Premorbid Reading Activity and Patterns of Cognitive Decline in Alzheimer Disease

Robert S. Wilson, PhD; David A. Bennett, MD; David W. Gilley, PhD; Laurel A. Beckett, PhD; Lisa L. Barnes, PhD; Denis A. Evans, MD

Background: Educational and occupational attainment have been associated with progression of Alzheimer disease in some studies. One hypothesis about this association is that education and occupation are markers for lifelong participation in cognitively stimulating activities like reading.

Objective: To assess the relation of premorbid reading activity with patterns of cognitive decline in Alzheimer disease.

Methods: During a 4-year period, 410 persons with Alzheimer disease had annual clinical evaluations, which included administration of 17 cognitive function tests from which global, verbal, and nonverbal summary measures were derived. At baseline, a knowledgeable informant was questioned about the affected person’s reading frequency and access to reading materials before dementia onset.

Results: A composite measure of premorbid reading activity was developed. It had moderately high internal consistency and was positively correlated with education and baseline level of cognitive function. In analyses that controlled for baseline cognitive function, education, and other demographic variables, higher level of premorbid reading activity was associated with more rapid decline on the global cognitive and verbal measures but not on the nonverbal measure.

Conclusions: These results suggest that both the extent and nature of premorbid cognitive experiences may affect how Alzheimer disease pathology is clinically expressed.

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Progressive decline in cognitive function is a defining feature of Alzheimer disease, but there are substantial differences in rates of progression. As a result, there is much interest in understanding factors that contribute to this variability, especially potentially modifiable ones. Previous research has suggested that level of educational or occupational attainment may be associated with rate of progression of Alzheimer disease, but the basis of this association is uncertain. One possibility is that educational and occupational attainment are markers for cognitively stimulating experiences occurring over the life span. If this is true, then the amount and nature of these experiences should be independently related to progression, even after considering the effects of education or occupation.

In the present study, we examined whether frequency of premorbid reading activity was related to rate of cognitive decline in Alzheimer disease. During a 4-year period, a large group of affected persons had annual evaluations that included detailed testing of verbal and nonverbal cognitive functions. As part of the baseline evaluation, an informant was interviewed about the participant’s typical reading frequency and access to materials that supported reading before the onset of memory and thinking problems. We developed a summary measure of premorbid reading activity from these questions and tested its association with rate of global cognitive decline using a growth curve approach. In addition, to see if the effect of reading experience was mainly confined to verbal skills, we repeated the analysis using summary measures of verbal and nonverbal abilities. Secondary analyses also examined the effects of education because of its use in prior research.

Results: A composite measure of premorbid reading activity was developed. It had moderately high internal consistency and was positively correlated with education and baseline level of cognitive function. In analyses that controlled for baseline cognitive function, education, and other demographic variables, higher level of premorbid reading activity was associated with more rapid decline on the global cognitive and verbal measures but not on the nonverbal measure.

Conclusions: These results suggest that both the extent and nature of premorbid cognitive experiences may affect how Alzheimer disease pathology is clinically expressed.

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PARTICIPANTS AND METHODS

PARTICIPANTS

Participants were recruited from the Rush Alzheimer’s Disease Center, as previously described. Eligibility was determined at baseline and required a clinical diagnosis of Alzheimer disease, a Mini-Mental State Examination (MMSE) score greater than 10, and community residence. These criteria were met by 492 people, and 410 agreed to participate. Informed consent was obtained from participants and family members, following procedures approved by the Institutional Review Board of Rush-Presbyterian-St Luke’s Medical Center.

At baseline, mean age was 75.5 years (SD, 7.3) and mean years of education completed was 12.0 (SD, 3.4). There were 274 women and 136 men; 61 persons were African American and 349 were white. The mean baseline MMSE score was 18.7 (SD, 4.3).

PROCEDURE

Clinical Evaluation

At baseline, each person had a uniform, structured clinical evaluation that was repeated annually for up to 4 years, with examiners blinded to previously collected data. Evaluation components included a medical history, neurologic examination, cognitive function assessment, and informant interview. Laboratory tests and brain scans were done at baseline only.

The diagnosis of Alzheimer disease was made by a board-certified neurologist and was based on the criteria of the joint working group of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association. These criteria require a history of cognitive decline and evidence of impairment in memory and cognition; 380 persons met criteria for probable Alzheimer disease and 30 met criteria for possible Alzheimer disease due to the presence of another condition that contributed to cognitive impairment. Exclusion of the possible subgroup did not change results, so it is included in all analyses in this article. As previously reported, 52 of 54 brain autopsies in this cohort have met CERAD (Consortium to Establish a Registry for Alzheimer’s Disease) pathological criteria for Alzheimer disease.

Assessment of Cognitive Function

Eighteen cognitive tests were administered at each evaluation. The MMSE was used for descriptive purposes. Because of the wide range of cognitive function in Alzheimer disease, floor and ceiling effects are often encountered on individual tests. To reduce these and other sources of measurement error, composite scores, based on several tests, were used in analyses. The primary outcome was a composite based on 17 individual tests of memory, language, and visuocostruction. To see if premorbid reading experience was more strongly related to verbal than nonverbal ability, summary verbal (based on 3 memory and 8 language tests) and nonverbal (based on 3 memory and 3 visuocostruction tests) measures were also formed. For each measure, raw scores were transformed to z scores, using the baseline mean and SD, and then averaged to yield the summary measure.

Assessment of Premorbid Reading Activity

We studied reading because it is an important cognitive skill that is commonly performed and readily observable. We assessed both reading frequency and the availability of reading resources in the home environment. At baseline, the person with the most daily contact with the participant underwent a structured interview that included 8 questions about the participant’s reading frequency and access to reading materials during adult life until approximately 5 years before the onset of memory and thinking problems. The informant estimated the typical daily hours spent reading books, magazines, and newspapers (none, <1 hour, 1 hour to less than 2 hours, 2 hours to less than 3 hours, ≥3 hours); number of books read annually (0, 1-5, 6-10, 11-50, >50); number of books in the home (<20, 20-49, 50-100, 101-249, ≥250); whether the home had a dictionary or bookcase; and whether the participant had a library card.

A composite measure of premorbid reading activity was formed by summing item scores. Missing scores on up to 4 items were permitted, in which case item scores were imputed by converting the person’s valid item scores to z scores, assigning the mean of these z scores to the missing item, and then converting that z score back to a raw score.

FOLLOW-UP PARTICIPATION

There were 141 deaths during the study. Of the 387 persons who survived to the first follow-up, 354 (91.5% of survivors) had at least 2 valid composite cognitive scores (mean of 3.8 scores per person) and therefore were eligible for longitudinal analyses. Further information about follow-up participation is published elsewhere.

DATA ANALYSIS

The frequencies of responses to the premorbid reading questionnaire items were examined. The associations among premorbid reading items were assessed with pairwise correlations, item-total correlations, and coefficient α to determine how best to form a summary measure. Pairwise correlations were used to assess the relation of the summary measure to demographic variables.

Random effects regression models were used to characterize individual paths of change in cognitive function during the study period and to test whether the reading measure and covariates were related to initial level of or rate of change in cognitive function. To simplify interpretation, centered versions of the premorbid reading measure (at a score of 8), age (at 75 years), and education (at 12 years) were used in all analyses. Change in each was assumed to follow the mean path except for random effects that caused the baseline level to be higher or lower and the rate of change to be faster or slower. The 2 random effects were assumed to follow a bivariate normal distribution and were used to estimate growth curves for each person, and these were plotted. Model assumptions regarding linearity, normality, independence of errors, and homoscedasticity of errors were examined graphically and analytically and found to be adequately met.
about premorbid reading (mean of 7.4 valid item scores per person). The remaining 48 persons were missing all (n=44) or more than half (n=4) of the reading items. They were equivalent in age, education, sex, race, and baseline MMSE to the subgroup for whom questionnaire data were available.

Correlations among the 8 premorbid reading items (Table 1) were positive and of modest size (median \( r = 0.25 \)). The correlations of each item with the total for the other 7 items ranged from 0.24 to 0.65 (median \( r = 0.45 \)). Given this evidence of shared item variance, a composite premorbid reading measure was formed by summing responses to the 8 items.

The distribution of the composite premorbid reading measure was approximately normal (Figure 1). Scores ranged from 0 to 21 (mean [SD] score, 8.00 [3.96]), with higher scores indicating more premorbid reading activity. Coefficient \( \alpha \) was .70, indicating moderately high internal consistency. There was a small negative correlation of premorbid reading score with age (\( r = -0.11, P < .05 \)) and a stronger positive correlation with education (\( r = 0.32, P < .01 \)). Premorbid reading scores were slightly lower for African Americans compared with white persons (\( t = 2.40, P < .05 \)) and equivalent in men and women (\( t = 0.04, P > .50 \)).

### Table 1. Correlations of Premorbid Reading Items With Other Items and Adjusted Item Totals

<table>
<thead>
<tr>
<th>Reading and Reading-Related Items</th>
<th>Newspaper Read</th>
<th>Magazine Read</th>
<th>Books Read/h</th>
<th>Books Read/y</th>
<th>No. of Books in Home Dictionary</th>
<th>Bookcase in Home Library Card Owned Total*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Read newspaper (daily hours)</td>
<td>0.44</td>
<td>0.26</td>
<td>0.04†</td>
<td>0.08†</td>
<td>0.11</td>
<td>0.13</td>
</tr>
<tr>
<td>Read magazine (daily hours)</td>
<td>0.56</td>
<td>0.23</td>
<td>0.22</td>
<td>0.18</td>
<td>0.26</td>
<td>0.13</td>
</tr>
<tr>
<td>Read book (daily hours)</td>
<td>0.04†</td>
<td>0.36</td>
<td>0.13</td>
<td>0.28</td>
<td>0.37</td>
<td>0.37</td>
</tr>
<tr>
<td>Read book (yearly total)</td>
<td>0.04†</td>
<td>0.07†</td>
<td>0.04†</td>
<td>0.29</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>No. of books in home</td>
<td>0.22</td>
<td>0.38</td>
<td>0.42</td>
<td>0.47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dictionary in home</td>
<td>0.33</td>
<td>0.20</td>
<td>0.25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bookcase in home</td>
<td>0.30</td>
<td>0.37</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Library card</td>
<td>0.43</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Refers to adjusted item total, which is the sum of scores on the other 7 items.
† \( P < .05 \); all other \( P < .05 \).

### Table 2. Summary of Random Effects Models Examining the Relation of Time, Premorbid Reading, and Their Interaction to the Global Measure of Cognitive Function

<table>
<thead>
<tr>
<th>Model Terms</th>
<th>Unadjusted Model</th>
<th>Adjusted Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>(-0.57)†</td>
<td>(-0.57)†</td>
</tr>
<tr>
<td>Premorbid reading</td>
<td>(0.04)†</td>
<td>(0.03)†</td>
</tr>
<tr>
<td>Premorbid reading × time</td>
<td>(-0.02)‡</td>
<td>(-0.01)‡</td>
</tr>
</tbody>
</table>

* The adjusted model included terms for age, education, sex, race, and their interactions with time.
† \( P < .01 \).
‡ \( P < .05 \).

Random effects models were used to see how the premorbid reading score was related to baseline level of cognitive function and rate of change. The initial analysis used the global cognitive measure, which ranged from −1.68 to 1.36 at baseline (mean [SD] score, 0.00 [0.57]), with higher scores indicating better cognitive function. The model included terms for study time in years, premorbid reading score, and their interaction (Table 2). There was an average annual decline of 0.57 units on the global cognitive score (95% confidence interval, −0.50 to −0.64). Premorbid reading score was positively correlated with baseline cognitive score. For each 1-point increase in reading score, baseline cognitive score was 0.04 units greater, on average. Premorbid reading score was also related to rate of cognitive decline, as shown by the interaction term in the model. For each 1-point increase in reading score, the annual rate of cognitive decline increased by 0.02 units. Thus, the average rate of global cognitive decline associated with a premorbid reading score of 13 (90th percentile) was about 19% faster than the average rate expected for a person with a reading score of 3 (10th percentile).

Because of the association of demographic variables with both cognitive test performance and premorbid reading score, the analysis was repeated with terms...
for age, education, sex, race, and their interactions with time (Table 2). Results were essentially unchanged.

These analyses were repeated using summary measures of verbal and nonverbal ability as the outcomes. At baseline, the verbal score ranged from –2.26 to 1.37 (mean [SD] score, 0.00 [0.61]), and the nonverbal score ranged from –2.67 to 1.43 (mean [SD] score, 0.00 [0.67]). Table 3 shows results from analyses adjusted for demographic variables. Baseline level of each score was positively related to the premorbid reading score. The average annual decline on the verbal score was 0.60 units and this rate increased by 0.02 units for each 1-point increase in premorbid reading score. The rate of nonverbal decline was substantial (0.48 units per year) but not significantly related to premorbid reading score ($P = .41$).

To visually examine these associations, the predicted paths of verbal and nonverbal decline during the 4-year period were plotted for persons with premorbid reading scores at the 10th and 90th percentiles (Figure 2). For the verbal measure, decline is about 40% faster in the more frequent reader compared with the less frequent reader. For the nonverbal measure, rates of decline in the 2 persons are similar.

### EDUCATION AND COGNITIVE DECLINE

The relation of education with cognitive function was examined in a similar series of analyses (Table 4). In an initial model with terms for years of education, time, and their interaction, more educational attainment was associated with higher baseline level of cognitive function and more rapid cognitive decline, but these associations were no longer significant when terms for other demographic variables, premorbid reading, and their interactions with time were added to the model. Similar results were obtained with the verbal and nonverbal outcome measures (data not shown). That is, education was related to baseline level of and rate of change in both measures, but these effects were no longer significant after adjusting for other demographic variables and premorbid reading. Comparable results were also obtained when education was dichotomized as 8 years or less and more than 8 years, as was done in a previous study.$^3$

**Table 3. Summary of Random Effects Models Using Verbal and Nonverbal Outcome Measures With Terms for Time, Premorbid Reading, and Their Interaction**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Model Terms</th>
<th>Estimate</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal</td>
<td>Time</td>
<td>-0.60†</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>Premorbid reading</td>
<td>0.02†</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Premorbid reading × time</td>
<td>-0.02†</td>
<td>0.01</td>
</tr>
<tr>
<td>Nonverbal</td>
<td>Time</td>
<td>-0.48†</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>Premorbid reading</td>
<td>0.03†</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Premorbid reading × time</td>
<td>-0.01</td>
<td>0.01</td>
</tr>
</tbody>
</table>

* Terms for age, education, sex, race, and their interactions with time were also included.
†$P < .01$.
‡$P < .05$.

**Figure 2. Average decline in verbal (A) and nonverbal (B) summary scores for persons with high (90th percentile) and low (10th percentile) premorbid reading frequency.**

**Table 4. Summary of Random Effects Models Examining the Relation of Time, Education, and Their Interaction to the Global Measure of Cognitive Function**

<table>
<thead>
<tr>
<th>Model Terms</th>
<th>Unadjusted Model</th>
<th>Adjusted Model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>SE</td>
</tr>
<tr>
<td>Time</td>
<td>-0.57†</td>
<td>0.03</td>
</tr>
<tr>
<td>Education</td>
<td>0.04†</td>
<td>0.01</td>
</tr>
<tr>
<td>Education × time</td>
<td>-0.02‡</td>
<td>0.01</td>
</tr>
</tbody>
</table>

* The adjusted model included terms for age, sex, race, premorbid reading and their interactions with time. †$P < .01$; all other $P > .05$.

**COMMENT**

In this study, 410 people with Alzheimer disease underwent annual clinical evaluations for 4 years. At baseline, knowledgeable informants were interviewed about the affected person’s reading activity before dementia onset, and a composite measure of premorbid reading activity was developed from these questions. In analyses controlling for baseline level of cognitive function and demographic variables, including education, greater premorbid reading activity was associated with more rapid decline on measures of global cognitive function and verbal ability but not on a measure of nonverbal ability. These results suggest that both the extent and nature of premorbid cognitive experiences may influence the rate at
which cognitive skills are eroded by Alzheimer disease pathology.

Knowledge about how premorbid cognitive experience and ability are related to rate of cognitive decline in Alzheimer disease has come mainly from studies of education and occupation, which are related to both frequency of cognitive activity\(^{18,22-24}\) and performance on cognitive tests.\(^{25}\) One study found more rapid cognitive decline in those with more education,\(^{4}\) one study found a similar trend,\(^{26}\) another study obtained a similar trend for education and a significant effect for occupation,\(^{3}\) and one study had a null result.\(^{27}\) In this study, more educational attainment was associated with more rapid cognitive decline in initial analyses, but this effect was not statistically significant after controlling for premorbid reading level and other demographic variables.

Measurement of premorbid patterns of cognitive activity in persons with Alzheimer disease is difficult. We focused on reading because it is an important, common, and observable cognitive skill. Our informant-reported measure of premorbid reading activity showed moderately good internal consistency, and its validity is supported by its positive correlations with educational attainment and baseline level of cognitive function. We also found that premorbid reading was related to verbal but not nonverbal decline, implying that the effects of cognitive activity are relatively selective, mainly impacting those functions relevant to participation in the activity.

We considered the possibility that the informant report about premorbid reading behavior might have been influenced by how severely cognition was impaired at baseline. Baseline level of cognition was controlled in analyses, however. Furthermore, such an effect would presumably attenuate the observed association between activity and cognitive decline because those with lower baseline cognition tended to decline more rapidly.\(^{11}\)

These results are consistent with the hypothesis, by Stern and colleagues\(^{1,2,3}\) and others,\(^{2,26}\) that dementia progression in Alzheimer disease is more rapid in those with more highly developed premorbid cognitive ability. This is because experience and practice over the life span are hypothesized to change cognitive skills in ways that make them less vulnerable to disruption by mild levels of brain disease.\(^{8,10,28}\) As a result, more Alzheimer disease pathology is needed to cause dementia in persons with higher levels of premorbid skill. Once dementia is clinically evident, however, the protective benefits of premorbid experience and skill are assumed to have substantially diminished, and because Alzheimer disease pathology is relatively more advanced in those with higher premorbid skill levels, they are hypothesized to decline more rapidly.

We found that premorbid reading was related to cognitive decline in persons who already exhibited clinical signs of Alzheimer disease. Little is known about the relation of cognitive activities such as reading with risk of developing Alzheimer disease.\(^{29,30}\) Our study did not address this question directly, but the results are consistent with the hypothesis that such experience may be protective through the mechanism discussed above.\(^{1,3,5,38}\) This possibility is also supported by reports that cognitive activity is associated with reduced cognitive decline in old age.\(^{31,32}\)

This study has several strengths. First, the diagnosis of Alzheimer disease was based on uniform application of accepted criteria and has been confirmed in more than 90% of autopsied cases. Second, follow-up participation exceeded 90%, reducing the chance of bias due to selective attrition. Third, substantial information was available about each person's cognitive function history because of the 4-year study period, an average of about 4 evenly spaced evaluations per person, and the detailed cognitive testing at each evaluation. Fourth, the growth curve approach allowed us to model baseline level of cognitive function and rate of change as separate random effects and to test the association of reading and other covariates with each.

Several limitations should also be noted. First, participants were selected from a specialty clinic. Because a nonrandom fraction of people with Alzheimer disease come to medical attention, the full ranges of premorbid reading activity, education, and cognitive function are probably not represented in this study. Longitudinal studies of population-based samples of affected persons will be needed to more securely estimate how premorbid patterns of reading and other cognitive activities are related to progression of Alzheimer disease. Second, it is possible that some characteristics related to premorbid reading activity, but perhaps less modifiable, may account for its association with cognitive decline. Third, although the verbal and nonverbal ability measures had similar baseline distributions and rates of change, they may not be psychologically equivalent, and this could have contributed to their differential association with reading.

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REFERENCES