Cognitive Profiles of Autopsy-Confirmed Lewy Body Variant vs Pure Alzheimer Disease

Donald J. Connor, PhD; David P. Salmon, PhD; Teresa J. Sandy, BS; Douglas Galasko, MD; Lawrence A. Hansen, MD; Leon J. Thal, MD

Objective: To compare the cognitive profiles of patients with autopsy-confirmed Alzheimer disease (AD), with or without concomitant Lewy bodies, on 2 dementia screening measures.

Methods: Profiles on subtests of the Mattis Dementia Rating Scale (range, 105-125) and of component items of the Mini-Mental State Examination were compared between 23 patients with uncomplicated AD and 23 patients with concomitant AD and Lewy body pathology (Lewy body variant [LBV]).

Results: Although the groups did not differ significantly regarding age, years of education, total Mini-Mental State Examination score, or total Mattis Dementia Rating Scale score, the AD group performed significantly worse than the LBV group on the Mattis Dementia Rating Scale Memory subscale \( (P<.005) \). In contrast, the LBV group demonstrated poorer performance than the pure AD group on the Initiation/Perseveration subscale \( (P<.02) \). The groups did not differ significantly on the Attention, Construction, or Conceptualization subscales. The same overall pattern of results was obtained when subgroups with mild to moderate and moderate to severe dementia were examined separately, with the additional finding that in the mild-to-moderate range patients with dementia and LBV performed worse than patients with pure AD on the Construction subscale.

Conclusions: The difference in pattern of cognitive deficits among patients with pure AD vs those with LBV is similar to that seen between AD and more subcortical/frontal dementias (eg, Huntington disease). This suggests that the concomitant Lewy body pathology significantly contributes to the presentation of the cognitive dysfunction in individuals with LBV.

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Dementia with Lewy bodies is a recently described condition in which autopsy examination of the brain of patients with dementia reveals diffusely distributed cortical and subcortical Lewy bodies. While some of these patients are found to possess only Lewy body pathology, most have concomitant Alzheimer disease (AD) pathologic features. Those patients with dementia and Lewy bodies who also manifest sufficient AD pathologic features to satisfy the National Institute on Aging autopsy criteria for AD and criteria from the Consortium to Establish a Registry for Alzheimer’s Disease for either “definite” or “probable” AD are referred to as having the Lewy body variant (LBV) of AD. While senile plaque distribution in LBV is similar to that in pure AD, neocortical neurofibrillary tangles are absent or rare, and entorhinal and hippocampal tangle counts are intermediate between those of elderly controls and patients with pure AD. Lewy bodies in LBV occur both neocortically and in the more common subcortical distribution (substantia nigra, locus ceruleus, substantia innominata, and dorsal vagus nucleus) typically associated with Parkinson disease. Clinically, both patients with dementia with Lewy bodies and LBV present with a progressive dementia and often develop mild extrapyramidal motor dysfunction (eg, bradykinesia, rigidity, or masked facies) and hallucinations early in the course of the disease. The pattern of cognitive deficits engendered by LBV is similar to that of AD in some respects, but a number of specific features distinguish the 2 groups. Although patients with LBV and AD exhibit similar deficits in memory and confrontation naming, preliminary studies have indicated that patients with prominent Lewy body burden display disproportionately severe deficits in attention, fluency, and visuospatial processing. As Hansen and colleagues suggest, patients with LBV appear to exhibit a com-
PATIENTS AND METHODS

PATIENTS

Twenty-three patients with autopsy-confirmed LBV and 23 patients with autopsy-confirmed AD, all of whom were diagnosed as having dementia at the time of their initial clinical evaluation, were included in the current study. All patients had been participants in the University of California, San Diego Alzheimer’s Disease Research Center (UCSD/ADRC) in San Diego through which they received yearly physical, neurologic, and neuropsychological assessments. Written informed consent for participation in the UCSD/ADRC longitudinal study was obtained from all patients (or their conservators) after the procedures of the study had been fully explained. Informed consent for autopsy was obtained from the next of kin immediately after the patient’s death. Three of 23 patients with LBV and 1 of the patients with AD were from the original study by Hansen et al.4

The procedures that were used to prepare and histologically analyze the brains of the patients have been described in detail previously.4 The neuropathologic diagnosis was made according to both the criteria suggested by the National Institute on Aging and the Consortium to Establish a Registry for Alzheimer’s Disease criteria for definite or probable AD. The neuropathologic diagnosis of LBV required satisfaction of the National Institute on Aging and the Consortium to Establish a Registry for Alzheimer’s Disease criteria for AD, as well as the presence of subcortical and cortical Lewy bodies (see Hansen and Samuel26 for detailed diagnostic and nosologic review of LBV). Braak stage was established by degree and spread of neurofibrillary tangle formation.15

The patients with LBV and AD selected for our study were pair matched in terms of level of dementia (MDRS total score), age, and years of education at the time of their initial ADRC evaluation. The MDRS scores of the patients with LBV and AD ranged from 80 to 125 of a possible 144 points. Matching on the MDRS total score was performed to ensure that any differences in group subtest profiles could be attributed to differences in the underlying nature of the 2 disorders, rather than to differences in global level of dementia. The MDRS total score is a more refined staging measure of dementia than the MMSE score, and matching on MMSE score can result in significant differences in the total MDRS score that would confound interpretation of the MDRS subscale profiles. While this matching causes some interdependence between the subscales, it does not preclude examination of different subscale profiles at equivalent levels of dementia. However, caution must be used in interpreting what specific cognitive abilities are differentially affected by the presence of the additional cortical and subcortical Lewy body burden (see the “Comment” section).

PROCEDURE

The MDRS24 and the MMSE25 were administered to each patient as part of a larger neuropsychological evaluation.

Only data from the patients’ initial ADRC evaluation were used in the analysis.

The MDRS is a standardized, 144-point mental status examination that consists of 5 subscales that assess Attention (37 points), Initiation/Perseveration (37 points), Construction (6 points), Conceptualization (39 points), and Memory (25 points). The MDRS was administered according to the standard procedures24 with the exception that all items were administered to all patients.

The MMSE is a standardized, 30-point scale that encompasses 11 component items: orientation to time (5 points), orientation to place (5 points), word registration (3 points), serial subtraction or backward spelling (5 points), word recall (3 points), naming (2 points), repetition (1 point), following commands (3 points), reading (1 point), writing (1 point), and copying a figure (1 point). Both the backward spelling of world and serial subtraction (7’s from 100) were administered to all patients and the best performance of the 2 items was included in the total MMSE score.

STATISTICAL ANALYSIS

The scores achieved by the patients with AD and LBV on the subscales of the MDRS were compared using multivariate analysis of variance with planned post hoc comparisons using the Fisher least significant difference test. Subscales demonstrating significant differences between patients with AD and LBV were submitted for individual item analysis using the Mann-Whitney U test. Since this group represents a broad range of cognitive impairment, additional exploratory analyses using multivariate analysis of variance were performed separately for patients with mild to moderate (MDRS score, 106-125) and moderate to severe (MDRS score, 80-105) dementia (ie, SD = 2.0 to 4.5 and SD = 4.6 to 8.3, respectively, from the mean normal control score as reported in the MDRS manual).28

The MDRS subscale scores of the patients with LBV and AD were submitted to a discriminate function equation that has been shown to effectively discriminate between patients with AD and patients with HD.14 Correctly and incorrectly classified patients were compared on demographic variables, time from assessment to death, and Braak stage of AD pathologic progression post mortem. A new discriminant function analysis using the MDRS subscale scores of patients with AD and LBV was also conducted to derive an equation that might optimally differentiate between patients with AD and LBV. The latter analysis should be considered exploratory because of the small sample size and ultimately must be validated with a larger sample.

The scores achieved by patients with LBV and AD on the 11 component items of the MMSE were compared using the nonparametric Mann-Whitney U test for continuous measures or the χ2 test for dichotomous measures as appropriate.

Combination of cortical and subcortical neuropsychological dysfunction.

Progressive dementing disorders that involve predominantly cortical (eg, AD) or subcortical (eg, Huntington disease [HD]) neurodegeneration manifest distinct patterns of cognitive deficits on detailed neuropsychological evaluation.13-15 Typically, patients with AD, a prototypical cortical dementia, present with severe memory impairment with additional deficits in language (ie, anemia), verbal fluency, abstract reasoning, and visuospatial abilities.15-17 In contrast, patients with HD, a typical subcortical dementia, usually demonstrate impaired atten-
tion, slowed cognitive processes, severe verbal fluency deficits, and a relatively moderate memory impairment. These distinct patterns of cognitive deficits are robust and have been detected even on brief, standardized mental status examinations. In view of the somewhat disparate nature of the cognitive deficits exhibited by patients with AD and LBV on detailed neuropsychological testing, it may be the case that these groups could be distinguished by their patterns of performance on mental status examinations that have been shown to discriminate between patients with cortical and subcortical dementia syndromes. That is, since patients with LBV appear to have a significant subcortical component to their cognitive dysfunction, aspects of their performance on mental status tests may resemble those of patients with HD or Parkinson disease.

To address this issue, our study compared the performances of patients with autopsy-confirmed LBV and pure AD on the Mattis Dementia Rating Scale (MDRS) and the Mini-Mental State Examination (MMSE). Patients with LBV and AD were matched on overall level of dementia, and their patterns of performance on the 5 MDRS subscales were compared. To determine whether the subcortical component of the cognitive dysfunction of patients with LBV is prominent enough to affect their classification as “cortical” or “subcortical,” the MDRS subscale scores of both groups were submitted to discriminant equations that have been shown to effectively differentiate between patients with AD and HD. Since these groups represent a broad range of cognitive impairment, the MDRS profiles of patients with AD and LBV were also analyzed over a mild-moderate and a moderate-severe range of dementia. Finally, the performance of patients with LBV and AD was compared on the components of the MMSE. This comparison was limited to patients with MMSE scores of 14 to 25, since this range of dementia has been shown to be most conducive to discriminating between patients with AD and HD with this task.

### RESULTS

Mean age, years of education, MDRS score, MMSE score, and time from evaluation to death for the 2 patient groups are presented in Table 1. As expected from the matching procedure, the LBV and AD groups did not differ significantly on any of the demographic features or overall level of dementia. Three patients with AD and 3 with LBV demonstrated significant depressive symptoms on clin-ical interview. A significantly higher proportion of patients with AD (18 of 20) than with LBV (8 of 20) achieved a Braak stage of 4 or higher, indicative of notable cortical neurofibrillary tangles formation.

### MATTIS DEMENTIA RATING SCALE

Multivariate analysis of variance revealed that the patterns of performance of the LBV and AD groups on the subscales of the MDRS were significantly different (P < .002). Post hoc comparisons of performance on the individual subscales (Fisher least significant difference test) showed that patients with LBV scored significantly higher than patients with AD on the Memory subscale (mean ± SD scores: AD, 10.8 ± 4.2; LBV, 15.3 ± 4.4; P < .001) but significantly lower on the Initiation/Perseveration subscale (mean ± SD scores: AD, 25.2 ± 5.0; LBV, 21.0 ± 5.9; P < .02). The groups did not differ significantly on the Attention, Construction, or Conceptualization subscales. The different patterns of performance produced by the 2 patient groups are presented in Figure 1. To facilitate comparison across the subscales, the scores are presented as a percentage of each subscale’s maximum possible score.

The performance of patients with LBV and pure AD on the individual items of the MDRS Memory subscale is shown in Table 2. Patients with AD scored significantly lower than patients with LBV on the orientation items (P < .01), on 1 of the free recall measures (sentence 1; P < .001), and marginally lower on the second recall measure (self-generated sentence; P < .06). The groups did not differ significantly on the word or design recognition items.

Table 2 also presents the performance of patients with LBV and AD on the individual items of the Initiation/Perseveration subscale. Although the mean scores of patients with LBV were lower than those of patients with AD on each item, the groups differed significantly only on the clothing-naming item (P < .01) that required gen-

### Table 1. Demographics and Level of Dementia*

<table>
<thead>
<tr>
<th></th>
<th>AD (n = 23)</th>
<th>LBV (n = 23)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>76.7 (5.7)</td>
<td>75.9 (5.2)</td>
<td>.61</td>
</tr>
<tr>
<td>Education, y</td>
<td>13.4 (3.0)</td>
<td>12.7 (2.7)</td>
<td>.43</td>
</tr>
<tr>
<td>Mattis Dementia Rating Scale score</td>
<td>104.5 (13.3)</td>
<td>104.7 (13.0)</td>
<td>.90</td>
</tr>
<tr>
<td>Mini-Mental State Examination score</td>
<td>18.6 (4.2)</td>
<td>19.5 (4.0)</td>
<td>.46</td>
</tr>
<tr>
<td>Time from cognitive evaluation to death, y</td>
<td>3.88 (1.6)</td>
<td>3.37 (1.7)</td>
<td>.30</td>
</tr>
</tbody>
</table>

*Values are mean (SD). AD indicates Alzheimer disease; LBV, Lewy body variant.

![Figure 1](https://example.com/figure1.png)

**Figure 1.** Mean (SEM) percentage of the maximum possible score on each subtest of the Mattis Dementia Rating Scale for patients with Alzheimer disease (AD) or the Lewy body variant (LBV). The groups differed significantly only on the Initiation/Perseveration and Memory subscales. Asterisk indicates P < .05; double asterisk, P < .01.
erating the names of articles of clothing, including those that the patient was wearing. Although performance on the graphomotor component of the Initiation/Perseveration subscale was not different for the 2 patient groups, a greater proportion of patients with LBV than with AD failed the most difficult item of that component (65% vs 30%, respectively; \( \chi^2 = 5.6; P < .02 \)), copying alternating figures presented in a ramparts or saw-tooth design.

### Subgroup With Mild to Moderate Dementia

The performances of patients with mild to moderate dementia (LBV score, mean ± SD MDRS, 116 ± 5.5; n = 11; and AD score, mean ± SD MDRS, 115 ± 7.5; n = 11) on the subscales of the MDRS are presented in Figure 2 (top). The scores are presented in terms of the percentage of the maximum possible score that could be achieved on each subscale. Overall multivariate analysis of variance revealed that the patterns of performance of the 2 groups were not significantly different (\( P > .10 \)). However, planned post hoc comparisons showed that patients with LBV scored significantly worse than patients with AD on the Initiation/Perseveration (mean ± SD scores: AD, 28.5 ± 3.8; LBV, 24.5 ± 4.4; \( P < .04 \)) and Construction (mean ± SD scores: AD, 5.5 ± 0.7; LBV, 4.3 ± 1.4; \( P < .02 \)) subscales. In contrast, patients with AD scored significantly lower than patients with LBV on the Memory subscale (mean ± SD scores: AD, 12.5 ± 5.1; LBV, 17.6 ± 2.7; \( P < .01 \)). The groups did not differ significantly on the Attention or Conceptualization subscales.

### Subgroup With Moderate to Severe Dementia

Figure 2 (bottom) also shows the performances of patients with moderate to severe dementia (LBV, mean ± SD MDRS score, 95 ± 9.0; n = 12; and AD, mean ± SD MDRS score, 95 ± 9.1; n = 12) on the MDRS subscales. As with the full group data, multivariate analysis of variance showed that the groups produced significantly different patterns of performance on the MDRS subscales (\( P < .02 \)). Planned post hoc comparisons revealed that patients with LBV scored significantly lower than patients with AD on the Initiation/Perseveration subscale (mean ± SD scores: AD, 22.1 ± 4.0; LBV, 17.8 ± 5.3; \( P < .04 \)), but significantly higher on the Memory subscale (mean ± SD scores: AD, 9.2 ± 2.3; LBV, 13.2 ± 4.7; \( P < .02 \)). The groups did not differ significantly on any other of the MDRS subscales.

### DISCRIMINANT FUNCTION ANALYSIS

To determine if the MDRS subscale profiles of patients with LBV and AD in this study were more typical of a cortical or subcortical dementia, their subscale scores were submitted to a discriminant equation using coefficients previously derived from a linear discriminant function analysis comparing the MDRS subscale scores of patients with AD vs HD. \( ^{22} \) Seventeen (74%) of 23 patients with AD were correctly classified as having cortical dementia by the discriminant equation, whereas only 9 (40%) of 23 patients with LBV were classified as having cortical dementia.

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**Table 2. Individual Items of the Memory and Initiation/Perseveration Subscales**

<table>
<thead>
<tr>
<th>Subscale Item</th>
<th>AD (Mean ± SD)</th>
<th>LBV (Mean ± SD)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Memory Subscale</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dog sentence</td>
<td>0.3 (0.56)</td>
<td>1.7 (1.43)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Own sentence</td>
<td>0.5 (1.08)</td>
<td>1.2 (1.37)</td>
<td>.06</td>
</tr>
<tr>
<td>Orientation</td>
<td>3.0 (2.22)</td>
<td>4.8 (2.15)</td>
<td>.01</td>
</tr>
<tr>
<td>Word recognition</td>
<td>4.0 (1.13)</td>
<td>4.1 (1.24)</td>
<td>.70</td>
</tr>
<tr>
<td>Design recognition</td>
<td>3.5 (0.85)</td>
<td>3.6 (0.86)</td>
<td>.70</td>
</tr>
<tr>
<td><strong>Initiation/Perseveration Subscale</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supermarket</td>
<td>10.2 (3.89)</td>
<td>8.2 (4.89)</td>
<td>.12</td>
</tr>
<tr>
<td>Clothing</td>
<td>7.2 (1.30)</td>
<td>5.9 (1.89)</td>
<td>.01</td>
</tr>
<tr>
<td>Repetition</td>
<td>1.9 (0.29)</td>
<td>1.7 (0.56)</td>
<td>.10</td>
</tr>
<tr>
<td>Alternating</td>
<td>2.6 (0.78)</td>
<td>2.2 (0.81)</td>
<td>.15</td>
</tr>
<tr>
<td>Graphomotor</td>
<td>3.3 (1.02)</td>
<td>2.9 (1.04)</td>
<td>.20</td>
</tr>
</tbody>
</table>

*Values are mean (SD). AD indicates Alzheimer disease; LBV, Lewy body variant.*
Patients with AD classified as having subcortical dementia (eg, HD-like) and patients with LBV classified as having cortical dementia (eg, AD-like) were not significantly different regarding demographics (age, education, or sex distribution) or level of dementia (as assessed by MMSE and MDRS total scores) from the correctly classified patients in their respective neuropathologically defined groups. However, patients with LBV classified as having an AD-like or cortical-like dementia had greater cortical AD-type neurofibrillary tangle pathologic features (Braak stage ≥4; \( \chi^2 = 4.4; P < .04 \)) than patients with LBV classified as having subcortical dementia. That is, those patients with LBV with significant cortical infiltration of neurofibrillary tangles were more often classified as having AD than those with tangles largely confined to the medial temporal lobe. This greater degree of AD pathologic features in patients with LBV who were classified as having cortical dementia is not simply a reflection of their having been tested at a more advanced stage of the disease than the other patients with LBV, since time from neuropsychological assessment to death was not different for the 2 subgroups (analysis of variance, \( P > .30 \)). Conversely, patients with AD misclassified as having subcortical dementia did not differ in Braak stage (\( \chi^2 = -.95; P > .30 \)) from the correctly classified patients with AD. The ability of the original AD vs HD discriminant function to differentiate patients with AD vs LBV was improved by adjusting the constant (from 8.2 to 7.02), a procedure that shifts the cutoff point to compensate for differences in degree of separation while keeping the relative pattern of variables that define the groups intact. This optimally adjusted discriminant function correctly classified 70% of patients with AD as having cortical dementia and 87% of patients with LBV as having subcortical dementia.

A new linear discriminant function analysis was performed to explore the maximal classification rate using the results of the MDRS profile in the present sample. As in previous studies, all 5 subscales were forced into the discriminant function analysis. With equal prior probability of group membership, the resulting equation,

\[
\text{Classification} = 0.154 (\text{Attention}) - 0.101 (\text{Construction}) + 0.040 (\text{Conceptualization}) - 0.162 (\text{Initiation}) + 0.191 (\text{Memory}) - 4.75
\]

correctly classified 82% of patients with LBV and 78% of patients with AD (canonical \( r = 0.64; P < .001 \); overall classification rate, 80%). When the 5 subscales were entered in a stepwise fashion, only the Memory and Initiation/Perseveration subscales were maintained in the significant discriminant function,

\[
\text{Classification} = 0.212 (\text{Memory Score}) - 0.137 (\text{Initiation/Perseveration Score}) + 0.391
\]

These 2 variables alone were able to correctly classify 78% of the autopsy-verified patients with LBV and 74% of patients with pure AD (canonical \( r = 0.61; P < .001 \); overall classification rate, 76%).

**MINI-MENTAL STATE EXAMINATION**

The performances of patients with LBV (\( n = 13 \)) and AD (\( n = 13 \)) (MMSE scores, 14-25) on the individual components of the MMSE are presented in **Figure 3**. Scores are presented in terms of the percentage of the total possible points achieved for each item. Patients with LBV scored significantly lower than patients with AD on the memory registration (\( P < .05 \)) and writing (\( P < .05 \)) components, whereas patients with AD scored significantly lower than patients with LBV on the temporal orientation (date; \( P < .005 \)) and free recall (3 words; \( P < .02 \)) items.

**COMMENT**

In this study, patients with autopsy-confirmed LBV and pure AD were differentiated by their performance on a simple dementia screening instrument (MDRS). Although matched for overall level of dementia, patients with AD performed worse than patients with LBV on the Memory subscale, whereas patients with LBV performed relatively worse than patients with AD on the Initiation/Perseveration subscale. This pattern is similar to that found in previous studies comparing patients with AD and HD, in which patients with AD were more impaired than patients with HD on the Memory subscale of the MDRS, but less impaired on the Initiation/Perseveration subscale. Rosser and Hodges recently replicated this finding and demonstrated that patients with progressive supranuclear palsy exhibit a pattern of deficits on the MDRS subscales identical to that of patients with HD. Similarly, patients with Parkinson disease who were equated to patients with AD in total MDRS score performed better than the patients with AD on the Memory subscale, but worse on the Construction subscale. Therefore, the cognitive deficits of patients with LBV appear to express characteristics of both subcortical and cortical dysfunction.

The possible subcortical contribution to the cognitive deficits of patients with LBV was further demonstrated by the finding that 60% of these patients were classified as having subcortical dementia when their MDRS subscale scores were submitted to a discriminant func-
tion that had been previously used to differentiate between patients with AD (cortical) vs HD (subcortical). In contrast, only 26% of patients with AD in our study were classified as having the HD-like pattern using these same discriminant equations. The significant improvement in LBV group classification (from 60% to 87%) with only a minimal loss in correct AD classification (from 74% to 70%) following adjustment of the coefficient is consistent with the proposition that patients with LBV are more likely to manifest an HD-like frontal/subcortical pattern on the MDRS compared to patients with AD. Although the observed degree of classification is far from perfect, it is impressive considering that the brains of individuals with LBV contain significant AD pathologic features, and in light of the fact that the original AD vs HD discriminant function was based on a sample clinically diagnosed as having AD, which most likely included some patients with LBV (since about 15%-20% of patients clinically diagnosed as having AD are found at autopsy to have had LBV). This possible contamination in the AD vs HD discriminant function may have contributed to the poorer classification of the patients with pure AD in our study compared with the AD vs HD study (AD correct, 74% vs 82%).

A NEW DISCRIMINANT function analysis also effectively distinguished patients with AD and LBV in this study. Despite the high degree of shared neuropathologic features in the 2 disorders, 78% of patients with AD and 82% of patients with LBV were correctly classified with this discriminant function equation. As would be expected from the multivariate analysis of variance, most of the power of this equation came from the Initiation/Perseveration and Memory subscales, which by themselves were able to correctly classify approximately 76% of all patients. However, these results must remain tentative until the equation can be validated with larger, independent, autopsy-verified groups of patients with AD and LBV.

Although analysis of individual items within a subscale must be approached with caution since they may represent divergent qualities, exploratory analyses indicated that patients with AD were relatively more impaired than patients with LBV on the Memory subscale’s orientation and free recall items, but not on the recognition task. That patients with LBV did not show the disproportionate improvement with recognition testing often observed in patients with a purely subcortical dementia syndrome is not surprising, since both groups performed near maximum on the recognition test (ceiling effect). Performance on the individual items of the Initiation/Perseveration subscale revealed few consistent or theoretically interpretable differences between patients with AD and LBV.

Analyses examining the pattern of MDRS performance in patients with LBV and AD with mild to moderate dementia and moderate to severe dementia demonstrated that the dissociation between the groups on the Memory and Initiation/Perseveration subscales was maintained across both ranges of severity. In addition, in the mild to moderate dementia range, patients with LBV were more impaired than patients with AD on the Construction subscale. This latter finding is consistent with the finding of poorer Construction subscale performance in patients with Parkinson disease than in patients with AD and with studies that have demonstrated visuospatial and constructional deficits in patients with LBV. The absence of this difference in the group with moderate to severe dementia appears to be due to the increased constructional deficits of the more impaired patients with AD. Interestingly, one of the most difficult items from the Initiation/Perseveration subscale that taps both constructional and executive abilities (ie, copying the raptures figure) was significantly more impaired in patients with LBV than with pure AD across the full MDRS range.

Comparison of the performance of patients with AD vs LBV on a more abbreviated screening instrument (MMSE) yielded results that were similar to those reported for patients with AD and HD matched on total MMSE score. In the study by Brandt et al, patients with AD were more impaired than those with HD in free recall (recalling 3 words after a 5-minute delay) and orientation (date), whereas patients with HD were more impaired than patients with AD in counting backward from 100 by 7’s and (in the MMSE total score, 15-19 range) memory registration and writing items. In our study, patients with AD performed worse than patients with LBV on the free recall and orientation items, whereas patients with LBV performed worse than patients with AD on the memory registration and writing items. Despite these significant differences between patients with AD and LBV, there are several factors that limit the significance of the results. The difference found on the recall item, for example, is confounded by the fact that none of the patients with AD, and only 5 of the 13 patients with LBV were able to recall any of the 3 words. In addition, our study failed to find the difference between groups on the serial subtraction item that was noted previously in the AD vs HD study. This may be due to a procedural difference, since our study accepted the highest score from either the serial subtraction or backward spelling items, while the AD vs HD study only used the serial subtraction item. Finally, the small sample size in our study (n = 13 per group), and the restricted range of scores for the instrument, precludes any definitive conclusion about differences between patients with LBV and AD on the individual components of the MMSE. Despite these limitations, the pattern of results obtained with the MMSE is consistent with the hypothesis that subcortical disfunction significantly influences the cognitive performance of patients with LBV.

In conclusion, the different patterns of performance on 2 different standardized screening devices for dementia (MDRS and MMSE) produced by patients with autopsy-verified AD and LBV are consistent with findings from preliminary studies using a more extensive battery of neuropsychological tests, and similar to the pattern of differences that have been observed between patients with AD and HD. That is, despite the fact that patients with LBV share much of the same underlying
neuropathologic features as patients with pure AD, the Lewy body burden can influence the pattern of cognitive deficits observed, especially in the early stages of the disease before the AD neuropathologic damage becomes predominant. While these differences in subscale profiles were significant, they were also relatively small and may be of limited clinical utility when applied to individual patients. Furthermore, these results need to be replicated with larger, independent, autopsyc-verified cohorts to establish their validity and reliability.

Despite these limitations, the results indicate that research investigating the nature of the cognitive deficits in patients with AD and other dementing disorders should take the existence of concomitant Lewy body patho-
logic features into account.

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calcium channel is ubiquitous in the brain, the channel is expressed most abundantly in the regions where patients who currently had SCA6 showed atrophy.

In conclusion, our results suggest that SCA6 affects the cerebellum and its afferent and efferent systems. Further study with larger numbers of subjects is necessary to elucidate the relationship between the CAG repeat length and atrophy or duration of illness.

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Correction

Incorrect Equation. In the July 1998 issue of the ARCHIVES (1998;55:994-1000) in the first equation on page 998 the coefficient value for conceptualization should have been +0.040 and not +040 as printed. Thus, the correct equation is: Classification = 0.154 (Attention) − 0.101 (Construction) + 0.040 (Conceptualization) − 0.162 (Initiation) + 0.191 (Memory) − 4.75.