Assessment of hallucinations in Parkinson’s disease using a novel scale


Objective – To assess hallucinations in Parkinson’s disease (PD), we developed a novel practical rating scale that evaluates five items including variety, frequency, and severity of hallucinations, caregiver burden levels, and psychiatric status at nighttime. Methods – Forty-one PD patients and their caregivers were examined regarding the status of the hallucinations associated with PD. Results – As a measure of internal consistency, the Tottori University Hallucination Rating Scale (TUHARS) has a Cronbach’s α of 0.88. Mini-Mental State Examination (MMSE) and Hoehn–Yahr stage were associated with the TUHARS scores in a multivariate regression analysis. Visual hallucinations are the most common. However, half of the patients who reported visual hallucinations also had other hallucinations. The scale scores in the PD patients with dementia (PDD) group were significantly greater than in the PD patients without dementia (PDnD) group. Conclusions – TUHARS appears to be a suitable and easily administered instrument for assessment of hallucinations in PD. PD patients experienced various kinds of hallucinations. Hallucinations may have a close relationship with cognitive decline in PD patients.

Introduction

The presence of psychosis in Parkinson’s disease (PD) represents a significant risk factor for permanent placement in a nursing home and increased mortality (1, 2). Hallucinations are one of the most common psychotic symptoms in PD, occurring in approximately 8–40% of PD patients (3–6). Hallucinations are mainly visual and may be of people, animals, insects, or inanimate objects; but may also be auditory, tactile, or cenesthetic (7, 8). A recent clinicopathological study has revealed a significant, though subtle, correlation of visual hallucinations with anti-parkinsonian drugs in PD patients and that visual hallucinations have a close relationship with Lewy body pathology (9). Several studies have reported a close relationship between visual hallucinations and the occurrence of dementia in PD (3, 4, 6, 10, 11). Burn et al. showed that the presence of visual hallucinations may predict a more rapid cognitive decline in Parkinson’s disease dementia (PDD) (12). It is important to assess hallucinations. However, there are currently few available rating scales for the evaluation of hallucinations in PD patients. The majority of rating scales for evaluation of hallucinations were developed for assessing psychosis in schizophrenia or dementia (13, 14). The Parkinson Psychosis Questionnaire (PPQ) (15) and the Parkinson Psychosis Rating Scale (PPRS) (16) have been reported as rating scales designed for assessing drug-induced psychosis in PD. However, these scales are not specific to hallucinations. We constructed an evaluation scale targeting the assessment of hallucinations in PD. Our scale evaluates the variety, frequency, and severity of hallucinations, the degree of caregiver burden, and the psychiatric status at nighttime including during sleep. In this study, we assessed the hallucinations of PD patients both quantitatively and qualitatively using our novel scale and report the utility of this scale.
Methods

Subjects

The subjects for this study comprised 41 patients in the Department of Neurology at Tottori University Hospital diagnosed as having idiopathic PD. Furthermore, these PD patients were divided into 31 PD patients without dementia (PDnD) and 10 PD patients with dementia (PDD). Table 1 shows the baseline characteristics of the patients. Assessments of these patients included a carefully examined medical history, physical examination, drug inventory, neurological examination, comprehensive cognitive evaluation with the use of the Mini-Mental State Examination (MMSE), neuroimaging assessments by computed tomography (CT) or magnetic resonance imaging (MRI) and single-photon emission computed tomography (SPECT) of the head, electric encephalography (EEG), 123I-metaidobenzylguanidine (MIBG) myocardial scintigraphy, and routine laboratory tests such as blood cell analysis and biochemical profile. Patients were examined by at least two Japanese Neurological Society Board-certified neurologists. The clinical diagnosis of PD was based on the Diagnostic and Statistical Manual of Mental Disorders, fourth edition-revised (DSM-IV) criteria (Code 294.1) (18). The ethics committee of Tottori University Faculty of Medicine approved the study, and all patients gave their informed consent to participate in the study.

Tottori University Hallucination Rating Scale

The TUHARS evaluates five items including variety, frequency, and severity of hallucination, caregiver burden level, and psychiatric status at nighttime (Appendix). Points are accumulated according to the severity of hallucinations. Patients and their caregivers were interviewed by a clinician as to whether the patient had experienced hallucinations using TUHARS. The TUHARS score was calculated as the total score of each question.

External validation

The PPQ was used to evaluate drug-induced psychosis in PD (15). The PPQ is a reliable and well-validated questionnaire that consists of four categories including (A) early symptoms/sleep disturbances, (B) hallucinations/illusions, (C) delusions, and (D) orientation. The part (B) section regarding hallucinations/illusions was applied for external validation.

Statistical analysis

Data analysis was conducted with SPSS for Windows version 11.5J (Chicago, IL, USA). The results are presented as mean ± standard deviation. Cronbach’s $\alpha$ was used to assess internal consistency. Intergroup differences were analyzed using a Mann–Whitney $U$-test. Categorical variables were examined using a chi-squared test. Correlation analysis was conducted using a Pearson correlation coefficient. Univariate and multivariate regression analyses were used to elucidate variables associated with the TUHARS score. The variables used in the multivariate analysis were selected using a forward stepwise model. We used a level of 95% ($P < 0.05$) as the criterion for statistical significance.

Results

Reliability and validity of the TUHARS

The TUHARS was able to completely evaluate the hallucinations of a patient within 5 min. As a comprehensive measure of internal consistency, TUHARS had a Cronbach’s $\alpha$ of 0.88. As a criterion related to validity, the total TUHARS score was significantly correlated with the score of hallucinations/illusions in the PPQ (Pearson correlation coefficient = 0.965, $P < 0.001$) (Fig. 1).

Table 1 Characteristics of the subjects

<table>
<thead>
<tr>
<th></th>
<th>PDnD</th>
<th>PDD</th>
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<tbody>
<tr>
<td>Number</td>
<td>31</td>
<td>10</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>9/23</td>
<td>2/8</td>
</tr>
<tr>
<td>Age at evaluation</td>
<td>68.7 ± 10.1 (65.0–72.4)</td>
<td>71.6 ± 7.7 (66.1–77.1)</td>
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<tr>
<td>(95% CI) years</td>
<td>60.4 ± 13.1 (55.5–65.2)</td>
<td>57.9 ± 12.1 (49.2–66.6)</td>
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<tr>
<td>Age at onset</td>
<td>8.3 ± 7.6 (5.5–11.1)</td>
<td>13.7 ± 6.6 (9.0–18.4)*</td>
</tr>
<tr>
<td>(95% CI) years</td>
<td>2.9 ± 0.8 (2.5–3.9)</td>
<td>3.5 ± 0.9 (2.9–4.1)*</td>
</tr>
<tr>
<td>Duration (95% CI), years</td>
<td>27.1 ± 2.9 (26.1–28.2)</td>
<td>23.8 ± 5.8 (19.7–27.9)</td>
</tr>
<tr>
<td>Hoenh–Yahr stage (95% CI)</td>
<td>289.3 ± 143.2 (n = 27)</td>
<td>415.0 ± 238.0 (n = 10)</td>
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<tr>
<td>MMSE (95% CI) years</td>
<td>8.1 ± 4.7 (n = 7)</td>
<td>0.95 ± 0.46 (n = 7)</td>
</tr>
<tr>
<td>Treatment (user number),</td>
<td>0.75 ± 0.43 (n = 3)</td>
<td>1.0 ± 1.3 (n = 10)</td>
</tr>
<tr>
<td>mg/day</td>
<td>1.0 (n = 1)</td>
<td>2.6 ± 1.3 (n = 10)</td>
</tr>
<tr>
<td>Levodopa/carbidopa</td>
<td>1.2 ± 0.78 (n = 8)</td>
<td>1.03 ± 0.87 (n = 4)</td>
</tr>
<tr>
<td>Dopamine agonist</td>
<td>150 ± 59.8 (n = 8)</td>
<td>150 (n = 1)</td>
</tr>
<tr>
<td>Bromocriptine</td>
<td>4.2 ± 1.9 (n = 12)</td>
<td>4.2 ± 1.4 (n = 3)</td>
</tr>
<tr>
<td>Pergolide</td>
<td>2.5 ± 1.3 (n = 8)</td>
<td>2.6 ± 1.3 (n = 10)</td>
</tr>
<tr>
<td>Cabergoline</td>
<td>1.03 ± 0.87 (n = 4)</td>
<td>1.0 ± 1.3 (n = 10)</td>
</tr>
<tr>
<td>Pramipexole</td>
<td>150 (n = 1)</td>
<td>150 ± 59.8 (n = 8)</td>
</tr>
<tr>
<td>Amantadine</td>
<td>4.2 ± 1.4 (n = 3)</td>
<td>4.2 ± 1.9 (n = 12)</td>
</tr>
<tr>
<td>Selegiline</td>
<td>6.6 (9.0–18.4)*</td>
<td>7.6 (5.5–11.1)</td>
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<td>*P &lt; 0.05 Mann–Whitney $U$-test PDnD vs PDD.</td>
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Data indicate mean ± SD. 95% CI, 95% confidence interval; PDnD, PD without dementia; PDD, PD with dementia; MMSE, Mini-Mental State Examination.
The univariate analyses demonstrated that duration of disease, Hoehn–Yahr stage, daily dose of \( L \)-dopa, and MMSE correlated with the TUHARS score. The multivariate analysis revealed that Hoehn–Yahr stage and MMSE independently predicted the TUHARS scores. The age at onset did not reach statistical significance although it was selected in a forward stepwise analysis (Table 2).

Assessment of hallucinations in PD patients with the TUHARS

As shown in Fig. 2, 31.4% of PD patients exhibited hallucinatory symptoms. Among the hallucinators, 42.9% had visual hallucinations only, 28.6% visual plus auditory hallucinations, 14.3% visual plus cenesthetic hallucinations, 7.1% visual plus auditory plus tactile hallucinations, and 7.1% auditory hallucinations only. The most frequent hallucinations were visual, but half of the patients who reported visual hallucinations also had other hallucinations including auditory, tactile, or cenesthetic hallucinations.

The average TUHARS score was 2.4 ± 4.6 in patients with PDDnD and 9.4 ± 7.0 in patients with PDD. Scores of patients with PDD were significantly higher than those of patients with PDDnD (Fig. 3). Caregiver burden scores were significantly correlated with those of TUHARS (Fig. 4).

Discussion

This study assessed the characteristics of hallucinations in patients with PD using a novel rating scale for the assessment of hallucinations associated with PD. It has been reported that vivid dreams and sleep disruption are associated with hallucinations in PD (19, 20), thus psychiatric status at nighttime, including during sleep, was included in our scale. Furthermore, the burden of the hallucinations on caregivers was also assessed. Our scale, TUHARS, has a Cronbach’s \( \alpha \) of 0.88, which indicates excellent internal constancy, and it is an easy-to-use scale. TUHARS significantly correlated with the hallucination/illusion scores of the PPQ as an external validator. The multivariate regression analysis revealed MMSE and Hoehn–Yahr stage as significant determinants of TUHARS. While the PPQ is designed to assess the whole spectrum of psychosis in PD, TUHARS is specifically intended for the assessment of hallucination. The PPRS was also designed to assess the severity of specific symptoms of drug-
induced psychosis in PD patients. Questions of the PPRS quantify the severity of psychosis based mainly on the frequency of symptoms, and assess visual hallucinations but not other types of hallucinations. The TUHARS is able to assess hallucinations in PD patients in more detail than the PPQ or the PPRS.

Using this novel scale, we assessed the characteristics of hallucinations in PD patients. In our study, 31.4% of the PD patients were found to exhibit hallucinatory symptoms. The most common hallucination was visual, and all of the PD patients, except one who had only auditory hallucinations, had experience of visual hallucinations. Auditory hallucinations were the second most common hallucination found by our study. Other kinds of hallucinations such as tactile and cencesthetic hallucinations, though not common, were experienced in combination with visual hallucinations. Our results were consistent with previous studies from the point of view that visual hallucinations were the most common and auditory hallucinations usually occur against a background of visual hallucinations (4, 19, 21). Tactile and cencesthetic hallucinations may also occur against a background of visual hallucinations (22). Olfactory hallucinations have rarely been described in PD (23, 24). Indeed, there was no PD patient with olfactory hallucinations in this series.

In a quantitative analysis, the TUHARS scores of the PDD patients were significantly higher compared with those of the PDnD patients and MMSE scores were inversely correlated with the TUHARS scores, showing a close relationship between hallucinations and cognitive declines in PD patients. MMSE scores of the PDD patients were relatively high in our study. The difference in MMSE scores between PDnD and PDD patients did not reach statistical significance. It is not easy to diagnose dementia in PD. Various kinds of cognitive impairments including visuo-spatial and executive functions as well as memory have been reported in PDD patients (25). For the diagnosis of dementia, we attached importance not only to MMSE, but also to the interview of the caregivers regarding the daily activity of their patients. Furthermore, clinical diagnosis of dementia was made strictly according to the same criteria of evaluation by at least two neurologists in order to improve the accuracy of the clinical diagnosis.

It is difficult to differentiate whether hallucinations are drug-induced or symptoms of dementia itself. Indeed, the daily doses of l-dopa in the PDD patients were greater than doses in PDnD patients, and univariate regression analysis showed that the daily dose of l-dopa correlated with the TUHARS score. However, the daily dose of l-dopa did not reach statistical significance in multivariate regression analysis. Prospective and retrospective studies have found that hallucinations were not associated with the dosage of dopaminergic medication (4, 26–28). These findings indicate that the etiology of hallucinations may be not only a simple dopaminergic adverse

Figure 3. Tottori University Hallucination Rating Scale (TUHARS) scores in Parkinson’s disease (PD) patients with (PDD) and without dementia (PDnD). The horizontal bar indicates the mean level. Statistical differences were calculated using the Mann–Whitney U-test.

Figure 4. Tottori University Hallucination Rating Scale (TUHARS) scores and caregiver burden levels. Caregiver burden levels significantly correlated with TUHARS scores.
event, but also symptoms occurring in the course of dementia itself.

This is a preliminary study, which showed the usefulness of our novel rating score (TUHARS) for hallucinations in PD patients and indicated that hallucinations may be closely related to cognitive decline in PD patients. However, there were some weaknesses in this study. The first was that we did not examine the test–retest and interrater reliability of the TUHARS. Secondly, our study was limited by its small sample size and cross-sectional design, and the value of validations was limited. Therefore, further studies with larger samples are necessary to more fully evaluate the reliability and external validity of the TUHARS and to examine the association of hallucinations with cognitive decline in a prospective design.

Acknowledgements

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References

Appendix

Tottori University Hallucination Rating Scale

This is a clinician-administered interview conducted with the patient and care giver. The TUHARS score is calculated as the total score of each question.

1. Has he/she experienced any of these hallucinations? (Please circle all that apply)
   Never (0).
   Visual hallucination: He/she reports seeing something (people, animals, objects) that is not seen by others (1).
   Auditory hallucination: He/she reports hearing something (noise, voice) that is not heard by others (1).
   Olfactory hallucination: He/she reports smelling something that is not smelt by others (1).
   Tactile hallucination: He/she reports feeling something touch him/her when in fact nothing is touching him/her (1).
   Cenesthetic hallucination: This is visceral in origin. He/she reports to feel bodily functions that are usually undetectable (2).

2. How frequently has he/she experienced hallucinations? (Please circle one applicable item)
   Up to three times per month (1).
   About once per week (2).
   Two or three times per week (3).
   Several times per week, but not everyday (4).
   More than once per day (5).

3. How severe are the hallucinations that he/she has experienced? (Please circle one applicable item)
   He/she can always tell they are not real (0).
   After having the hallucination explained by the family, he/she can tell they are not real (1).
   After having the hallucination explained by the family, he/she still believes they are real (2).
   He/she has experienced hallucinations with delusions (3).
   He/she has experienced hallucinations with delusions and emotional change (for example fear, excitement, gratification) (4).

4. How much extra burden has been imposed on you because of the hallucinations? (Please circle one applicable item)
   None at all (0).
   Though we must pay attention to the patient, it doesn't interfere with regular tasks and housekeeping (1).
   We must pay attention to the patient and there are some problems with completing our housekeeping and other tasks (2).
   We must pay a lot of attention to the patient and we have moderate problems with completing our housekeeping and other tasks (3).
   We must always attend the patient and we cannot do our housekeeping and other tasks (4).

5. Has he/she experienced any hallucinations during the night? (Please circle one applicable item)
   Yes (1).
   No (0).

6. Please answer this question if you answered ‘yes’ to question 5. (Please circle one applicable item)
   He/she has experienced ambiguous hallucinations like dreams (1).
   He/she has experienced vivid hallucinations, but he/she can understand that they are ‘hallucinations’ (2).
   He/she has experienced vivid hallucinations, but he/she cannot understand that they are ‘hallucinations’ (3).
   He/she has tried to talk to or communicate with the hallucinations (4).

7. Please answer this question if you answered ‘no’ to question 5. Has he/she experienced any vivid dreams during the night? (Please circle one applicable item)
   Yes (1).
   No (0).