Depression and parkinsonism in older Europeans: results from the EURODEP concerted action

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Objective: The prevalence rate of depression among patients with Parkinson’s disease (PD) has been estimated at 25%, although prevalence figures range between 7–76%. Relatively few studies on PD and depression are based on random samples in the general population. Some depressive symptoms can also be understood as symptoms of parkinsonism, and the current study aims to describe which ‘overlap’ symptoms can be identified in a community sample.

Methods: Data are employed from the EURODEP collaboration. Nine study centres, from eight western European countries, provided data on depression (most GMS-AGECAT), depressive symptoms (EURO-D items and anxiety), parkinsonism (self-report of PD or clinical signs of PD), functional disability and dementia diagnosis.

Results: Data were complete for 16 313 respondents, aged 65 and older; 306 (1.9%) reported or had signs of parkinsonism. The rate of depression was about twice as high among respondents with parkinsonism (unadjusted Odds Ratio 2.44, 95% Confidence Interval 1.88–3.17), also among those without functional disability. ‘Overlap’ symptoms between parkinsonism and depression, were represented by motivation and concentration problems, appetite problems and especially the symptom of fatigue (energy loss). However, principal component analysis showed that these ‘overlap’ symptoms loaded on different factors of the EURO-D scale.

Conclusions: As among clinical patients with PD, depression is highly common in community dwelling older people with parkinsonism, even among those without functional disability. Although fatigue did not strongly relate to motivational symptoms, both types of ‘overlap’ symptoms possibly trigger a final common pathway towards a full depressive syndrome. Copyright © 2009 John Wiley & Sons, Ltd.

Key words: depression; Parkinson; parkinsonism; epidemiology; symptoms; disability; community

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Introduction

Patients with Parkinson’s disease (PD) frequently suffer from depression. In the literature, the prevalence figures of depression among Parkinson patients vary, with a range between 7 and 76% (Veazey et al., 2005). Reasons for this wide range should be sought in that different diagnostic criteria for depression have been applied and that studies are based on different types of populations. Reijnders et al. (2007) conclude in a recent review that the few existing population studies report lower prevalence rates for depression (around 8%) than studies in outpatient or inpatient samples (around 24%). In a study from US, a national registration by Veteran Affairs was used to compute prevalence figures of PD and comorbid depression (Chen et al., 2007). Over 41,000 males had the diagnosis of PD. The prevalence of depression, based on ICD-codes, amounted to 18.5%. As a rule of thumb, one major textbook of neurology (Victor and Ropper, 2001) states that depression occurs in about one quarter of the cases, especially presenting with signs of weakness and fatigue.

The overlap between PD and depression is acknowledged by virtually all scholars in the field of PD and depression: several of the DSM-IV diagnostic symptoms of depression are common in PD. The symptoms with the most pronounced overlap are psychomotor retardation, loss of energy (or fatigue) and loss of interest (Hoogendijk et al., 1998), along with disabilities with eating, sleep problems and difficulties with concentration. With respect to non-overlapping symptoms, Ehrt et al. (2006) described that depressed PD patients reported less sadness than depressed people without PD, less anhedonia and less feelings of guilt. Others fail to find differences between the manifestation of depression in patients with and without PD (Merschdorf et al., 2003).

Most insights about the epidemiology of depression and PD are based on samples consisting of patients with PD who are already under regular neurological treatment. Nevertheless, patients with parkinsonism with less medical consumption may be overlooked, leading to a selection bias. Assuming that some patients with parkinsonism may appear to be relatively passive in health care seeking, random population-based samples may provide additional insights in the epidemiology of parkinsonism and depression. With a prevalence of PD of about 2% in those above the age of 65, a relatively large survey sample is needed for a population-based study. The EURODEP collaboration was established to examine the geographical variation and risk factors of depression in older people (Copeland et al., 1999a). Fourteen centres from 11 European countries contributed with data. In over half of these centres, information on parkinsonism was available, providing a sufficient sample size for a study on parkinsonism and depression. Depression among PD patients has a unique relation with physical disability (Brown et al., 1988; Weintraub et al., 2004). Therefore, a population-based study may further be utilised to examine the association between parkinsonism and depression with increasing levels of disability.

The current study, based on the EURODEP dataset, aims (1) to describe the strength of the association between parkinsonism and depression, among community dwelling older Europeans, also in the subgroups with no, some or severe physical disability and (2) to examine whether symptoms of depression differ between those with and without parkinsonism.

Methods

Samples

The EURODEP Concerted Action is a consortium of 14 research groups from 11 European countries all engaged in population-based research into the epidemiology of late-life depression (Copeland et al., 1999a). Basic demographic characteristics of the nine study-samples with data available for the present study, including data on parkinsonism, are summarised in Table 1. The overall sample size of this pooled EURODEP data set amounts to 16,313 respondents. All participating studies adhered to standards according to local or university ethical committees. More detailed information on sampling-frame, interview procedures and non-response have been described elsewhere (Copeland et al., 1999a; Braam et al., 2004).

Measures

Outcome variable.

Depressive syndrome. In six of the centres, depression was assessed using the Geriatric Mental State-AGECAT package (GMS-AGECAT; Copeland et al., 1986). The GMS is a semi-structured interview schedule designed for use with older people. AGECAT is a computerised diagnostic algorithm which uses scores on GMS items to produce a level of confidence of a diagnosis (and its clinical relevance, levels 3 and higher) within the syndrome cluster of depression, pertaining to the month preceding the examination.
In two centres (Bordeaux region and Antwerp region), the Center for Epidemiologic Studies Depression Scale (CES-D) was used to assess depressive symptoms in the previous week. The CES-D is a 20-item self-report scale designed to measure depressive symptoms in the community (Radloff, 1977). Items were coded in four response categories, ranging from 0 (‘rarely or none of the time’) to 3 (‘most of or all the time’), yielding a score range of 0–60. CES-D scores were dichotomised, using the criterion score of 20 and higher, as indicative of a clinically relevant depressive syndrome. The higher criterion score level, instead of 16 which is generally used, has been chosen for two reasons. First, the 20 and higher score corresponded best with a GMS-diagnosis of depression in Berlin, the only EURODEP centre with both the GMS-AGECAT and the CES-D. Second, a higher cut-off criterion has been advised to apply in studies among respondents with somatic conditions, which pertained to PD in particular (Naarding et al., 2002). In Gothenburg, depression was diagnosed using a structured interview including all DSM-IIIR symptoms and signs of depression during the month preceding the examination (Skoog et al., 1993).

The depressive symptoms measure in the current study is the EURO-D scale (Prince et al., 1999). This harmonised depressive symptom scale has been developed to facilitate analyses in the pooled EURODEP data set, because not all centres used the same depression assessment procedure. The EURO-D scale comprises twelve items: depressive affect, pessimism, wishing death, guilt, sleep, lack of interest, irritability, appetite problems, fatigue/energy loss, concentration difficulties, lack of enjoyment and tearfulness (0 is ‘not present’; 1 is ‘present’, range 0–12).

In addition, an algorithm based on the DSM-IV was applied to the EURO-D items, with either ‘depressive affect’, ‘lack of interest’ or ‘lack of enjoyment’ as key symptoms, and at least five of the other symptoms, but excluding ‘pessimism’ and ‘tearfulness’ (which do not belong to the DSM-IV items on depression). A DSM-IV based procedure provides a more stringent depression definition compared to the GMS (Newman et al., 1998; Schaub et al., 2003).

Anxiety. Feelings of anxiety, a common psychiatric symptom in PD (Veazey et al., 2005) were assessed using the item in the GMS, the CES-D or the DSM-III interview in Gothenburg. Answers were dichotomised in the same way as the EURO-D items.

Parkinsonism. Self-reports were obtained from interviews with the participating respondents on a range of chronic conditions, including PD (Braam et al., 2005).
Between the centres, the types of questions varied, as is summarised in Table 2. In most centres, respondents were asked whether they were diagnosed with PD. In Bordeaux, the presence of core symptoms of PD, tremor and stiffness/rigidity, was chosen as a measure: when answers on both signs were positive, the presence of parkinsonism was assumed to be plausible. In Berlin, the presence of parkinsonism was observed by the physician who carried out the interview and examination. As it is uncertain whether all participants who reported to have PD suffer from idiopathic PD (as defined by the UK Brainbank criteria), and no other diagnostic assessment was available, the focus of the current study is on parkinsonism in a broader sense, including both PD and PD related disorders.

Functional disability. For functional disability, several versions of ‘activities of daily living’ scales were employed in the different participating centres. To obtain comparable measures, total scores of each scale were trichotomised into ‘no’, ‘intermediate’ or ‘high’ levels of disability. The measure of disability has been described in detail in a previous article (Braam et al., 2005).

Demographic variables. These include gender, age, marital status and education. Marital status was categorised as ‘married’ versus ‘non-married’ (never married, divorced or separated, or widowed). Education was assessed in several ways: years or levels of education, or classifications into ‘lower’, ‘intermediate’ and ‘higher’. To maintain maximal variability, a range of index-scores was computed, dividing the score by the number of categories used in the centre, resulting into values between 0 and 1.

Dementia. In most centres, dementia was diagnosed using the Geriatric Mental State Examination (GMS; Copeland et al., 1986), employing the AGECAT algorithm to derive diagnoses of dementia. In the remaining centres, closely resembling procedures were employed: in Belgium the Cambridge Mental Disorder of the Elderly Examination (CAMDEX) was used in a sub-sample, whereas MMSE scores <24 served as adjunct criterion; in France and Sweden, a diagnosis of dementia was based on a clinical interview using the DSM-III-R criteria.

Statistical procedures

Depression rates are given for the total sample, are also specified for the six samples with the GMS-AGECAT

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diagnostic procedure, and are expressed for the total sample as depression rates according to the DSM-IV algorithm using EURO-D items. The association between parkinsonism and depression is analysed using $\chi^2$ tests. Logistic regression analysis, computing Odds Ratios (OR) and 95% confidence intervals (95% CI) has been used for analyses where adjustment is required for demographic variables, study-centre (for cross-national differences and variations in assessment procedures between the centres), and functional disability.

To identify the symptoms that belong to a depressive syndrome but also to parkinsonism (‘overlap’ items) Odds Ratios are computed for the associations between parkinsonism and each of the 12 EURO-D items (as the dependent variable). Next, in a second model, the OR is adjusted for sum-score of the remaining 11 EURO-D symptoms. When a specific EURO-D item is significantly associated with parkinsonism, also after adjustment for the presence of other depressive symptoms, the symptom is considered to represent an ‘overlap’ symptom. The association between parkinsonism and feelings of anxiety is examined in the same way.

Finally, principal component analyses (PCA) are performed (Dunteman, 1989), to verify whether ‘overlap symptoms’ identified so far represent one underlying Parkinson–depression component. PCA involves a mathematical procedure that transforms a number of possibly correlated variables into a smaller number of uncorrelated variables called principal components. The first principal component accounts for as much of the variability in the data as possible, and each succeeding component accounts for as much of the remaining variability as possible. Following a Varimax rotation (a mathematical convenience to make the coefficients unique), a Promax rotation is applied to obtain the most accurate results. Analyses have been carried out using SPSS version 15.0 for windows. In general, PCA is applied using ordinal-scale item scores. As the EURO-D items are dichotomous, the results by PCA are re-analysed based on tetrachoric correlations computed using the package Polycor from the programme R (http://www.r-project.org).

Results
Sample characteristics

The basic demographics are summarised in Table 1. The distributions across the samples have been described in a previous publication (Braam et al., 2004). The variations of the levels of functional disability partly depend on the age-distribution, and partly on the assessment procedures (Braam et al., 2005).

The prevalences of reports on parkinsonism are summarised in Table 2. In total, the number of probable cases with parkinsonism in the pooled sample amounts to 306 (1.9%). There is no difference according to sex ($\chi^2 = 0.6$, df = 1, $p = 0.431$). The highest rate of parkinsonism is in the age group between 80 and 85 ($\chi^2 = 78$, df = 5, $p < 0.001$).

**Parkinsonism and depression: rates and associations**

Among respondents with parkinsonism, the depression rate amounts to 25.8% compared to 12.5% among those without parkinsonism ($\chi^2 = 50$, df = 1, $p < 0.001$). When only data are considered from the six GMS centres, the prevalence of depression is 22.2% among respondents with parkinsonism compared to 12.4% among those without parkinsonism ($\chi^2 = 16$, df = 1, $p < 0.001$). Applying the DSM-IV depression algorithm to the EURO-D items, the prevalence of depression was 12.3% among respondents with parkinsonism and 4.4% among those without parkinsonism ($\chi^2 = 43$, df = 1, $p < 0.001$).

In Table 3, the results are shown after excluding respondents with dementia: the depression rate among respondents with parkinsonism amounts to 27.7% compared to 12.3% in respondents without parkinsonism. In GMS centres, the rates are 22.6 and 12.3%, respectively (OR 2.14, 95% CI 1.45–3.15, Wald = 15, $p < 0.001$, adjusted for demographics). Using the DSM-IV algorithm, the depression rates are 12.2 and 4.0% (OR 3.17, 95% CI 2.15–4.67, Wald = 34, $p < 0.001$, adjusted for demographics).

After adjustment for functional disability, the association between parkinsonism and depression shows a slight decrease in strength but remains statistically significant. In this multivariate model, the strength of the association (as expressed by the Wald values) with depression is lower for parkinsonism (OR 2.00, 95% CI 1.48–2.69, Wald 21, $p < 0.001$) than for functional disability (OR 2.40, 95% CI 2.19–2.63, Wald 354, $p < 0.001$) and sex (female vs. male: OR 2.32, 95% CI 2.06–2.62, Wald 186, $p < 0.001$), and is similar to marital status (unmarried vs. married: OR 1.33, 95% CI 1.18–1.49, Wald 23, $p < 0.001$) and education (OR 0.44, 95% CI 0.32–0.60, Wald 26, $p < 0.001$). For ‘study centre’, a pronounced association
is found (Wald 167, \( p < 0.001 \); details on request). There are no significant interactions between sex and parkinsonism in their association with depression (\( p = 0.486 \), results on request) or between age (<80 years vs. 80+ years) and parkinsonism (\( p = 0.357 \)).

Association between parkinsonism and depression according to levels of functional disability

As shown in the lower panel of Table 3, the depression rates increase with increase in levels of disability, up to 44.2% among those with parkinsonism and severe disability. This rate corresponds with an OR amounting to 5.65 (95% CI 3.26–9.78, Wald = 38, \( p < 0.001 \)), comparing to respondents without parkinsonism and without disability. When analysed within the groups with the same levels of disability (Table 3), the net association between parkinsonism and depression is still statistically significant in the group without functional disability, but not among those with some or severe disability, which may be due to relatively low numbers of respondents with parkinsonism and disability. There is no significant interaction between functional disability and parkinsonism in their association with depression (\( p = 0.378 \); results on request).

Types of depressive symptoms: identifying overlap with symptoms of parkinsonism

As shown in Table 4, only four EURO-D items do not have a significant association with parkinsonism: wishing death, irritability, sleeping problems and tearfulness. After adjustment for the presence of the remaining 11 EURO-D items, significant associations are found for lack of interest, appetite problems, fatigue and concentration problems. Fatigue represents the most evident overlap symptom. Parkinsonism has a modest association with feelings of anxiety, as shown in the lowest line of Table 4. After adjustment for EURO-D score, the association loses significance.

The results of the PCA are shown in Table 5. Both from the ordinal PCA and from the PCA based on tetrachoric correlations, four components are distinguished among respondents with parkinsonism. The first contains the items pertaining to cognitive functioning and motivation (lack of interest, concentration problems, lack of enjoyment). Affective symptoms contribute to the second component together with appetite problems. Fatigue and irritability load together with sleep problems on a third component. The fourth component includes the item on feelings of guilt and some items with double loadings. Summarising, the PCA results show that the ‘overlap’ symptoms load on different components of the EURO-D scale.

Discussion

The current study, based on data from the EURODEP concerted action, aimed to provide population based insights into depression and depressive symptomatology in older adults with a report on parkinsonism. For the six centres that used the same diagnostic procedure (GMS-AGECAT), the depression rate among respondents with parkinsonism amounted to 21.7% (22.6% in the non-demented). Applying a stringent DSM-IV algorithm, the depression rate was 12.3%. These rates fit with the estimates reported by the literature (Victor and Ropper, 2001; Leentjens, 2004; Veazey et al., 2005; Reijnders et al., 2007). There was a more than twofold risk of depression among respondents with

Table 3 Rates of depression and association between parkinsonism and depression in the pooled EURODEP sample (cases of dementia excluded), as well as stratified for subgroups according to levels of functional disability

<table>
<thead>
<tr>
<th></th>
<th>No parkinsonism</th>
<th>Parkinsonism</th>
<th>Parkinsonism regressed on depression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( N )</td>
<td>Depression rate</td>
<td>( N )</td>
</tr>
<tr>
<td>Complete sample</td>
<td>14,988</td>
<td>12.3%</td>
<td>260</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(2.00 (1.48–2.69)&lt;sup&gt;b,c&lt;/sup&gt;)</td>
<td></td>
</tr>
<tr>
<td>Subgroups for levels of functional disability</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without</td>
<td>12,634</td>
<td>10.6%</td>
<td>166</td>
</tr>
<tr>
<td>Some</td>
<td>1,526</td>
<td>17.2%</td>
<td>42</td>
</tr>
<tr>
<td>Severe</td>
<td>828</td>
<td>29.3%</td>
<td>52</td>
</tr>
</tbody>
</table>

OR, Odds ratio; 95% CI, 95% confidence interval.

<sup>a</sup>Adjusted for demographics and study-centre.

<sup>b</sup>Adjusted for demographics, study-centre and functional disability.

<sup>c</sup>Association between parkinsonism and depression in the GMS centres: OR 1.62, 95% CI 1.07–2.45, Wald 5, \( p < 0.021 \); association between parkinsonism and depression according to the DSM-IV algorithm based on EURO-D items: OR 2.22, 95% CI 1.48–3.32, Wald 15, \( p < 0.001 \).
parkinsonism, also after adjustment for effects by functional disability. When applying a more stringent depression definition based on DSM-IV, the strength of the association between parkinsonism and depression increased. Furthermore, for those without functional disability, the association between parkinsonism and depression remained clearly significant. At least four of the symptoms under study emerged to be more prevalent among respondents with parkinsonism, irrespective of the presence of other depressive symptoms: 'loss of interest', 'appetite problems', 'concentration problems' and most pronounced the item of 'fatigue/energy loss'. Analysing the distribution and covariance of these 'overlap' symptoms in more detail showed that the 'overlap' items loaded on three different components of the EURO-D scale. Therefore, no one-dimensional parkinsonism–depression component could be distilled.

One approach to understand the overlap dilemma has been described by Kirsch-Darrow et al. (2006), who emphasised that apathy may be a core feature of parkinsonism in the absence of depression. Apathy can be defined as lack of motivation not attributable to diminished levels of consciousness, cognitive

### Table 4

<table>
<thead>
<tr>
<th>Euro-D item</th>
<th>OR (95% CI)</th>
<th>Wald</th>
<th>p</th>
<th>Euro-D item</th>
<th>OR (95% CI)</th>
<th>Wald</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressed mood</td>
<td>1.71 (1.32–2.23)</td>
<td>16.0</td>
<td>.000</td>
<td>1.13 (0.83–1.54)</td>
<td>0.6</td>
<td>.426</td>
<td></td>
</tr>
<tr>
<td>Pessimism</td>
<td>1.74 (1.28–2.38)</td>
<td>12.2</td>
<td>.000</td>
<td>1.11 (0.78–1.59)</td>
<td>0.3</td>
<td>.556</td>
<td></td>
</tr>
<tr>
<td>Wishing death</td>
<td>1.40 (0.88–2.21)</td>
<td>2.0</td>
<td>.158</td>
<td>0.76 (0.46–1.27)</td>
<td>1.1</td>
<td>.290</td>
<td></td>
</tr>
<tr>
<td>Guilt</td>
<td>1.58 (1.05–2.37)</td>
<td>4.9</td>
<td>.027</td>
<td>1.09 (0.71–1.68)</td>
<td>0.2</td>
<td>.685</td>
<td></td>
</tr>
<tr>
<td>Sleep</td>
<td>1.39 (1.06–1.81)</td>
<td>5.7</td>
<td>.017</td>
<td>0.92 (0.69–1.24)</td>
<td>0.3</td>
<td>.597</td>
<td></td>
</tr>
<tr>
<td>Lack of interest</td>
<td>2.06 (1.52–2.78)</td>
<td>22.2</td>
<td>.000</td>
<td>1.41 (1.00–1.99)</td>
<td>3.9</td>
<td>.048</td>
<td></td>
</tr>
<tr>
<td>Irritability</td>
<td>1.08 (0.77–1.53)</td>
<td>0.2</td>
<td>.653</td>
<td>0.73 (0.50–1.06)</td>
<td>2.8</td>
<td>.096</td>
<td></td>
</tr>
<tr>
<td>Appetite problems</td>
<td>2.09 (1.53–2.86)</td>
<td>21.2</td>
<td>.000</td>
<td>1.61 (1.15–2.23)</td>
<td>7.9</td>
<td>.005</td>
<td></td>
</tr>
<tr>
<td>Fatigue / Energy loss</td>
<td>2.85 (2.19–3.71)</td>
<td>60.8</td>
<td>.000</td>
<td>2.40 (1.80–3.20)</td>
<td>35.6</td>
<td>.000</td>
<td></td>
</tr>
<tr>
<td>Concentration</td>
<td>1.97 (1.45–2.70)</td>
<td>18.2</td>
<td>.000</td>
<td>1.42 (1.01–1.99)</td>
<td>4.1</td>
<td>.042</td>
<td></td>
</tr>
<tr>
<td>Lack of enjoyment</td>
<td>2.18 (1.56–3.05)</td>
<td>20.7</td>
<td>.000</td>
<td>1.42 (0.96–2.09)</td>
<td>3.0</td>
<td>.081</td>
<td></td>
</tr>
<tr>
<td>Tearfulness</td>
<td>1.17 (0.87–1.57)</td>
<td>1.9</td>
<td>.314</td>
<td>0.76 (0.55–1.07)</td>
<td>2.6</td>
<td>.103</td>
<td></td>
</tr>
</tbody>
</table>

OR: Odds ratio; 95% CI: 95% confidence interval.

aAdjusted for demographics, study-centre, and functional disability.
bAdjusted for demographics, study-centre, and functional disability and sum of the (remaining) EURO-D item.

### Table 5

<table>
<thead>
<tr>
<th>Principal components analysis</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eigenvalue</td>
<td>3.2</td>
<td>1.3</td>
<td>1.1</td>
<td>1.1</td>
</tr>
<tr>
<td>Variance explained</td>
<td>27%</td>
<td>11%</td>
<td>9%</td>
<td>8%</td>
</tr>
<tr>
<td>Depressed mood</td>
<td>0.58</td>
<td>0.58</td>
<td>0.31</td>
<td>0.73</td>
</tr>
<tr>
<td>Pessimism</td>
<td>8.3%</td>
<td>8.3%</td>
<td>8.3%</td>
<td>8.3%</td>
</tr>
<tr>
<td>Wishing death</td>
<td>0.58</td>
<td>0.31</td>
<td>0.72</td>
<td>0.72</td>
</tr>
<tr>
<td>Guilt</td>
<td>0.73</td>
<td>0.43</td>
<td>0.43</td>
<td>0.43</td>
</tr>
<tr>
<td>Sleep problems</td>
<td>0.34</td>
<td>0.44</td>
<td>0.44</td>
<td>0.44</td>
</tr>
<tr>
<td>Lack of interest</td>
<td>0.78</td>
<td>0.44</td>
<td>0.31</td>
<td>0.58</td>
</tr>
<tr>
<td>Irritability</td>
<td>0.78</td>
<td>0.74</td>
<td>0.31</td>
<td>0.58</td>
</tr>
<tr>
<td>Appetite problems</td>
<td>0.48</td>
<td>0.62</td>
<td>0.51</td>
<td>0.53</td>
</tr>
<tr>
<td>Fatigue / Energy loss</td>
<td>0.38</td>
<td>0.38</td>
<td>0.38</td>
<td>0.38</td>
</tr>
<tr>
<td>Concentration problems</td>
<td>0.58</td>
<td>0.58</td>
<td>0.58</td>
<td>0.58</td>
</tr>
<tr>
<td>Lack of enjoyment</td>
<td>0.75</td>
<td>0.75</td>
<td>0.75</td>
<td>0.75</td>
</tr>
<tr>
<td>Tearfulness</td>
<td>0.55</td>
<td>0.35</td>
<td>0.35</td>
<td>0.35</td>
</tr>
</tbody>
</table>

At least four of the symptoms under study emerged to be more prevalent among respondents with parkinsonism, irrespective of the presence of other depressive symptoms: 'loss of interest', 'appetite problems', 'concentration problems' and most pronounced the item of 'fatigue/energy loss'. Analysing the distribution and covariance of these 'overlap' symptoms in more detail showed that the 'overlap' items loaded on three different components of the EURO-D scale. Therefore, no one-dimensional parkinsonism–depression component could be distilled.

One approach to understand the overlap dilemma has been described by Kirsch-Darrow et al. (2006), who emphasised that apathy may be a core feature of parkinsonism in the absence of depression. Apathy can be defined as lack of motivation not attributable to diminished levels of consciousness, cognitive

### Table 5

Results from principal components analyses for respondents with parkinsonism; factor loadings higher than 30 (Left: Promax rotation with Kaiser normalisation; Right: based on tetrachoric correlations), cases of dementia excluded
impairment or emotional distress (Marin et al., 1991; Robert et al., 2002). With respect to the symptom of fatigue, it is difficult in the current study to specify to which degree this symptom pertains to rigidity and akinetism. There exists some evidence, however, that depression in PD is more common among those with the akinetic-rigid subtype, than among those with the tremor-dominant subtype (Starkstein et al., 1998). Furthermore, fatigue has been shown to have a pronounced association with a poor patient quality of life (Brown et al., 2005; Havlíková et al., 2008).

The impression may rise that the overlap-symptoms contribute to a depressive syndrome that should not be considered to be a ‘true’ depression. The impression of an ‘as-if’ depression should be discarded, however, as too simplistic. Early stages of PD are known to affect the locus coeruleus and the amygdala (Braak et al., 2003), which have key roles in the noradrenergic system: dysfunction of this system is known to be related to depressive disorder. Indeed, Remy et al. (2005) showed a decrease of catecholaminergic transmission in the locus coeruleus and amygdala in patients with PD and depression. It may be hypothesised that either the cognitive or the vegetative symptoms or both, raised by PD, may induce a complete depressive syndrome. The depression might then represent the result of a final common pathway, induced by (early) cerebral pathology.

Although the strength of the current approach was that it was population based, and therefore also probably included more older adults with parkinsonism, irrespective of their care-seeking behaviour, several limitations of the study need further consideration. First, the reliability of interview data on PD is uncertain, and no systematic diagnostic algorithms could be employed. The prevalence figures of parkinsonism do however closely correspond with results from the five-centre (one shared with the current study) EUROPARKINSON initiative (Rijk et al., 1997). Nevertheless, there is no way to know whether the PD assessment in the current study pertains to idiopathic PD or to secondary PD (e.g. stroke induced). Second, in spite of sufficient statistical power, the current process of secondary analyses, with pooling of data-samples in different national settings, and for some variables with different methods, may have led to a loss of specificity, probably at the expense of more robust findings. Another limitation is that the available depression assessment was not uniform, which limited the comparability to other studies.

The current approach aimed to facilitate the estimation of risk of depression in groups with different levels of functional disability. However, it was not possible to account for disease duration or for disease stages, as are frequently applied to PD. In the literature, it has been mentioned that the relationship between PD and depression does not need to be linear. Instead, a ‘triphasic’ relationship has been suggested, with higher frequencies of depression in the advancing stage of the illness, as well as higher frequencies in the more incapacitating stages (Brown and Jahanshahi, 1995). In the current study, the results did not follow this triphasic relationship, although the results suggested that the net-association between parkinsonism and depression was somewhat more pronounced for those without functional disability. Other PD specific characteristics were, however, not assessed, such as systematic information on symptomatic motor treatment or whether the respondent was interviewed during ‘on’ or ‘off’ periods. For example, there is some risk that L-dopa may provoke depression (Victor and Ropper, 2001). Depression treatment strategies were not known as well, although the evidence-based knowledge about the effectiveness of antidepressants in PD is still a developing field of research (e.g. Veazey et al., 2005).

James Parkinson (1817) characterised PD as a tedious and most distressing malady. For treatment studies in the future, it might be advisable to evaluate the effects of psychological interventions and of medication not only for depression as a phenomenon as such, but also for the evident ‘overlap’ symptoms on the one hand, and symptoms of affective suffering such as thoughts about death or feelings of guilt on the other hand.

## Conflict of interest

No conflict of interest.

## Key points

- There is twofold risk on depression among those with parkinsonism, also among those without functional disability.
- Depressive symptoms that significantly co-occur with parkinsonism, also after multivariate adjustment, are motivation and concentration problems, appetite problems and fatigue/energy loss.
- Principal component analysis demonstrates that these ‘overlap’ symptoms do not constitute a one-dimensional parkinsonism-depression sub-syndrome.
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