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The utility of the Cambridge Behavioural Inventory in neurodegenerative disease

C Wedderburn, H Wear, J Brown, S J Mason, R A Barker, J Hodges, C Williams-Gray

ABSTRACT
We investigated the utility of the Cambridge Behavioural Inventory (CBI), a carer-completed questionnaire, in a large cohort with Parkinson’s disease (PD) (n = 215). In a sub-cohort of 112 patients with PD, the CBI was found to be a valid instrument compared with the Neuropsychiatric Inventory, PDQ-39 and UPDRS, with high internal consistency. Furthermore, in the whole cohort, the CBI was sensitive to changes in behaviour with disease progression. Comparison between CBI scores in PD and other neurodegenerative diseases, including Huntington’s disease (HD) (n = 75), Alzheimer’s disease (AD) (n = 96) and fronto-temporal fronto-temporal dementia (fvFTD) (n = 64), revealed distinct profiles for each disease. Predominant deficits were “sleep” and “self care” in PD; “memory” in HD and AD; and “motivation” and “stereotypic behaviours” in fvFTD. The CBI is a robust, easy-to-use and valid instrument, which has the capacity to discriminate between neurodegenerative diseases, and may be of value in monitoring therapeutic interventions.

Neurodegenerative disorders, such as Parkinson’s disease (PD), Huntington’s disease (HD), Alzheimer’s disease (AD) and frontotemporal dementia (FTD), are a major cause of morbidity and mortality. Although these disorders manifest with a range of cognitive, motor and behavioural problems, the latter have important implications in terms of quality of life and care burden. Although several studies have described the pattern of behavioural deficits in FTD and AD, as well as HD, such deficits in PD are less well studied, and systematic cross-disease comparisons in large numbers of patients are lacking.

The Cambridge Behavioural Inventory (CBI) is an 81-item questionnaire that is divided into 13 subsections: memory; orientation and attention; everyday skills; self-care; mood; beliefs; challenging behaviour; disinhibition; eating habits; sleep; stereotypic behaviours; motivation; and insight. Items are scored on a scale from 0 to 4, with higher scores indicating more frequent problems. It is completed by a family member or close friend, thus allowing the collection of large amounts of clinically important data without placing demands on the clinician’s time. The behavioural component derives from an earlier questionnaire that was shown to discriminate between FTD and AD. The CBI leans heavily on the interview-based Neuropsychiatric Inventory (NPI), but assesses a wider range of symptoms. The CBI also incorporates components of the General Health Questionnaire, as well as containing a section that is designed to assess activities of daily living (ADLs).

A recent preliminary study investigating the utility of the CBI in FTD and AD indicated acceptable test-retest reliability, good concurrent validity and the expected group discrimination, but was limited by small group sizes. The CBI has not been validated for use in patients with PD. We have undertaken an extensive study that aims (i) to evaluate the psychometric properties of the CBI, incorporating well-established statistical procedures, in a large cohort of patients with PD, and (ii) to compare the behavioural deficits in PD with those found in other common neurodegenerative disorders, specifically HD, AD and FTD.

METHODS
CBI questionnaires were completed by caregivers of patients with PD and HD attending clinics at the Cambridge Centre for Brain Repair, and carers of patients with AD and FTD attending the Memory and Cognitive Disorders clinic. All patients met strict diagnostic criteria: idio-pathic patients with PD fulfilled UKPDS Brain Bank criteria; patients with HD had genetically confirmed disease; patients with AD met National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association criteria; and patients with FTD fulfilled consensus criteria and had what we have referred to as the behavioural or fronto-temporal variant of FTD (fvFTD). The study was approved by the Cambridge Local Research Ethics Committee.

In a sub-cohort of patients with PD—who were part of an extensive epidemiological study—NPI, Unified Parkinson’s Disease Rating Scale (UPDRS) and Parkinson’s Disease Questionnaire (PDQ-39) scores had been completed at the same time as the CBI. The validity of the questionnaire in PD was assessed by comparison with these three well-established instruments using a correlation matrix with bivariate Spearman’s rank correlation coefficients at a 0.01 level of significance. Internal consistency was analysed in the whole data set using Cronbach’s alpha. The sensitivity of the CBI to change in disease duration and functional ability, as measured by the Schwab and England scale (S&E), was assessed in the PD cohort using a cross-sectional approach. Patients were stratified into subgroups on the basis of disease duration and S&E scores. CBI profiles were based on the proportion of patients with “frequently occurring/severe deficits” on each item and compared using repeated measures analyses of variance (RMANOVA), with CBI subsection as a within-subject factor and disease duration or S&E.
score as between-subject factors. A similar strategy was used to compare the distribution of behavioural deficits in PD, HD, AD and fvFTD and to investigate the utility of the CBI in discriminating between the four diseases.

RESULTS
Patient characteristics

Questionnaires from a total of 450 patients were included in the study: 215 with PD, 75 with HD, 96 with AD and 64 with fvFTD. There were, as anticipated, significant differences between disease groups in terms of age (ANOVA, F = 45.5, p < 0.001), Mini Mental State Examination (MMSE) score (F = 9.26, p < 0.001) and gender (F = 7.65, p < 0.001). In particular, the HD cohort was considerably younger, and MMSE scores were well preserved in PD and HD, reflecting, in part, the insensitivity of the instrument to frontostriatal dysfunction. In terms of gender, male predominance is well established in PD and fvFTD, which is reflected in this unselected population. Total CBI scores also differed significantly across groups, with fvFTD being most affected (F = 61.14, p < 0.001) (see table 1).

Validity of the CBI

For the subcohort of 112 patients with PD for whom relevant data were available, correlations between CBI subsection scores and NPI, UPDRS and PDQ-39 subscale scores are shown in table 2. As expected, most subsections in the CBI correlated well with the relevant scales in the comparative instruments, indicating good concurrent validity. Using all available data, 8 subsections (memory, orientation and attention, everyday skills, self-care, mood, beliefs, motivation, and insight and awareness) were found to have high internal consistency (α > 0.8), and the Cronbach’s alpha score for the whole CBI was 0.95. The alpha score fell below 0.7, which is the recommended level for group comparisons in research situations,27 in only one subsection—sleep.

Sensitivity of the CBI

Behavioural profiles in subgroups of patients with PD, stratified according to functional impairment and disease duration (fig 1A and 1B), reveal that, although the pattern of behavioural deficits appears stable, the frequency of deficits increases as disease duration and disability progress. RMANOVA confirmed a main effect of both disease duration (F = 4.5, p = 0.004) and S&E functional independence score (F = 9.5, p < 0.001) on CBI profile.

Cross-disease comparison

Comparison of behavioural profiles across the four diseases (fig 1c) using RMANOVA confirmed significant between-group differences (F = 37.3, p < 0.001). Pairwise post-hoc comparisons were explored using the Tukey’s honestly significant difference (HSD) test. fvFTD patients showed the highest prevalence of behavioural symptoms, with notably high endorsement of stereotypic behaviours and motivation subsections. The percentage of fvFTD patients with severe deficits was also significantly greater than any of the other diseases in four further CBI subsections: mood, challenging behaviours, disinhibition and eating habits (p < 0.05). Memory and orientation and attention deficits were common in patients with AD, with prevalence being comparable to those in patients with fvFTD. Severe deficits in ADLs were also common. Deficits in patients with PD

Table 1 Demographic, cognitive and behavioural data

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>N</th>
<th>Age (years)</th>
<th>Disease duration (years)</th>
<th>CBI score</th>
<th>MMSE score</th>
<th>Gender (M/F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD</td>
<td>215</td>
<td>68.3 (37.1–90.1)</td>
<td>4.60 (0.1–19.8)</td>
<td>35 (1–140)</td>
<td>27.2 (8–30)</td>
<td>137/78</td>
</tr>
<tr>
<td>HD</td>
<td>75</td>
<td>52.4 (21–79.8)</td>
<td>4.07 (0.1–12)</td>
<td>62 (2–189)</td>
<td>25.1 (12–30)</td>
<td>33/42</td>
</tr>
<tr>
<td>AD</td>
<td>96</td>
<td>67.0 (47–90)</td>
<td>5.30 (1.5–24)</td>
<td>78 (6–230)</td>
<td>17.9 (4–27)</td>
<td>53/43</td>
</tr>
<tr>
<td>fvFTD</td>
<td>64</td>
<td>62.0 (43–81)</td>
<td>9.62 (3–28)</td>
<td>114 (10–227)</td>
<td>21.2 (2–30)</td>
<td>47/17</td>
</tr>
</tbody>
</table>

Values are expressed in mean (range).

AD, Alzheimer’s disease; CBI, Cambridge Behavioural Inventory; F, female; fvFTD, frontal variant frontotemporal dementia; HD, Huntington’s disease; M, male; MMSE, Mini Mental State Examination; PD, Parkinson’s disease.

Table 2 Spearman’s rho coefficients (r) for correlations between CBI subsections and NPI, UPDRS and PDQ-39 subscales in PD (n = 112), demonstrating concurrent validity of the CBI

<table>
<thead>
<tr>
<th>CBI subscale</th>
<th>NPI subscale</th>
<th>r</th>
<th>UPDRS (I and II) subscale</th>
<th>r</th>
<th>PDQ-39 subscale</th>
<th>r</th>
<th>UPDRS (III) subscale</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory</td>
<td>–</td>
<td>–</td>
<td>Intellectual impairment</td>
<td>0.56</td>
<td>Cognitions</td>
<td>0.38</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Orientation and attention</td>
<td>–</td>
<td>–</td>
<td>Intellectual impairment</td>
<td>0.54</td>
<td>Cognitions</td>
<td>0.58</td>
<td>Motor score</td>
<td>0.28</td>
</tr>
<tr>
<td>Everyday skills</td>
<td>–</td>
<td>–</td>
<td>Activities of daily living</td>
<td>0.45</td>
<td>Activities of daily living</td>
<td>0.42</td>
<td>Motor score</td>
<td>0.30</td>
</tr>
<tr>
<td>Self-care</td>
<td>–</td>
<td>–</td>
<td>Activities of daily living</td>
<td>0.58</td>
<td>Activities of daily living</td>
<td>0.66</td>
<td>Motor score</td>
<td>0.44</td>
</tr>
<tr>
<td>Mood</td>
<td>Depression</td>
<td>0.44</td>
<td>Depression</td>
<td>0.36</td>
<td>Emotional well-being</td>
<td>0.50</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Beliefs</td>
<td>Hallucinations</td>
<td>0.58</td>
<td>Thought disorder</td>
<td>0.40</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Challenging behaviour</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Disinhibition</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Eating habits</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Sleep</td>
<td>Night-time behaviour</td>
<td>0.31</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Motor score</td>
<td>0.28</td>
</tr>
<tr>
<td>Stereotypic and motor behaviour</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Motivation</td>
<td>Apathy</td>
<td>0.52</td>
<td>Motivation/initiation</td>
<td>0.48</td>
<td>–</td>
<td>–</td>
<td>Motor score</td>
<td>0.26</td>
</tr>
<tr>
<td>Insight/awareness</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
</tbody>
</table>

Highest correlations significant at the 0.01 level are shown.

CBI, Cambridge Behavioural Inventory; NPI, Neuropsychiatric Inventory; PDQ-39, Parkinson’s Disease Questionnaire; UPDRS, Unified Parkinson’s Disease Rating Scale.
and HD were comparable in frequency across the majority of subsections. However, patients with HD had a significantly higher percentage of severe deficits in the memory, mood, motivation and stereotypic behaviours subsections compared with patients with PD. Sleep impairment was the most common symptom affecting patients with PD, followed by impaired ADLs.

**DISCUSSION**

This study shows that the CBI is a useful and valid instrument for assessing behavioural deficits in PD and is able to discriminate between a range of neurodegenerative disorders, including PD, HD, AD and fvFTD.

Interestingly, the CBI revealed strikingly different profiles of behavioural impairment across the four neurodegenerative diseases. The fvFTD profile encompassed a full repertoire of behavioural deficits, with impairment in the motivation and stereotypic behaviours subsections being most prominent. These results were in keeping with those previously reported. In patients with AD, impairments in memory, orientation and attention and motivation were most common, as anticipated from the literature. Patients with PD and HD had similar behavioural profiles, although certain subsections, including memory, motivation, mood and stereotypic behaviours, were affected more commonly in patients with HD, in keeping with the prominent cognitive and behavioural deficits in the earliest stages of this disorder. Patients with PD appeared to be the least impaired overall. Self-care difficulties in this group presumably reflect motor disability. Sleep disorder was also prominent, as anticipated.

Although the utility of the CBI has been explored previously in patients with AD and fvFTD, this is the first study to formally demonstrate its validity and sensitivity in patients with PD. We used three separate instruments to evaluate the concurrent validity of the CBI, involving carer (NPI), patient (PDQ-39) and clinician (UPDRS) input. This comprehensive approach was adopted, in part, because the CBI covers a wider range of behavioural symptoms than each of these instruments alone. In addition, our results suggest that not only clinicians, but also patients, recognise the behavioural repercussions of PD reported by the carer, in spite of the relatively high deficits in insight recorded using the CBI.

Another important measure of the validity of any questionnaire is its internal consistency, which measures how closely questions within a particular subsection correlate with one another. The internal consistency of the CBI was generally high, with Cronbach’s alpha being suboptimal only for the sleep subsection, probably reflecting the inclusion of only two questions in this section, which may benefit from expansion.

Our data suggest that the CBI is sensitive to changes in functional status and disease duration in PD. Of interest is the observation that the behavioural deficits experienced in early PD become more frequent with disease progression without any change in the pattern of deficits. This indicates that certain behaviours, such as disinhibition and challenging behaviour, are rarely seen, even in later stages of PD. Further studies designed to examine the sensitivity of the CBI using a longitudinal prospective approach are now underway in order to explore whether the CBI is truly a useful instrument for monitoring disease progression.

Behavioural questionnaires are increasingly recognised as an important method of assessing the impact of disease in the individual. Identification of behavioural and neuropsychiatric disturbances as primary manifestations of dementia make it...
imperative that valid, easy-to-use instruments are available for their accurate detection and quantification, particularly in an ageing society. The CBI is just such an instrument and has the advantage of evaluating a wide range of psychopathology. As a carer-completed questionnaire, it provides an important insight into the issues that are most significant to the patient’s daily life, and allows a large amount of data to be collected without encroaching on the clinician’s time in a busy clinical setting. Furthermore, it is able to distinguish between different neurodegenerative diseases, indicating that it may have some diagnostic value. If its apparent sensitivity to disease progression is confirmed in longitudinal studies, it may prove to be a useful instrument for evaluating treatment efficacy.

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Competing interests: None declared.

REFERENCES


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