on a four-point Likert scale (0–3) that are rated based on feelings/thoughts/behaviors over the last 2 weeks. Higher scores indicate greater levels of symptom severity. The literature supports the reliability and construct, convergent, discriminant, and content validity of the BDI-II.[17] The BDI-II has been validated within samples of patients with PD, and a cutoff score of 13 or 14 has been recommended as a marker of clinically significant depression.[18]

Mood measures: apathy scale. The Apathy Scale (AS) is a 14-item questionnaire that assesses symptoms of motivation, interest, and emotional blunting using a four-point Likert scale, ranging from 0 (not at all) to 3 (a lot).[7] The AS has been recommended for use with patients with PD by a Movement Disorders Task Force, and the recommended clinical cutoff is 14.[19] Higher scores indicate greater levels of symptom pathology. Studies have demonstrated good support for the reliability and construct validity of the AS in PD.[7,20]

Mood measures: trait scale of the state trait anxiety inventory. Symptoms of chronic anxiety were assessed using the trait subscale of the State Trait Anxiety Inventory (STAI-T).[21] The STAI-T consists of 20 items on a four-point Likert scale (1–4), with higher scores indicating greater levels of symptom pathology. The STAI is a well-established measure with strong reliability and construct and concurrent validity.[21] A Movement Disorder Society Task Force suggested the STAI as a measure of anxiety within PD.[22]

Statistical Analyses

The initial set of analyses used total scores on the BDI-II, AS, STAI-T, and overall QoL score on the PDQ-39. First, correlations were conducted to understand the relationship among measures of mood symptom severity (BDI-II, AS, and STAI-T total scores) and overall QoL (PDQ-SI). Second, significant differences among correlations between QoL and mood symptom severity were examined using Williams' t tests.[23] Third, stepwise regressions were used to determine which mood symptoms contributed to overall QoL independent of differences in age, global cognitive ability (Dementia Rating Scale II total scaled score), and disease severity (Unified Parkinson's Disease Rating Scale motor score). To control for potential influence of age, cognitive performance, and disease severity on QoL, the following variables were forced into the first block in the regression model: age, Dementia Rating Scale II total scaled score, and Unified Parkinson's Disease Rating Scale motor score. Then, total scores from the three mood/motivation measures (BDI-II total score, AS total score, and STAI-T total score) were entered with stepwise entry in the last block.

A second set of analyses used factor scores derived from BDI-II and AS items, according to the procedure of Kirsch-Darrow et al.,[12] and the trait anxiety score from the STAI to examine the relationship with QoL. This approach was taken to better characterize pure apathy and pure depression from overlapping symptoms. Calculations were based on a factor analysis conducted by Kirsch-Darrow et al.[12] and were used in place of total scores, yielding four predictors: 1) pure dysphoria, 2) pure apathy, 3) decreased interest (common to both apathy and depression), and 4) somatic symptoms. To investigate the contribution of these derived mood factors and STAI-T on PD-specific QoL domains, nine separate stepwise regression analyses were conducted to investigate the independent contribution of the mood factors on the total PDQ-39 score and each of the eight PDQ-39 subdomains: activities of daily living, communication, social, cognition, emotion, stigma, discomfort, and mobility. Once again, age, global cognitive functioning (Dementia Rating Scale total), and disease severity were entered into the first block of the regression analyses to control for potential influences, followed by mood variables entered into the second block in stepwise fashion.

TABLE 2. Descriptives of Mood Questionnaires and PDQ-39

	Range	Mean (Standard Deviation)
BDI-II total	1–34	9.9 (7.4)
Apathy Scale total	0–31	10.8 (6.5)
STAI-Trait total	20–71	35.8 (11.0)
PDQ Summary Index	5–81	34.1 (19.4)
Mobility	0–100	38.9 (27.8)
ADL	0–100	35.6 (24.3)
Emotional Well-Being	0–88	27.6 (21.9)
Stigma	0–94	25.0 (24.0)
Social	0–75	13.2 (17.7)
Cognitions	0–75	28.4 (18.8)
Communication	0–75	24.9 (20.9)
Discomfort	0–92	38.3 (21.8)

ADL: activity of daily living; BDI-II: Beck Depression Inventory-II; PDQ: Parkinson's Disease Questionnaire-39; STAI: State-Trait Anxiety Inventory.

RESULTS

Descriptives

Table 1 depicts demographic and disease characteristics of the 107 patients with PD. As a group, the majority were male (69%), Caucasian (95%), tremor predominant (68.2%), and in the mid-stages of PD disease severity based on the Hoehn and Yahr staging system. Participants ranged in age from 42 to 86 years (mean=64 years, SD=8.6) and were well educated overall (mean=15 years, SD=2.8). Results for mood symptoms revealed that levels of depression severity ranged from no symptoms to severe levels, although the overall mean was below the clinical cutoff (Table 2). Similarly, self-ratings of apathy (AS) and anxiety (STAI-T) ranged from no symptoms to clinically significant levels. The average PDQ-SI total score was 34.1 (SD=19.4). Difficulties were reported to be greatest within the domain of mobility, followed by discomfort, activities of daily living, cognitions, emotional well-being, stigma, communication, and social.

Correlations

Reductions in overall QoL were associated with increased levels of anxiety ($r=0.494$, $p<0.01$), depression ($r=0.476$, $p<0.01$), and apathy ($r=0.241$, $p<0.05$). Positive and moderate to strong correlations were present between measures of depression, anxiety, and apathy (Table 3). Positive correlations between derived factor scores also ranged from moderate to strong (Table 4). Williams' t tests revealed that the correlation between depression and QoL was significantly stronger than the correlation between apathy and QoL [Williams' $t(104)=3.13$, $p=0.002$]. Similarly, the correlation between anxiety and QoL was stronger than the correlation between apathy and QoL [Williams' $t(104)=3.15$, $p=0.002$]. The correlations between QoL and either anxiety or depression were not significantly different.

Regression Analyses: Predicting Overall QoL (PDQ-39 Summary Index)

To determine which mood predictors contributed independently to overall QoL over and above that of age, global cognitive ability, and disease severity, a stepwise regression was conducted in which overall QoL (PDQ-SI) was regressed on BDI-II, AS, and STAI-T total scores, after controlling for age, Dementia Rating Scale total, and Unified Parkinson's Disease Rating Scale motor scores. Collinearity diagnostics (tolerance >0.2 and variation inflation factor <5) were appropriate for all regression analyses, indicating that multicollinearity was not present among predictors. Although the overall model was significant [$R^2=0.279$, $F(1,102)=9.88$, $p<0.001$], trait anxiety contributed the most variance in overall QoL scores (R^2 change=0.251, beta=0.472, $p<0.001$), and neither depression nor apathy significantly contributed to variance over and above that of trait anxiety.

To disentangle unique and overlapping symptoms of depression and apathy, factor scores were used in further regression analyses in place of BDI-II and AS total scores (Table 5). Again, trait anxiety contributed the most independent variance to overall QoL, followed by pure dysphoria and decreased interest (i.e., overlapping symptoms of depression and apathy). Pure apathy, somatic symptoms, age, Unified Parkinson's Disease Rating Scale, and Dementia Rating Scale total scores did not significantly contribute to overall QoL.

TABLE 3. Correlations Between Mood Symptom Severity (Total Scores)

	BDI-II Total Score	AS Total Score
AS total score	0.622[a]	
STAI-T total score	0.779[a]	0.560[a]

AS: Apathy Scale.
[a] $p<0.001$.

Regression Analyses: Predicting Domain-Specific QoL (PDQ-39 subscales)

Finally, each subscale of the PDQ-39 was inspected to determine which of the five mood factors independently contributed to domain-specific QoL (activities of daily living, communication, social, cognition, emotion, stigma, discomfort, mobility). As shown in Table 5, trait anxiety was the best independent predictor of activities of daily living, communication, emotion, stigma, discomfort, and mobility domains. Pure dysphoria was the best independent predictor for the social and cognition domains and the second strongest independent predictor for the emotion domain. Pure apathy contributed significantly to communication. Overlapping symptoms of depression and apathy (i.e., decreased interest factor) significantly contributed to activities of daily living, emotion, and stigma. Last, somatic symptoms contributed significantly to the social domain.

DISCUSSION

This retrospective study including 107 patients with PD found that self-reported QoL was related to mood symptoms, primarily trait anxiety. However, further inspection revealed separate mood factors to contribute significantly to various domains of QoL. Although trait anxiety was the

TABLE 4. Correlations Among Mood Symptom Severity (Factor Scores)

	Trait Anxiety	Pure Dysphoria	Pure Apathy	Reduced Interest (Overlapping Items)
Pure dysphoria	0.722[a]			
Pure apathy	0.568[a]	0.482[a]		
Reduced interest (overlapping items)	0.635[a]	0.598[a]	0.702[a]	
Somatic symptoms	0.619[a]	0.509[a]	0.600[a]	0.683[a]

[a] $p<0.001$.

primary contributor to a majority of QoL domains (activities of daily living, communication, emotion, stigma, discomfort, and mobility), separate and overlapping factors of depression and apathy contributed to a number of QoL domains (activities of daily living, communication, social, cognition, emotion, and stigma). This study was unique in its ability to examine how separate factors of these mood disturbances contributed to various domains of QoL affected by PD.

Past studies examining the impact of anxiety and depression have found the presence of either mood symptom to be indicative of worse QoL.[5] Usually, symptoms of depression show a slightly stronger relationship with QoL than anxiety; however, this finding has not always been replicated.[24] A review of determinants of QoL revealed that both anxiety and depression are strongly related to QoL, but fewer studies of QoL examine anxiety than depression, on the order of 2:1.[25]

Regarding apathy, our finding of a significant correlation between apathy and QoL is consistent with a past study,[11] in which five separate domains of QoL (i.e., mobility, self-care, usual activities, pain, and mood) were found to be significantly related to apathy. However, the current study suggests that a majority of the variance in this relationship might be explained by overlapping symptoms of apathy with either anxiety or depression (e.g., reduced interest in learning new things, loss of interest, loss of pleasure, indecisiveness), rather than by symptoms that are unique to apathy (e.g., motivation, indifference, putting forth effort, relying on others to initiate daily activity). This is consistent with past findings that failed to show a relationship between the Apathy Evaluation Scale and the PDQ-8 (short form of PDQ-39) independent of depression.[12]

A previous review questioned the clinical importance of apathy and whether it was linked to meaningful outcomes.[10] Although apathy may only show a small relationship to QoL, there are at least two reasons why apathy should continue to be considered a useful construct in PD. First, apathy has been shown to significantly predict other meaningful outcomes including cognition/dementia status, disease severity, and functional abilities, with some of these studies specifying a contribution of apathy over and above that of depression.[12,26–29] Second, although apathy may not be related to self-reported QoL, caregiver QoL has yet to be thoroughly investigated. The impact of mood functioning among patients with PD has been linked to caregiver distress, and nonmotor symptoms have been shown to account for about twice as much variance in caregiver distress compared with motor symptoms.[30,31] At least one study to date has shown that caregivers of apathetic patients with PD experience a greater degree of caregiver burden compared with those who care for nonapathetic patients with PD.[32] A similar relationship between apathy and caregiver distress has also been reported among nondemented elderly individuals[33] and patients with other neurodegenerative disorders including Alzheimer's disease, Lewy body dementia, and fronto-temporal dementia.[34–36]

There are several limitations in the current study. First, a convenience sample of nondemented patients receiving outpatient clinical care was used and may limit the generalizability of these findings. Second, as with all cross-sectional studies, the directionality of the relationships cannot be specified. It is possible that having worse QoL may contribute to patients developing depressed, apathetic, or anxious phenotypes or that the inverse is true and that mood disturbances lead to worse QoL. The use of a cross-sectional sample also limits the ability to inspect the trajectory/changes in mood symptoms and QoL across different stages of PD. Additionally, there are concerns about the validity of the subdomains of the PDQ-39.[37] Future studies could benefit from using additional clinical measures of QoL and mood functioning, including a mixture of state/trait measures and DSM-V diagnoses. Next, we did not look at factors within the STAI measure to exclude items within this anxiety measure that overlap with depression or apathy. Bieling

TABLE 5. Stepwise Regression Analyses Evaluating the Contribution of Mood Factors on QoL

	Criterion	Predictor	Beta	Significance	R^2
1	Overall QoL	Anxiety	0.400	0.002	0.215
		Dysphoria	0.316	0.012	0.029
		Decreased interest	−0.247	0.027	0.033
2	QoL-ADL	Anxiety	0.390	0.002	0.056
		Decreased interest	−0.246	0.048	0.035
3	QoL-communication	Age	−0.192	0.049	0.049
		Anxiety	0.277	0.009	0.168
		Apathy	0.249	0.019	0.041
4	QoL-social	Dysphoria	0.292	0.005	0.169
		Somatic	0.270	0.009	0.053
5	QoL-cognition	Dysphoria	0.413	0.000	0.162
6	QoL-emotion	Anxiety	0.463	0.000	0.268
		Dysphoria	0.333	0.006	0.030
		Decreased interest	−0.282	0.009	0.043
7	QoL-stigma	Anxiety	0.448	0.000	0.067
		Decreased interest	−0.304	0.012	0.053
8	QoL-discomfort	Anxiety	0.293	0.002	0.083
9	QoL-mobility	Anxiety	0.319	0.001	0.098

Only significant predictors shown. QoL: quality of life.

et al.[38] reported that the trait scale of the STAI includes items assessing depression and negative affect in addition to pure anxiety. As a result, our measure of anxiety was not a measure of pure anxiety and likely accounted for some overlapping symptoms of depression, less likely apathy, when entered into the regression, thus reducing the observed influence of other mood factors in our model. However, the presence of sufficient collinearity diagnostics suggests that anxiety scores did not significantly reduce the ability to detect unique effects of apathy or depression. Last, as mentioned previously, this study was unable to account caregiver QoL, which may be affected by the patient's mood symptoms in a unique way.

Overall, common mood disturbances are indicative of worse QoL among patients with PD. Although anxiety may have the most detrimental effect on QoL, symptoms of depression and apathy may be linked to specific domains of QoL. Apathy, depression, and anxiety may respond differently to separate pharmaceutical and behavioral therapies.[9] The investigation of the relationship between separate mood components and QoL may have implications for interventions (i.e., which treatment might be most effective among individuals with comorbid disorders) and targeted outcomes of future intervention trials.

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