

Visual perception in Parkinson disease dementia and dementia with Lewy bodies

U. P. Mosimann, G. Mather, K. A. Wesnes, et al. *Neurology* 2004;63;2091-2096 DOI 10.1212/01.WNL.0000145764.70698.4E

This information is current as of December 13, 2004

The online version of this article, along with updated information and services, is located on the World Wide Web at: http://www.neurology.org/content/63/11/2091.full.html

Neurology [®] is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright . All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.



Visual perception in Parkinson disease dementia and dementia with Lewy bodies

U.P. Mosimann, MD; G. Mather, PhD; K.A. Wesnes, PhD; J.T. O'Brien, DM; D.J. Burn, MD; and I.G. McKeith, MD

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 visuoperceptual 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. NEUROLOGY 2004;63:2091–2096

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.¹ 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 overrepresented in PDD and DLB² and both disorders show similar fluctuation of attention³ and response to cholinergic therapy.^{4,5}

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,^{6,7} whereas other studies found no differences.^{8,9} Similar inconsistencies have been found when perception of PD patients was compared with healthy controls.¹⁰ Since operationalized criteria to define the clinical boundaries between PD and PDD or PDD and DLB require refinement, these inconsistencies may be partly due to diagnostic heterogeneity. When DLB was compared with AD, studies consistently reported greater

Additional material related to this article can be found on the *Neurology* Web site. Go to www.neurology.org and scroll down the Table of Contents for the December 14 issue to find the title link for this article.

visual impairment in DLB¹¹ and a recent study found similar impairments in pentagon copying in DLB and PDD.¹² 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.¹³ 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.14 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 occipitoparietal pathway, required for spatial vision and motion perception.¹⁴ 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

From the Institute for Ageing and Health (Drs. Mosimann, O'Brien, Burn, and McKeith), Newcastle upon Tyne; Psychology Department (Dr. Mather), Life Sciences School, University of Sussex, Brighton; and Cognitive Drug Research Ltd. (Dr. Wesnes), Oxon, UK.

Supported by the UK Medical Research Council, the Swiss National Science Foundation, and the Swiss Parkinson Foundation. Cognitive Drug Research (CDR) provided the test battery and computers required for free.

G.M. received a research grant in excess of \$10,000 from CDR for the programming of the test battery used in the present study. K.A.W. is the Chief executive of CDR. I.G.M. has previously received research support from CDR.

Received May 8, 2004. Accepted in final form August 13, 2004.

Address correspondence and reprint requests to Dr. Urs P. Mosimann, Institute for Ageing and Health, Wolfson Research Centre, Newcastle General Hospital, Newcastle upon Tyne NE4 6BE, UK; e-mail: u.p.mosimann@ncl.ac.uk

Copyright © by AAN Enterprises, Inc. Unauthorized reproduction of this article is prohibited

Table 1	Demographics	and clinical	description	of the	sample
---------	---------------------	--------------	-------------	--------	--------

	NC, n = 25	PD, n = 24	PDD, n = 24	DLB, n = 20	AD, n = 23	Between-group comparison
Age, y	75.5 ± 5.9	76.9 ± 5.4	75.2 ± 6.2	77.6 ± 6.9	77.8 ± 6.8	NS
Education, y	14.2 ± 2.1	12.9 ± 1.8	13.6 ± 1.6	13.7 ± 1.9	13.4 ± 1.0	NS
Female, %	44	21	25	45	48	NS
Estimated dementia onset, y	NA	NA	4.0 ± 1.9	3.2 ± 2.1	5.4 ± 1.7	$p = 0.001^*$
MMSE (max. 30)	29.0 ± 1.3	28.1 ± 1.4	20.8 ± 3.8	19.4 ± 5.2	20.0 ± 5.4	p < 0.0001†
Estimated onset parkinsonism, y	NA	6.3 ± 5.1	8.3 ± 5.0	2.8 ± 1.7	NA	NS
UPDRS motor score (max. 108)	1.6 ± 1.8	29.8 ± 11.1	37.8 ± 12.7	29.2 ± 17.3	6.7 ± 6.5	p < 0.0001‡
NPI (max. 144)	0.0 ± 0.2	3.9 ± 5.1	17.8 ± 14.5	15.5 ± 12.0	11.0 ± 11.8	p < 0.0001†
Fluctuation (max. 21)	0.0 ± 0.0	1.3 ± 2.2	6.0 ± 4.2	4.8 ± 4.0	2.0 ± 2.9	p < 0.0001§
Bristol-ADL (max. 60)	0.0 ± 0.0	3.1 ± 5.7	19.4 ± 10.9	21.7 ± 11.2	13.1 ± 10.1	$p < 0.0001 \P$

Values are mean \pm 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 AD: p = 0.047; DLB vs AD: p = 0.001.

 \dagger PDD vs PD < 0.0001.

 \ddagger PD vs NC < 0.0001; PDD vs AD: p < 0.0001; DLB vs AD: p < 0.0001.

§ PDD vs PD < 0.0001; PDD vs AD: p = 0.001; DLB vs AD: p = 0.027.

 \P PDD vs PD < 0.0001; DLB vs AD: p = 0.026.

NC = normal controls; PD = non-demented Parkinson disease; PDD = Parkinson disease dementia; DLB = Dementia with Lewy bodies; AD = Alzheimer disease; NS = not significant (<math>p > 0.05); MMSE = Mini-Mental State Examination; UPDRS = Unified Parkinson Disease Rating Scale; NPI = Neuropsychiatric Inventory; Fluctuation = One Day Fluctuation Assessment Scale; Bristol-ADL = Bristol Activities of Daily Living scale.

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,^{15,16} 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.² Characteristics of the sample are summarized in table 1. The UK PD Society Brain Bank Clinical Diagnostic Criteria¹⁷ 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-ADRDA)18 for AD, and the DLB Consensus guidelines for DLB,19 following the recommendation that patients with parkinsonian features preceding cognitive impairment for more than 12 months should be diagnosed with PDD.¹⁹ PDD patients had to have PD for more than 12 months before developing dementia.¹⁹ 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).²⁰ 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 (PDD: 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 $(CAMCOG)^{21}$ and for the purpose of this study, tests assessing apraxia were analyzed separately from tests measuring visuoconstructional ability, i.e., praxis and construction scores. CAMCOG visual construction in-

cluded spiral, pentagon, three-dimensional house and clock copying. 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).²² A cutoff score of more than 6 in the one-day fluctuation assessment scale defined fluctuation.23 The Neuropsychiatric Inventory (NPI)²⁴ 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)²⁵ 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

2092 NEUROLOGY 63 December (1 of 2) 2004

Copyright © by AAN Enterprises, Inc. Unauthorized reproduction of this article is prohibited

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.

<u>Angle discrimination task.</u> The task was a simplified version of Benton's task.²⁷ Our task used 5 (instead of 11) standard lines at 30 deg (instead of 18 deg) intervals, with subjects judging one 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.²⁸ In each trial a series of four unique pictures of animals, utensils, clothing, or fruits were presented on the screen and 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.²⁹ 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.³⁰ In each trial, two squares were presented side-by-side, one containing a dot and the other five different numbers at random position. 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 Vaina³¹ as closely as possible. In each trial, two black squares $(70 \times 70 \text{ mm})$ 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 velocity ratios were 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.

<u>Visual counting task</u>. This task is a modified version of the visual counting task used by Fujimori et al.³² 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 visual pathway, mean errors of the overlapping figure and form perception tasks were calculated (object-form perception score). The mean errors in motion, dot position, and visual counting tasks were a measure of the impairment in the dorsal visual 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 correlative analysis. All reported p values were two-tailed and a pvalue 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 $0.37 \pm$ $0.18; AD\, 0.42 \pm 0.17) (ANOVA: NS)$ 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 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, objectform, and space-motion perception are summarized in the figure, A through C. Visual discrimination scores (zvalues) 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

December (1 of 2) 2004 NEUROLOGY 63 2093

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

Values are mean \pm 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.

 $\ddagger NC vs PD: p = 0.01.$

§ 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.

 \parallel 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 (<math>p > 0.05).

group did not differ from PDD but tended to be more impaired compared to AD (post-hoc Bonferroni tests: DLB vs AD: p = 0.074). PD was similar to controls but less impaired than PDD in all scores (post-hoc Bonferroni tests for all: p < 0.0001). The PDD group made more errors in object-form perception compared to space-motion perception (paired sample *t*-test: p < 0.0001), a difference also found in the DLB group (paired sample *t*-test: p < 0.0001) but not in the AD group (paired sample *t*-tests: NS). The raw data of all tasks are summarized in table E-1 on the *Neurology* Web site.

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, spacemotion 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 spacemotion 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.

2094 NEUROLOGY 63 **December (1 of 2) 2004**

Copyright © by AAN Enterprises, Inc. Unauthorized reproduction of this article is prohibited

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

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

Values are mean \pm SD.

DLB = Dementia with Lewy bodies; PDD = Parkinson disease dementia; NS = not significant (<math>p > 0.05); MMSE = Mini-Mental State Examination.

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^{33,34} and functional imaging studies have reported hypoperfusion in the occipital and parietal lobes, occipital changes consistently exceeding those found in AD.^{15,16} 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^{35,36} and are unlikely to be discovered during routine neurologic examination or by ordinary high contrast visual acuity testing.

The dissociation between performance in objectform 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 finds support in studies reporting profound cholinergic deficits and greater Lewy body density in the temporal lobes.^{34,37,38} However, it is possible that the differences observed are partly related to nonspecific visuocognitive 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.¹⁰ The better perfusion seen on SPECT imaging in DLB/PDD in the ventral stream compared with the dorsal stream¹⁶ 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 task³⁹ and in the line orientation task.⁴⁰ Barnes and David⁴¹ 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,^{39,40} the number of demented patients without hallucinations in this study was small (n = 8).

The neuropsychological (CAMCOG) data confirm previous findings showing that visuoconstructional abilities are more impaired in PDD and DLB compared to AD and that memory function is relatively preserved.^{11,42,43} 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 study⁴⁴ which 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 also correlated with 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.

References

- Aarsland D, Andersen K, Larsen JP, Lolk A, Kragh-Sorensen P. Prevalence and characteristics of dementia in Parkinson disease: an 8-year prospective study. Arch Neurol 2003; 60:387–392.
- Burn DJ, Rowan EN, Minett T, et al. Extrapyramidal features in Parkinson's disease with and without dementia and dementia with Lewy bodies: a cross-sectional comparative study. Mov Disord 2003;18:884-889.
- Ballard CG, Aarsland D, McKeith I, et al. Fluctuations in attention: PD dementia vs DLB with parkinsonism. Neurology 2002;59:1714–1720.
- Aarsland D, Laake K, Larsen JP, Janvin C. Donepezil for cognitive impairment in Parkinson's disease: a randomised controlled study. J Neurol Neurosurg Psychiatry 2002;72:708-712.
- McKeith I, Del Ser T, Spano P, et al. Efficacy of rivastigmine in dementia with Lewy bodies: a randomised, double-blind, placebo-controlled international study. Lancet 2000;356:2031–2036.
- Starkstein SE, Sabe L, Petracca G, et al. Neuropsychological and psychiatric differences between Alzheimer's disease and Parkinson's disease with dementia. J Neurol Neurosurg Psychiatry 1996;61:381-387.
- Mohr E, Litvan I, Williams J, Fedio P, Chase TN. Selective deficits in Alzheimer and parkinsonian dementia: visuospatial function. Can J Neurol Sci 1990;17:292–297.
- Gnanalingham KK, Byrne EJ, Thornton A, Sambrook MA, Bannister P. Motor and cognitive function in Lewy body dementia: comparison with Alzheimer's and Parkinson's diseases. J Neurol Neurosurg Psychiatry 1997;62:243–252.
- 9. Pillon B, Dubois B, Ploska A, Agid Y. Severity and specificity of cognitive impairment in Alzheimer's, Huntington's, and Parkinson's diseases and progressive supranuclear palsy. Neurology 1991;41:634-643.
- Crucian GP, Okun MS. Visual-spatial ability in Parkinson's disease. Front Biosci 2003;8:s992–997.
- Collerton D, Burn D, McKeith I, O'Brien J. Systematic review and meta-analysis show that dementia with Lewy bodies is a visualperceptual and attentional-executive dementia. Dement Geriatr Cogn Disord 2003;16:229-237.
- Cormack F, Aarsland D, Ballard C, Tovee MJ. Pentagon drawing and neuropsychological performance in dementia with Lewy bodies, Alzheimer's disease, Parkinson's disease and Parkinson's disease with dementia. Int J Geriatr Psychiatry 2004;19:371–377.
- Wurtz RH, Kandel ER. Central visual pathways. In: Kandel ER, Schwartz JH, Jessell TM, eds. Principles of neural science. Fourth ed. New York: McGraw-Hill, 2000;523–547.
- Ungerleider LG, Haxby JV. 'What' and 'where' in the human brain. Curr Opin Neurobiol 1994;4:157–165.
- Donnemiller E, Heilmann J, Wenning GK, et al. Brain perfusion scintigraphy with 99mTc-HMPAO or 99mTc-ECD and 1231-beta-CIT single-photon emission tomography in dementia of the Alzheimer-type and diffuse Lewy body disease. Eur J Nucl Med 1997;24:320-325.
 Firbank MJ, Colloby SJ, Burn DJ, McKeith IG, O'Brien JT. Regional
- Firbank MJ, Colloby SJ, Burn DJ, McKeith IG, O'Brien JT. Regional cerebral blood flow in Parkinson's disease with and without dementia. Neuroimage 2003;20:1309–1319.
- Gibb WR, Lees AJ. The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease. J Neurol Neurosurg Psychiatry 1988; 51:745-752.
- McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 1984; 34:939-944.
- McKeith IG, Galasko D, Kosaka K, et al. Consensus guidelines for the clinical and pathologic diagnosis of dementia with Lewy bodies (DLB): report of the consortium on DLB international workshop. Neurology 1996;47:1113–1124.
- Folstein MF, Folstein SE, McHugh PR. "Mini-mental state." A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-198.

- Roth M, Tym E, Mountjoy CQ, et al. CAMDEX. A standardised instrument for the diagnosis of mental disorder in the elderly with special reference to the early detection of dementia. Br J Psychiatry 1986;149:698–709.
- Fahn S, Elton R, UPDRS program members. Unified Parkinson's disease rating scale. Florham Park, NJ: Macmillan Healthcare Information, 1987.
- Walker MP, Ayre GA, Cummings JL, et al. The Clinician Assessment of Fluctuation and the One Day Fluctuation Assessment Scale. Two methods to assess fluctuating confusion in dementia. Br J Psychiatry 2000; 177:252–256.
- Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. Neurology 1994;44:2308-2314.
- Bucks RS, Ashworth DL, Wilcock GK, Siegfried K. Assessment of activities of daily living in dementia: development of the Bristol Activities of Daily Living Scale. Age Ageing 1996;25:113-120.
- Kaernbach C. Simple adaptive testing with the weighted up-down method. Percept Psychophys 1991;49:227-229.
- Benton AL, Varney NR, Hamsher KD. Visuospatial judgment. A clinical test. Arch Neurol 1978;35:364-367.
- De Renzi E, Scotti G, Spinnler H. Perceptual and associative disorders of visual recognition. Relationship to the side of the cerebral lesion. Neurology 1969;19:634-642.
- Caplan B, Caffery D. Fractionating block design: development of a test of visuospatial analysis. Neuropsychology 1992;6:385–394.
- Warrington EK, James M. Visual apperceptive agnosia: a clinicoanatomical study of three cases. Cortex 1988;24:13–32.
- Vaina LM. Selective impairment of visual motion interpretation following lesions of the right occipito-parietal area in humans. Biol Cybern 1989;61:347-359.
- Fujimori M, Imamura T, Yamashita H, Hirono N, Mori E. The disturbances of object vision and spatial vision in Alzheimer's disease. Dement Geriatr Cogn Disord 1997;8:228-231.
- Bohnen NI, Kaufer DI, Ivanco LS, et al. Cortical cholinergic function is more severely affected in parkinsonian dementia than in Alzheimer disease: an in vivo positron emission tomographic study. Arch Neurol 2003;60:1745-1748.
- Harding AJ, Broe GA, Halliday GM. Visual hallucinations in Lewy body disease relate to Lewy bodies in the temporal lobe. Brain 2002; 125(Pt 2):391-403.
- Nguyen-Legros J. Functional neuroarchitecture of the retina: hypothesis on the dysfunction of retinal dopaminergic circuitry in Parkinson's disease. Surg Radiol Anat 1988;10:137–144.
- Bodis-Wollner I, Tagliati M. The visual system in Parkinson's disease. Adv Neurol 1993;60:390-394.
- Perry EK, Irving D, Kerwin JM, et al. Cholinergic transmitter and neurotrophic activities in Lewy body dementia: similarity to Parkinson's and distinction from Alzheimer disease. Alzheimer Dis Assoc Disord 1993;7:69–79.
- Tiraboschi P, Hansen LA, Alford M, et al. Cholinergic dysfunction in diseases with Lewy bodies. Neurology 2000;54:407–411.
- Mori E, Shimomura T, Fujimori M, et al. Visuoperceptual impairment in dementia with Lewy bodies. Arch Neurol 2000;57:489-493.
- Simard M, van Reekum R, Myran D. Visuospatial impairment in dementia with Lewy bodies and Alzheimer's disease: a process analysis approach. Int J Geriatr Psychiatry 2003;18:387–391.
- Barnes J, David AS. Visual hallucinations in Parkinson's disease: a review and phenomenological survey. J Neurol Neurosurg Psychiatry 2001;70:727-733.
- Emre M. Dementia associated with Parkinson's disease. Lancet Neurol 2003;2:229–237.
- McKeith I, Mintzer J, Aarsland D, et al. Dementia with Lewy bodies. Lancet Neurol 2004;3:19–28.
- Walker Z, Allen RL, Shergill S, Katona CL. Neuropsychological performance in Lewy body dementia and Alzheimer's disease. Br J Psychiatry 1997;170:156-158.

Copyright © by AAN Enterprises, Inc. Unauthorized reproduction of this article is prohibited.

Visual perception in Parkinson disease dementia and dementia with Lewy bodies U. P. Mosimann, G. Mather, K. A. Wesnes, et al. *Neurology* 2004;63;2091-2096 DOI 10.1212/01.WNL.0000145764.70698.4E

Updated Information & Services	including high resolution figures, can be found at: http://www.neurology.org/content/63/11/2091.full.html
Supplementary Material	Supplementary material can be found at: http://www.neurology.org/neurology/suppl/2004/11/16/63.11.209 1.DC1.html
References	This article cites 41 articles, 17 of which you can access for free at: http://www.neurology.org/content/63/11/2091.full.html##ref-list-1
Citations	This article has been cited by 28 HighWire-hosted articles: http://www.neurology.org/content/63/11/2091.full.html##otherart icles
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Dementia with Lewy bodies http://www.neurology.org//cgi/collection/dementia_with_lewy_b odies Parkinson's disease with dementia http://www.neurology.org//cgi/collection/parkinsons_disease_wit h_dementia Parkinson's disease/Parkinsonism http://www.neurology.org//cgi/collection/parkinsons_disease_par kinsonism Visual processing http://www.neurology.org//cgi/collection/visual_processing
Permissions & Licensing	Information about reproducing this article in parts (figures,tables) or in its entirety can be found online at: http://www.neurology.org/misc/about.xhtml#permissions
Reprints	Information about ordering reprints can be found online: http://www.neurology.org/misc/addir.xhtml#reprintsus

This information is current as of December 13, 2004

