Visual perception in Parkinson disease dementia and dementia with Lewy bodies

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Abstract—Objective: To quantify visual discrimination, space-motion, and object-form perception in patients with Parkinson disease dementia (PDD), dementia with Lewy bodies (DLB), and Alzheimer disease (AD). Methods: The authors used a cross-sectional study to compare three demented groups matched for overall dementia severity (PDD: n = 24; DLB: n = 20; AD: n = 23) and two age-, sex-, and education-matched control groups (PD: n = 24, normal controls [NC]: n = 25). Results: Visual perception was globally more impaired in PDD than in nondemented controls (NC, PD), but was not different from DLB. Compared to AD, PDD patients tended to perform worse in all perceptual scores. Visual perception of patients with PDD/DLB and visual hallucinations was significantly worse than in patients without hallucinations. Conclusions: Parkinson disease dementia (PDD) is associated with profound visuo-perceptual impairments similar to dementia with Lewy bodies (DLB) but different from Alzheimer disease. These findings are consistent with previous neuroimaging studies reporting hypoactivity in cortical areas involved in visual processing in PDD and DLB.

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Parkinson disease (PD) is associated with a higher risk of developing dementia compared to healthy elderly controls; longitudinal studies suggest that up to 78% of PD patients will develop dementia after nearly two decades of motor symptoms. Once dementia is established, clinical symptoms of PD dementia (PDD) may show, apart from a longer duration of motor features, considerable overlap with dementia with Lewy bodies (DLB). The postural instability-gait type of parkinsonism is over-represented in PDD and DLB and both disorders show similar fluctuation of attention and response to cholinergic therapy. Studies comparing visual perception and visual construction of PDD with Alzheimer disease (AD) have revealed contradictory results. Some studies report PDD to be more impaired, whereas other studies found no differences. Similar inconsistencies have been found when perception of PD patients was compared with healthy controls. Since operationalized criteria to define the clinical boundaries between PD and PDD or PD and DLB require refinement, these inconsistencies may be partly due to diagnostic heterogeneity. When DLB was compared with AD, studies consistently reported greater visual impairment in DLB and a recent study found similar impairments in pentagon copying in DLB and PDD. Some of these studies used construction tasks as evidence, but this may not be legitimate given the motor impairments in these patients. Studies quantifying visual perception of DLB and PDD using tasks without motor requirements are lacking.

Peripheral structures such as the retina, the optic nerve and tract, and primary visual cortex are multimodal in their function, whereas the visual association cortex is more specialized. Low-level visual discrimination is mainly processed in visual area V1/ V2, whereas high-level visual functions require additional activation of large extrastriatal cortical networks. Two visual pathways can be distinguished: the ventral occipito-temporal pathway, which is required for detailed analysis and identification of objects and forms, and the dorsal occipito-parietal pathway, required for spatial vision and motion perception. Task selection of the present study took these theoretical considerations into account. We aimed to quantify perceptual differences in PDD, DLB, and AD patients matched for overall dementia severity, and in non-demented controls (PD and NC). We tested visual discrimination, object-form perception, and space-motion perception to assess impairments in different visual cortical pathways. Since PDD and DLB have combined motor...
and visuoperceptual impairments, all tasks used in the present study did not require motor responses and were not time driven. Based on previous neuroimaging findings, we hypothesized similar visual impairments in PDD and DLB and expected impairments to exceed those of matched AD patients.

Methods. Subjects. All subjects were recruited from the Newcastle MRC prospective outpatient cohort. Characteristics of the sample are summarized in Table 1. The UK PD Society Brain Bank Clinical Diagnostic Criteria were used to make the diagnosis of PD, the National Institute of Neurologic and Communicative Disorders and Stroke and AD and Related Disorders Association (NINCDS-ADRD) for AD, and the DLB Consensus guidelines for DLB, following the recommendation that patients with parkinsonian features preceding cognitive impairment for more than 12 months should be diagnosed with PDD. PDD patients had to have PD for more than 12 months before developing dementia. Patients were required to have a caregiver providing regular care and support and to score at least 10 on the Mini-Mental State Examination (MMSE). Subjects with coexisting medical illness or a history of visual impairment due to cataract, glaucoma, or macular degeneration were excluded. The only antiparkinsonian medication allowed was levodopa. Patients stabilized on cholinesterase inhibitors (ChE-I) were eligible for the study provided they were on a stable dose for more than 3 months. The percentage of demented patients on long-term ChE-I was not different between the diagnostic groups (PD: 58%; DLB: 65%, and AD: 69%). All patients with PDD were treated with levodopa, but only 43% of DLB were on dopaminergic treatment. Of 146 subjects invited, 118 gave written informed consent; 2 patients had to be excluded because they did not understand the task instructions. The local research ethics committee granted ethical approval.

Procedure. Global cognitive impairment was assessed with the Cambridge Cognitive Examination (CAMCOG) and for the purpose of this study, tests assessing apraxia were analyzed separately from tests measuring visuconstructional ability, i.e., praxis and construction scores. CAMCOG visual construction included spiral, pentagon, three-dimensional house and clock copy. Parkinsonism in DLB was defined as bradykinesia, plus one or more of rest tremor, muscular rigidity, and postural instability without other explanation. Severity of extrapyramidal features was assessed with the Unified PD Rating Scale (UPDRS) motor score (part III). A cutoff score of more than 6 in the one-day fluctuation assessment scale defined fluctuation. The Neuropsychiatric Inventory (NPI) was used to determine whether a subject was experiencing recurrent visual hallucinations during the month previous to the assessment. Analyzing questions 2 or 3 in the hallucination section of the NPI identified recurrent visual hallucinations. In patients with recurrent visual hallucinations, the caregiver agreed with either of these questions and reported a frequency and severity of at least one. The Bristol Activities of Daily Living Scale (Bristol-ADL) was used to assess impairments in activities of daily living. The neuro-ophthalmologic assessment included external inspection of the eyes, assessment of pupil reactions, light reflex (penlight), measurement of near vision (Landolt broken rings, test distance 40 cm), assessment of ocular movements, and estimation of the visual field by confrontation test. The red reflex and ocular fundus were assessed with direct ophthalmoscopy.

Assessment of visual perception. Visuoperceptual tasks were presented in a multiple-choice format on a 14-inch computer screen in a standardized, darkened environment. Subjects sat 40 cm in front of the computer screen. Tasks were not time driven, subjects responded verbally, and the examiner handled all buttons. The instruction of each task was read while an example was presented on the screen. Once the correct answer was given, the task started and no further feedback was given. Different random arrangements of stimulus presentation were used in each task. The assessment lasted about 30 to 45 minutes. Figure E-1 on the Neurology Web site (www.neurology.org) gives an overview of all tasks used.

Visual discrimination. Length and size discrimination tasks. Pairs of lines/circles were presented side-by-side on the screen and subjects had to decide which of the lines/circles, left or right, were longer/larger. The stimulus field dimensions were 140 mm wide and 150 mm tall. Reference stimulus (70 mm) and comparison
stimulus were separated by 70 mm and the position of the longer line/larger circle varied randomly. To eliminate cues based on the absolute position of the stimulus features such as end-lines, the position of each stimulus was randomly jittered from trial to trial with a diameter of 7 mm. The test used an adaptive psychophysical procedure to find the stimulus difference required for a subject to achieve reliable discrimination. Each correct response led to a decrease in the stimulus difference for the next trial (by 1 mm), and each incorrect response led to an increase in the difference for the next trial (by 3 mm). As a result, the test converged on an estimate of the threshold, expressed as difference of size or length (in %), that the subject detected with 75% accuracy.26 Thirteen trials were presented in each task.

Angle discrimination task. The task was a simplified version of Benton's task.27 Our task used 5 (instead of 11) standard lines at 30° orientation, and subjects judged whether their angle matched the angle of the comparison line (instead of two) in each trial. The stimulus field dimensions were 180 mm wide and 150 mm tall. Twenty trials were presented. Subjects were required to match the angle of the single line to one of five lines forming a semicircle.

Object and form perception. Overlapping figures task. This overlapping figures task was described by De Renzi et al.27 In each trial a series of four unique pictures of animals, utensils, clothing, or furniture were presented on the screen. Subjects decided which of the four pictures was included in the simultaneously presented overlapping figure. The stimulus field dimensions were 180 mm wide and 150 mm tall. Thirteen trials were presented.

Form perception task. This task was based on the WAIS-R block design subtest.27 Two boxes with slightly different forms were presented side-by-side and the subject had to decide in which quadrant the two boxes were different. Stimuli were not matched systematically for mean luminance. Each box was 60 mm wide and 60 mm tall, and the two boxes were separated by 20 mm. Thirteen trials were presented.

Space and motion perception. Dot position task. This task is based on the dot position task of Warrington and James.28 In each trial, two squares were presented side-by-side, one containing a dot and the other filled with numbers at random positions. The position of the dot exactly matched the position of a number and the subject was required to name this number. Each square was 70 × 70 mm and the squares were separated by 30 mm. Thirteen trials were presented.

Motion perception task. The stimuli for this task were designed to match those used in Vaina29 as closely as possible. In each trial, two black squares (70 × 70 mm) were presented side-by-side on the screen, separated by 30 mm. Each square contained 12 small (3 mm diameter) white dots in random positions, moving in random directions and bouncing off the sides of the square. Within a square all dots moved with the same velocity, but the dots moved with different velocities in the two squares. Four velocities were presented: 15 mm/second, 20 mm/second, 44.8 mm/second, and 60 mm/second. The computer-generated velocity ratio was the ratio of two different velocities presented in a trial: 1.33 = 20/15; 2.24 = 44.8/20; 3 = 60/20. When the ratio was 3, for example, all dots in one square moved at three times faster than the dots in the other square. The side on which each velocity appeared was selected randomly. There were 12 trials—i.e., four presentations of each velocity ratio—and subjects determined which of the two squares contained the faster moving dots.

Visual counting task. This task is a modified version of the visual counting task used by Fujimori et al.27 The stimulus in each trial consisted of 10 to 12 colored shapes (white, green, blue, triangles and squares). There were between 1 and 5 target stimuli in each trial (average 3.5). In each of the 13 trials the subject needed to count the number of shapes containing one of five possible attributes (e.g., how many squares). The stimulus field dimensions were 80 × 80 mm.

Data analysis. Outcome measures were errors (in percent) in all tasks except the line and size discrimination tasks. Standardized z-values were calculated to compare thresholds in the size/length discrimination tasks and percentage of errors in the angle discrimination task. The mean of the three z-values was the discrimination score. To get a measure of the impairment in the ventral pathway (space-motion perception score). The Statistical Package for Social Sciences (SPSS Version 11) was used for statistical analysis. The distribution of the data was examined for normality (Kolmogorov-Smirnov test). Provided the data did not deviate from normal distribution, the five groups were compared with parametric tests (i.e., one-way analysis of variance (ANOVA)) and subsequently post hoc Bonferroni tests were used for two-group comparisons. Means and SD were calculated to represent central tendency and dispersion. Pearson-rank-correlation was used for a correlational analysis. All reported p values were two-tailed and a p value of less than 0.05 was considered statistically significant.

Results. Demographic characteristics. The five groups were well matched with respect to age, sex, and education and the three dementia groups did not differ in global cognitive impairment (see table 1). Compared to the AD group, the DLB and PDD groups had higher UPDRS motor scores, higher fluctuation scores, shorter dementia duration, and greater impairment in activities of daily living (Bristol ADL). No differences in these scores were found when DLB was compared with PDD. The frequencies of the core clinical features-fluctuation of cognition (PDD 54%; DLB 35%; AD 8%), recurrent visual hallucinations (PDD 75%; DLB 90%; AD 8%), and extrapyramidal features (PDD 100%; DLB 85%; AD 13%)—were similar in the DLB and PDD groups (chi square or Fisher’s exact t-test: p > 0.05; NS) but different from AD (Fisher’s exact t-test for comparison PDD vs AD and DLB vs AD: p < 0.05). Visual acuity did not differ between groups (controls 0.40 ± 0.16; PD 0.40 ± 0.14; PDD 0.34 ± 0.11; DLB 0.37 ± 0.18; AD 0.42 ± 0.17) (ANOVA: NS) and other neuro-ophthalmologic assessments did not reveal impairments interfering with perceptual testing.

Table 2 summarizes CAMCOG data. One-way ANOVA revealed significant group differences in all except the praxis score. PD was similar to controls and different from PDD in all but the CAMCOG abstract thinking score. In abstract thinking PD were similar to PDD and more impaired than controls. Group comparison did not reveal any differences between PDD and DLB. Compared to AD, PDD and DLB patients were significantly less impaired in memory scores, but more impaired in the visual construction scores, and the DLB group scored lower in the perception score compared to AD. Visual construction CAMCOG scores did not correlate with UPDRS-motor scores in PDD group (Pearson correlation: r = −0.190, p > 0.05, NS) but correlated in the DLB group (Pearson correlation: r = −0.612, p = 0.007).

Visual perception. Results for discrimination, object-form, and space-motion perception are summarized in the figure, A through C. Visual discrimination scores (z-values) were different between the groups (ANOVA: p < 0.0001) and DLB and PDD patients were more impaired than AD (post-hoc Bonferroni tests: DLB vs AD: p = 0.007; PDD vs AD: p = 0.051), but were not different from each other (post-hoc Bonferroni tests PDD vs DLB: NS) (see figure 1A). Between-group differences were also found in object-form and space-motion perception (ANOVA: p < 0.0001). The impairment in object-form perception (see figure 1B) of PDD and DLB patients was greater compared with AD patients (post-hoc Bonferroni tests: DLB vs AD: p = 0.003; PDD vs AD: p = 0.001), but not different in DLB and PDD patients (post-hoc Bonferroni tests PDD vs DLB: NS). Space-motion perception (see figure 1C) revealed a similar pattern of impairment in that the DLB...
Table 2 CAMCOG data

<table>
<thead>
<tr>
<th></th>
<th>NC, n = 25</th>
<th>PD, n = 24</th>
<th>PDD, n = 24</th>
<th>DLB, n = 20</th>
<th>AD, n = 23</th>
<th>Between-group comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orientation (max. 10)</td>
<td>9.7 ± 0.6</td>
<td>9.4 ± 1.0</td>
<td>7.0 ± 2.3</td>
<td>5.8 ± 2.5</td>
<td>5.0 ± 2.3</td>
<td>( p &lt; 0.0001^*)</td>
</tr>
<tr>
<td>Attention (max. 7)</td>
<td>6.5 ± 1.1</td>
<td>6.1 ± 1.1</td>
<td>3.7 ± 2.2</td>
<td>3.6 ± 2.5</td>
<td>4.8 ± 2.3</td>
<td>( p &lt; 0.0001^{†})</td>
</tr>
<tr>
<td>Abstract thinking (max. 8)</td>
<td>7.4 ± 1.1</td>
<td>4.8 ± 2.2</td>
<td>4.1 ± 2.2</td>
<td>4.3 ± 2.9</td>
<td>4.9 ± 2.1</td>
<td>( p &lt; 0.0001^{‡})</td>
</tr>
<tr>
<td>Language and calculation (max. 32)</td>
<td>30.3 ± 1.7</td>
<td>28.8 ± 2.1</td>
<td>22.6 ± 4.2</td>
<td>23.1 ± 3.9</td>
<td>24.3 ± 3.6</td>
<td>( p &lt; 0.0001^{†})</td>
</tr>
<tr>
<td>Praxis (max. 6)</td>
<td>5.5 ± 0.8</td>
<td>5.4 ± 0.9</td>
<td>4.8 ± 1.6</td>
<td>4.9 ± 0.9</td>
<td>5.0 ± 0.8</td>
<td>NS</td>
</tr>
<tr>
<td>Visual construction (max. 6)</td>
<td>5.6 ± 0.6</td>
<td>5.0 ± 0.9</td>
<td>2.0 ± 1.7</td>
<td>1.8 ± 1.6</td>
<td>3.4 ± 1.6</td>
<td>( p &lt; 0.0001^{§})</td>
</tr>
<tr>
<td>Perception (max. 9)</td>
<td>7.9 ± 1.3</td>
<td>7.3 ± 1.1</td>
<td>5.2 ± 2.1</td>
<td>4.0 ± 2.2</td>
<td>6.3 ± 1.6</td>
<td>( p &lt; 0.0001^{¶})</td>
</tr>
<tr>
<td>Memory (max. 27)</td>
<td>23.6 ± 1.8</td>
<td>23.0 ± 2.6</td>
<td>16.7 ± 4.8</td>
<td>14.9 ± 4.9</td>
<td>9.8 ± 4.8</td>
<td>( p &lt; 0.0001^{</td>
</tr>
<tr>
<td>CAMCOG total (max. 105)</td>
<td>96.4 ± 5.0</td>
<td>89.4 ± 8.2</td>
<td>67.3 ± 13.7</td>
<td>61.9 ± 15.9</td>
<td>63.6 ± 14.7</td>
<td>( p &lt; 0.0001^{†})</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

Post-hoc Bonferroni tests compared NC vs PD, PDD vs PD, PDD vs DLB, PDD vs AD, and DLB vs AD, and significant group differences are reported:

* PDD vs PD: \( p < 0.0001\); PDD vs AD: \( p = 0.004\).
† PDD vs PD: \( p < 0.0001\).
‡ NC vs PD: \( p = 0.01\).
§ PDD vs PD: \( p < 0.0001\); PDD vs AD: \( p = 0.006\); DLB vs AD: \( p = 0.002\).
¶ PDD vs PD: \( p < 0.0001\); DLB vs AD: \( p < 0.0001\).
|| PDD vs PD: \( p < 0.0001\); PDD vs AD: \( p < 0.001\); DLB vs AD: \( p = 0.003\).

CAMCOG = Cambridge Cognitive Examination Scale; NC = normal controls; PD = non-demented Parkinson disease; PDD = Parkinson disease dementia; DLB = Dementia with Lewy bodies; AD = Alzheimer disease; NS = not significant \( (p > 0.05)\).

There were few patients without recurrent hallucinations (RVH) in the DLB and PDD groups; therefore the PDD and DLB groups were pooled to compare patients with and without hallucinations. Results are shown in table 3. Global cognitive impairment of patients with visual hallucinations (MMSE) was not different from patients without hallucinations and the two groups did not differ with regard to education, frequency of extrapyramidal symptoms, or fluctuation. Patients with RVH were significantly more impaired in visual discrimination, space-motion perception, and object-form perception compared to patients without visual hallucinations.

Within each dementia group, patients on ChE-I did not perform differently compared to patients not taking ChE-I in visual discrimination, object-form perception, or space-motion perception. DLB patients taking levodopa did not differ in any visual score compared to those patients not taking levodopa; such comparison was not feasible in PDD, since all patients were taking levodopa.

Figure. (A through C) Mean and 95% CI of the discrimination score (A), of errors in object-form perception (B), and errors in space-motion perception (C). There was no difference in any of these scores between the DLB and PDD groups, but DLB and PDD tended to perform worse compared to AD patients. PDD and DLB patients made more errors in object-form perception than in space-motion perception. NC = normal controls; PD = Parkinson disease; PDD = PD dementia; DLB = Dementia with Lewy bodies; AD = Alzheimer disease.
Discussion. We assessed visual perception in patients with PDD and DLB compared with AD and two control groups—NC and nondemented PD patients. PDD and DLB had similar visuoperceptual impairments but were more impaired compared to patients with AD. Visual perception of PDD/DLB patients with visual hallucinations was worse than in patients without hallucinations.

Combined retinal and cortical changes need to be addressed to understand the extent of perceptual impairment affecting all test scores. PDD and DLB are both associated with profound cortical cholinergic deficits and cortical Lewy body pathology in areas involved in visual perception and functional imaging studies have reported hypoperfusion in the occipital and parietal lobes, occipital changes consistently exceeding those found in AD. These findings suggest abnormal function of visual cortical areas. Additional retinal changes cannot be excluded, since some visual abnormalities, such as impaired contrast vision, are mediated by disruption of dopaminergic processes in the retina and are unlikely to be discovered during routine neurologic examination or by ordinary high contrast visual acuity testing.

The dissociation between performance in object-form and space-motion perception found in PDD and DLB but not in AD patients may indicate a deficit in the ventral visual pathway in these groups. This finding is consistent with studies reporting profound cholinergic deficits and greater Lewy body density in the temporal lobes. However, it is possible that the differences observed are partly related to non-specific visuoconstructive deficits. Object-form perception tasks may be more sensitive than space-motion perception tasks because they may contain more visual information or require more complicated solution strategies. The better perfusion seen on SPECT imaging in DLB/PDD in the ventral stream compared with the dorsal stream does not necessarily equate with better function, since it may reflect compensatory increase in activity in structurally altered brain areas.

Visual impairments in DLB patients with visual hallucination exceed those without hallucination, especially in the overlapping figure task and in the line orientation task. Barnes and David compared visual imagery, visual perception, and recognition memory in nondemented PD patients with and without hallucinations and found that PD patients with visual hallucinations were more impaired in object perception. In the present study, hallucinating DLB/PDD patients were more impaired in all visual scores compared to patients without hallucinations. The interpretation of this finding needs caution, because as in previous studies, the number of demented patients with hallucinations in this study was small (n = 8).

The neuropsychological (CAMCOG) data confirm previous findings showing that visuoconstructual abilities are more impaired in PDD and DLB compared to AD and that memory function is relatively preserved. In contrast to most previous studies, which reported additional frontal impairment in PDD and DLB, we did not find differences in the attentional scores. The numerical tasks used to assess attention in the CAMCOG battery may be insensitive to detect group differences within demented patients. One study compared the cognitive profile of AD and DLB patients using the CAMCOG battery also did not find attentional differences. Since CAMCOG visual construction scores in DLB as well as the severity of extrapyramidal motor symptoms, it is likely that some of the visual constructional impairment is related to motor impairment in the DLB group. This underpins the need for tasks that are independent of motor function when testing visual perception in patients with combined extrapyramidal and cognitive impairment.

Acknowledgment
The authors thank the patients and controls for their participation, Lorraine Bowman for help with testing, Daniel Collerton for help with data analysis, Simon Kometa for statistical advice, and Jordan Bowen for help with recruiting.

Table 3 Comparison of DLB/PDD patients with and without recurrent visual hallucinations (RVH)

<table>
<thead>
<tr>
<th></th>
<th>DLB/PDD without RVH, n = 8</th>
<th>DLB/PDD with RVH, n = 36</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>78.5 ± 8.5</td>
<td>75.8 ± 6.1</td>
<td>NS</td>
</tr>
<tr>
<td>Education, y</td>
<td>14.0 ± 1.9</td>
<td>13.6 ± 1.7</td>
<td>NS</td>
</tr>
<tr>
<td>MMSE (max. 30)</td>
<td>21.8 ± 4.2</td>
<td>19.8 ± 4.5</td>
<td>NS</td>
</tr>
<tr>
<td>Parkinsonism, %</td>
<td>100</td>
<td>92</td>
<td>NS</td>
</tr>
<tr>
<td>Fluctuation, %</td>
<td>38</td>
<td>47</td>
<td>NS</td>
</tr>
<tr>
<td>Discrimination, z-values</td>
<td>−0.09 ± 0.6</td>
<td>0.65 ± 0.88</td>
<td>p = 0.030</td>
</tr>
<tr>
<td>Errors object-form perception, %</td>
<td>22.1 ± 19.5</td>
<td>39.8 ± 19.6</td>
<td>p = 0.031</td>
</tr>
<tr>
<td>Errors space-motion perception, %</td>
<td>6.5 ± 5.5</td>
<td>17.6 ± 13.4</td>
<td>p = 0.028</td>
</tr>
</tbody>
</table>

Values are mean ± SD.
DLB = Dementia with Lewy bodies; PDD = Parkinson disease dementia; NS = not significant (p > 0.05); MMSE = Mini-Mental State Examination.
References


