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Quality of Life in Parkinson's Disease: The Relative Importance of the Symptoms

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Abstract: A body of literature now exists, which demonstrates that idiopathic Parkinson's disease (PD) has a major negative impact on quality of life (QoL), and that depression and cognitive impairment are among the main predictors of poor QoL in this disorder. Relatively little work has been done to assess the differential contribution of the specific symptoms of PD to QoL, which was the aim of this study. One hundred thirty patients with PD completed a booklet of questionnaires, which included the PDQ39 as a disease-specific measure of QoL, a symptom checklist, a mobility checklist, as well as patient ratings of disease stage and disability. The results indicated that the contribution of physical, medication-related, and cognitive/psychiatric symptoms to QoL can be significant. Sudden unpredictable on/off states, difficulty in dressing, difficulty in walking, falls, depression, and confusion were PD symptoms, which significantly influenced QoL scores. Among the mobility problems associated with PD, start hesitation, shuffling gait, freezing, festination, propulsion, and difficulty in turning had a significant effect on QoL scores. In addition to depression and anxiety, the major predictors of QoL were shuffling, difficulty turning, falls, difficulty in dressing, fatigue, confusion, autonomic disturbance particularly urinary incontinence, unpredictable on/off fluctuations, and sensory symptoms such as pain. The implications of these results for the medical management of PD are discussed. © 2008 Movement Disorder Society

Key words: Parkinson's disease; quality of life; mobility; symptoms; depression.

In the last decade there has been a "paradigm shift " in the assessment of chronic neurological disorders such as Parkinson's disease (PD). Previously, following treatment, the focus was on documenting changes in motor symptoms using scales such as the United PD Rating Scale.[1] Now, there is increasing recognition that examining the impact of the illness, and its medical or surgical treatment, on the daily life, psychological well-being of the patient and their ability to perform their occupational and social roles is equally important. This had led to the emergence of quality of life (QoL) measures as important tools for quantifying the "true" impact of chronic illness. Consequently, more recent studies, such as those quantifying the effect of surgical treatments, such as deep brain stimulation (DBS), have used QoL as a primary outcome measure (for review, see Ref. 2).

There is now a body of literature, which has established that PD, like many other chronic neurological disorders, has a negative impact on the QoL of patients.[3–7] Interestingly, in PD nonmotor symptoms such as depression and cognitive impairment are major predictors of QoL.[5–8] Other investigators have examined the effect of specific PD symptoms such as tremor, rigidity and bradykinesia,[4] medication-related complications,[9] insomnia,[10] fatigue,[11] and sweating.[12] However, to date, the *relative* contributions of the different PD symptoms to the patient's QoL have not been investigated. This is important for several reasons. First, if the paradigm shift noted earlier is to have a true influence, symptoms that are shown to have the greatest impact on the QoL of PD patients should be targeted for medical management alongside treatment of the primary motor symptoms. Second, it is possible that the impact on QoL of surgical techniques such as DBS of the subthalamic nucleus

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(STN) is mediated by improving the physical aspects of QoL[13] or by amelioration of depression.[14] Third, if those symptoms perceived by PD patients as having the most negative influence on their daily life e.g., freezing, are not greatly improved by surgical intervention; then, despite relieving rigidity, bradykinesia, tremor, and dyskinesias, surgical interventions (lesions or DBS) of the STN or the internal segment of the pallidum may disappoint the patients at some level and reduce the positive impact of these surgical techniques on their QoL.[15] In light of these, the primary aim of this article is to consider the relative importance of specific PD symptoms to the QoL of the patients. The contribution of anxiety to QoL in PD has not been investigated so far, and so we examined this in addition to depression and mobility-related problems, such as postural instability and falls, which we have previously shown to be important for QoL in PD.[3,7]

PATIENTS AND METHODS

Sample

This study was approved by the Ethics Committee of the National Hospital for Neurology and Neurosurgery (NHNN) and the Institute of Neurology; informed consent was obtained from all participants. Patients who had recently attended PD clinics at the NHNN were invited to participate, 68% of whom responded, and an advertisement was placed in the newsletter of the Parkinson's Disease Society, to which 60 patients replied. The majority of questions could be answered by marking the chosen response. One hundred thirty patients (84 men) completed the questionnaires, their mean age was 66.7 (SD 8.52), the mean number of years since diagnosis was 9.28 (SD 6.48), and the mean number of years of illness was 12.1 (SD 7.94).

Stage of Illness and Disability

The self-administered measures of disease stage and of disability were modified versions of the Hoehn and Yahr (H&Y) scale[16]; with stage 1 indicating mild parkinsonism and stage 5 indicating the most severe disease, and the Schwab and England (S&E) scale[17]; with 10 indicating complete independence and 0 indicating complete dependence).

QoL

QoL was assessed with the PDQ-39[4] which produces eight subscores (mobility, activities of daily living [ADL], emotional wellbeing, stigma, social support, cognition, communication, and bodily discomfort, and one summary index (the PDQ39-SI). Higher scores reflect poorer QoL (range 0–100).

PD Symptoms Checklist

Patients indicated whether they had experienced each of 29 symptoms, from five clusters: motor, medication related, cognitive/neuropsychiatric, autonomic, and sensory (fully listed in Table 2). Each symptom was rated as none = 0, mild = 1, moderate = 2, severe = 3 when on and off medication.

Mobility Checklist

Patients indicated whether they had experienced specific mobility symptoms (fully listed in Table 3). The terms start hesitancy, shuffling, freezing, festination, propulsion, and retropulsion were explained in simple terms. Each symptom was rated as 0 = absent, 1 = mild, 2 = moderate, 3 = severe when on and off medication.

Measures of Mood

Depressive and anxiety symptoms were assessed using the 21 item Beck depression inventory (BDI)[18] and Beck anxiety inventory (BAI)[19] questionnaires, respectively.

RESULTS

Self-rated H&Y stage data were unavailable for 4 PD patients (3.1% of sample), and 3 PD patients (2.3%) rated themselves as having no tremor or slowness (stage 0) when on medication. The remaining patients were distributed as follows: stage 1 = 11 (8.5%); stage 1.5 = 15 (11.5%); stage 2 = 30 (23.1%); stage 2.5 = 15 (11.5%); stage 3 = 14 (10.8%); stage 4 = 32 (24.6%); stage 5 = 6 (4.6%).

Effect of Stage of Illness on PDQ39-SI and Subscores

Table 1 provides data concerning the PDQ39-SI and the eight subscores according to H&Y stages 0 to 2.5 (early PD with little or no balance or mobility problems) versus 3 to 5 (late PD with balance and mobility problems). As expected, one-way ANOVAs revealed that patients in the later stages of PD had significantly higher scores (poorer QoL) than patients with early PD on the PDQ39-SI, and all domains of the PDQ39 except bodily discomfort.

Effect of Specific PD Symptoms on PDQ39-SI

Table 2 provides information regarding significant differences in PDQ39-SI scores as a function of presence or absence (in the "on" state) of each of the 29 symptoms or signs of PD. Differences were tested using one-way ANOVAs with a strict criterion of $P < 0.0017$.

Effect of Mobility Symptoms on PDQ39-SI

The mean PDQ39-SI as a function of the presence or absence (in the "on" state) of key mobility

TABLE 1. *Mean (SD) scores on the eight PDQ39 domains and PDQ39-SI as a function of Hoehn & Yahr[16] stage of illness, comparing stages 1 to 2.5 with stages 3 to 5*

	H&Y ≤ 2.5 (N = 74)	H&Y ≥ 3 (N = 52)	Statistical results
Mobility	33.1 (26.1)	62.9 (24.9)	$F(1,113) = 37.3$, $P < 0.0005$
ADL	30.2 (23.1)	49.3 (24.4)	$F(1,119) = 19.2$, $P < 0.0005$
Emotional wellbeing	22.5 (18.6)	36.9 (25.4)	$F(1,118)=12.9$, $P < 0.0005$
Stigma	22.3 (23.8)	33.7 (28.3)	$F(1,121)=5.84$, $P = 0.017$
Social support	10.1 (15.6)	19.0 (19.8)	$F(1,97)=6.34$, $P = 0.013$
Cognition	26.8 (21.4)	37.6 (20.6)	$F(1,117)=7.50$, $P = 0.007$
Communication	23.4 (23.3)	37.7 (22.1)	$F(1,121)=11.9$, $P = 0.001$
Bodily discomfort	40.2 (26.9)	48.2 (25.9)	$F(1,120)=2.70$, $P = 0.103$
PDQ39-SI	25.2 (15.1)	39.6 (17.5)	$F(1,80)=15.8$, $P < 0.0005$

problems are shown in Table 3. Differences were tested using one-way ANOVAs with a strict $P < 0.0045$ criterion.

TABLE 2. *Mean (SD) quality of life (PDQ39-SI) scores as a function of the presence/absence of each of 29 PD symptoms*

Mean PDQ39-SI score (SD)	Symptom absent	Symptom present	*P* value
Motor			
Slowness of movement	13.8 (3.81)	33.5 (17.4)	0.014
Stiffness	27.8 (13.6)	33.0 (18.4)	0.370
Tremor	31.4 (20.3)	32.6 (17.0)	0.788
Falls	25.7 (13.9)	39.8 (19.0)	<0.0005
Loss of balance	31.0 (20.0)	32.3 (17.3)	0.808
Difficulty in dressing	20.1 (14.0)	38.0 (16.8)	<0.0005
Difficulty in walking	18.9 (10.1)	35.8 (17.9)	<0.0005
Medication-related			
Drug induced dyskinesia	29.7 (15.1)	33.2 (18.5)	0.377
End of dose deterioration	24.1 (13.1)	33.6 (17.5)	0.038
Unpredictable "on/offs"	23.9 (12.7)	37.9 (17.5)	0.001
Cognitive/psychiatric			
Fatigue	22.4 (13.0)	34.2 (18.3)	0.025
Depression	25.4 (12.4)	40.4 (19.5)	<0.0005
Memory problems	27.8 (16.3)	36.7 (18.5)	0.029
Confusion	26.3 (14.3)	40.5 (18.9)	<0.0005
Hallucinations (visual)	29.2 (16.3)	38.5 (19.6)	0.037
Hallucinations (auditory)	31.0 (17.9)	35.9 (17.0)	0.395
Sex drive (increased)	31.5 (16.5)	31.8 (20.1)	0.934
Sex drive (decreased)	27.8 (15.1)	41.0 (19.1)	0.002
Autonomic			
Nausea	31.3 (18.6)	34.5 (14.8)	0.462
Vomiting	31.7 (18.0)	36.1 (13.7)	0.481
Dizziness or fainting	29.8 (15.3)	38.9 (21.0)	0.037
Sweating attacks	31.7 (19.6)	32.2 (15.8)	0.896
Bladder frequency	26.9 (13.3)	34.2 (19.1)	0.113
Bladder urgency	28.2 (15.5)	33.3 (18.8)	0.261
Urinary incontinence	27.9 (17.1)	40.2 (16.9)	0.005
Faecal incontinence	29.7 (16.1)	42.0 (21.6)	0.018
Constipation	27.2 (17.1)	35.6 (17.5)	0.041
Sensory			
Pain	28.4 (13.6)	35.5 (21.0)	0.091
Headache/migraine	29.6 (16.3)	40.8 (21.1)	0.028

P values are given from one-way ANOVA, with a Bonferroni correction applied such that significance is set at $P \leq 0.0017$.

Predictors of PDQ39-SI: Regression Analyses

Predictors of QoL were identified through multiple regression analyses with PDQ39-SI as the dependent variable. First, age of PD onset, H&Y staging, S&E disability ratings, and duration of illness were entered as independent variables. These factors cumulatively accounted for 42.9% of the variance in PDQ39-SI scores. Only the contribution of the S&E ratings reached significance (β coefficient = −0.600, $t = -6.16$, $P < 0.0005$).

Based on *a priori* hypotheses, BDI and BAI, in that order, were entered as independent variables into a stepwise linear regression. BDI accounted for 40.8% of the variance of QoL, while anxiety as measured on the BAI accounted for a further 17.0% of variance of QoL scores (adjusted R^2 of 0.408 and 0.578, respectively; BDI: β = 0.409, $t = 4.78$, $P < 0.0005$; and BAI: β = 0.478, $t = 5.59$, $P < 0.0005$).

Further linear stepwise regression analyses were performed for each cluster of the PD symptoms checklist. The severity (0–3) of PD symptoms in the on state were entered as independent variables. The severity of items from the mobility checklist (on state) were also added as independent variables in a separate analysis. The summary of these regression analyses are shown in Table 4.

A final stepwise linear regression was performed, with all the factors that had been shown to be predictors of QoL in previous regressions as independent variables. These were as follows: S&E rating, BDI, BAI, from the PD symptom checklist (on state): falls, difficulty in dressing, depression, confusion, fatigue, unpredictable on–off states, urinary incontinence, constipation, headache, and pain, from the mobility symptoms (on state): difficulty turning and shuffling gait. The result of this analysis is shown at the end of Table 4.

DISCUSSION

The present study specifically assessed the relative contribution of PD symptoms to QoL. The most striking

TABLE 3. *Mean (SD) quality of life (PDQ39-SI) scores as a function of the presence/absence of each of 11 mobility-related symptoms*

	Symptom absent	Symptom present	*P* value
Difficulty in turning	22.5 (14.1)	38.2 (17.0)	<0.0005
Festination	25.2 (12.4)	38.7 (18.8)	<0.0005
Freezing	22.8 (11.9)	36.6 (17.6)	<0.0005
Shuffling gait	21.6 (9.84)	36.2 (18.5)	<0.0005
Start hesitation	23.9 (12.6)	36.0 (17.7)	0.002
Propulsion	23.6 (12.7)	35.1 (17.3)	0.003
Balance difficulties	24.3 (16.3)	35.5 (17.4)	0.010
Difficulty rising from a chair	23.6 (13.0)	35.2 (18.2)	0.014
Lack of arm swing	26.7 (15.2)	34.4 (18.2)	0.085
Retropulsion	30.1 (14.9)	39.6 (27.9)	0.128
Stooped posture	26.1 (12.0)	32.5 (18.3)	0.214

P values are given from one-way ANOVA, with a Bonferroni correction applied such that significance is set at $P \leq 0.0045$.

finding was an explanation of a considerable proportion of the variance of QoL through physical and autonomic symptomotology, medication-related complications, as well as cognitive/psychiatric problems. Also, increased severity of PD was associated with poorer QoL, not just overall, but on all domains of QoL with the exception of bodily discomfort.

That such a wide range of PD symptoms are linked to poorer QoL is clearly relevant to its medical management, as it is currently posited that interventions such as DBS of the STN only improve physical aspects of QoL[13] or improve QoL via reduction of depression.[14] We have corroborated previous findings that overall QoL deteriorates with advancing disease,[3,20] and additionally shown that later stages of illness are associated with poorer QoL in all domains of the PDQ39 except bodily discomfort. Disability, indexed by S&E ratings, emerged as a significant predictor of QoL.

TABLE 4. *A summary table of the multiple linear stepwise regression analyses, with the PDQ39-SI as the dependent variable and the five symptom clusters of the PD symptoms checklist, and the mobility checklist, as the independent variables. The independent variables for final combined analysis were those symptoms found to be significant predictors of QoL in the previous regressions*

Symptom cluster	Adjusted R^2	β coefficient	*t* value	*P* value
Motor	0.470			
Falls		0.331	3.65	0.001
Difficulty in dressing		0.535	5.90	<0.0005
Cognitive/psychiatric	0.418			
Depression		0.270	2.60	0.011
Confusion		0.304	2.90	0.005
Fatigue		0.300	2.87	0.005
Medication-related	0.219			
Unpredictable on–off states		0.479	4.79	<0.0005
Autonomic	0.291			
Urinary incontinence		0.408	3.98	<0.0005
Constipation		0.339	3.30	0.002
Sensory	0.116			
Headache		0.258	2.27	0.027
Pain		0.236	2.08	0.042
Mobility checklist	0.292			
Shuffling gait		0.353	2.94	0.004
Difficulty turning		0.278	2.32	0.023
Combined	0.789			
BDI		0.367	4.79	<0.0005
BAI		0.202	2.79	0.007
Schwab & England rating		-0.329	-4.53	<0.0005
Difficulty in turning		0.155	2.20	0.032
Shuffling gait		0.162	2.26	0.028

Physical Symptoms

The deterioration of manual dexterity as a result of worsening rigidity and tremor with progressing PD obviously affects everyday activities such as cutting food, pill-taking, and simple housework. Correspondingly, tremor, rigidity, and bradykinesia have been shown to correlate strongly with poorer QoL.[4] Our findings highlight the importance of mobility problems to QoL in PD, as found in previous studies,[3,7] not only on the mobility subscale of the PDQ39, but also on overall QoL in PD.

Shuffling, difficulty turning, falls, and difficulty in dressing emerged as significant predictors of QoL. Shuffling and difficulty turning are likely to contribute to falls, which in turn have an obvious influence on QoL in PD through injury and resulting in time in hospital,[21] or social stigma and embarrassment from falling in public. Also, the fear of falling[22] can prevent PD patients from taking part in activities, further restricting their QoL. The ability to dress and undress oneself is a major indicator of a person's functional independence, and an inability to do so increases the patients' dependence on their carers and affects their QoL. Simple interventions to facilitate everyday activities are therefore an important strategy[23] for improving QoL.

Medication-Related Symptoms

Increasing dyskinesia severity has previously been associated with increased depression,[24] and health care costs,[25] in addition to poorer QoL, particularly in older patients.[9] In this study unpredictable on–off states were found to influence QoL in PD. Attempts to improve QoL through reduction of these medication-related complications must obviously be balanced against continued, effective amelioration of primary PD symptoms. However, even patients on high doses of levodopa without dyskinesias are liable to experience poorer QoL in relation to advanced disease.[26] More optimistically, posteroventral pallidotomy[27] and DBS[2,14] have a beneficial effect on QoL, likely due, in part, to post-surgical reduction of L-dopa and its associated complications.

Neuropsychiatric/Neurocognitive Symptoms

Our finding that depression has a serious impact on QoL in PD supports previous studies.[5–8] However, across these studies, the overlap between items assessing emotional wellbeing on QoL scales and depression scales is a possible source of shared variance between depression and QoL measures. Our novel finding here was that, once the contribution of depression to QoL was taken into account, self-rated anxiety on the BAI accounted for a further 17% of the variance of QoL. This additional contribution of anxiety to QoL in PD has not been previously recognized, possibly because anxiety is relatively under-investigated in PD,[28] despite being present in up to 38% of PD patients.[29] Many symptoms of PD can give rise to anxiety: the unpredictability of function and mood swings associated with on–off fluctuations,[30] the disturbance of posture and balance, and risk of falls when walking.[21,22] Anxiety can worsen the motor symptoms of PD,[31] which can, reciprocally, lead to greater anxiety. This anxiety can manifest as "fear of falling," which has been reported by 46% of patients,[22] and can lead to avoidance of mobility, particularly venturing outside the home, and hence, social isolation and poorer QoL.

As has been proposed for depression in PD,[32] anxiety may be more likely at specific points in the course of the illness, such as immediately after diagnosis, at the time of development of mobility problems or on–off fluctuations, or when key roles/skills are lost. The increasing evidence that anxiety and depression impair QoL in PD, means that an appreciation of the timescale for depression and anxiety in the course of PD is important to facilitate their direct medical, although not necessarily pharmacological,[33] treatment.

The contribution of fatigue to poorer QoL in PD had been previously noted,[11] and has been rated as among the most disabling symptoms of PD by a large percentage of patients.[34] Consistent with previous findings of cognitive impairment as a predictor of QoL in PD,[3,6] confusion and, at a less significant level, memory problems, visual hallucinations, and reduced sex drive were found here to significantly influence QoL. Hallucinations are common symptoms in PD and are associated with worse cognitive function, greater depression, and more severe disease,[35] and, with delusions, are associated with increased nursing home placement.[36] Such neuropsychiatric symptoms are also major predictors of depression and emotional distress in caregivers,[37] highlighting the importance of their management.

Autonomic Symptoms

Many autonomic symptoms are scarcely covered by available rating scales, and their impact on patients' QoL may, therefore, be missed. In the current study, none of the autonomic symptoms had a highly significant effect on QoL scores, although urinary or faecal incontinence, constipation, and dizziness or fainting significantly affected QoL at a less stringent criterion. The emergence of urinary incontinence and constipation as predictors of QoL, support the findings of Sakakibara et al. (2001)[38] and their conclusion that "*amelioration of pelvic organ*

dysfunction. . . should be a primary target in the treatment of patients with PD."

Sensory Symptoms

We found that pain and headache contribute to poor QoL in PD, corroborating previous findings using the SF-36 QoL questionnaire.[39] In the literature, as many as two thirds of patients report pain, with muscle stiffness, which becomes more problematic with disease progression, as a likely cause.[8] While L-dopa improves some types of pain in PD, such as off pain, alternative approaches such as relaxation training, distraction, and mindfulness may prove helpful in reducing or coping with pain in PD, even in patients *"optimally treated by a neurologist."*[39]

CONCLUSIONS

Postal questionnaire studies such as this allow collation of data from a large cohort of patients on a wide range of measures. The compromise for such breadth is that the patients' responses are not confirmed by clinicians. For the H&Y and S&E scales, a strong agreement between self-ratings and clinician ratings has been shown.[40] The PDQ39, BDI, and BAI are also well-established measures.[4,18,19] The PD symptom checklist and mobility checklist, specifically designed for this study, are being validated. As noted for depression, a particular issue with studies of the effect of PD symptoms on QoL is that many, e.g., difficulty in dressing, are included as items within the PDQ39 itself, as these problems are *assumed* to impact QoL. However, this does not invalidate our findings, since not all items that are present in both PDQ39 and symptom checklists emerge as strong predictors of QoL e.g., memory problems. With these limitations in mind, this study provided a useful analysis of the effects of different symptoms on QoL in PD, which identifies worthwhile targets for disease management.

In summary, there are many facets to the patient's "journey " from the initial communication of the diagnosis that influence their QoL. Our results suggest that the nonmotor symptoms across all clusters should be targeted for intervention, either medically, or through alternative approaches such as cognitive-behavioral methods, as this should result in a substantial improvement of the QoL of PD patients. The impact on QoL of certain mobility problems, including shuffling, difficulty turning and falls, that are relatively resistant to medical treatment, means that these features of PD are likely to warrant more innovative multidisciplinary rehabilitation approaches. This, in a way, requires a further "paradigm shift."

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REFERENCES

1. Schrag A, Jahanshahi M, Quinn N. What contributes to quality of life in patients with Parkinson's disease? J Neurol Neurosurg Psychiatry 2000;69:308-312.
2. Fahn S, Elton RL; For the UPDRS Development Committee. Unified Parkinson's disease rating scale. In: Fahn S, Marsden CD, Calne D, Goldstein M, editors. Recent developments in Parkinson's disease, Vol. 2. Florham Park: MacMillan Healthcare Information; 1987. p 153-163.
3. Diamond A, Jankovic J. The effect of deep brain stimulation on quality of life in movement disorders. J Neurol Neurosurg Psychiatry 2005;76:1188-1193.
4. Peto V, Jenkinson C, Fitzpatrick R, et al. The development and validation of a short measure of functioning and well-being for individuals with Parkinson's disease. Qual Life Res 1995;4:241-248.
5. Martinez-Martin P. An introduction to the concept of "quality of life in Parkinson's disease". J Neurol 1998; 245 (Suppl 1): S2–S6.
6. Kuopio AM, Marttila RJ, Helenius H, Toivonen M, Rinne UK. The quality of life in Parkinson's disease. Mov Disord 2000;15:216-223.
7. Schrag A, Selai C, Jahanshahi M, Quinn NP. The EQ-5D—a generic quality of life measure—is a useful instrument to measure quality of life in patients with Parkinson's disease. J Neurol Neurosurg Psychiatry 2000;69:67-73.
8. Karlsen KH, Larsen JP, Tandberg E, Maeland JG. Influence of clinical and demographic variables on quality of life in patients with Parkinson's disease. J Neurol Neurosurg Psychiatry 1999;66: 431-435.
9. Chapuis S, Ouchchane L, Metz O, Gerbaud L, Durif F. Impact of the motor complications of Parkinson's disease on the quality of life. Mov Disord 2005;20:224-230.
10. Caap-Ahlgren M, Dehlin O. Insomnia and depressive symptoms in patients with Parkinson's disease. An interview study of patients living at home. Arch Gerontol Geriatr 2001;32:23-33.
11. Herlofson K, Larsen JP. The influence of fatigue on health-related quality of life in patients with Parkinson's disease. Acta Neurol Scand 2003;107:1-6.
12. Swinn L, Schrag A, Viswanatha R, Bloem BR, Lees A, Quinn N. Sweating dysfunction in Parkinson's disease. Mov Disord 2003; 18:1459-1463.
13. Drapier S, Raoul S, Drapier D, et al. Only physical aspects of quality of life are significantly improved by bilateral subthalamic stimulation in Parkinson's disease. J Neurol 2005;252:583-588.
14. Troster AI, Fields JA, Wilkinson S, Pahwa R, Koller WC, Lyons KE. Effect of motor improvement on quality of life following subthalamic stimulation is mediated by changes in depressive symptomatology. Stereotact Funct Neurosurg 2003;80:43-47.
15. Baron MS, Vitek JL, Bakay RAE, et al. Treatment of advanced Parkinson's disease by posterior GPi pallidotomy: 1-year results of a pilot study. Ann Neurol 1996;40:355-366.
16. Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. Neurology 1967;17:427-442.
17. Schwab RS, England AC. Projection technique for evaluating surgery in Parkinson's disease. In: Gillingham FJ, Donaldson IML, editors. Third symposium on Parkinson's disease. Edinburgh: Livingstone; 1969. p 152-157.
18. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psych 1961;4:561-571.
19. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol 1988; 56:893-897.

20. Chrischilles EA, Rubenstein LM, Voelker MD, Wallace RB, Rodnitzky RL. The health burdens of Parkinson's disease. Mov Disord 1998;13:406-413.
21. Wielinski CL, Erickson-Davis C, Wichmann R, Walde-Douglas M, Parashos SA. Falls and injuries resulting from falls among patients with Parkinson's disease and other parkinsonian syndromes. Mov Disord 2005;20:410-415.
22. Bloem BR, Grimbergen YA, Cramer M, Willemsen M, Zwinderman AH. Prospective assessment of falls in Parkinson's disease. J Neurol 2001;248:950-958.
23. Beattie A, Caird FI. The occupational therapist and the patient with Parkinson's disease. BMJ 1980;280:1354-1355.
24. Pechevis M, Clarke CE, Vieregge P, et al. Effects of dyskinesias in Parkinson's disease on quality of life and health-related costs: a prospective European study. Eur J Neurol 2005;12:956-963.
25. Maurel F, Lilliu H, Le Pen C. Social and economic cost of L-Dopa-induced dyskinesias in patients with Parkinson's disease. Rev Neurol (Paris) 2001;157:507-514.
26. Behari M, Srivastava AK, Pandey RM. Quality of life in patients with Parkinson's disease. Parkinsonism Relat Disord 2005;11:221-226.
27. Zimmerman GJ, D'Antonio LL, Iacono RP. Health related quality of life in patients with Parkinson's disease two years following posteroventral pallidotomy. Acta Neurochir (Wien) 2004;146: 1293-1299.
28. Jahanshahi M. The psychosocial impact of Parkinson's Disease and its clinical management. In: Playford D, editor. Neurological Rehabilitation of Parkinson's Disease. (Queen Square Neurological Rehabilitation Series). London: Martin Dunitz, 2003. p. 25-47.
29. Stein MB, Heuser IJ, Juncos JL, Uhde TW. Anxiety disorders in patients with Parkinson's disease. Am J Psychiatry 1990;147:217-220.
30. Menza MA, Sage J, Marshall E, Cody R, Duvoisin R. Mood changes and "on-off" phenomena in Parkinson's disease. Mov Disord 1990;5:148-151.
31. Marsh L. Anxiety disorders in Parkinson's Disease. Int Rev Psychiatr 2000;12:307-318.
32. Brown R, Jahanshahi M. Depression in Parkinson's disease: a psychosocial viewpoint. Adv Neurol 1995;65:61-84.
33. Macht M, Schwarz R, Ellgring H. Patterns of psychological problems in Parkinson's disease. Acta Neurol Scand 2005;111:95-101.
34. Friedman J, Friedman H. Fatigue in Parkinson's disease. Neurology 1993;43:2016-2018.
35. Holroyd S, Currie L, Wooten GF. Prospective study of hallucinations and delusions in Parkinson's disease. J Neurol Neurosurg Psychiatry 2001;70:734-738.
36. Goetz CG, Stebbins GT. Mortality and hallucinations in nursing home patients with advanced Parkinson's disease. Neurology 1995;45:669-671.
37. Aarsland D, Larsen JP, Karlsen K, Lim NG, Tandberg E. Mental symptoms in Parkinson's disease are important contributors to caregiver distress. Int J Geriatr Psychiatry 1999;14:866-874.
38. Sakabira R, Shinotoh H, Uchiyama T, et al. Questionnaire-based assessment of pelvic organ dysfunction in Parkinson's disease. Auton Neurosci 2001; 92:76-85.
39. Quittenbaum BH, Grahn B. Quality of life and pain in Parkinson's disease: a controlled cross-sectional study. Parkinsonism Relat Disord 2004;10:129-136.
40. Schrag A, Jahanshahi M, Quinn NP. What contributes to depression in Parkinson's disease? Psychol Med 2001;31:65-73.