Published in final edited form as:

Eur J Neurol. 2013 April ; 20(4): 663–670. doi:10.1111/ene.12019.

Major life events and development of major depression in Parkinson's disease patients

Naja Hulvej Rod, MS, PhD¹, Yvette Bordelon, MD, PhD³, Alex Thompson, MD, PhD⁴, Erin Marcotte, PhD², and Beate Ritz, MD, PhD^{2,3}

¹Department of Public Health, University of Copenhagen, Copenhagen, Denmark

²Department of Epidemiology, School of Public Health, UCLA, Los Angeles, CA, USA

³Department of Neurology, School of Medicine, UCLA, Los Angeles, CA, USA

⁴Department of Psychiatry and Behavioral Sciences, University of Washington and Group Health Cooperative, Seattle, WA, USA

Abstract

Background—Non-motor symptoms including depression are important features of Parkinson's disease (PD). We aim to address the relation between major life events and depression among PD patients free of depressive symptoms at baseline.

Methods—New-onset PD patients from California were recruited in 2001-2007 and followed-up for 3-4 years. The participants (n=221) were examined by neurologists and responded to comprehensive interviews that included major life events, social support, and coping measures from validated scales. Major depression was assessed using the Structured Clinical Interview for the DSM-IV depression module (SCID).

Results—More than half of all patients had experienced major life events since diagnosed with PD and 22 patients developed a major depression. Number of life events was associated with risk of depression in an exposure-dependent manner, with each additional event being associated with a 56 % higher risk of depression (95 % CI: 1.23-1.98). Most individual life events were associated with a two to eight-fold higher risk of depression. Patients with low social support or coping capacities seemed to be particularly susceptible to developing depression after experiencing major life events.

Conclusions—Life events play an important role for onset of depression in PD patients; an effect that seems to be modulated by social support and coping capacities and these factors may therefore be important to assess in order to identify PD patients at high risk of depression and provide effective interventions.

Keywords

Life change events; Psychological stress; Depression; Parkinson disease; Prospective studies

INTRODUCTION

Parkinson's disease (PD) is a movement disorder traditionally characterized by its motor symptoms including bradykinesia, resting tremor, stiffness, and postural instability.(1) Non-

Correspondence to: Naja Hulvej Rod (nahuro@sund.ku.dk), Department of Public Health, University of Copenhagen, Øster Farimagsgade 5, Postbox 2099, 1014 Copenhagen K, Denmark, Tel: (+45) 3532 6735, Fax: (+45) 3535 1181.

Conflicts of interests: None

motor symptoms such as depression are important features of the disease with a major negative impact on quality of life.(2;3) Depression may affect up to half of patients with PD, (4;5) and has been associated with a more rapid deterioration in cognitive and motor functions.(6) The underlying mechanisms of depression in PD patients are complex and may include a combination of genetic factors, PD-specific factors such as changes in the brain structure and signalling by neurotransmitters, and psychosocial issues.(3;7) Clinical observations indicate that stress may lead to the onset and accelerate the progression of Parkinsonian symptoms,(8) and it is increasingly accepted that depression in PD patients is not exclusively dependent on a simple relationship with disability, but may also include psychosocial factors such as self-esteem, coping styles and practical support.(7) Major life events are clearly linked to major depression and many studies have shown that depressive episodes are preceded by a variety of life events.(9;10) Studies suggest that while most people successfully handle a stressful life event, problems arise when stressors accumulate. (11) Having a chronic neurological condition like PD is stressful since most patients experience changes in social activities, work, relationships, physical mobility, and general independence. Superimposed on the chronic stress of suffering from PD are major life events expected to occur in any aging population. We hypothesize that major life events may be related to development of major depression in PD patients and that social support and coping abilities may counteract or prevent the occurrence of depression. Here, we aim to address whether type and number of life events are related to development of major depression among 221 new-onset PD patients free of severe depressive symptoms at baseline, who were ascertained in a population-based manner and followed for an average of 3-4 years. Furthermore, we address whether the association between life events and incidence of depression is modified by social support and coping. To our knowledge, this is the first study to address the effect of major life events on onset of major depression in PD patients.

MATERIAL AND METHODS

Case recruitment

New-onset PD patients (diagnosed within three years) who resided in Fresno, Tulare, and Kern Counties, California were recruited for the Parkinson's, Environment and Gene (PEG) study between 2001 and early 2007 through neurology offices, clinics, and public service announcements. Cases were eligible if they had lived in California for at least five years, were not in the last stages of a terminal illness, and were confirmed as having clinically probable or possible PD by a UCLA movement disorder specialist. Diagnostic criteria, explained in detail elsewhere, (12) were based on those recommended previously.(13) A diagnosis of clinically probable or possible PD was confirmed if patients met the following criteria: 1) manifestation of at least two of the following: resting tremor, bradykinesia, or cogwheel rigidity; 2) no suggestion of a parkinsonian syndrome due to trauma, brain tumor, infection, cerebrovascular disease, other known neurologic disease, or treatment with dopamine-blocking or dopamine-depleting agents; 3) no atypical features such as prominent oculomotor palsy, cerebellar signs, vocal cord paresis, severe orthostatic hypotension, pyramidal signs, amyotrophy, or limb apraxia; 4) asymmetric onset; and 5) if treatment with levodopa had been initiated, symptomatic improvement after treatment. Probable cases met criteria one through four plus/minus criterion five. Possible cases had at least one sign from criterion one and fulfilled criteria two and three. Although sometimes included in criterion one, postural reflex impairment was excluded since it usually occurs late in PD and may typically occur early in other parkinsonian disorders, such as progressive supranuclear palsy and vascular parkinsonism. Of 1,167 patients initially contacted, 604 were not eligible because their diagnosis date did not fall within the three years prior to contact (n= 397), they never received an idiopathic PD diagnosis (n=73), they lived outside the tri-county area

(n=134). Of those first recruited, 473 (84 %) were examined by a UCLA movement disorder specialist at least once. A diagnosis of probable or possible idiopathic PD was established at baseline in 379 examined patients and those who received other diagnoses such as PD with dementia or Parkinsonism with other neurodegenerative diseases were excluded. Figure 1 depicts the data collection procedure.

Follow-up

To follow progression of motor and non-motor manifestations of PD, the participants of the PEG study were invited to participate in a follow-up study and a total of 254 patients from the original cohort were enrolled, examined and interviewed between June 2007 and June 2009. Of the original 379 patients, 70 died before the follow-up examination resulting in a participation proportion of 82 % among those alive and eligible at follow-up. During the re-examination, 12 of the patients were re-diagnosed as not having idiopathic PD, leaving 242 PD cases with full or partial follow-up data. Of these 221 were fully assessed with the geriatric depression scale (GDS), the SCID clinical evaluation for a major depressive episode, and did not have severe depressive symptoms (GDS score<10) at baseline. The UCLA IRB (#G06-07-055) approved the study; all subjects provided informed consent.

Major life events

At follow-up, the patients were asked whether they had experienced a set of different life events since they were diagnosed with PD. The life event scale we employed was a shorter and modified form of the Social Readjustment Rating Scale developed by Holmes and Rahe. (14) The list of life events included questions on both *acute life events* (spouse died, someone close other than spouse died, separated or divorced, laid off or fired from work, someone close had sudden illness or injury, lost home, retired, assaulted or robbed, involved in serious accident) and more *chronic life events* (serious arguments with someone at home, serious problem with friend, relative or neighbour, serious illness other than PD, financial crisis). The PD patients were asked to report if each life event had happened to them as well as to indicate how much it had upset them (did not happen; happened and did not upset me; happened and upset me somewhat; happened and upset me very much).

Depression

Depressive symptoms at baseline were assessed by the short form of the Geriatric Depression Scale.(15;16) The scale ranges from 0 to 15 and according to the literature a score above 9 indicates major depressive symptoms.(16) The GDS avoids many symptoms overlapping between depression and PD and has previously been validated in PD patients with high discriminant validity and internal consistency.(15;17) The presence of major depression at follow-up was determined using the Structured Clinical Interview for the DSM-IV-TR depression module (SCID), the “gold standard” method for diagnosis of major depression based on the DSM-IV_TR.(18) Research Assistants, trained and supervised by a psychiatrist (AT), conducted the interviews. Due to limited statistical power severity of the depressive symptoms will not be addressed at follow-up. The SCID was only administered at follow-up, which is why the GDS rating scale is used to exclude people with severe depressive symptoms at baseline.

Other covariates

UCLA movement disorder specialists examined all potential PD cases and carried out the Unified Parkinson’s Disease Rating Scale (UPDRS) Motor Scale. Whenever possible, the examinations were performed in the practically defined “off” state (i.e. the patient had not taken PD medications overnight) in order to allow for the most accurate diagnosis of idiopathic PD in the early stages of PD. Subjects also answered a standardized questionnaire

supplemented by an interview ascertaining demographic and other risk factor information. In the present analysis we included self-reported information on race (white/other), PD in first degree relative (yes/no) and formal education (< 12 years, 12 years, > 12 years). Social support was assessed with a short five-item form of the Medical Outcomes Study (MOS) Social Support Scale, which measures the perceived availability, if needed, of various components of social support.(19) The scale includes questions on how often the patient had someone available to 1) take him/her to the doctor, if needed; 2) have a good time with; 3) to hug him/ her; 4) prepare meals if unable to do it themselves; and 5) understand his/ hers problems. High social support was defined as reporting all or most of the time to have someone available for support with at least four of the above-mentioned aspects. The 13-item short form of the Sense of Coherence (SOC) Scale was used to capture global subjective states of coping with everyday life problems (20). Coping is the way an individual reacts to problems and conflicts, such as major life events. The scale has a seven-point response format, with a greater number of points representing a stronger SOC. The scores range from 13 to 91. The stronger the SOC, the more likely it is that the person will be able to cope successfully with stressful situations. The scale has a high validity and homogeneity.(20) There is no well-established cut-point for the SOC, and we considered PD patients with a total score below the 20th percentile as having a low sense of coherence and all others as having high sense of coherence. Due to limited statistical power, we were unable to formally investigate statistical interactions between life events and sub-scales of the total SOC score.

Statistical methods

We evaluated the associations between number and type of major life event and risk of developing major depression using logistic regression models. A multivariate model was fitted to adjust for potential confounding by baseline covariates. Potential confounders were identified by drawing Directed Acyclic Graphs (21) and included sex, age at baseline, race, family history of PD in first degree relative, length of follow-up, education and UPDRS motor score at baseline. In secondary analyses, we evaluated the joint effects of major life events and social support as well as the joint effects of major life events and sense of coherence. In sensitivity analyses we excluded participants with a history of depression prior to PD diagnosis. History of depression was based on self-reported doctor diagnosed history of depression and intake of antidepressants. Finally, the best cut-off point for the GDS is debated in the literature,(22;23) and we therefore also tried to exclude participants with depressive symptoms based on a lower cut-off point (GDS>5) at baseline.

RESULTS

Baseline characteristics

The mean age of PD patients at baseline was 69 years, ranging from 37 to 90 years. The PD patient sample had a mean UPDRS motor score of 19 and a mean Mini Mental State Exam (MMSE) score of 28 at baseline. Half of the patients reported having experienced two or more major life events since they were diagnosed with PD and only nine percent reported no life events. Younger age and longer follow-up since PD diagnosis were associated with reporting more life events (Table 1). Number of life events showed no associations with sex, race, family history of PD, education, UPDRS motor score, or MMSE score at baseline.

Major life events and major depression

During an average of 3.4 years of follow-up, 22 of the 221 eligible PD patients without depression at baseline (defined as GDS<10) developed a major depressive episode. Number of life events was associated with higher risk of depression in a dose-response manner, with each additional event increasing the odds of developing depression by 56 percent (95 % CI:

1.23-1.98) (Table 2). Number of upsetting events had a slightly stronger association with development of depression (for each additional event: OR=1.63, 95 % CI: 1.27-2.09). Both acute life events (OR=1.83; 95 % CI: 1.25-2.68) and more chronic life events (1.99; 1.32-3.01) were associated with higher risk of major depression. Most of the individual life events were associated with higher risk of major depression, although we had low statistical power to address these associations (Table 2). Thirty-three individuals had a history of depression prior to PD diagnosis. Exclusion of these individuals from the analyses did not markedly change the risk estimates (data not shown). Excluding individuals based on a lower cut-off point for defining depression a baseline (GDS>5) resulted in forty-seven instead of sixteen individuals with depressive symptoms being excluded at baseline. This more strict criterion reduced the statistical power of the analyses, but made the risk estimates slightly stronger, e.g. each additional life event were associated with an OR of 1.60 (95 % CI: 1.19-2.15) for developing depression during follow-up.

Major life events and depression: modification by social support and coping

Both social support and coping seemed to modify the risk of developing major depression associated with major life events. As shown in Figure 2, PD patients who had experienced three or more life events and at the same time reported low social support had a 13-times higher risk of developing depression (OR=13.7; 95 % CI: 3.46-53.9) compared to those PD patients who had experienced 0-2 life events and reported high social support. The joint effects were even more pronounced for the combination of having experienced three or more life events and having low sense of coherence (OR=43.4; 95 % CI: 9.70-195) (Figure 3). Even though this risk estimate was only based on 12 cases of depression, it clearly indicates that coping behaviours modify the associations of major life events and depression in PD. However, due to limited statistical power, we did not perform a formal statistical test for interaction.

DISCUSSION

In this study of PD progression, we followed a population-based cohort of 221 new-onset PD patients free of depression at baseline and found that 10 percent developed a major depressive episode during an average of 3.4 years of follow-up. We also found that both number and type of major life events as well as degree to which events were perceived as upsetting to be associated with a higher risk of developing depression in PD. Those with low social support or low coping capacities seemed to be particularly susceptible to depression after experiencing major life events. More than half of our PD patient population reported having experienced two or more major life events since they were diagnosed with PD while only nine percent reported no life events during this interval, making major life events common occurrences in the course of PD.

Most previous studies on markers for depression in PD patients have focused on disease-specific factors such as age of onset, disease duration, and severity of symptomatology, without taking general risk factors for depression into account.(24;25) In a cross-sectional study of 160 PD patients, Leentjens et al. showed that risk factors for depression in the general population were more important in predicting onset of depression in PD patients than disease-specific factors.(26) An association between major life events and depression is well established in the general population,(27;28) and our results emphasise the importance of including such general risk factors in the assessment of depression in PD patients.

Whether the association between major life events and depression is causal or arises from covariates influencing both the reporting of life events and depression is an ongoing debate. (28;29) In support of a causal role, Kendler and colleagues have found a moderate causal effect of stressful life events on risk of major depression in detailed analyses including a co-

twin control design and propensity score matching.(29) Access to social support and various coping strategies have also previously been found to modify the relation between life events and depression.(27) The results from the present study are in line with these previous findings, but distinguish themselves by, for the first time, also being relevant for and applicable to a population of patients experiencing the progression of a chronic and deteriorative disease process known to be associated with a high risk of depression.

Strengths and limitations

Comprehensive neurological and clinical tests within 3 years of first diagnosis and again after almost four years of follow-up on average combined with validated measures of depression, major life events, social support and coping allowed us to comprehensively address the relation between major life events and new onset of major depression in a relatively large sample of population-based PD patients.

Information on major life events was retrospectively collected in the sense that information on life events was gathered after onset of depression. This is by far the most common way of obtaining information on major life event, but one may still be concerned about the temporality between major life events and depression. Depression may precede and possibly cause some events (e.g. being fired due to poor performance) and there may also be issues of differential recall accuracy among depressed and non-depressed patients. We cannot exclude the possibility of such bias, but we would expect many of the major events to be recalled accurately regardless of depression (e.g. spouse died, lost home, retired). More problematic are the measures of social support and sense of coherence, which were only assessed at follow-up. Both measures may be highly affected by a person's mood state, and cause and effect are hard to disentangle for these measures. Baseline measures of such constructs would have been preferable, but were unfortunately not available in the present study. We only considered major life events after diagnosis of PD. While we expect these events to have the largest impact on development of depression following PD, life events occurring earlier in life may also have some effect, which we were unfortunately not able to account for in the present study.

The “kindling” hypothesis, which states that psychosocial stressors play a greater role when people first experience depression than during recurrences of depression, has some empirical support.(30) In a sensitivity analysis, we excluded individuals with a history of depression prior to PD diagnosis and found no changes in the risk estimates. Although family history of depression is not expected to be highly related to major life events, a family history of depression could make some PD patients more prone to develop depression. Unfortunately, information on this variable was not available in the present study.

It is important to distinguish between stressors and stress. A stressor is an external stimulus that can potentially cause stress depending on the individual's perception of the threat the stressor poses. We used information on major life events that are expected to create stress in most individuals regardless of personality, coping styles and social support. However, for some individuals the event itself may reduce stress, such as for example a divorce from an abusive spouse. We included information on the degree to which each event was perceived as upsetting in order to accommodate such differences in impact of the events.

Conclusion

We find life events to play an important role for onset of depression in PD patients. Both the experience of life events and onset of depression are common problems in the course of PD, making it important to acknowledge the problem and their relationship as well as identify factors that may mitigate the harmful effects of life events. We find social support and

coping capacities to be promising in this regard. The primary care physician may be in a good position to identify PD patients at high risk of depression by including life events as part of standard patient assessment as well as help increase the patients' social support and coping capabilities by referral to formal supportive interventions for people with PD such as psychotherapy and family and patient support groups.

Acknowledgments

Funding sources for study: This work was supported by National Institute of Environmental Health Science [ES10544, U54ES12078, 5P30 ES07048], National Institute of Neurological Disorders and Stroke [NS 038367], and Department of Defense Prostate Cancer Research Program [051037]; in addition, initial pilot funding was provided by the American Parkinson's Disease Association. Naja Hulvej Rod was supported by the Danish Health Insurance Foundation [grant no. 2009B126] and the Danish Medical Research Council [grant no. 09-062115].

References

1. Burch D, Sheerin F. Parkinson's disease. *Lancet*. 2005 Feb 12; 365(9459):622–7. [PubMed: 15708109]
2. Reijnders JS, Ehrt U, Weber WE, Aarsland D, Leentjens AF. A systematic review of prevalence studies of depression in Parkinson's disease. *Mov Disord*. 2008 Jan 30; 23(2):183–9. [PubMed: 17987654]
3. Aarsland D, Pahlhagen S, Ballard CG, Ehrt U, Svenningsson P. Depression in Parkinson disease-epidemiology, mechanisms and management. *Nat Rev Neurol*. 2011; 8(1):35–47. [PubMed: 22198405]
4. Richard IH. Anxiety disorders in Parkinson's disease. *Adv Neurol*. 2005; 96:42–55. [PubMed: 16383211]
5. Lieberman A. Depression in Parkinson's disease -- a review. *Acta Neurol Scand*. 2006 Jan; 113(1):1–8. [PubMed: 16367891]
6. Uekermann J, Daum I, Peters S, Wiebel B, Przuntek H, Muller T. Depressed mood and executive dysfunction in early Parkinson's disease. *Acta Neurol Scand*. 2003; 107(5):341–8. [PubMed: 12713526]
7. Brown R, Jahanshahi M. Depression in Parkinson's disease: a psychosocial viewpoint. *Adv Neurol*. 1995; 65:61–84. [PubMed: 7872153]
8. Metz GA. Stress as a modulator of motor system function and pathology. *Rev Neurosci*. 2007; 18(3-4):209–22. [PubMed: 18019607]
9. Paykel ES. Life events and affective disorders. *Acta Psychiatr Scand Suppl*. 2003; 418:61–6. [PubMed: 12956817]
10. Tafet GE, Smolovich J. Psychoneuroendocrinological studies on chronic stress and depression. *Ann N Y Acad Sci*. 2004 Dec.1032:276–8. [PubMed: 15677427]
11. Miller, T. The assessment of stressful life events. In: Goldberger, L.; Breznitz, S., editors. *Handbook on stress Theoretical and clinical aspects*. New York: The Free Press; 1993. p. 161-73.
12. Kang GA, Bronstein JM, Masterman DL, Redelings M, Crum JA, Ritz B. Clinical characteristics in early Parkinson's disease in a central California population-based study. *Mov Disord*. 2005; 20(9):1133–42. [PubMed: 15954133]
13. Hughes AJ, Ben-Shlomo Y, Daniel SE, Lees AJ. What features improve the accuracy of clinical diagnosis in Parkinson's disease: a clinicopathologic study. *Neurology*. 1992 Jun; 42(6):1142–6. [PubMed: 1603339]
14. Holmes TH, Rahe RH. The Social Readjustment Rating Scale. *J Psychosom Res*. 1967; 11(2):213–8. [PubMed: 6059863]
15. Ertan FS, Ertan T, Kiziltan G, Uygucil H. Reliability and validity of the Geriatric Depression Scale in depression in Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 2005 Oct; 76(10):1445–7. [PubMed: 16170093]
16. Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. *Clin Gerontol*. 1986; 5:165–73.

17. Schrag A, Barone P, Brown RG, et al. Depression rating scales in Parkinson's disease: critique and recommendations. *Mov Disord.* 2007; 22(8):1077–92. [PubMed: 17394234]
18. First, M.; Spitzer, R.; Gibbon, M.; Williams, J. Structured clinical interview for DSM-IV-TR axis I disorders e patient edition (SCID-I/P, 4/2005 revision). New York: Biometrics Research Department, New York State Psychiatric Institute; 2005.
19. Sherbourne CD, Stewart AL. The MOS social support survey. *Soc Sci Med.* 1991; 32(6):705–14. [PubMed: 2035047]
20. Antonovsky A. The structure and properties of the sense of coherence scale. *Soc Sci Med.* 1993; 36(6):725–33. [PubMed: 8480217]
21. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. *Epidemiology.* 1999; 10(1):37–48. [PubMed: 9888278]
22. Almeida OP, Almeida SA. Short versions of the geriatric depression scale: a study of their validity for the diagnosis of a major depressive episode according to ICD-10 and DSM-IV. *Int J Geriatr Psychiatry.* 1999; 14(10):858–65. [PubMed: 10521885]
23. Fountoulakis KN, Tsolaki M, Iacovides A, et al. The validation of the short form of the Geriatric Depression Scale (GDS) in Greece. *Aging.* 1999; 11(6):367–72. [PubMed: 10738851]
24. Tandberg E, Larsen JP, Aarsland D, Laake K, Cummings JL. Risk factors for depression in Parkinson disease. *Arch Neurol.* 1997; 54(5):625–30. [PubMed: 9152120]
25. Schrag A, Jahanshahi M, Quinn NP. What contributes to depression in Parkinson's disease? *Psychol Med.* 2001; 31(1):65–73. [PubMed: 11200961]
26. Leentjens AF, Lousberg R, Verhey FR. Markers for depression in Parkinson's disease. *Acta Psychiatr Scand.* 2002; 106(3):196–201. [PubMed: 12197857]
27. Kessler RC. The effects of stressful life events on depression. *Annu Rev Psychol.* 1997; 48:191–214. [PubMed: 9046559]
28. Kendler KS, Karkowski LM, Prescott CA. Causal relationship between stressful life events and the onset of major depression. *Am J Psychiatry.* 1999; 156(6):837–41. [PubMed: 10360120]
29. Kendler KS, Gardner CO. Dependent stressful life events and prior depressive episodes in the prediction of major depression: the problem of causal inference in psychiatric epidemiology. *Arch Gen Psychiatry.* 2010; 67(11):1120–7. [PubMed: 21041613]
30. You S, Conner KR. Stressful life events and depressive symptoms: influences of gender, event severity, and depression history. *J Nerv Ment Dis.* 2009; 197(11):829–33. [PubMed: 19996721]

Figure 1.
Flow-chart of the data collection procedure

Figure 2. Joint effects of major life events and social support on risk of major depression among 221 Parkinson's disease patients free of severe depressive symptoms at baseline

Figure 3. Joint effects of major life events and sense of coherence (SOC) on risk of major depression among 221 Parkinson's disease patients free of severe depressive symptoms at baseline

Table 1
Descriptive characteristics of 221 Parkinson's disease patients participating in the UDALL study

	Study population (n=221)	Number of life events				P-value
		0-1 (n=74)	2-3 (n=89)	4-5 (n=36)	6+ (n=22)	
Depression at follow-up (SCID); n (%)	22 (10)	1 (1)	7 (8)	6 (17)	8 (36)	<0.001
Age at baseline, yrs; mean (sd)	69 (10)	71 (9)	70 (9)	67 (10)	67 (10)	0.03
Women; n (%)	94 (43)	28 (38)	38 (43)	15 (42)	13 (59)	0.37
White; n (%)	177 (80)	61 (82)	69 (78)	30 (83)	17 (77)	0.81
Family history of PD in first degree relative; n (%)	35 (16)	8 (11)	17 (18)	5 (14)	6 (27)	0.27
Length of follow-up, yrs; mean (sd)	3.4 (2)	3.3 (2)	3.1 (2)	4.0 (2)	4.0 (2)	0.03
<12 yrs of education; n (%)	37 (17)	10 (14)	19 (21)	2 (6)	6 (27)	0.10
UPDRS motor score at baseline; mean (sd)	19 (10)	18 (8)	20 (10)	20 (9)	21 (11)	0.16
MMSE score at baseline; mean (sd)	28 (3)	28 (2)	27 (3)	28 (2)	28 (3)	0.95

Table 2

Odds ratio of major depression according to number and type of life events among 221 Parkinson's disease patients free of major depressive symptoms at baseline

	Cases/n *	Sex- and age-adjusted OR (95 % CI)	Fully adjusted** OR (95 % CI)
Number of life events (continuous)	22/221	1.54 (1.24; 1.92)	1.56 (1.23; 1.98)
Number of upsetting life events (continuous)	22/221	1.63 (1.30; 2.05)	1.63 (1.27; 2.09)
Number of acute life events (continuous)	22/221	1.78 (1.27; 2.49)	1.83 (1.25; 2.68)
Number of chronic life events (continuous)	22/221	1.97 (1.34; 2.90)	1.99 (1.32; 3.01)
Type of life event			
Spouse died	5/21	3.27 (1.00; 10.7)	3.62 (0.97; 13.6)
Someone close other than spouse died	19/124	2.00 (0.86; 4.67)	2.11 (0.87; 5.08)
Serious arguments with someone at home	10/46	3.56 (1.40; 9.05)	3.38 (1.28; 8.95)
Serious problem with friend, relative or neighbour	8/42	2.42 (0.92; 6.33)	2.38 (0.85; 6.62)
Separated or divorced	2/12	1.61 (0.31; 8.26)	1.31 (0.22; 7.77)
Serious arguments or problems at work	3/13	3.40 (0.80; 14.4)	3.84 (0.87; 16.9)
Laid off or fired from work	1/6	1.57 (0.17; 14.6)	2.63 (0.26; 26.9)
Serious illness or injury other than PD	12/92	1.72 (0.70; 4.25)	1.71 (0.68; 4.34)
Financial crisis	8/29	4.28 (1.57; 11.7)	4.41 (1.48; 13.1)
Someone close had sudden serious illness or injury	12/83	2.02 (0.82; 5.01)	2.18 (0.84; 5.62)
Lost home	5/10	9.41 (2.41; 36.7)	12.9 (2.11; 78.8)
Retired	10/66	2.31 (0.89; 6.02)	2.35 (0.86; 6.42)
Assaulted or robbed	2/9	2.42 (0.45; 13.0)	1.31 (0.20; 8.53)
Involved in a serious accident	6/24	3.35 (1.14; 9.85)	2.98 (0.94; 9.40)

* Cases and number of persons within each exposure category.

** Adjusted for sex, age at baseline, race, family history of PD in first degree relative, length of follow-up, baseline UPDRS motor score, and education.