Absence of Effect of Depression on Cognitive Performance in Early-Stage Alzheimer Disease

Kimberly K. Powlishta, PhD; Martha Storandt, PhD; Tammy A. Mandernach, BA; Ellen Hogan, MA; Elizabeth A. Grant, PhD; John C. Morris, MD

Background: Depression can interfere with the normal expression of cognitive abilities in adults of all ages, but it is unclear if depression in demented people, which is common, is associated with reduced cognitive performance beyond the effect of the dementia itself.

Objective: To determine if depression adds to the cognitive deficit in dementia.

Design: Performance on psychometric tests of memory and other cognitive function was correlated with the number of depressive features reported by the individual and by a knowledgeable collateral source, as well as the judgment of a research clinician as to whether the person was depressed.

Setting: An Alzheimer disease research center.

Participants: The convenience sample included individuals with very mild (Clinical Dementia Rating, 0.5; n = 167 [mean age, 76.03 years]) or mild (Clinical Dementia Rating, 1; n = 155 [mean age, 78.41 years]) Alzheimer disease who were enrolled in ongoing longitudinal studies at the center.

Main Outcome Measures: Psychometric measures of memory and cognition.

Results: Depression was present in 15% of the very mild and 24% of the mild dementia groups. There was no relation between the clinicians’ diagnoses of depression and psychometric scores. Little relation was found between performance on the cognitive tests and the number of depressive features (maximum, 9) reported by the individual or collateral source. The few statistically significant (P<.05) correlations were modest (r=.21).

Conclusion: Depression does not worsen cognitive test performance beyond the effect of dementia.

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REPORTED DEPRESSION IS COMMON in people with dementia. Epidemiological data indicate prevalence rates of 30% to 50% for significant depressive symptoms among people with dementia of the Alzheimer type (DAT).1 Rates of depression may be higher in the earlier stages of Alzheimer disease.2 Even in cognitively normal younger or older adults, depression can interfere with the normal expression of cognitive abilities. Although the results of studies are somewhat mixed, slowed mental processing and deficits in attention and executive function seem to be more likely in depressed than in nondepressed individuals in the absence of dementia.3,4 Individuals with late-onset depression have more significant cognitive impairment.5 We know less, however, about whether depression in demented people is associated with reduced cognitive performance beyond the effect of the dementia itself. That is, if dementia severity were held constant, would depressed demented people perform more poorly than nondepressed demented people? Addressing this question was the primary goal of the present study.

Individuals who are diagnosed as having depression and dementia are reported to have excess impairment in functional abilities.6-10 Results of studies looking at specific cognitive abilities have been less definitive. Most of these studies11-15 found no difference in cognitive performance between depressed DAT patients and nondepressed DAT patients. A single study16 found patients with DAT and depression performed worse than DAT patients without depression on tasks of attention and psychomotor speed. Therefore, one reason for the conflicting reports may be related to the measures of cognition examined. Depression may have an added effect on timed tasks or measures of attention but not on tests of memory, which is already severely affected by dementia. Also, it is possible that an added effect of depression may be seen in some stages of dementia but not others.7

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In this study, we used information about the stage of dementia in groups of people with similar degrees of dementia severity and examined performance on several specific neuropsychological tests. We expected to see the greatest cognitive impairment in demented people with depression on those cognitive tasks shown previously to be especially susceptible to the effects of depression in cognitively normal younger and older adults. Therefore, a second goal of the present study was to determine whether diagnosed depression or reports of depressive features in demented individuals were associated with additional impairment in performance, particularly on timed tasks or tasks requiring effortful attention.

## METHODS

### SAMPLE

Data were available for 322 individuals withDAT who were enrolled in a longitudinal study at an Alzheimer disease research center in a midwestern urban area and who came in for an annual evaluation between October 21, 1996, and March 27, 2002. Only the first assessment during that period was included for individuals who returned for more than 1 assessment. Other data from many of these participants have appeared in numerous publications from the center. The project was approved by a university institutional review board.

Experienced clinicians assessed each older adult for the presence and severity of dementia using the Clinical Dementia Rating (based on a 90-minute semistructured interview with the research participant and a knowledgeable collateral source (usually a spouse or adult child), followed by a neurological examination of the participant. The diagnosis of DAT was based on a history of gradual onset and progressive cognitive impairment and was comparable to that specified in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Diag nostic accuracy for Alzheimer disease as verified by postmortem examination in 207 individuals is 93%. If these features had occurred in the participant. Previous work has suggested that the collateral source is important to the diagnosis of depression in demented individuals.

### PSYCHOMETRIC BATTERY

Participants completed a 2-hour battery of standard psychometric tests approximately 2 weeks after clinical evaluation. Psychometricians were unaware of the results of the clinical evaluation or prior psychometric testing. The tests included the mental control, logical memory, digit span (forward and backward), and associate learning subtests of the Wechsler Memory Scale; Visual Retention Test (Form C, 10-second exposure and Form D, copying); Boston Naming Test; word fluency for S and P (60 seconds allowed for each letter); information, block design, and digit symbol subtests of the Wechsler Adult Intelligence Scale; Trail-Making Test A and C; and Crossing-off. The standard tests were administered according to their manuals except for the Boston Naming Test, for which all items were administered and no cues were given. A high score indicates good performance on all tests except the Trail-Making Test, for which the score was time; a cutoff of 180 seconds was used.

In addition to the scores for each test in the battery, a factor score was computed using all the tests in the battery. The means, standard deviations, and weights used to compute this composite were based on a principal components analysis of 81 nondemented individuals that revealed a single component accounting for 37% of the variance.

### STATISTICAL ANALYSIS

Because dementia severity affects level of performance on the psychometric tests, correlations between the psychometric scores and the 3 indexes of depression (clinician’s judgment and number of depressive features reported by the participant and collateral source) were computed for the very mildly and mildly demented groups separately.

The correlations between the psychometric scores and the measures of depression are shown in Table 2. The only anticipated pattern of poorer performance in timed or attention-requiring tests was in the mildly demented group. Poorer performance on 3 timed tests (block design, digit symbol, and Trail-Making A) was modestly correlated with reports of more depressive features by the participants. The value of the participant’s report of depressive features is important in light of the lack of the

### TABLE 1. SAMPLE CHARACTERISTICS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Very Mild Dementia (n = 167)</th>
<th>Mild Dementia (n = 155)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>76.03 (8.13)</td>
<td>78.41 (8.07)</td>
</tr>
<tr>
<td>Education, y</td>
<td>13.54 (3.44)</td>
<td>12.27 (3.22)</td>
</tr>
<tr>
<td>Mini-Mental State Examination score, range 1-90</td>
<td>25.13 (3.02)</td>
<td>21.03 (3.90)</td>
</tr>
<tr>
<td>Men, %</td>
<td>44</td>
<td>29</td>
</tr>
</tbody>
</table>

*Data are given as mean (SD) unless otherwise indicated.

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expected correlations (Table 2) between the timed and attentational test results and the clinician’s diagnosis of depression or the number of depressive features reported by the collateral source. The clinician and the collateral source may have difficulty differentiating depression from cognitive impairment, especially as the cognitive impairment progresses. The correlations among the 3 reports of depression (from the participant, collateral source, and clinician) ranged from 0.36 to 0.42 in the very mild dementia group. In the mild dementia group the reports of depressive features by the collateral and clinical sources were similarly related (r = 0.43), but the depression scores provided by participants were less strongly related to those of the collateral source (r = 0.20) and clinician (r = 0.25). It has long been noted that the differential diagnosis of depression and dementia in older adults can be difficult because symptoms of depression and dementia overlap considerably.20,21,29 Therefore, some older individuals may appear to have dementia when they are depressed instead. The present results indicate a related problem. That is, features of depression include diminished interest in work or hobbies and indecisiveness, which could be mistaken as impairments in functional activities resulting from cognitive impairment. These overlapping symptoms may make it difficult to determine whether a demented individual has depression as well. It is therefore important to give credence to the demented person’s reports of symptoms of depression. It is somewhat surprising, however, that this modest pattern of correlation between the demented individual’s report of depressive features and performance on timed tests was seen in the mildly demented group rather than in the very mildly demented group, in whom one might expect greater insight. Therefore, although these modest correlations occurred where they were expected to, it is possible that they represent type I errors, given the large number of correlations computed.

Our results show that there was little relation between the indexes of depression and performance on this battery of psychometric tests. Those correlations that were statistically significant at α = 0.05 were small in magnitude (≤0.21). It appears that the deleterious effect of major depression on test performance seen in nondemented individuals is superseded by the global effect of the dementia in people with Alzheimer disease.

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Author Contributions: Study concept and design: Powlishta, Storandt, and Morris. Acquisition of data: Powlishta, Grant, and Morris. Analysis and interpretation of data: Powlishta, Storandt, Morris, Mandernach, and Hogan. Drafting of the manuscript: Powlishta, Storandt, Mandernach, and Hogan. Critical revision of the manuscript for important intellectual content: Storandt, Morris, and Mandernach. Statistical expertise: Powlishta, Storandt, and Hogan. Obtained funding: Morris. Administrative, technical, and material support: Grant and Morris. Study supervision: Morris.

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### Table 2. Correlations Between Scores on Psychometric Measures and 3 Types of Reports of Depression for 2 Demented Groups

<table>
<thead>
<tr>
<th>Psychometric Measure</th>
<th>Very Mildly Demented</th>
<th>Mildly Demented</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Clinician*</td>
<td>Self</td>
</tr>
<tr>
<td>Mental control</td>
<td>−0.02</td>
<td>−0.08</td>
</tr>
<tr>
<td>Logical memory</td>
<td>−0.03</td>
<td>0.02</td>
</tr>
<tr>
<td>Digit span forward</td>
<td>0.08</td>
<td>0.04</td>
</tr>
<tr>
<td>Digit span backward</td>
<td>−0.12</td>
<td>−0.15</td>
</tr>
<tr>
<td>Associate learning</td>
<td>−0.02</td>
<td>0.08</td>
</tr>
<tr>
<td>Benton (10-second delay)</td>
<td>0.02</td>
<td>−0.02</td>
</tr>
<tr>
<td>Benton (copy)</td>
<td>0.07</td>
<td>0.03</td>
</tr>
<tr>
<td>Boston Naming</td>
<td>0.05</td>
<td>−0.03</td>
</tr>
<tr>
<td>Word fluency</td>
<td>−0.08</td>
<td>−0.11</td>
</tr>
<tr>
<td>Information</td>
<td>−0.04</td>
<td>−0.10</td>
</tr>
<tr>
<td>Block design</td>
<td>−0.07</td>
<td>−0.08</td>
</tr>
<tr>
<td>Digit symbol</td>
<td>−0.02</td>
<td>−0.14</td>
</tr>
<tr>
<td>Trail-Making A</td>
<td>−0.02</td>
<td>0.06</td>
</tr>
<tr>
<td>Crossing-off</td>
<td>0.16†</td>
<td>0.11</td>
</tr>
<tr>
<td>Factor score</td>
<td>0.00</td>
<td>−0.07</td>
</tr>
</tbody>
</table>

*Clinician judgments were coded 1 if depression was present, 0 if absent.
†P<.05.

### REFERENCES
