

The Progression of Cognition, Psychiatric Symptoms, and Functional Abilities in Dementia With Lewy Bodies and Alzheimer Disease

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Background: Although dementia with Lewy bodies (DLB) may be one of most common forms of dementia, relatively little is known about its cognitive and functional course.

Objective: To compare change over time in general cognitive status, memory test performance, psychiatric symptoms, neurological signs, and functional abilities in patients with probable DLB and probable Alzheimer disease (AD).

Design: Twenty-eight patients who met diagnostic criteria for DLB were recruited into the study from 3 sites. Patients with AD (n=55) were selected from a larger cohort and matched 2 to 1 to the patients with DLB on age and baseline global cognitive status. Patients were followed up at 6-month intervals for an average of 6.2 visits and assessed at each visit with tests of global cognitive functioning and verbal learning and memory and measures of psychiatric, neurological, and functional status.

Results: At the baseline evaluation, patients with DLB performed more poorly on a measure of constructional

praxis and all measures of functional status. They also had more severe psychiatric symptoms and neurological signs than the AD group. Despite these initial differences, generalized estimating equations applied to regression analyses with repeated measures determined that the only difference between the 2 groups in change in cognitive test performance was on a measure of recognition memory; patients with AD declined, while patients with DLB remained relatively stable. Patients with DLB had relatively stable behavioral symptoms and visual illusions, whereas patients with AD had a significant increase in these symptoms over time. Neurological and functional changes over time were similar in the 2 groups.

Conclusions: Both baseline and longitudinal differences between patients with DLB and patients with AD were noted; these have implications for clinical diagnosis and treatment.

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DEMENTIA WITH LEWY BODIES (DLB) is characterized clinically by widespread cognitive loss, marked fluctuations in cognitive functioning, visual hallucinations, extrapyramidal signs (EPS), and sensitivity to typical neuroleptics.¹ Pathological studies suggest that DLB may be the second most common form of dementia,¹ though it is often misdiagnosed clinically as probable Alzheimer disease (AD).²⁻⁴ Prospective longitudinal studies comparing patients who meet clinical diagnostic criteria for DLB with matched patients with AD may help refine the concept of DLB and improve clinical diagnosis. The purpose of the current study was to compare, cross-sectionally and longitudinally, a group of patients with DLB with a well-matched sample of patients with probable AD on

measures of cognition and function that have been implicated in both forms of dementia.

Although cross-sectional studies have suggested similarities between DLB and AD in overall level of cognitive dysfunction, patients with DLB are reported to have more pronounced executive, attentional, and visuospatial deficits early in the course of the dementia.⁵⁻¹⁸ Several studies suggest that patients with DLB perform better than patients with AD on verbal recall tasks,^{5-9,14} but others have found no differences.^{11,19} Patients with DLB may have more difficulty with the free recall of declarative information in the context of relatively intact recognition memory.^{18,20} There have been fewer studies comparing progression of cognition in DLB and AD, and their results have been somewhat equivocal. In 3 studies, the rate of decline in global

cognitive function was similar in AD and DLB²¹⁻²⁴; another noted faster decline in DLB.²⁰ With regard to everyday functioning, 1 retrospective study found that patients with DLB were more likely to be institutionalized than patients with AD. However, both groups displayed a similar time to reaching an end point of moderate to severe functional impairment, as measured by the Blessed Dementia Rating Scale (BDRS).²⁵

In the current study, we evaluated differences between well-matched patients with AD and DLB in the progression of global cognitive function, declarative memory, and functional status. Because EPS and psychiatric symptoms are increased in DLB and are associated with poorer cognitive and functional outcome,²⁶⁻³¹ we expected that patients with DLB would decline at a faster rate than patients with AD.

METHODS

We studied patients from the second cohort of the Predictors Study. Recruitment of this cohort was initiated in 1997 following the same methods as the first Predictors cohort, which has been described previously.^{24,32} In this new cohort, patients with DLB were recruited and followed up using the same procedures. Two hundred eleven subjects with probable AD and 28 with DLB were recruited into the cohort at 3 sites: Columbia University, Johns Hopkins University, and Massachusetts General Hospital. All patients were diagnosed in a consensus conference with at least 2 faculty physicians specializing in dementia and 1 faculty neuropsychologist present. Alzheimer disease was diagnosed according to established criteria for probable AD.³³ Dementia with Lewy bodies was diagnosed according to the 1996 Consensus Guidelines¹ for probable DLB.

Specific details of the general inclusion/exclusion criteria have been described previously.³² Although the original study procedures excluded patients scoring lower than 30 (of a possible 57 points) on the Columbia modified Mini-Mental State Examination (mMMS),^{34,35} for the purposes of the current study, some patients with a lower mMMS score were followed up. To ensure that any differences between the groups could be attributed to the disorders themselves and not to differences in baseline global cognitive impairment, the patients with AD and DLB were matched 2 to 1 based on their baseline mMMS score and age. For the matching procedure, the 2 groups were first subdivided into quartiles based on age and baseline mMMS score of the patients with DLB. We then randomly selected 2 patients with AD for every 1 patient with DLB, yielding a sample of 55 patients with AD and the original 28 patients with DLB (for 1 of the patients with DLB, there was only 1 patient with AD who met the matching criteria).

The project was approved by the institutional review board at each of the 3 sites. All patients and their proxy decision makers provided written informed consent.

NEUROPSYCHOLOGICAL ASSESSMENT

Subjects were evaluated once every 6 months. Global cognitive functioning was assessed using the mMMS,³⁵ a modified version of the Folstein Mini-Mental State Examination³⁴ that includes the digit span forward and backward from the Wechsler Adult Intelligence Scale-Revised,³⁶ as well as additional attention/calculation (eg, serial 7s, summation), general knowledge (eg, current and past 4 presidents), language (eg, repetition, command, object naming), and construction items (eg, construction of shapes). The maximum score on the mMMS is 57. Items of the

mMMS are grouped into 5 cognitive domains: orientation, short-term memory, long-term memory, language, and visuoconstruction.³⁷ The mMMS was administered at each follow-up visit.

Verbal memory was evaluated with the Hopkins Verbal Learning Test-Revised (HVLTR).³⁸ The primary dependent variables for the HVLTR are total recall across 3 trials, percentage of retention at delay, number of correct items on a yes/no recognition trial, and number of false-positive responses on the recognition trial. The HVLTR was administered annually; counterbalanced alternate forms were used.

ASSESSMENT OF NEUROLOGICAL SIGNS

Extrapyramidal signs were assessed with items from the Unified Parkinson's Disease Rating Scale.^{26,39,40} Eleven EPS domains included speech, tremor, rigidity, bradykinesia, gait, posture, and facial appearance. The items were rated on a scale of 0 (normal) to 4 (maximum impairment). The dependent variable for these analyses was total EPS score (range, 0-44). Only EPS that were not considered drug induced were included in these analyses.

PSYCHIATRIC SYMPTOM ASSESSMENT

Psychiatric symptoms and behaviors were assessed using the Columbia University Scale for Psychopathology in Alzheimer's Disease,^{24,41} an informant-based rating scale. Most scale items were scored dichotomously (ie, present or absent). For the primary analyses, patients received 1 point for each domain in which they had significant symptoms (ie, psychosis [delusions, hallucinations, and illusions], behavioral symptoms, and depression), with a maximum score of 3. Follow-up analyses examined the presence of 5 psychiatric symptoms: delusions, hallucinations, illusions (misperceptions), behavioral symptoms, and depression.

FUNCTIONAL ASSESSMENT

Functional capacity was assessed using the 2 parts of the BDRS.⁴² Part 1 assesses instrumental activities of daily living (IADL) and has a maximum score of 7, indicating the lowest level of function. Part 2 measures basic activities of daily living (ADL) (ie, eating, dressing, and toileting) and has a maximum score of 9.

DEPENDENCY ASSESSMENT

Level of functional dependence was assessed using the Dependence Scale.^{43,44} The scale is based on informant interviews, specifically targeting the informant's impression of the amount of assistance required by the patient in everyday tasks. The total score was used with a maximum of 15, indicating the highest degree of dependency.

STATISTICAL ANALYSIS

Group differences at baseline were examined with independent sample *t* tests and Pearson χ^2 tests. The rate of change in verbal memory, global cognitive function, Dependence Scale score, IADL score, ADL score, EPS, and psychiatric symptom sum was compared across groups by applying generalized estimating equations (GEEs) to regression analyses with repeated measures.⁴⁵ The group diagnosis (ie, AD or DLB) was used as the independent variable, with the AD group as the reference group. Therefore, for interactions between group and time, the β values in the GEE analyses represent the change during 1 year in the patients with DLB above and beyond that of the patients with AD. The GEE analyses were repeated, with baseline scores that differed be-

Table 1. Demographic and Baseline Clinical Characteristics of Patients With Probable AD and DLB*

	AD (n = 55)	DLB (n = 28)	Statistical Test
Age at intake, y	73.09 ± 8.26	73.46 ± 7.56	$t_{81} = -0.20; P = .84$
Education, y	14.27 ± 2.98	14.43 ± 3.44	$t_{81} = -0.21; P = .83$
Sex, No. M/F	21/34	19/9	$\chi^2 = 6.5; P = .01$
Duration of illness, y	4.42 ± 2.37	4.54 ± 2.34	$t_{74} = -0.20; P = .84$
Visit at last follow-up, No.	6.20 ± 3.51	5.93 ± 3.31	$t_{81} = 0.34; P = .74$
mMMS at baseline	39.02 ± 7.58	38.11 ± 8.32	$t_{81} = 0.50; P = .62$
Orientation	6.33 ± 2.60	5.82 ± 2.60	$t_{80} = 0.85; P = .40$
Short-term memory	15.26 ± 3.30	14.39 ± 3.55	$t_{80} = 1.1; P = .28$
Long-term memory	2.24 ± 2.17	2.61 ± 2.01	$t_{80} = -0.74; P = .46$
Language	14.04 ± 2.53	14.29 ± 2.73	$t_{80} = -0.41; P = .68$
Visuoconstructive ability	1.81 ± 0.92	1.26 ± 1.13	$t_{78} = 2.35; P = .02$
Total learning	13.15 ± 4.60	10.86 ± 4.34	$t_{65} = 1.93; P = .058$
% of retention	23.09 ± 31.84	30.38 ± 36.51	$t_{65} = -0.83; P = .41$
Recognition hits	9.04 ± 2.88	8.38 ± 2.36	$t_{65} = 0.92; P = .36$
False alarms	4.39 ± 2.80	3.14 ± 1.82	$t_{65} = 1.87; P = .07$
IADL	2.65 ± 1.41	3.90 ± 1.81	$t_{79} = -3.39; P = .001$
ADL	0.11 ± 0.10	0.24 ± 0.22	$t_{79} = -3.58; P = .001$
Dependence Scale sum	4.94 ± 2.10	6.81 ± 3.41	$t_{78} = -3.0; P = .004$
EPS sum	1.58 ± 3.17	11.30 ± 7.42	$t_{71} = -7.88; P < .001$
Psychiatric symptoms, No. of patients/total No. of patients	0.89 ± 0.86	1.96 ± 0.93	$t_{71} = -5.0; P < .001$
Delusions	13/54	15/25	$\chi^2 = 9.64; P = .002$
Hallucinations	2/54	11/25	$\chi^2 = 20.2; P < .001$
Depression	12/54	12/25	$\chi^2 = 5.37; P = .02$
Behavioral symptoms	21/54	20/25	$\chi^2 = 11.7; P = .001$
Illusions	1/52	8/25	$\chi^2 = 14.8; P < .001$

Abbreviations: AD, Alzheimer disease; ADL, basic activities of daily living; DLB, dementia with Lewy bodies; EPS, extrapyramidal signs; IADL, instrumental activities of daily living; mMMS, modified Mini-Mental State Examination.

*Values are presented as mean ± SD unless otherwise indicated. Most of the significant effects remain significant after correction for multiple comparisons, with the exception of depression scores and visuoconstructive abilities.

tween the 2 groups held as covariates. Additional analyses to examine the longitudinal contribution of each of the 4 individual psychiatric domains were performed by applying GEE to logistic regression analyses with repeated measures.^{45,46} These analyses provide estimates of the odds of the occurrence of an outcome dependent on the values of the covariates. The outcomes included presence of delusions, hallucinations, behavioral symptoms, and depression.

Cox proportional hazards models were calculated for the following dichotomous outcomes: entry into a nursing home and progression to severe dementia, as measured by a Clinical Dementia Rating (CDR) of 3. The time variable was duration between the initial visit and development of the outcome variable or time to last evaluation in patients who did not develop the outcome of interest. Diagnostic group was the predictor for these outcomes.

RESULTS

Clinical and demographic characteristics of the AD and DLB groups are presented in **Table 1**. By design, the 2 groups did not differ on baseline mMMS score or age. They also did not differ in number of years of education or estimated duration of illness at the baseline visit. The DLB group had a greater proportion of men.

BASELINE COMPARISONS

The DLB group performed significantly worse than the AD group on the constructional domain of the mMMS.

Scores on the other mMMS domains did not significantly differ between groups. As expected from the diagnostic criteria for DLB,¹ the DLB group had more severe Unified Parkinson's Disease Rating Scale scores, higher psychiatric symptom sums, and a higher proportion of positive cases in each of the psychiatric domains. Specifically, at baseline, the DLB group exhibited more paranoid, misidentification, and other delusions than the AD group. They also experienced more auditory and visual hallucinations and exhibited more physical threats, agitation, and confusion than the AD group.

On the HVLTR, at baseline, there were nonsignificant trend level differences on total learning, with the DLB group scoring slightly lower scores than the AD group. There were no differences in percentage of retention after a delay or in recognition hits after a delay. There was a nonsignificant trend for patients with DLB to have fewer false-positive errors than patients with AD.

The DLB group had significantly higher scores on both IADL and ADL of the BDRS, indicating lower functioning. The DLB group had significantly higher total dependence scores, indicating greater need for assistance.

LONGITUDINAL ANALYSES

Cognitive Decline

β and P values for all longitudinal analyses are presented in **Table 2**. Both the total mMMS score and its

Table 2. Results of GEE Analyses Comparing Patients With DLB and AD*

	Estimated β (P Value)		
	Time	Diagnosis	Time \times Diagnosis
mMMS score	-3.93 \pm 0.64 ($P < .001$)	-2.18 \pm 2.04 ($P = .29$)	-0.57 \pm 1.43 ($P = .69$)
Orientation	-0.87 \pm 0.14 ($P < .001$)	-1.0 \pm 0.57 ($P = .08$)	0.16 \pm 0.43 ($P = .70$)
Short-term memory	-1.42 \pm 0.25 ($P < .001$)	-1.68 \pm 0.80 ($P = .04$)	0.11 \pm 0.55 ($P = .84$)
Long-term memory	-0.33 \pm 0.10 ($P = .002$)	-0.019 \pm 0.45 ($P = .97$)	0.22 \pm 0.22 ($P = .32$)
Language	-1.49 \pm 0.21 ($P < .001$)	-0.64 \pm 0.74 ($P = .39$)	0.036 \pm 0.61 ($P = .95$)
Visuoconstructive abilities	-0.29 \pm 0.045 ($P < .001$)	-1.04 \pm 0.21 ($P < .001$)	0.27 \pm 0.15 ($P = .08$)
Total learning score	-1.8 \pm 0.31 ($P < .001$)	-2.62 \pm 1.38 ($P = .06$)	0.96 \pm 1.01 ($P = .34$)
% of retention	-2.46 \pm 1.69 ($P = .15$)	2.86 \pm 9.86 ($P = .77$)	4.05 \pm 5.65 ($P = .47$)
Recognition hits	0.79 \pm 0.23 ($P = .001$)	-0.71 \pm 0.72 ($P = .32$)	1.12 \pm 0.36 ($P = .002$)
False alarms	-0.16 \pm 0.17 ($P = .35$)	-0.57 \pm 0.66 ($P = .39$)	0.36 \pm 0.34 ($P = .29$)
EPS sum	0.85 \pm 0.34 ($P = .01$)	12.6 \pm 1.9 ($P < .001$)	1.05 \pm 1.14 ($P = .36$)
Psychiatric symptoms	0.077 \pm 0.036 ($P = .03$)	1.12 \pm 0.18 ($P < .001$)	-0.23 \pm 0.06 ($P < .001$)
Delusions	0.19 \pm 0.097 ($P = .05$)	1.83 \pm 0.47 ($P < .001$)	-0.28 \pm 0.17 ($P = .09$)
Hallucinations	0.20 \pm 0.11 ($P = .06$)	2.73 \pm 0.53 ($P < .001$)	-0.13 \pm 0.21 ($P = .53$)
Depression	-0.048 \pm 0.10 ($P = .65$)	0.93 \pm 0.41 ($P = .02$)	-0.21 \pm 0.20 ($P = .29$)
Behavioral symptoms	0.22 \pm 0.092 ($P = .02$)	1.75 \pm 0.49 ($P < .001$)	-0.47 \pm 0.20 ($P = .02$)
Illusions	0.39 \pm 0.17 ($P = .02$)	3.76 \pm 0.70 ($P < .001$)	-0.77 \pm 0.23 ($P < .001$)
IADL	0.65 \pm 0.06 ($P < .001$)	1.41 \pm 0.40 ($P < .001$)	-0.32 \pm 0.23 ($P = .16$)
ADL	0.075 \pm 0.008 ($P < .001$)	0.19 \pm 0.046 ($P < .001$)	-0.033 \pm 0.023 ($P = .15$)
Dependence Scale sum	1.15 \pm 0.13 ($P < .001$)	0.83 \pm 0.31 ($P = .007$)	-0.22 \pm 0.43 ($P = .60$)

Abbreviations: AD, Alzheimer disease; ADL, basic activities of daily living; DLB, dementia with Lewy bodies; EPS, extrapyramidal signs; GEE, generalized estimating equation; IADL, instrumental activities of daily living; mMMS, modified Mini-Mental State Examination.

*Values presented are overall progression of the cognitive, neurological, and functional variables collapsed across the 2 groups (main effect of time), differences between the 2 groups collapsed across time (main effect of diagnosis), and differences in the rate of decline between the 2 diagnostic groups (time \times diagnosis interaction). Values are presented as estimated $\beta \pm$ SE.

cognitive domain scores significantly decreased over time in both groups at a similar rate. With respect to the HVLT-R, both groups showed a significant, similar decrease in total learning scores over time. For percentage of retention after a delay, neither the main effect of time nor the group \times time interaction was statistically significant. However, for recognition hits, there was a significant effect of time as well as a group \times time interaction indicating a greater decrease in scores over time in the AD than in the DLB group (**Figure 1**). However, although the 2 groups showed differential patterns of change on the recognition test, cross-sectional and longitudinal measures of discriminability⁴⁷ did not differ between the 2 groups. It is therefore possible that differences in recognition memory performance could be partially due to differential changes in response bias.

EPS and Psychopathologic Features

Extrapyramidal signs increased over time in both groups. However, the group \times time interaction was not statistically significant. This finding was not altered when controlling for baseline EPS. There were significant main effects of time and diagnosis for total psychiatric symptoms, with patients with DLB exhibiting greater overall symptoms. However, these effects were modified by an interaction, indicating a slight increase over time in the patients with AD (**Figure 2**). The group \times time interaction remained significant after controlling for baseline psychiatric symptoms (estimated $\beta \pm$ SE = -0.21 \pm 0.06; $P = .001$). This finding appeared to be due to an increased risk of developing behavioral symptoms and illusions in the AD group.

We conducted a more detailed analysis of the presence of visual hallucinations. At baseline, none of the patients with AD had visual hallucinations, whereas 11 (44%) of the patients with DLB did ($\chi^2 = 27.60$; $P < .001$). A Kaplan-Meier regression equation demonstrated that the median number of visits to reach the end point of being rated as having visual hallucinations was 5.63 (SE = 1.12) for patients with AD and 0.55 (SE = 0.10) for patients with DLB.

Functional Activities

Both IADL and ADL scores became significantly worse over time, but at a similar rate for the 2 groups. The sum of the Dependence Scale scores significantly increased over time in both groups at a similar rate. Controlling for baseline dependence scores did not affect the results.

Cox Regression Analyses

There was no differential risk between the 2 groups of reaching the outcome of entry into a nursing home (risk ratio, 0.593 [95% confidence interval, 0.226-1.556]) nor of reaching severe dementia as defined by a CDR of 3 (risk ratio, 0.877 [95% confidence interval, 0.291-2.638]).

COMMENT

Cognitive and functional differences between carefully matched patients with probable AD and probable DLB were examined in cross-sectional and longitudinal analyses. At their initial visit, patients with DLB were more impaired

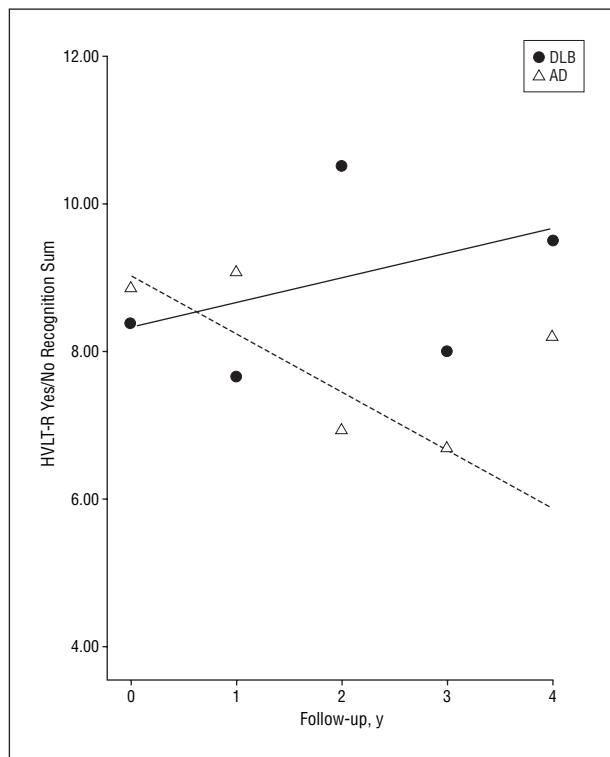


Figure 1. Predicted values of Hopkins Verbal Learning Test–Revised (HVLT-R) yes/no recognition sum over time in patients with dementia with Lewy bodies (DLB) and Alzheimer disease (AD). Lines indicate predicted values. The triangles and dots represent calculated means at each year for patients with AD and patients with DLB, respectively.

on a test of constructional praxis, had greater functional deficits, and had more psychiatric symptoms and EPS than did patients with AD. These findings are consistent with previous studies that also found greater deficits in spatial cognition in DLB^{5,10,12,14-17} as well as more psychopathologic features and EPS.^{1,15,48-52} We did not confirm previous findings of better performance on verbal recall in the patients with DLB than the patients with AD.^{5-7,9,14,15}

Performance on a measure of recognition memory declined more rapidly in patients with AD than in patients with DLB, although at baseline the 2 groups were similar. No differences were seen in the false-positives measure. These findings are consistent with previous studies that found patients with DLB to have similar or less severe impairment in recognition memory than patients with AD.^{9,10,18,51,53,54} At initial evaluation, patients with DLB exhibited more psychiatric symptoms than did patients with AD. There was a significant difference in the progression of these features, with an increase in behavioral symptoms in the AD group and a decrease in the DLB group. Previous reports have established that psychiatric symptoms in AD increase with the severity of the disease,^{24,55,56} and findings from the current study suggest that patients with AD eventually exhibit a similar degree of psychiatric symptoms as patients with DLB.

Although at first evaluation patients with DLB were significantly more impaired on measures of ADL and showed greater dependence on caregivers, there were no significant differences in the rate of decline between the 2 groups. Another study similarly found no differences

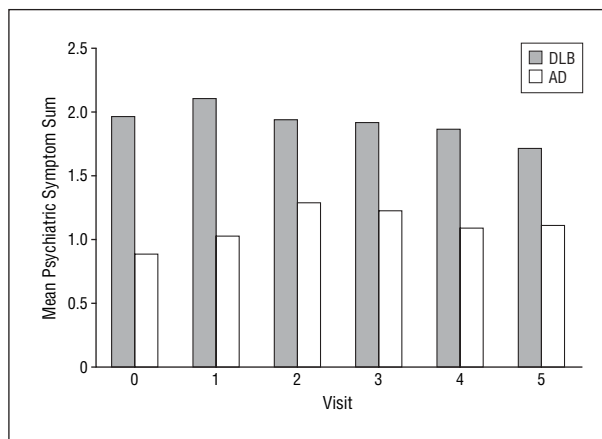


Figure 2. Mean values of psychiatric symptom sums in patients with Alzheimer disease (AD) and dementia with Lewy bodies (DLB).

in the frequency of development of severe functional impairment between patients with AD and those with DLB.²⁵

The results suggest that differences between patients with DLB and AD appear most pronounced early in the course of the disease. At more advanced stages of dementia, patients with AD and DLB may appear very similar on the domains assessed in the current study. In milder stages of dementia, the presence of EPS, psychiatric symptoms, and constructional deficits suggests a diagnosis of DLB, whereas psychiatric symptoms that emerge in later stages do not. Recognition memory, on the other hand, is more likely to be similar in the 2 groups of patients during early stages and to diverge at later stages, with patients with AD progressing more rapidly.

We used a stratified, random sample-matching procedure based on age and baseline mMMS scores. There are advantages and disadvantages to this approach. Well-matched samples allow for the comparison of the progression of symptoms between groups beginning from a similar baseline level of functioning. This approach assumes that global measures of cognition are good correlates of disease severity and that matched samples are similar in degree of pathological features. Domains that might be more affected in DLB, such as attention or executive functioning, are underrepresented on both the mMMS and its parent instrument, the Mini-Mental State Examination. Thus, as an index of global disease severity, these measures may have different utility in AD and DLB.

In a similar vein, it is important to consider the referral source of clinic-based studies involving DLB. Patients with DLB recruited from memory disorders programs may have different presenting symptoms and a different course than those referred from movement disorders programs, psychiatry clinics, or from population-based samples. If memory dysfunction is not among the more salient initial problems in DLB, those patients referred from memory clinics may be more advanced in the course of the disease.

A limitation of the current study was the neuropsychological battery used. Although several neurocognitive domains were assessed, more detailed evaluation of specific areas of function is required to better characterize the longitudinal differences between patients with AD and DLB. The attention domain has been particularly implicated in DLB.^{8,14} Future prospective studies should incorporate more

detailed neuropsychological measures that would more directly assess all relevant cognitive domains.

Seven of the patients with DLB in this study have come to autopsy; 6 met autopsy diagnostic criteria for either "pure" DLB or DLB with concomitant AD pathological features and 1, for Parkinson disease with diffuse cortical and subcortical distribution of Lewy bodies. Autopsy data were available for 6 patients with AD in the current study; 4 met autopsy criteria for AD only and 2, for AD with some Lewy body pathological features, which is consistent with other reports of autopsy-verified samples. While these findings suggest that the patients were accurately diagnosed clinically, there is still the possibility of some cross-contamination between the AD and DLB groups.

The current study is among the largest prospective analyses of patients with probable DLB. However, there is still the possibility that some of the negative findings were due to lack of sufficient power to detect statistical differences between groups. For example, on the measure of free verbal recall, the group \times time interaction was not statistically significant but indicated that patients with DLB recalled approximately 1 more word per year than did patients with AD ($\beta=0.96$). Consideration of the magnitude of differences between groups would suggest that the effect sizes of the negative findings in the current study had little clinical significance; that is, although statistical differences may have been detected with a larger sample, the effect sizes were of small magnitude. Nonetheless, future studies should be conducted to replicate the stability of these findings.

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