Visuoperceptual Impairment in Dementia With Lewy Bodies

Etsuro Mori, MD, PhD; Tatsuo Shimomura, MD; Misato Fujimori, PhD; Nobutsugu Hirono, MD, PhD; Toru Imamura, MD, PhD; Mamoru Hashimoto, MD, PhD; Satoshi Tanimukai, MD, PhD; Hiroaki Kazui, MD, PhD; Tokiji Hanihara, MD, PhD

Background: In dementia with Lewy bodies (DLB), vision-related cognitive and behavioral symptoms are common, and involvement of the occipital visual cortices has been demonstrated in functional neuroimaging studies.

Objectives: To delineate visuoperceptual disturbance in patients with DLB in comparison with that in patients with Alzheimer disease and to explore the relationship between visuoperceptual disturbance and the vision-related cognitive and behavioral symptoms.

Design: Case-control study.

Setting: Research-oriented hospital.

Patients: Twenty-four patients with probable DLB (based on criteria of the Consortium on DLB International Workshop) and 48 patients with probable Alzheimer disease (based on criteria of the National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer’s Disease and Related Disorders Association) who were matched to those with DLB 2:1 by age, sex, education, and Mini-Mental State Examination score.

Main Outcome Measures: Four test items to examine visuoperceptual functions, including the object size discrimination, form discrimination, overlapping figure identification, and visual counting tasks.

Results: Compared with patients with probable Alzheimer disease, patients with probable DLB scored significantly lower on all the visuoperceptive tasks (P < .04 to P < .001). In the DLB group, patients with visual hallucinations (n = 18) scored significantly lower on the overlapping figure identification (P = .01) than those without them (n = 6), and patients with television misidentifications (n = 5) scored significantly lower on the size discrimination (P < .001), form discrimination (P = .01), and visual counting (P = .007) than those without them (n = 19).

Conclusions: Visual perception is defective in probable DLB. The defective visual perception plays a role in development of visual hallucinations, delusional misidentifications, visual agnosias, and visuoconstructive disability characteristic of DLB.

Arch Neurol. 2000;57:489-493

Dementia with Lewy bodies (DLB) is increasingly being recognized as a common cause of dementia in elderly people and is the second most common type after Alzheimer disease (AD). In 1996, the Consortium on DLB International Workshop proposed criteria for clinical and pathological diagnosis. In addition to progressive dementia, other criteria specific to the clinical features of DLB are parkinsonism, fluctuating cognitive functions, and complex visual hallucinations.

Since publication of the criteria, clinical studies have been conducted to delineate neuropsychiatric, neuropsychological, and neuroimaging features that distinguish DLB from AD. In addition to visual hallucinations, vision-related behavioral symptoms including visual agnosia and delusional misidentification are common in DLB. Compared with AD, visuospatial and visuoconstructive disabilities are disproportionately severe. Recently, radio-nuclear studies have demonstrated that glucose metabolism and blood flow are significantly decreased in the occipital lobes, including the primary visual cortex and visual association cortex, in DLB as compared with AD. The involvement of the visual cortex may cause dysfunction of elementary visual sensation, which may be involved in development of visual cognitive deficits and vision-related behavioral symptoms. However, only 1 limited study has examined visuoperceptual function in patients with DLB. In the present study, we addressed problems in visual perception in patients with probable DLB, and compared them with patients with probable AD.

The results of visuoperceptual assessment are summarized in Table 1. The performance was invariably lower in the patients with DLB than in those with AD.
PATIENTS AND METHODS

Patients with probable DLB or AD were recruited from those who were given a short-term admission to the infirmary of the Hyogo Institute for Aging Brain and Cognitive Disorders, Himeji, Japan, a research-oriented hospital for dementia, for investigation from April 1, 1997, to March 31, 1998. All patients were examined comprehensively by both neurologists (E.M., T.S., N.H., and T.I.) and psychiatrists (M.H., S.T., H.K., and T.H.) and underwent standard neuropsychological examinations, routine laboratory tests, electroencephalography, cranial magnetic resonance imaging, cerebral magnetic resonance angiography, and radionuclear neuroimaging studies. Uncorrected and corrected distant visual acuity testing and Goldmann perimetry were performed by an ophthalmometrician (T.S., T.I., M.H., S.T., H.K., or T.H.). Behavioral and cognitive changes were assessed with a structured interview for a caregiver, the Neuropsychiatric Inventory, \textsuperscript{13} and with monitoring during the patient’s hospital stay by staff physicians. Staff physicians also closely monitored significant fluctuation of cognition, recurrent visual hallucinations, and spontaneous parkinsonism, and any 2 of them are necessary for a diagnosis of probable DLB. We excluded patients with a clinical history of parkinsonism longer than 12 months before dementia developed (“Parkinson disease with dementia” as designated by the consortium criteria). A sensitivity of 75% and a specificity of 79% have been documented in a preliminary validation study of the DLB International Workshop criteria. \textsuperscript{16} In the present study, patients with AD who fulfilled any 1 of the 3 DLB criteria were excluded.

The DLB group consisted of 24 patients. The mean (± SD) age was 74.0 ± 5.8 years for the 11 women and 13 men. The mean educational attainment was 9.1 ± 2.3 years. The mean duration of illness (the interval from the moment of the nearest caregiver’s awareness of the patient’s cognitive abnormality to the assessment) was 24.7 ± 20.4 months, and the mean score (the best performance in repeated measures) on the MMSE was 19.1 ± 4.1. Of the 24 patients, 6 had fluctuating cognition and parkinsonism, 4 had fluctuating cognition and visual hallucinations, 2 had visual hallucinations and parkinsonism, and 12 had all 3 features.

The AD group consisted of 48 patients (2 sets of 24 patients) with probable AD who were matched 2:1 to the patients with DLB on the basis of sex, age, and severity of cognitive disturbances represented by their MMSE score. The mean age was 74.0 ± 7.2 years for the 22 women and 26 men. The mean educational attainment was 8.8 ± 2.0 years. The mean duration of dementing illness was 31.9 ± 21.5 months, and the mean MMSE score was 19.1 ± 3.5.

Corrected visual acuity was comparable between the DLB and AD groups (range, 20/70 to 20/20; median, 20/30 in the worse eye; \( \chi^2 = 1.37; P = .50 \), Friedman 2-way analysis of variance [ANOVA]). There was no significant difference in the scores for the Alzheimer’s Disease Assessment Scale \textsuperscript{17} between the DLB and AD groups (\( \chi^2 = 3.10; P = .21 \), Friedman 2-way ANOVA); the mean total scores were 28.2 ± 10.8 in the patients with DLB and 23.9 ± 8.9 in the patients with AD. Global severity of dementia as demonstrated by the Clinical Dementia Rating \textsuperscript{18} was comparable between the DLB and AD groups (\( \chi^2 = 2.94; P = .23 \), Friedman 2-way ANOVA); Clinical Dementia Rating scales of 0.5, 1, 2, and 3 were obtained by 2, 8, 11, and 3 patients, respectively, in the probable DLB group, and by 6, 23, 16, and 3 patients, respectively, in the probable AD group.

ASSESSMENT OF VISUAL PERCEPTION

We used 4 test items to examine various aspects of the patients’ visual perception, a subset of the object and spatial vision test battery. \textsuperscript{17} The discrimination of object size task was used to examine elementary visual perception, the form
discrimination task was used to examine more complex visuo perceptual function that requires analysis of 2-dimen sional visual stimuli, the overlapping figure identification task was used to examine the abilities to actively extract concrete shapes and to recognize objects, and the visual counting task was used to examine the ability to explore and identify the spatial relation of visual stimuli to count targets without du plication or omission. Specific brain regions have been as sumed to be involved in the performance of these tests: the occipital visual association cortex for size discrimination, the occipitotemporal visual association cortex for form discrimination, and the occipitoparietal cortex for visual counting.  

The assessments were performed while subjects were free of neuroleptic and neurotropic agents and not in a state of confusion or with active hallucinations. Subjects were al lowed to wear their own glasses when requested. Test in structions were given repeatedly as needed to ensure the pa tients’ comprehension. Furthermore, no time limits were given for the tasks to exclude the influence of psychomotor slowing resulting from parkinsonism on the performance in the visuo cognitive tests. In a previous study, cognitively healthy subjects (8 women and 2 men; age, 72.6 ± 5.1 years; education, 8.9 ± 0.8 years) achieved almost full scores in all these tasks.  

**DISCRIMINATION OF SIZE**  
The task stimuli consisted of 6 sets of lines and 6 sets of circles printed on separate sheets of paper (12 sheets). Three of the sets of lines consisted of parallel (horizontal) lines with lengths of 5.5 and 14.5 cm; 5.5, 14.5, and 21.5 cm; and 6, 10, 16, and 21.5 cm. The other 3 sets consisted of nonparallel lines with lengths of 5.5 and 14.5 cm; 5.5, 14.5, and 21.5 cm; and 6, 10, 15, and 20.5 cm. Three of the sets of circles were arranged in rows, and the other 3 sets were arranged randomly. The diameters of the circles in both sets were 4 and 7 cm; 3.5, 6, and 8 cm; and 3.5, 6, 7, and 9 cm. For each of the 12 sheets of paper, the subject was asked to point out the longer (in the sets of 2 lines), the longest and shortest (in the sets of 3 or 4 lines), the larger (in the sets of 2 figures), or the largest and the smallest (in the sets of 3 or 4 figures). One point was given for each correct an swer, and the total score ranged from 0 to 20. 

**DISCRIMINATION OF FORM**  
The task stimuli consisted of 20 sheets, each with 4 line drawn geometric figures. Three of the figures were the same and the fourth was distorted or rotated. The subjects were instructed to point to the odd figure. The maximum score was 20. 

**OVERLAPPING FIGURE IDENTIFICATION**  
The subjects were shown 3 sets of overlapping line drawings individually. The first set contained 3 simple geometric figures, the second contained 4 man-made objects, and the third contained 5 fruits (a total of 12 objects). The subjects were asked to identify each figure; in the first and second sets, to either name, describe, or trace the object by finger; and in the third set, to match each fruit with one of 8 nonoverlapping drawings printed on another sheet. The maximum score was 12. 

**VISUAL COUNTING**  
The task stimuli consisted of 14 sheets, each with 5 to 12 figures (circles, triangles, or both) of 1 or 2 colors (red or blue). Patients were shown the sheets one at a time, and were asked to count the number of figures with a specified color (red or blue) or form (circle or triangle), or to count the total number of objects. The score was the number of attributes identified correctly. The maximum score was 38. 

**VISUAL HALLUCINATIONS, MISIDENTIFICATIONS, AND CONSTRUCTIONAL ABILITY IN DLB**  
In the DLB group, visual hallucinations and delusional misidentifications were assessed during an interview with the caregiver by means of the Neuropsychiatric Inventory and were monitored during the patient’s hospital stay by staff physicians. The Capgras type, phantom boarder, house misidentifications (the patient’s belief that the house is not his or her own house), and television misidentifications (the belief that television figures are actually present in the home) were included in delusional misidentifications. 

**STATISTICAL ANALYSIS**  
Statistical analyses were carried out with the Statistica version 4.1 software package (StatSoft Inc, Tulsa, Okla) with a significance level set at P<.05. The nonparametric Friedman 2-way ANOVA was used for the matched group comparison (1 set of AD and 2 sets of DLB). The 2-tailed Mann Whitney test was used for analyses of group difference, and the Kendall τ test was used for correlational analyses.

The differences in visuo perceptual dysfunction between the 2 diseases probably represent the different distributions of vulnerable regions. The visuo perceptual dysfunction in DLB can be attributed to accentuated damage in the occipital lobes. Albin et al demonstrated that regional glucose metabolism was decreased in the occipital association cortex and primary visual area in 6 patients with autopsy-proved DLB. In recent studies by Imamura and Ishii and their colleagues, using fludeoxyglucose F 18 and positron emission tomography, the glucose metabolic rate in the occipital cortices was found to be significantly lower in patients with probable DLB than in controls with probable AD matched for age, sex, disease...
Defective visual perception, resulting in illusions in- 
formation images are spatially and dimensionally distinct from 
sion misidentifications are likely to link to the patients'
dimensional misidentification syndrome. In particular, televi-
sional misidentifications are likely to link to the patients'
difficulty in visually recognizing size and form, as television 
images are spatially and dimensionally distinct from 
real-world images. Defective visual perception and visual 
illusions reportedly occur after lesions of the occipital, oc-
cipitoparietal, or occipitotemporal regions.21 Complex or 
formed visual hallucinations are indicative of lesions in 
the visual association areas or their connections with the 
temporal lobe. In a recent study by Imamura et al23 using 
positron emission tomography, where regional cerebral 
glucose metabolism was compared among patients who 
had DLB with visual hallucinations, DLB without visual 
hallucinations, and AD without visual hallucinations, they 
found that visual hallucinations were associated with a rela-
tively preserved metabolism in the right temporoparietal 
association cortices and severe hypometabolism in the pri-
mary and secondary visual cortices in DLB. In addition to 
defective visual processing, brainstem lesions that appear 
to affect ascending cholinergic and serotonergic pathways 
may underlie visual hallucinations.

Retrospective studies of patients with DLB have demon-
strated that these patients have greater impairment on 
visuocognitive and visuospatial tests than patients with 
AD.24-26 In a previous case-control study by Shimomura et 
al,7 where patients with DLB were compared with patients 
with probable AD who had comparable global dementia se-
verity, disproportionately severe visuocognitive and vi-
suospatial dysfunction in DLB was found. Walker et al27 
demonstrated that patients with DLB performed worse than those 
with AD who were similar in overall degree of cognitive im-
pairment on the praxis subtest of the Cambridge Cognitive 
Examination, including visuocognitive tasks. Furthermore, 
Gnanalingham et al28 pointed out the usefulness of the 
lock clock test that assesses executive and visuospatial 
functioning in differentiating DLB from AD: patients with 
AD do well on the “copy” part of the test despite doing poorly 
on the “draw” part, while patients with DLB do equally poorly 
on both parts of the test. However, the defective visuo-
ceptual ability should be taken into consideration when 
visuocognitive and visuospatial deficits in DLB are in-
terpreted. Since a relationship between visuo perceptual 
performance and constructive performance was demonstrated 
in this study, visuoperceptual deficits underlie the severe 
visuocognitive deficits in DLB or explain a part of them.

The mechanism of occipital involvement and visuo-
ceptual deficits in DLB is highly speculative. In a re-
cent postmortem study, occipital and inferotemporal 
cortical degeneration was found in a patient with DLB and 
unexplainable familiarity.29 Defective visual input caused by 
visual system lesions may result in hallucinations from de-
fective visual processing or an abnormal cortical release 
phenomenon.30 The finding in a study by McShane et al12 
that poor eyesight is correlated with the severity of the vi-
ual hallucinations in DLB supports this hypothesis. The 
association between visual hallucinations and the score 
on the overlapping figure identification task demonstrated 
in the present study is interesting, because interpreting 
blurred images with top-down visual processing would 
be involved both in overlapping figure identification and 
in generation of visual hallucinations. Similarly, defective 
visual perception would contribute partially to the delu-
sional misidentification syndrome. In particular, tele-
vision misidentifications are likely to link to the patients' 
difficulty in visually recognizing size and form, as television 
images are spatially and dimensionally distinct from 
real-world images. Defective visual perception and visual 
illusions reportedly occur after lesions of the occipital, oc-
cipitoparietal, or occipitotemporal regions.21 Complex or 
formed visual hallucinations are indicative of lesions in 
the visual association areas or their connections with the 
temporal lobe. In a recent study by Imamura et al23 using 
positron emission tomography, where regional cerebral 
glucose metabolism was compared among patients who 
had DLB with visual hallucinations, DLB without visual 
hallucinations, and AD without visual hallucinations, they 
found that visual hallucinations were associated with a rela-
tively preserved metabolism in the right temporoparietal 
association cortices and severe hypometabolism in the pri-
mary and secondary visual cortices in DLB. In addition to 
defective visual processing, brainstem lesions that appear 
to affect ascending cholinergic and serotonergic pathways 
may underlie visual hallucinations.

Retrospective studies of patients with DLB have demon-
strated that these patients have greater impairment on 
visuocognitive and visuospatial tests than patients with 
AD.24-26 In a previous case-control study by Shimomura et 
al,7 where patients with DLB were compared with patients 
with probable AD who had comparable global dementia se-
verity, disproportionately severe visuocognitive and vi-
suospatial dysfunction in DLB was found. Walker et al27 
demonstrated that patients with DLB performed worse than those 
with AD who were similar in overall degree of cognitive im-
pairment on the praxis subtest of the Cambridge Cognitive 
Examination, including visuocognitive tasks. Furthermore, 
Gnanalingham et al28 pointed out the usefulness of the 
lock clock test that assesses executive and visuospatial 
functioning in differentiating DLB from AD: patients with 
AD do well on the “copy” part of the test despite doing poorly 
on the “draw” part, while patients with DLB do equally poorly 
on both parts of the test. However, the defective visuo-
ceptual ability should be taken into consideration when 
visuocognitive and visuospatial deficits in DLB are in-
terpreted. Since a relationship between visuo perceptual 
performance and constructive performance was demonstrated 
in this study, visuoperceptual deficits underlie the severe 
visuocognitive deficits in DLB or explain a part of them.

The mechanism of occipital involvement and visuo-
ceptual deficits in DLB is highly speculative. In a re-
cent postmortem study, occipital and inferotemporal 
cortical degeneration was found in a patient with DLB and 
unexplainable familiarity.29 Defective visual input caused by 
visual system lesions may result in hallucinations from de-
fective visual processing or an abnormal cortical release 
phenomenon.30 The finding in a study by McShane et al12 
that poor eyesight is correlated with the severity of the vi-
ual hallucinations in DLB supports this hypothesis. The 
association between visual hallucinations and the score 
on the overlapping figure identification task demonstrated 
in the present study is interesting, because interpreting 
blurred images with top-down visual processing would 
be involved both in overlapping figure identification and 
in generation of visual hallucinations. Similarly, defective 
visual perception would contribute partially to the delu-
sional misidentification syndrome. In particular, tele-
vision misidentifications are likely to link to the patients' 
difficulty in visually recognizing size and form, as television 
images are spatially and dimensionally distinct from 
real-world images. Defective visual perception and visual 
illusions reportedly occur after lesions of the occipital, oc-
cipitoparietal, or occipitotemporal regions.21 Complex or 
formed visual hallucinations are indicative of lesions in 
the visual association areas or their connections with the 
temporal lobe. In a recent study by Imamura et al23 using 
positron emission tomography, where regional cerebral 
glucose metabolism was compared among patients who 
had DLB with visual hallucinations, DLB without visual 
hallucinations, and AD without visual hallucinations, they 
found that visual hallucinations were associated with a rela-
tively preserved metabolism in the right temporoparietal 
association cortices and severe hypometabolism in the pri-
mary and secondary visual cortices in DLB. In addition to 
defective visual processing, brainstem lesions that appear 
to affect ascending cholinergic and serotonergic pathways 
may underlie visual hallucinations.

Retrospective studies of patients with DLB have demon-
strated that these patients have greater impairment on 
visuocognitive and visuospatial tests than patients with 
AD.24-26 In a previous case-control study by Shimomura et 
al,7 where patients with DLB were compared with patients 
with probable AD who had comparable global dementia se-
verity, disproportionately severe visuocognitive and vi-
suospatial dysfunction in DLB was found. Walker et al27 
demonstrated that patients with DLB performed worse than those 
with AD who were similar in overall degree of cognitive im-
pairment on the praxis subtest of the Cambridge Cognitive 
Examination, including visuocognitive tasks. Furthermore, 
Gnanalingham et al28 pointed out the usefulness of the 
lock clock test that assesses executive and visuospatial 
functioning in differentiating DLB from AD: patients with 
AD do well on the “copy” part of the test despite doing poorly 
on the “draw” part, while patients with DLB do equally poorly 
on both parts of the test. However, the defective visuo-
ceptual ability should be taken into consideration when 
visuocognitive and visuospatial deficits in DLB are in-
terpreted. Since a relationship between visuo perceptual 
performance and constructive performance was demonstrated 
in this study, visuoperceptual deficits underlie the severe 
visuocognitive deficits in DLB or explain a part of them.

The mechanism of occipital involvement and visuo-
ceptual deficits in DLB is highly speculative. In a re-
cent postmortem study, occipital and inferotemporal 
cortical degeneration was found in a patient with DLB and 

a left homonymous hemianopia.27 The degeneration was characterized by a disproportionately large number of neuroribillary tangles and likely was the cause of the patient’s visual field defect. However, in general, the pathologic features of DLB (including the Lewy bodies) hardly affect the occipital lobes.28,29 Psychomotor slowing accompanied by parkinsonism is unlikely to explain the low performance on the visuoconstructive tasks, since the tests were untimed measures. Because spontaneous motor features of parkinsonism in DLB are generally mild,1 poor performance on the tasks would not be attributable to other motor components of parkinsonism. Nonmotor components of parkinsonism would be more involved. Occipital glucose hypometabolism has also been reported in patients with Parkinson disease both with and without dementia.30,31 Bodis-Wollner32 speculated that dysfunction of the occipital visual cortices was attributed to dopaminergic systems in the visual pathway, and abnormal visual input from the retina, caused by a retinal dopamine deficiency, might explain the dysfunction. Degeneration of dopaminergic cells in the retina of patients with Parkinson disease was indicated, and dopaminergic treatment improved abnormal visual contrast sensitivity.33,34 On the other hand, Bohnen et al35 found that patients with Parkinson disease showed glucose metabolic reduction in the occipital lobe, which correlated with motor dysfunction, and suggested a pathophysiological association between nigrostriatal dysfunction and occipital glucose hypometabolism. In either case, a common pathologic process in the dopaminergic system among Lewy body diseases would be conceivable. On the other hand, involvement of the occipital cholinergic system also has been assessed. The activity of a cholinergic enzyme, choline acetyltransferase, is reportedly lower in the temporoparietal and occipital cortices in Parkinson disease both with and without dementia.30,31 Kuhl et al.36 using single photon emission computed tomography and iodine 123–labeled iodobenzovesamicol, an in vivo marker of the vesicular acetylcholine transporter, found that the presynaptic cholinergic terminal density was reduced in the parietal and occipital cortices in Parkinson disease without dementia.

In conclusion, both elementary and higher-order visuoconstructive functions are affected in patients with probable DLB as compared with patients with probable AD. Our results suggest that these deficits reflect dysfunction of the visual cortices and play a role in development of the vision-related behavioral and cognitive symptoms in DLB.

Accepted for publication October 29, 1999.

This work was supported in part by a Comprehensive Research on Aging and Health research grant, Ministry of Health and Welfare, Tokyo, Japan.

Reprints: Etsuro Mori, MD, PhD, Department of Clinical Neurosciences, Hyogo Institute for Aging Brain and Cognitive Disorders, Saisai-ko 520, Himeji 670-0981, Japan (e-mail: mori@hiabcd.go.jp).

REFERENCES


