Loss of Calculation Abilities in Patients With Mild and Moderate Alzheimer Disease

Roy C. Martin, PhD; Shannon M. Annis, MS; Laurie Z. Darling, BA; Virginia Wadley, PhD; Lindy Harrell, MD, PhD; Daniel C. Marson, JD, PhD

**Background:** Calculation deficits are a common early manifestation of Alzheimer disease (AD).

**Objective:** To investigate oral and written calculation skills in AD patients using quantitative and qualitative methods.

**Design:** Comparison among controls, patients with mild AD, and patients with moderate AD on measures of arithmetic skill.

**Setting:** Tertiary care university medical center.

**Participants:** Twenty patients with AD (11 with mild AD, 9 with moderate AD) and 23 elderly controls.

**Main Outcome Measures:** Tests of oral arithmetic (Wechsler Adult Intelligence Scale–Third Edition [WAIS-III] Arithmetic subtest) and written arithmetic (Wide Range Achievement Test-3 [WRAT-3] Arithmetic subtest) were administered, and overall group differences were examined. Errors on selected WRAT-3 problems were qualitatively analyzed across groups using a set of error codes.

**Results:** Patients with mild and moderate AD performed significantly below controls on both oral and written arithmetic tasks (P<.001). Patients with moderate AD performed worse than those with mild AD on written arithmetic (P<.002) but not on oral arithmetic tasks. On selected WRAT-3 problems, single- and multidigit addition and subtraction operations and single-digit division operations were preserved in patients with mild AD. In contrast, only single-digit addition was preserved in patients with moderate AD. Errors of operation substitution and number position were the most common error types observed in AD patients. Patients with moderate AD displayed multiple error types and high incidence rates compared with controls, while patients with mild AD exhibited error types and incidence rates intermediate to controls and patients with moderate AD.

**Conclusions:** A decline in calculation abilities is one of the hallmark cognitive features of AD. Patients with mild AD maintain relative preservation of simple written calculation skills but demonstrate marked impairment as task complexity increases. Patients with moderate AD demonstrate global impairments extending to the simplest arithmetic skills. These findings suggest that loss of calculation abilities in AD is both hierarchical (by arithmetic operation) and a function of disease severity.

Arch Neurol. 2003;60:1585-1589

CALCULATION DEFICITS can occur early in the course of Alzheimer disease (AD) and can have substantial consequences for everyday functioning. Relative to controls, AD patients demonstrate deficits in both written and oral arithmetic skills. The extent of the calculation deficits in AD patients may correlate with dementia severity, and cortical regions associated with calculation abilities demonstrate degeneration. Calculation abilities in AD may deteriorate in a hierarchical manner, beginning with more complex arithmetic skills and extending eventually to more basic operations, although atypical preservation of arithmetic skills has also been noted.

In one study, AD patients performed equivalently with controls on simple single-digit arithmetic problems but demonstrated severe impairment on multiple-step arithmetic problems. However, the hierarchical nature of calculation loss in AD has not been systematically examined across dementia stage. In addition, little is known about the types and incidence rates of calculation errors across dementia stage in AD.

We built on prior case and group studies by conducting both quantitative and qualitative analyses of dyscalculia in AD across dementia stage, employing commonly used arithmetic measures. We first investigated oral and written calculation.
performance in patients with mild and moderate AD, using 2 well-standardized clinical measures. We then used a subset of written arithmetic problems and examined group performance on basic mathematical operations (addition, subtraction, multiplication, and division). Finally, we examined qualitative error types on written arithmetic problems to highlight changing calculation deficits in mild and moderate AD.

METHODS

SUBJECTS

Patients with Alzheimer disease were diagnosed using National Institute of Neurological and Communication Disorders and Stroke—Alzheimer’s Disease and Related Disorders Association criteria by 2 board certified neurologists in a memory disorders clinic at a tertiary care university medical center. Patients with AD were subdivided into mild (n = 11) and moderate (n = 9) AD subgroups according to published criteria, with mild AD defined as a Mini-Mental State Examination (MMSE) score greater than 20, and moderate AD defined as an MMSE score between 10 and 20.4 One AD patient with an MMSE score of 8 was included in the moderate group based on the diagnostic consensus of the treating neurologists. Controls were recruited from community advertisements. Controls had MMSE scores equal to or greater than 1 SD below the mean for their age and education. Informant reports for controls verified no cognitive impairment history. Participants were screened for medications and medical and psychiatric conditions that might affect cognition. Informed consent was obtained from all subjects and from AD caregivers as part of this institutional review board–approved research.

MEASUREMENTS AND PROCEDURES

Participants were administered the Wechsler Adult Intelligence Scale–Third Edition (WAIS-III) Arithmetic subtest15 and the Wide Range Achievement Test–3 (WRAT-3) Arithmetic subtest.16 Test problems ranged in difficulty from simple calculation items to problems requiring knowledge of percentages, probability, and algebraic principles. The WAIS-III Arithmetic subtest is a psychometric component of the WAIS-III Working Memory Index and the WAIS-III Verbal Intelligence score.15 The WRAT-3 Arithmetic subtest is a 55-item test of written arithmetic with separate written (40 items) and oral (15 items) sections.16

WRAT-3 Analyses by Arithmetic Operation

A subset of 21 written WRAT-3 items provided specific information on the breakdown of operational knowledge (addition, subtraction, multiplication, and division). Arithmetic problems 1 through 19, 22, and 29 from the WRAT-3 were used. Single-digit (n = 10) and multiple-digit (n = 11) problems were included. Seven of the 20 AD patients completed all 21 problems, 5 patients completed 20 of 21 problems, and all patients but 3 attempted 16 or more problems. Of the controls, 21 of 23 individuals completed all 21 problems. The study sample was assumed to have premorbid educational and everyday experience with all 21 problems, since all study participants had at least ninth-grade education, and each subset item fell below a seventh-grade difficulty level.

WRAT-3 Error Analysis

We also conducted analyses of error types on the selected WRAT-3 problems. Error codes were based on previously described arithmetic error types7,16-19 but were expanded for this study. Coding was conducted by one of us (S.A.). In cases where error source was ambiguous, no error code was assigned. Different error codes could be applied within one problem, but multiple instances of a single error type within a problem were coded only once. The following error codes and definitions were used:

- Factual errors: Incorrect application of an arithmetic table fact (eg, 6 × 7 = 48) (all 10 single-digit problems).
- Borrowing errors: For subtraction problems that required borrowing, participants either omitted the borrowing procedure or performed it incorrectly (problems 12 and 16).
- Carrying errors: For addition and multiplication problems that required carrying, the participant either omitted the carrying procedure or performed it incorrectly (problems 9, 15, 17, and 22).
- Operation substitution: Substitution of one arithmetic operation for another (eg, 4 × 3 = 7) (all 21 problems).
- Positional errors: Misplaced answers in relation to the problem space or misaligned columns (all 21 problems).
- Perseveration errors: Participants either copied a digit from one of the operands or wrote the same number multiple times (all 21 problems).
- Zero errors: Misuse or misunderstanding of the properties of zero (problem 29).

RESULTS

DEMOGRAPHIC COMPARISONS

Controls and patients did not differ significantly in age or years of education (Table 1). As expected, the mean MMSE score in the control group was significantly higher than that for either AD subgroup (P < .001).

STANDARDIZED ARITHMETIC TESTS

The AD subgroups performed inferiorly to controls (P < .001) on both oral and written arithmetic tests (Table 1). Age and education level were not related to group effects for either test. Patients with moderate AD performed significantly worse than patients with mild AD on WRAT-3 Arithmetic (P < .002), but similarly on WAIS-III Arithmetic. The total number of problems attempted on the WRAT-3 Arithmetic subtest differed significantly between the AD subgroups and controls (P < .001). Patients with mild AD attempted a mean (SD) of 28.0 (1.3) problems, patients with moderate AD attempted 17.8 (1.4) problems, and controls attempted 32.8 (0.8) problems. The MMSE score correlated significantly with AD patient performance on WAIS-III Arithmetic (r = 0.42;
vision problems. Patients with moderate AD performed worse than controls on single-digit addition and multiple-digit multiplication and division. The AD group were higher than for controls across 5 of the 7 operations except single-digit addition, and performed significantly worse than controls only on the more complex single- and multiple-digit multiplication and division problems. In contrast, patients with moderate AD showed a higher proportion of errors of all types except factual and zero errors. Errors were recorded in at least 1 control subject across 5 of the 7 error categories, albeit at lower rates than either AD subgroup.

Error Analyses

Table 3 presents error rates on the selected WRAT-3 problems. Examples of each error type are shown in the Figure. Positional errors, operation substitutions, perseverations, borrowing errors, and carrying errors were produced more frequently in patients with moderate AD compared with controls. The mean error rates for the mild AD group were higher than for controls across 5 of the 7 error categories. When AD patients made operation substitution errors, addition was the operation most often substituted (90% of the occurrences of operation substitution).

Compared with controls, patients with mild and moderate AD exhibited a higher proportion of group members making errors across all error types (except borrowing errors in mild AD) (Table 4). Compared with the mild AD group, patients with moderate AD exhibited a higher proportion of errors of all types except factual and zero errors. Errors were recorded in at least 1 control subject across 5 of the 7 error categories, albeit at lower rates than either AD subgroup.

Our findings support the view that dyscalculia occurs early in AD and progresses. Patients with AD demonstrated significant loss of oral and written calculation abilities relative to controls and produced a variety of specific errors. Given that the WAIS-III Arithmetic subtest is a complex auditory cognitive task simultaneously tapping language, attention, working memory, and construction abilities, it is not surprising that both patient groups performed poorly. Regarding written arithmetic abilities, patients with mild AD differed significantly from controls only on the more complex single- and multiple-digit multiplication and division problems. In contrast, patients with moderate AD showed global impairment relative to controls on all written arithmetic problems except single-digit addition, and performed inferior to patients with mild AD on all problems except single-digit addition and multiple-digit division.

In general, calculation errors were affected by problem complexity (ie, single digit vs multiple digit) and op-

Table 1. Demographic Information and Group Comparisons**†

<table>
<thead>
<tr>
<th>Table 1. Demographic Information and Group Comparisons**†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Possible Score, Range</strong></td>
</tr>
<tr>
<td>Controls (n = 23)</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Age, y</td>
</tr>
<tr>
<td>Education</td>
</tr>
<tr>
<td>Sex, M/F</td>
</tr>
<tr>
<td>Race, White/African American</td>
</tr>
<tr>
<td>MMSE score</td>
</tr>
<tr>
<td>WAIS-III Arithmetic# standard score</td>
</tr>
<tr>
<td>WRAT-3 Arithmetic** standard score</td>
</tr>
</tbody>
</table>

Abbreviations: AD, Alzheimer disease; MMSE, Mini-Mental State Examination; NA, not applicable; WAIS-III, Wechsler Adult Intelligence Scale–Third Edition; WRAT-3, Wide Range Achievement Test–3.

*Data are given as mean (SD) unless otherwise indicated.
†A $t$ test was employed to determine group differences.
‡Control mean differed significantly from mild AD mean at $P<.01$ using the least significant difference (LSD) post hoc test.
§Control mean differed significantly from mild AD mean at $P<.001$ using the LSD post hoc test.
¶Control mean differed significantly from moderate AD mean at $P<.01$.
‖Control mean differed significantly from moderate AD mean at $P<.001$.
#Mild SD mean differed significantly from moderate AD mean at $P<.01$.
¶¶Mild SD mean differed significantly from moderate AD mean at $P<.001$.
¶¶¶Mild SD mean differed significantly from moderate AD mean at $P<.01$.
§Control mean differed significantly from moderate AD mean at $P<.05$.
§§Mild SD mean differed significantly from moderate AD mean at $P<.05$ using the least significant difference (LSD) post hoc test.
||Control mean differed significantly from moderate AD mean at $P<.001$.
¶¶¶¶Mild SD mean differed significantly from moderate AD mean at $P<.01$.
**Control mean differed significantly from moderate AD mean at $P<.01$ using the LSD post hoc test.

P<.05, overall WRAT-3 Arithmetic ($r=0.56$; $P<.01$), and the WRAT-3 problem subset ($r=0.48$; $P<.02$).

Performance on Mathematical Operations by Group

On the WRAT-3 subset, patients with mild AD performed equivalently with controls on single-digit addition, subtraction, and division, and on multiple-digit addition and subtraction problems (Table 2). Patients with mild AD performed worse than controls on single-digit multiplication and multiple-digit multiplication and division problems. Patients with moderate AD performed significantly worse than controls on all problems except single-digit addition. Patients with moderate AD performed significantly worse than patients with mild AD on single-digit division and on multiple-digit problems of addition, subtraction, and multiplication. The AD subgroups showed no differences in the multiple-digit division problems.

Table 2. Group Comparisons for WRAT-3 Specific Operations

<table>
<thead>
<tr>
<th>Table 2. Group Comparisons for WRAT-3 Specific Operations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WRAT-3 Selected Problem Subset</strong></td>
</tr>
<tr>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Single-digit operations</td>
</tr>
<tr>
<td>Addition</td>
</tr>
<tr>
<td>Subtraction</td>
</tr>
<tr>
<td>Multiplication</td>
</tr>
<tr>
<td>Division</td>
</tr>
<tr>
<td>Multiple-digit operations</td>
</tr>
<tr>
<td>Addition</td>
</tr>
<tr>
<td>Subtraction</td>
</tr>
<tr>
<td>Multiplication</td>
</tr>
<tr>
<td>Division</td>
</tr>
<tr>
<td>All problems</td>
</tr>
</tbody>
</table>

Abbreviations: AD, Alzheimer disease; WRAT-3, Wide Range Achievement Test–3.

*WRAT-3 problem subset selected to illustrate group performance by arithmetic operation and problem difficulty (see the “Methods” section).
†Mild SD mean differed significantly from moderate AD mean at $P<.01$.
‡Mild SD mean differed significantly from moderate AD mean at $P<.05$.
§Control mean differed significantly from mild AD mean at $P<.05$ using the least significant difference (LSD) post hoc test.
¶Control mean differed significantly from moderate AD mean at $P<.001$.
¶¶Mild SD mean differed significantly from moderate AD mean at $P<.01$.
¶¶¶Mild SD mean differed significantly from moderate AD mean at $P<.001$.
**Control mean differed significantly from mild AD mean at $P<.01$ using the LSD post hoc test.
Errors of operation substitution, arithmetic facts, carrying, and position were more frequently observed in AD patients relative to controls, while errors of perseveration and borrowing were unique to AD patients. These results indicate that a wide range of calculation skills, such as arithmetic fact knowledge, progressively deteriorates in AD. The diverse range of arithmetic errors by AD patients likely reflects the gradual deterioration of multiple cognitive functions, including loss of semantic meaning of specific arithmetic operations.7,23,24

The clinical implications of this study are limited, owing to sample size and the restricted problem set for error analyses. Nonetheless, this study contributes new information about the progressive loss of calculation abilities in AD. Future studies incorporating a longitudinal design with a broader range of calculation tasks and cognitive measures can further enhance our understanding of dyscalculia in primary dementias such as AD.

Accepted for publication February 4, 2003.

Author contributions: Study concept and design (Drs Martin, Wadley, and Marson, and Ms Annis and Darling); acquisition of data (Ms Annis and Drs Harrell and Marson); analysis and interpretation of data (Drs Martin, Wadley, and Marson, and Ms Annis and Darling); drafting of the manuscript (Drs Martin, Wadley, and Marson, and Ms Annis); critical revision of the manuscript for important intellectual content (Drs Martin, Harrell, and Marson, and Ms Annis); statistical expertise (Drs Martin and Marson); obtained funding (Drs Harrell and Marson); administrative, technical, and material support (Ms Annis and Drs Harrell and Marson); study supervision (Drs Wadley and Marson).

The research was supported by grant R01MH55247-07A2 from the National Institute of Mental Health, Bethesda, Md (Dr Marson), and from the Alzheimer’s Disease Research Center (Dr Harrell) and Project 2 (1P50 AG16582-01) (Dr Marson), National Institute on Aging, Bethesda.

We gratefully acknowledge the manuscript review and comments of Randall Griffith, PhD.
REFERENCES