Behavioural disorders, disability and quality of life in Parkinson’s disease

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Abstract

Background: although non-motor symptoms of Parkinson’s disease (PD) are known to adversely affect disability and health-related quality of life, the impact that specific disorders of reward and motivation have remains unclear. Impulse control disorders are more likely in those with a younger disease onset although there is no strong evidence to date that apathy is related to age of onset or correlated with a longer duration of disease.

Objective: to examine the effects of apathy and impulse control disorders on disability and health-related quality of life.

Methods: a total of 99 non-demented participants with PD (35 with impulse control disorders, 26 with apathy and 38 with neither behavioural complication) were assessed using the Unified Parkinson’s Disease Rating Scale (Activities of Daily Living component) and the Schwab–England scale to evaluate disability, and the PDQ (eight items) to assess quality of life.

Results: quality of life was reduced in both behavioural groups compared with participants without either condition. Disability was greater in the group with apathy. Variation in disability score (56%, P < 0.001) was explained by greater levels of apathy, depression, motor impairment and longer disease duration. Variation in quality of life score (54%, P < 0.001) was explained by higher levels of impulsivity, depression, dopaminergic load, motor complications, working memory problems and younger age at onset.

Conclusion: apathy and impulsivity negatively impact on disability and health-related quality of life, emphasising the importance of effective diagnosis and management of these PD-related behavioural disturbances.

Keywords: Parkinson’s disease, disability, quality of life, impulse control disorders, apathy, elderly

Introduction

It is now accepted that in Parkinson’s disease (PD), a neurodegenerative motor disorder, non-motor features (including autonomic symptoms, sleep and sensory disturbances) are almost ubiquitous and often pre-date the motor features of the disorder [1]. In particular, neuropsychiatric symptoms can be burdensome to patients and carers alike, with negative effects on quality of life and an increased risk of care home admission [2]. The most common neuropsychiatric complications include depression, anxiety, cognitive impairment and psychosis [3]. However, there is growing recognition of the so-called ‘behavioural disorders’, including impulse control disorders (ICDs) and apathy [2, 4]. The impact of these behavioural disorders is not well understood, particularly since ICDs have only recently been fully described. The aim of this study was to ascertain the extent to which apathy and ICDs affect disability and health-related quality of life (HRQoL).

ICDs, which occur in about 14% of those with PD [5], were first described in detail in the early 2000s [6, 7]. They constitute a group of psychiatric disorders which may manifest as pathological gambling, hypersexuality, compulsive shopping, and binge eating, as well as the dopamine
dysregulation syndrome (DDS). In DDS, a PD patient may become addicted to increasing amounts of antiparkinsonian medication [5]. The aetiology of these behaviours has been linked to the use of dopamine agonists [5, 8] and they are associated with motor fluctuations and higher levels of anxiety [9]. A cross-sectional study has shown that ICDs are associated with a younger age of disease onset, even after controlling for the increased rate of dopamine agonist usage in younger patients [8]. Apathy, on the other hand, presents with a lack of initiative or flat affect, as well as indifference or a paucity of emotional responsiveness [10]. The prevalence of apathy, which is distinct from depression, has been reported in up to 70% of PD sufferers [2] and is associated with depression and motor and cognitive impairment. In those with PD, comparison of those with apathy to those without has not shown a significant difference in age, although nonsignificant associations have been shown towards a longer duration of disease in those with apathy [10, 11]. Both ICDs and apathy likely involve PD-related disruptions to reward and motivation neural pathways [9, 12, 13].

The impact of the neuropsychiatric symptoms of PD on both disability [14] and HRQoL has been well documented, in particular, as it relates to depression [15] and cognitive impairment [16]. However, the extent of disability in PD varies widely [17] and several other factors need to be considered. In particular, behavioural disturbances may play a role. This current study compares the impact of ICDs and apathy on both disability and HRQoL in PD.

**Methods**

This study was approved by the North Manchester regional ethics committee and informed consent was obtained for each participant. The work was supported by Parkinson’s UK.

**Participants**

Ninety-nine participants with idiopathic PD were included in the study. All met UK Brain Bank criteria [18] for PD and those meeting the clinical diagnostic criteria for dementia associated with PD [19] were excluded. Patients with apathy or ICDs (together with PD controls) were actively recruited from a large number of tertiary and secondary care neurology and elderly care units in Greater Manchester, Lancashire, Merseyside and parts of Cumbria; some patients self-referred. For these reasons the study does not aim to determine incidence and prevalence. Within this sample, 35 had a clinical diagnosis of ICD, 26 had a diagnosis of apathy and the remaining 38 had neither behavioural disturbance (‘PD-control’). ICD was defined by clinical examination and whether they met one or more of the following criteria for the ICDs: (i) provisional criteria for homeostatic dysregulation syndrome in PD [6]; and/or (ii) Diagnostic and Statistical Manual IV, Text Revision [20] criteria for pathological gambling, pathological shopping or hypersexuality. For those with a diagnosis of pathological gambling, a score above five on the South Oaks Gambling Screen [21], a reliable and valid indicator of probable pathological gambling, was also required. Of those with an impulsivity disorder, pathological gambling was most frequent (12 patients, 34%), followed by hypersexuality (nine patients, 26%), compulsive shopping (five patients, 14%), overeating (three patients, 9%) and DDS (three patients, 9%). The remaining three patients presented with other impulsive behaviours, such as punding. The apathy group was defined by a cut-off score of ≥14 on the Apathy Scale [22], which has validity for determining clinically significant apathy in PD.

**Measures of clinical variables**

PD symptoms were assessed using the motor subscale of the Unified Parkinson’s Disease Rating Scale (UPDRS III) [23], rated during the ‘on’ medication state, as well as complications of therapy subscale (UPDRS IV). Levodopa equivalent drug doses (LEDD) were calculated using a previously described formula [24]. The levodopa equivalent drug dose of dopamine agonists only (LEDD-DA) was calculated using the same formula. Mood and anxiety were assessed using the Hospital Anxiety and Depression Scale (HADS) [25]. Apathy was assessed using the Apathy Evaluation Scale (AES)-Clinician version [26] and impulsivity was measured using the Barratt Impulsiveness Scale (BIS-11) [27]. Cognitive measures were the Mini-mental State Exam [28] for global cognition, and two measures of executive function, the n-back (working memory) [29] and the FAS variant of the Controlled Oral Word Association task (verbal fluency) [30].

**Measures of impact**

Disability was measured in two ways: (i) UPDRS-ADL subscale [23] and (ii) the Schwab–England scale [31]. The UPDRS-ADL scale is a 13-item scale that rates the ability to carry out daily tasks such as dressing and using a cutlery on a scale of 0–4 per item. It has a range of 0–52, with higher scores indicating greater impairment. It was designed specifically for assessing those with a diagnosis of PD and encompasses such items as the ability to eat and drink, move, toilet, dress, undertake hygiene routines and communicate. The Schwab–England scale rates ADL ability on a scale of 0–100% with 100% being completely independent and with no disability. This scale is a useful global measure of independence and performance on ADLs and has been used to compare the degree of disability in PD compared with non-PD samples such as osteoarthritis [10].

HRQoL was measured using the Parkinson’s Disease Questionnaire-8 item version (PDQ-8) [32], which is a well-validated abbreviated version of the PDQ-39 [33]. The PDQ-8 was derived based on one item from each of eight domains from the original scale encompassing core aspects of functioning: mobility; ADLs; emotional well-being;
The disease was 93.87 (SD 65.85) months with Hoehn–Toms was 55.39 (SD 11.58) years while the mean duration of behaviour groups. The mean age of onset of motor symp- 

However, this increased proportion may be explained by the selection of patients to optimise numbers in the different be-

Finally, forced entry linear regression models were created using either disability or HRQoL as the dependent variables and key clinical variables, including apathy and impulsivity, as independent variables.

Results

Descriptive measures

The entire sample had a mean age of 63.23 (SD 10.67) years, ranging from 26 to 86 years. In the general population, PD is about 1.5 times more likely to occur in males than females [34]. In this study, 70% of participants were male. However, this increased proportion may be explained by the selection of patients to optimise numbers in the different beha-

Mean behavioural, cognitive and psychiatric rating scale scores for the three behavioural groups are outlined in Table 1. Briefly, as expected, the apathy group was significantly higher than both comparison groups on loss of motiv-

Quality of life, as measured by PDQ-8 scores also correlated strongly with several variables. In particular, there was a negative correlation between age of onset and PDQ-8 score (P = 0.02), suggesting that those with younger onset PD have a greater impact on their quality of life. Motor severity (UPDRS motor), complications of therapy (e.g. dyskinesia, on/off symptoms), and higher dopaminergic load (LEDD; P < 0.001–0.03 for these variables). Both dis-

Impact measures

The mean overall UPDRS-ADL score for the entire study group was 14.63 (SD 5.28) with a median of 15 and the

mean Schwab–England score was 77.09 (SD 13.06), with a median of 80. The apathy group had significantly greater levels of disability compared with the PD controls as well as the ICD groups, as seen on both the UPDRS-ADL scale (P < 0.001) and the Schwab–England scale (P < 0.001). Furthermore, the ICD group had significantly greater levels of disability compared with the control group on the Schwab–England scale (P = 0.04). On the PDQ-8, the (single index) mean score for the entire study sample was 20.75 (SD 10.97), with a median of 20.83. Both ICD and apathy had significantly higher PDQ-8 scores compared with the PD controls (P < 0.001). The two beha-

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Mean age of onset of motor symptoms was 55.39 (SD 11.58) years while the mean duration of the disease was 93.87 (SD 65.85) months with Hoehn–Yahr score ranging from 1 to 4 (mean 2.31, SD 0.7). Dopamine replacement therapy ranged between 0 and 609.75 mg/day (mean 141.5, SD 165.01) LEDD. The mean MMSE score for the entire sample was 28.45 (SD 1.75). Thirty-three percent of the sample had the maximum MMSE scores of 30/30, 30% scored 29/30, 27% scored between 26 and 28 percent of the sample had the maximum MMSE scores of 30/30, 30% scored 29/30, 27% scored between 26 and 28 for the entire sample was 28.45 (SD 1.75). Thirty-three

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For HRQoL, a highly significant model (P < 0.001) also resulted, in which 54% of the variance in PDQ-8 scores were accounted for by higher dopaminergic load, more complications from therapy, younger age of onset, higher levels of depression, more impaired working memory and higher levels of impulsiveness.

More complications from therapy and greater cognitive problems account for larger impairments in both quality of

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**Table 1. Demographic and clinical characteristics of Parkinson’s disease study participants compared across three behavioural groups (impulse control disorders, apathy and controls)**

<table>
<thead>
<tr>
<th></th>
<th>Impulse control disorders (n = 35)</th>
<th>Apathy (n = 26)</th>
<th>Control (n = 38)</th>
<th>Statistics*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Motor and treatment response characteristics</strong></td>
<td></td>
<td></td>
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<tr>
<td>Unified Parkinson’s disease</td>
<td>26.85 (9.97)</td>
<td>37.54 (11.38)</td>
<td>24.11 (10.41)</td>
<td>F = 13.07; df = 2; P &lt; 0.001</td>
</tr>
<tr>
<td>Rating Scale (UPDRS) Part III—Motor</td>
<td>4.71 (3.33)</td>
<td>3.62 (3.40)</td>
<td>2.68 (2.99)</td>
<td>H(2) = 9.22; P = 0.01</td>
</tr>
<tr>
<td>UPDRS complications of therapy</td>
<td>25.88 (12.43)</td>
<td>46.57 (11.90)</td>
<td>21.68 (4.78)</td>
<td>F(2) = 44.69; P &lt; 0.001</td>
</tr>
<tr>
<td><strong>Degree of motivation/impulsiveness</strong></td>
<td></td>
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<tr>
<td>Apathy scale (AES-C)</td>
<td>25.88 (12.43)</td>
<td>46.57 (11.90)</td>
<td>21.68 (4.78)</td>
<td>H(2) = 44.69; P &lt; 0.001</td>
</tr>
<tr>
<td>Impulsiveness (BIS-11)</td>
<td>66.95 (13.12)</td>
<td>57.08 (9.68)</td>
<td>54.03 (10.63)</td>
<td>F = 12.88; P &lt; 0.001</td>
</tr>
<tr>
<td><strong>Psychiatric measures</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Hospital anxiety and depression score—anxiety component</td>
<td>8.60 (4.34)</td>
<td>5.96 (4.02)</td>
<td>4.29 (3.51)</td>
<td>H(2) = 17.55; P &lt; 0.001</td>
</tr>
<tr>
<td>Hospital Anxiety and Depression Score—depression component</td>
<td>6.48 (3.59)</td>
<td>9.15 (3.37)</td>
<td>4.03 (2.77)</td>
<td>H(2) = 28.12; P &lt; 0.001</td>
</tr>
<tr>
<td><strong>Cognitive measures</strong></td>
<td></td>
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<tr>
<td>Mini-Mental State Examination (MMSE)</td>
<td>28.94 (1.33); 25–30</td>
<td>27.23 (2.21); 24–30</td>
<td>28.84 (1.31); 25–30</td>
<td>H(2) = 13.70; P &lt; 0.001</td>
</tr>
<tr>
<td>Working memory (n-back)</td>
<td>16.50 (3.48)</td>
<td>13.39 (3.19)</td>
<td>17.00 (3.42)</td>
<td>H(2) = 13.94; P &lt; 0.001</td>
</tr>
<tr>
<td>Verbal fluency (FAS)</td>
<td>45.77 (13.52)</td>
<td>35.16 (9.66)</td>
<td>40.71 (13.48)</td>
<td>H(2) = 11.30; P = 0.004</td>
</tr>
<tr>
<td><strong>Impact measures</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Disability—UPDRS Part II—Activities of Daily Living</td>
<td>13.91 (5.14)</td>
<td>18.23 (4.10)</td>
<td>12.79 (4.95)</td>
<td>H(2) = 10.44; P &lt; 0.001</td>
</tr>
<tr>
<td>Disability—Schwab–England*</td>
<td>79.29 (9.86)</td>
<td>63.46 (12.39)</td>
<td>84.21 (8.26)</td>
<td>F = 39.41; P &lt; 0.001</td>
</tr>
<tr>
<td>Quality of life—Parkinson’s Disease Questionnaire (8) score</td>
<td>23.75 (10.71)</td>
<td>25.00 (9.65)</td>
<td>14.76 (9.65)</td>
<td>H(2) = 16.28; P &lt; 0.001</td>
</tr>
</tbody>
</table>

*ANOVA or Kruskal–Wallis for three-group comparison, with post hoc Bonferroni or Mann–Whitney U for two-group comparisons.

aLower score indicates greater disability.
life and disability. In addition, older age at onset, longer disease duration, more severe motor symptoms and greater levels of apathy account for increased disability, whereas greater dopaminergic load, impulsivity and younger age at onset account for impairments in HRQoL. These models are shown in Table 3.

**Discussion**

This study examined the impact of behavioural disturbances such as apathy or impulsivity on HRQoL and disability in PD. Several significant findings emerged, in particular that the presence of these syndromes had a significant impact on both outcomes. Specifically, apathy was associated with greater disability, whereas impulsivity was associated with worse HRQoL. To date, there has been no mention in the literature of the impact of ICDs or impulsiveness on either of these outcomes hence the current findings are of particular interest.

ICDs can have devastating consequences on the lives of PD sufferers and their carers [9]. For example, pathological gambling can result in huge financial losses [35] and uncharacteristic sexual practices may adversely implicate partners. The added impact of such adverse behavioural changes on a chronic degenerative disease significantly adds to the strain on personal and occupational relationships. Apathy, through its manifestations of poor motivation and indifference can lead to individuals withdrawing from relationships, occupations, hobbies and pastimes [2]. As was shown in this study, those with apathy are more likely to be cognitively impaired, and this combination can result in situations where individuals are less able to adapt to physical deterioration. They may be unable to comply with or actively seek therapy or support programmes, thus forming a vicious cycle with a further decline in mobility. Carers and loved ones may misinterpret the apathy as laziness or lack of self-motivation, causing resentment or relationship difficulties.

Several significant associations with the outcome measures emerged from this study. First, age at assessment and age of disease onset was younger in those with worse HRQoL, but older in those with greater disability. Older age and older age of disease onset may result in greater levels of disability due to associations with greater co-morbidity with non-PD conditions and with worse motor functioning [14, 15, 36]. Younger age Alzheimer disease sufferers has been associated with more impaired HRQoL, possibly due to younger people having greater difficulties adapting to a chronic degenerative disease when diagnosed in the prime of life [37]. Previous findings in PD also support an association with both younger age and younger age of disease onset and more impaired HRQoL, when using a more extensive QoL measure than was used in the current study [15, 38].

Second, this study found strong associations between more impaired motor function overall, as well as motor

### Table 2. Bivariate Spearman’s/Pearson’s rho correlation between clinical variables and disability (UPDRS Activities of Daily Living Scale and Schwab-England scale) and health-related quality of life (Parkinson’s Disease Questionnaire-8 item version) in Parkinson’s disease

<table>
<thead>
<tr>
<th>Clinical variable</th>
<th>Co-efficient</th>
<th>P-value</th>
<th>Co-efficient</th>
<th>P-value</th>
<th>Co-efficient</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apathy score AES-C</td>
<td>0.36</td>
<td>&lt;0.001</td>
<td>-0.55</td>
<td>&lt;0.001</td>
<td>0.23</td>
<td>0.04</td>
</tr>
<tr>
<td>Impulsiveness BIS-11</td>
<td>0.14</td>
<td>0.17</td>
<td>-0.09</td>
<td>0.37</td>
<td>0.43</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Demographic</td>
<td></td>
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<tr>
<td>Age at time of assessment</td>
<td>0.22</td>
<td>0.02</td>
<td>-0.447</td>
<td>&lt;0.001</td>
<td>-0.08</td>
<td>0.51</td>
</tr>
<tr>
<td>Disease variables</td>
<td></td>
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<tr>
<td>Age at onset of motor symptoms</td>
<td>0.044</td>
<td>0.664</td>
<td>-0.252</td>
<td>0.01</td>
<td>-0.26</td>
<td>0.02</td>
</tr>
<tr>
<td>Duration of disease</td>
<td>0.29</td>
<td>0.004</td>
<td>-0.38</td>
<td>&lt;0.001</td>
<td>0.18</td>
<td>0.11</td>
</tr>
<tr>
<td>UPDRS motor</td>
<td>0.58</td>
<td>&lt;0.001</td>
<td>-0.44</td>
<td>&lt;0.001</td>
<td>0.27</td>
<td>0.02</td>
</tr>
<tr>
<td>UPDRS complications of therapy</td>
<td>0.30</td>
<td>0.002</td>
<td>-0.21</td>
<td>0.04</td>
<td>0.52</td>
<td>&lt;0.001</td>
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<tr>
<td>Medication factors</td>
<td></td>
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<tr>
<td>Mean LEDD</td>
<td>0.22</td>
<td>0.03</td>
<td>-0.32</td>
<td>0.001</td>
<td>0.36</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean LEDD-DA only</td>
<td>-0.09</td>
<td>0.35</td>
<td>0.25</td>
<td>0.01</td>
<td>0.13</td>
<td>0.21</td>
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<tr>
<td>Psychiatric factors</td>
<td></td>
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<tr>
<td>HADS depression</td>
<td>0.32</td>
<td>0.002</td>
<td>-0.53</td>
<td>&lt;0.001</td>
<td>0.47</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HADS anxiety</td>
<td>0.09</td>
<td>0.41</td>
<td>-0.14</td>
<td>0.16</td>
<td>0.53</td>
<td>&lt;0.001</td>
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<tr>
<td>Cognitive factors</td>
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<tr>
<td>MMSE</td>
<td>-0.221</td>
<td>0.02</td>
<td>0.230</td>
<td>0.02</td>
<td>-0.02</td>
<td>0.88</td>
</tr>
<tr>
<td>N-back</td>
<td>-0.41</td>
<td>&lt;0.001</td>
<td>0.35</td>
<td>0.001</td>
<td>-0.15</td>
<td>0.16</td>
</tr>
<tr>
<td>FAS</td>
<td>-0.12</td>
<td>0.25</td>
<td>0.13</td>
<td>0.22</td>
<td>-0.02</td>
<td>0.88</td>
</tr>
</tbody>
</table>

*UPDRS ADL*: Unified Parkinson’s Disease Rating Scale, Activities of Daily Living subscale.

*Lower scores indicate greater disability.*

*PDQ-8*: Parkinson’s Disease Questionnaire-8 item version.
complications, and both greater disability and more impaired HRQoL. These findings are further supported by the strong associations of HRQoL with higher dopaminergic load.

Third, in both the ICD and the apathy group, depression levels were high, suggesting a common link between these behavioural groupings, psychiatric symptoms and the outcomes of interest. Namely, higher levels of depression were associated with negative outcomes in both disability and HRQoL, and anxiety appeared to play a negative role in HRQoL. Psychiatric factors, in particular depression and anxiety, have previously been shown to be strong predictors of the outcomes of either disability or HRQoL [14, 39].

Finally, the pattern of cognitive impairment across the outcomes is also noteworthy. Disability was associated with greater impairment in working memory (n-back). This supports the notion that key underlying factors determining disability are cognitive and psychiatric in nature, as well as being related to motor function and disease severity. Global cognitive measures did not appear to be associated with HRQoL, however more impaired working memory was also associated with greater impairment in this outcome. Working memory deficits, in the context of relatively intact global cognitive function, may impact on QoL due the specific nature of the deficit and its relationship to executive dysfunction and the ability to complete daily tasks efficiently.

A potential limitation to this study is that due to its cross-sectional methodology, the direction of causality is difficult to determine. Nonetheless, a strength is that this is the first direct comparison of the impact of the behavioural disorders of apathy and ICDs in PD in a non-demented community-based sample and the associations described were supported by linear regression models. These models showed that older age at disease onset was related to worse disability, whereas younger age at diagnosis was related to worse HRQoL. Depression negatively impacted both disability and HRQoL, with motor impairment more strongly impacting the former and working memory deficits the latter.

In conclusion, the PD-related behavioural complications of apathy and ICDs have significant implications for those affected. These findings strengthen the need to diagnose and manage behavioural complications of PD in a timely and accurate manner.

Key points
- In those with behavioural complications of PD, disability and quality of life are significantly yet differentially affected.
- ICDs are more likely to impair well-being, and apathy more likely to detrimentally impact on functioning.
- These findings strengthen the need to diagnose behavioural complications of PD in a timely and accurate manner.

Conflicts of interest
None declared.
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