Linguistic Ability in Early Life and Cognitive Function and Alzheimer's Disease in Late Life

Findings From the Nun Study

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Objective.—To determine if linguistic ability in early life is associated with cognitive function and Alzheimer's disease in late life.

Design.— Two measures of linguistic ability in early life, idea density and grammatical complexity, were derived from autobiographies written at a mean age of 22 years. Approximately 58 years later, the women who wrote these autobiographies participated in an assessment of cognitive function, and those who subsequently died were evaluated neuropathologically.

Setting.—Convents in the United States participating in the Nun Study; primarily convents in the Milwaukee, Wis, area.

Participants.—Cognitive function was investigated in 93 participants who were aged 75 to 95 years at the time of their assessments, and Alzheimer's disease was investigated in the 14 participants who died at 79 to 96 years of age.

Main Outcome Measures.—Seven neuropsychological tests and neuropathologically confirmed Alzheimer's disease.

Results.—Low idea density and low grammatical complexity in autobiographies written in early life were associated with low cognitive test scores in late life. Low idea density in early life had stronger and more consistent associations with poor cognitive function than did low grammatical complexity. Among the 14 sisters who died, neuropathologically confirmed Alzheimer's disease was present in all of those with low idea density in early life and in none of those with high idea density.

Conclusions.—Low linguistic ability in early life was a strong predictor of poor cognitive function and Alzheimer's disease in late life.

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LOW ATTAINED education is associated with poor health and function in older adults[1-3] and a higher risk of Alzheimer's disease and dementia.[4-8] Individuals with low education may be more likely to develop dementia and other diseases because of lifestyle differences associated with education, such as nutrition, alcohol consumption, and occupational exposures. An alternate explanation is suggested by the threshold model of dementia.[8-11] This model proposes that individuals will exhibit dementia only if their cognitive or neurological reserve capacity falls below a specific threshold (eg, a critical volume of functional brain tissue). Thus, neurocognitive reserve developed in early life may buffer elderly individuals from the consequences of dementia.

Education may reflect the extent of cognitive ability and neurological development in early life and hence the availability of neurocognitive reserve in late life. Linguistic ability in early life may be a better marker than education of important aspects of cognitive ability, neurocognitive development, and neurologic reserve in early life. A high level of linguistic ability in early life may act as a buffer to cognitive decline by facilitating mnemonic processes for encoding, organizing, and retrieving information.[12-15] Kemper and colleagues[16-18] have shown that linguistic ability may be assessed by analyzing the form and content of oral and written language samples to reveal how normal aging and the progression of Alzheimer's disease affect linguistic ability. This research suggests that working memory limitations in healthy adults affect their ability to develop and use complex grammatical constructions, leading to a decline in grammatical complexity in late life. The progression of Alzheimer's disease is associated with declines in both grammatical complexity and density of ideas expressed in sentences. In the current study, we investigated the relationship of linguistic ability in early life to cognitive function and neuropathologically confirmed Alzheimer's disease in late life in a subset of the Nun Study population who had handwritten autobiographies from early life.

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METHODS

Study Population

Participants in the Nun Study are members of the School Sisters of Notre Dame religious congregation. In 1991 to 1993, American sisters born before 1917 were asked to join the Nun Study, a longitudinal study of aging and Alzheimer's disease. Of the 1027 eligible sisters, 678 (66%) agreed to participate and gave informed written consent. Participants and nonparticipants did not differ significantly by country of birth, age, race, or annual mortality rate. The participation rate in the Nun Study is relatively high given that all participants agreed to brain donation at death as well as annual assessments of cognitive and physical function.

We investigated the relationship of linguistic ability in early life to cognitive function and Alzheimer's disease in late life in a subset of 93 participants in the Nun Study. All 93 participants in the study were white and born in the United States and had handwritten autobiographies from early life on file in the convent archives.

Linguistic Ability

Autobiographies found in the archives were used to characterize the level of linguistic ability in early life. After an average of 4 years of training in the convent, each sister wrote an autobiography a few weeks before taking her religious vows. Archival information from the convent indicated that each sister was asked to "write a short sketch of her own life. This account should not contain more than two to three hundred words and should be written on a single sheet of paper ... include the place of birth, parentage, interesting and edifying events of one's childhood, schools attended, influences that led to the convent, religious life, and its outstanding events."

To ensure that autobiographies were composed by the sisters themselves, we used only handwritten autobiographies. We discovered a high percentage of handwritten autobiographies for participants in the Nun Study who were born in the United States and who joined the Milwaukee Province during 1931 to 1939. For the 103 sisters in this group, 93 (90%) had handwritten autobiographies (two had typed autobiographies and autobiographies of eight sisters could not be located). Ten sisters were recently interviewed, and they confirmed that their handwritten autobiographies were completed without the assistance of others.

Two indicators of linguistic ability were derived from each autobiography: idea density[19,20] and grammatical complexity.[18] Prior studies suggest that idea density is associated with educational level, vocabulary, and general knowledge, whereas grammatical complexity is associated with working memory, performance on speeded tasks, and writing skill.[16,18,21-24]

In the current analysis, the mean idea density and grammatical complexity scores of each sentence were computed for the last 10 sentences of each autobiography. Idea density was defined as the average number of ideas expressed per 10 words. Ideas corresponded to elementary propositions, typically a verb, adjective, adverb, or prepositional phrase. Complex propositions that stated or inferred causal, temporal, or other relationships between ideas also were counted. Grammatical complexity was computed using the Developmental Level metric originally developed by Rosenberg and Abbeduto[25] and modified by Cheung and Kemper.[18] The Developmental Level metric classifies sentences according to eight levels of grammatical complexity, ranging from zero (simple one-clause sentences) to seven (complex sentences with multiple forms of embedding and subordination).

All autobiographies were scored for idea density and grammatical complexity by a single coder who was blinded to the age and cognitive function of each sister. Ten autobiographies also were scored independently by a second coder. The coders had a high level of agreement in scoring (ie, the intercoder correlation was 0.88 for idea density and 0.93 for grammatical complexity). Idea density and grammatical complexity also had a high degree of reliability. New handwritten autobiographies were elicited from 47 of the 93 Milwaukee sisters who survived to 1995. The linguistic scores for the autobiographies written in the 1930s and those written in 1995 were highly correlated (ie, 0.73 for idea density and 0.62 for grammatical complexity).

Cognitive Function

Cognitive function was assessed by a battery of seven neuropsychological tests.[26] These tests assessed memory, concentration, language, visuospatial ability, and orientation to time and place. Poor performance on these tests corresponded to the bottom quartile of the distribution of test scores for the 678 sisters in the source population (ie, <3 for Delayed Word Recall; <7 for Word Recognition; <13 for Word List Memory; <10 for Verbal Fluency; <9 for Constructional Praxis; <10 for Boston Naming; and <24 for the Mini-Mental State Exam).

Neuropathologic Evaluation

Senile plaques and neurofibrillary tangles were quantitated in the CA1 and subiculum of the hippocampus, inferior parietal lobule (Brodmann areas 39/40), middle temporal gyrus (area 21), and middle frontal gyrus (area 9). Using the 10 most involved fields of each region, Bielschowsky-stained sections were used to count the number of senile plaques per 10× field (2.35 mm^2) and the number of neurofibrillary tangles per 20× field (0.586 mm^2).

Diagnosis of Alzheimer's Disease

Participants in the study who had Alzheimer's disease had both intellectual decline prior to death consistent with dementia and neuropathologic evidence of Alzheimer's disease.

Intellectual decline prior to death consistent with dementia was based on cognitive and physical function data collected at each sister's last functional assessment prior to death. To be considered as having intellectual decline consistent with dementia, a sister had to meet each of the following three conditions: (1) impaired memory (ie, <4 on Delayed Word Recall); (2) impairment in at least one other area of cognition (ie, <11 on Verbal Fluency, <12 on Boston Naming, or <9 on Constructional Praxis); and (3) impairment in social functioning as indicated by an inability to perform at least one of three tasks of daily living (ie, dressing, using a telephone, and handling money). Cut-points for determining impairments in memory and other areas of cognition were based on the fifth to 10th percentile scores for nondemented older adults,[27] and the inability to perform tasks of daily living was determined by performance-based tests.[28,29]

Neuropathologic evidence of Alzheimer's disease was based primarily on the presence of neurofibrillary tangles in the neocortex (ie, parietal, temporal, and frontal lobes), since recent studies indicate that neurofibrillary tangles in the neocortex may be better markers of the cognitive deficits of Alzheimer's disease than are senile plaques.[30-32] These studies, as well as the Nun Study, show that the density of neurofibrillary tangles in the neocortex is strongly associated with the severity of the cognitive deficits of Alzheimer's disease. In addition to the presence of neurofibrillary tangles in the neocortex, all Alzheimer's disease cases had abundant senile plaques in the neocortex and met the diagnostic criteria for Alzheimer's disease described by Khachaturian.[33]

Statistical Methods

Means, SDs, and Pearson correlation coefficients were calculated using standard methods.[34] Unadjusted odds ratios were calculated using a logit estimator of the ratio and its precision-based confidence intervals.[35] Adjusted odds ratios were computed by logistic regression, and adjusted means were computed by least squares regression.[36]

RESULTS

The distribution of the primary variables used in this analysis are described in Table 1. The 93 Milwaukee sisters in this study wrote their autobiographies at an average age of 22 years and had their cognitive function assessed an average of 58 years later, when they were 75 to 87 years old. Excerpts from the autobiographies of the two sisters with the greatest difference in linguistic ability are presented in Table 2. These excerpts illustrate the method used to compute idea density and grammatical complexity, the two indicators of linguistic ability used in this study.

Correlations between the primary variables used in this analysis showed a significant association between idea density and grammatical complexity (correlation=0.45; $P<.001$) and a significant association between idea density and years of education (correlation=0.27; $P<.01$). The correlations also indicated that neither idea density nor grammatical complexity was associated with the age at which the au-

tobiography was written or the age at which cognitive function was assessed.

Least squares regression was used to assess the associations between linguistic ability in early life and cognitive function in late life. Findings from a series of regression analyses are shown in Table 3 and relate linguistic ability in early life, age, and education scores to scores for the Mini-Mental State Examination, a widely used test of global cognitive functioning. These analyses indicate that cognitive function was associated with idea density, grammatical complexity, and years of education. Idea density, however, had the strongest association with cognitive function as indicated by the percent of the variance explained (Table 3).

To control more strictly for education and occupation, regression analyses were repeated in a subgroup who all had high school diplomas when they wrote their autobiographies, achieved bachelor's degrees sometime during their lives, and were teachers most of their lives. Findings on these 85 college-educated teachers were similar to the findings on the total population of 93 sisters described in Table 3. For regression analyses that included age, years of education, idea density, and grammatical complexity, the changes in the Mini-Mental State Examination score with each unit change in linguistic ability among the college-educated teachers were 2.68 (95% CI, 1.56 to 3.80; $P<.001$) for idea density and 2.02 (95% CI, 0.06 to 3.98; $P<.05$) for grammatical complexity.

Other analyses presented in Table 4 describe the associations between the two linguistic measures and poor performance on seven cognitive tests. In these analyses, sisters with idea density in the bottom third of the distribution (the 33.3 percentile value or lower described in Table 1) were classified as low in idea density, and those in the top two thirds of the distribution were classified as high in idea density. Grammatical complexity was classified by the same procedure. Of the 93 sisters, 34 had low idea density and 32 had low grammatical complexity in their autobiographies. Findings in Table 4 indicate that idea density and grammatical complexity in early life had strong associations with each of the seven cognitive function tests. The associations between linguistic ability in early life and cognitive function in late life were stronger and more consistent for idea density than for grammatical complexity. These findings on the 93 sisters were not materially different when the analyses were restricted to the subgroup of 85 college-educated teachers (results not shown).

The last series of analyses were conducted on sisters who died. There were 14 deaths that occurred in the 93 Milwaukee sisters. Five had neuropathologically confirmed Alzheimer's disease. Low idea density in early life was present in 100% of those with Alzheimer's disease, compared with 0% in those without Alzheimer's disease ($P<.001$).

Because of the small number of deaths, we studied an additional 11 sisters from other convents who died and had handwritten autobiographies. Five had neuropathologically confirmed Alzheimer's disease. Low idea density in early life was

Table 1.—Distribution of Primary Variables for 93 Milwaukee, Wis, Sisters in the Nun Study Who Had Handwritten Autobiographies*

Variable	Mean	SD	Minimum	Percentile 33.3	Percentile 50.0	Percentile 66.7	Maximum
Idea density	7.0	1.2	3.9	6.8	7.2	7.6	9.3
Grammatical complexity	2.6	0.7	1.1	2.3	2.6	2.8	5.0
Years of education attained in life	16.5	2.5	8.0	16.0	18.0	18.0	20.0
Age when autobiography written	22.0	2.9	18.9	20.3	21.1	22.4	32.4
Age when cognitive function assessed	79.9	3.0	75.6	78.1	79.4	80.4	87.3
Mini-Mental State Examination score	26.0	7.4	0.0	28.0	28.0	29.0	30.0

*Idea density refers to the average number of ideas (propositions) expressed per 10 words. Grammatical complexity refers to a score ranging from 0 (simple one-clause sentences) to 7 (complex sentences with multiple forms of embedding and subordination). Mini-Mental State Examination scores ranged from 0 (poorest global cognitive function) to 30 (best global cognitive function).

Table 2.—Examples of the Computation of Idea Density (ID) and Grammatical Complexity (GC)*

Sister A	Sister B
I was born in Eau Claire, Wis, on May 24, 1913 and was baptized in St James Church. (ID=3.9; GC=0)	The happiest day of my life so far was my First Communion Day which was in June nineteen hundred and twenty when I was but eight years of age, and four years later in the same month I was confirmed by Bishop D. D. McGavick. (ID=8.6; GC=7)
Two of the boys are dead. (ID=3.3; GC=0)	I visited the capitol in Madison and also the Motherhouse of the Franciscan Sisters of Perpetual Adoration at Duluth which visit increased my love for Notre Dame, because it was and is Notre Dame. (ID=9.1; GC=7)
I prefer teaching music to any other profession. (ID=5.0; GC=5)	Now I am wandering about in "Dove's Lane" waiting, yet only three more weeks, to follow in the footprints of my Spouse, bound to Him by the Holy Vows of Poverty, Chastity, and Obedience. (ID=9.1; GC=7)

*Of the 93 Milwaukee sisters, sisters A and B had the lowest and highest scores on ID and GC. Each of their autobiographies contained 10 sentences, and this table includes their first, fifth, and 10th sentences. Ideas expressed in sister A's first sentence were (1) I was born; (2) born in Eau Claire Wis; (3) born on May 24, 1913; (4) I was baptized; (5) was baptized in church; (6) was baptized in St James Church; and (7) I was born . . . and was baptized. There were 18 words or utterances in that sentence. The ID for that sentence was 3.9 (ie, 7 ideas divided by 18 words and multiplied by 10 to yield a score of 3.9 ideas per 10 words). Sister A died with neuropathologically confirmed Alzheimer's disease; sister B is alive without cognitive impairment. To ensure anonymity, all dates and proper nouns in each autobiography were changed.

Table 3.—Change in Mini-Mental State Examination (MMSE) Score With Each One-Unit Change in Variables in Different Regression Models*

Model	Variables	Changes in MMSE Score per Unit Change in Variable (95% CI)	Percentage of Variance in MMSE Score Explained by Model (r^2)
1	Age, y	−0.20 (−0.70 to 0.30)	1
2	Age, y	−0.12 (−0.60 to 0.35)	13
	Education, y	1.05 (0.48 to 1.61)†	
3	Age, y	−0.11 (−0.56 to 0.35)	20
	Grammatical complexity	4.78 (2.76 to 6.81)†	
4	Age, y	−0.01 (−0.41 to 0.40)	37
	Idea density	3.59 (2.61 to 4.57)†	
5	Age, y	0.01 (−0.39 to 0.40)	40
	Idea density	3.03 (1.96 to 4.09)†	
	Grammatical complexity	2.34 (0.39 to 4.30)‡	
6	Age, y	0.04 (−0.35 to 0.42)	45
	Education, y	0.62 (0.14 to 1.09)§	
	Idea density	2.70 (1.64 to 3.77)†	
	Grammatical complexity	2.31 (0.42 to 4.21)‡	

*Units of analyses used were years of age at the functional assessment, years of education, idea density score (ie, number of ideas per 10 words), grammatical complexity score (ranging from 0 for simple one-clause sentences to 7 for complex sentences with multiple forms of embedding and subordination), and MMSE score (ranging from 0 for poorest global cognitive function to 30 for best global cognitive function). Least squares regression was used for this analysis. CI indicates confidence interval.
†$P\leq.001$ for the association of a variable with an MMSE score.
‡$P\leq.05$ for the association of a variable with an MMSE score.
§$P\leq.01$ for the association of a variable with an MMSE score.

Table 4.—Poor Performance on Cognitive Tests in Late Life by Linguistic Ability Demonstrated in Autobiographies Handwritten in Early Life*

Measure of Linguistic Ability	Measure of Poor Cognitive Performance	Percent With Poor Cognitive Performance by Level of Linguistic Ability		Unadjusted Odds Ratio of Poor Performance in Low vs High Linguistic Ability Groups (95% CI)	Multivariate-Adjusted Odds Ratio of Poor Performance in Low vs High Linguistic Ability Groups (95% CI)†
		Low	High		
Idea density	Mini-Mental State Examination	35	2	31.6 (3.9-257.9)‡	30.8 (2.6-362.7)§
	Delayed Word Recall	41	3	20.0 (4.2-95.6)‡	15.3 (3.0-78.3)‡
	Word Recognition	26	2	20.9 (2.5-173.7)‡	15.8 (1.8-138.3)§
	Word List Memory	32	3	13.6 (2.8-66.3)‡	8.9 (1.7-47.2)§
	Verbal Fluency	21	3	7.4 (1.4-38.0)§	7.3 (1.2-42.8)‖
	Constructional Praxis	24	3	8.8 (1.7-44.2)§	5.4 (1.0-30.7)
	Boston Naming	24	5	5.7 (1.4-23.4)§	3.2 (0.7-15.4)
Grammatical complexity	Mini-Mental State Examination	34	3	15.5 (3.2-75.5)‡	16.3 (2.0-130.9)§
	Delayed Word Recall	34	8	5.9 (1.8-18.9)§	4.1 (1.0-16.5)‖
	Word Recognition	22	5	5.4 (1.3-22.7)§	3.8 (0.8-19.1)
	Word List Memory	28	7	5.6 (1.6-19.9)§	3.5 (0.8-16.0)
	Verbal Fluency	19	5	4.5 (1.0-19.2)‖	2.7 (0.5-13.3)
	Constructional Praxis	22	5	5.4 (1.3-22.7)§	2.7 (0.5-13.4)
	Boston Naming	28	3	11.5 (2.3-57.5)‡	8.1 (1.5-45.2)‖

*These findings were based on the 93 Milwaukee sisters. Poor performance refers to the bottom quartile of performance on cognitive tests based on the scores for the 678 participants in the Nun Study. Low linguistic ability refers to the 33.3 percentile or lower for idea density (34 sisters with low vs 59 with high) and grammatical complexity (32 with low, 61 with high). CI indicates confidence interval.
†Adjusted for age at the functional assessment and years of attained education.
‡$P \leq .001$ for ratio of the odds of poor cognitive performance in low vs high linguistic ability group.
§$P \leq .01$ for ratio of the odds of poor cognitive performance in low vs high linguistic ability group.
‖$P \leq .05$ for ratio of the odds of poor cognitive performance in low vs high linguistic ability group.

Table 5.—Neurofibrillary Tangles in Different Regions of the Brain by Linguistic Ability Demonstrated in Autobiographies Written in Early Life*

Region of Brain	Idea Density	Percent With One or More Neurofibrillary Tangles	Unadjusted Mean No. of NeurofibrillaryTangles per 0.586 mm² (95% CI)	Multivariate-Adjusted Mean No. of Neurofibrillary Tangles Per 0.586 mm² (95% CI)
Temporal lobe	Low	90†	9.4 (6.7-12.1)‡	8.8 (6.1-11.5)‡
	High	29	0.5 (0-2.9)	1.0 (0-3.4)
Parietal lobe	Low	90‡	6.2 (3.5-8.9)†	5.1 (2.4-7.8)§
	High	14	0.3 (0-2.7)	1.1 (0-3.3)
Frontal lobe	Low	80§	6.0 (3.3-8.7)†	5.1 (2.4-7.8)§
	High	31	0.3 (0-2.7)	1.0 (0-3.4)
Subiculum	Low	100§	22.7 (14.1-31.3)†	22.6 (13.0-32.2)†
	High	57	3.8 (0-10.5)	3.8 (0-10.9)
CA1	Low	75	15.8 (7.2-24.4)§	21.6 (13.4-29.8)†
	High	50	4.8 (0-10.9)	1.9 (0-7.4)

*These findings were based on 24 of the 25 sisters with neuropathologic evaluations (complete lesion counts in all brain regions could not be determined for one sister). There were 10 sisters with low idea density and 14 with high idea density. Least squares regression was used to adjust for age at death and years of education. CI indicates confidence interval. Subiculum and CA1 are regions of the hippocampus.
†$P \leq .01$ for proportion with one or more neurofibrillary tangles (or the mean lesion count) in low vs high linguistic ability group.
‡$P \leq .001$ for proportion with one or more neurofibrillary tangles (or the mean lesion count) in low vs high linguistic ability group.
§$P \leq .05$ for proportion with one or more neurofibrillary tangles (or the mean lesion count) in low vs high linguistic ability group.

present in 80% of those with Alzheimer's disease compared with 33% of those without Alzheimer's disease (P=.14).

When findings in both groups of sisters were combined, 10 of these 25 sisters had neuropathologically confirmed Alzheimer's disease. Low idea density in early life was present in 90% of those with Alzheimer's disease compared with 13% in those without Alzheimer's disease (P<.001). Further evidence of the association between low idea density and Alzheimer's disease is presented in Table 5. These findings indicate that those with low idea density had substantially more neurofibrillary tangles in the hippocampus and neocortex that did those with high idea density.

All of these analyses were repeated for grammatical complexity. The results indicate only weak negative associations of grammatical complexity with neuropathologically confirmed Alzheimer's disease and with neurofibrillary tangles in the hippocampus and neocortex. For example, among the 14 Milwaukee sisters who died, low grammatical complexity was present in 80% of those with Alzheimer's disease compared with 67% in those without Alzheimer's disease (P=.61).

COMMENT

Our findings support a strong relationship between cognitive ability in early life, as indicated by linguistic ability, and cognitive function and Alzheimer's disease in late life. Low idea density in autobiographies, written at an average age of 22 years, significantly increased the risk of both poor cognitive function and Alzheimer's disease 58 years later. These associations also were found in a subset of sisters who were college-educated and who were teachers most of their lives. Thus, it seems unlikely that our findings were attributable to confounding by education or occupation.

We suspect that this relationship of linguistic ability in early life to cognitive function and Alzheimer's disease in late life has more to do with cognitive ability in early life than with lifestyle and environmental risk factors present in the sisters during mid and late adult life. Sisters in our study had the same reproductive and marital histories; had similar social activities and support; did not smoke or drink excessive amounts of alcohol; had similar occupations, income, and socioeconomic status; lived in

the same houses and ate food prepared in the same kitchens; and had equal access to preventive and medical care services. While this background limits the generalizability of the results, it also provides a unique opportunity to avoid many of the usual confounding factors in such studies. Because Catholic sisters represent a unique population of well-educated women, our findings need to be confirmed in other studies.

Sisters with low linguistic ability in early life may have had less neurocognitive reserve capacity when they entered the convent. This reduced reserve capacity may have made them more vulnerable later in life to the consequences of the neuropathology of Alzheimer's disease. This was our hypothesis prior to analyzing the data. That is, we expected that high linguistic ability (a potential indicator of brain reserve) would prevent those with abundant neurofibrillary tangles and senile plaques of Alzheimer's disease from expressing the symptoms of the disease. However, only one sister met the neuropathologic criteria for Alzheimer's disease but did not show intellectual decline consistent with dementia. This sister, who had high idea density, was therefore not diagnosed as having Alzheimer's disease. Thus, the relationships between linguistic ability in early life and Alzheimer's disease we observed appeared to be almost entirely attributable to the neuropathologic component of Alzheimer's disease rather than to reserve capacity of the brain. Those with low idea density in early life had an excessive number of neurofibrillary tangles in the neocortex and hippocampus. Therefore, after examining the data, we postulated that low linguistic ability in early life may be an early expression of Alzheimer's disease neuropathology.

However, this hypothesis is only plausible if low linguistic ability is associated with relatively subtle neuropathologic changes in early life that precede the senile plaques and neurofibrillary tangles of Alzheimer's disease. Recent findings from an autopsy study of individuals who were aged 20 to 100 years[37] showed that the neurofibrillary tangles and neuropil threads found in Alzheimer's disease develop over approximately five decades. Nonetheless, it is not known whether such neuropathologic changes might manifest in early life and produce low linguistic ability in early life or whether low linguistic ability in early life accelerates the development of the neuropathologic lesions of Alzheimer's disease later in life. Further research is needed to confirm our findings and test alternate hypotheses. Regardless of the mechanism, our findings indicate that low linguistic ability in early life is a potent marker of both Alzheimer's disease risk and the extent of Alzheimer's disease lesions present at death.

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References

1. Snowdon DA, Ostwald SK, Kane RL. Education, survival, and independence in elderly Catholic sisters, 1936-1988. *Am J Epidemiol.* 1989;130:999-1012.
2. Snowdon DA, Ostwald SK, Kane RL, Keenan NL. Years of life with good and poor mental and physical function in the elderly. *J Clin Epidemiol.* 1989;42:1055-1066.
3. Pincus T, Callahan LF, Burkhauser RV. Most chronic diseases are reported more frequently by individuals with fewer than 12 years of formal education in the age 18-64 United States population. *J Chronic Dis.* 1987;40:865-874.
4. Zhang M, Katzman R, Salmon D, et al. The prevalence of dementia and Alzheimer's disease in Shanghai, China: impact of age, gender, and education. *Ann Neurol.* 1990;27:428-437.
5. Fratiglioni L, Grut M, Forsell Y, et al. Prevalence of Alzheimer's disease and other dementias in an elderly urban population: relationship with age, sex, and education. *Neurology.* 1991;41:1886-1892.
6. D'Arcy C. Education and socio-economic status as risk factors for dementia: data from the Canadian Study of Health and Aging. *Neurobiol Aging.* 1994;15:S40.
7. Stern Y, Gurland B, Tatemichi TK, Tang MX, Wilder D, Mayeux R. Influence of education and occupation on the incidence of Alzheimer's disease. *JAMA.* 1994;271:1004-1010.
8. Mortimer JA, Graves AB. Education and other socioeconomic determinants of dementia and Alzheimer's disease. *Neurology.* 1993;43:S39-S44.
9. Roth M. The association of clinical and neuropsychological findings and its bearing on the classification and aetiology of Alzheimer's disease. *Br Med Bull.* 1986;42:42-50.
10. Mortimer JA. Do psychosocial risk factors contribute to Alzheimer's disease? In: Henderson AS, Henderson JH, eds. *Etiology of Dementia of the Alzheimer's Type.* Chichester, England: John Wiley & Sons Inc; 1988:39-52.
11. Gatz M, Lowe B, Berg S, Mortimer J, Pedersen N. Dementia: not just a search for the gene. *Gerontologist.* 1994;34:251-255.
12. Cropley AJ. *Lifelong Education: A Psychological Analysis.* New York, NY: Pergamon Press Inc; 1977.
13. Lazar I, Darlington R, Murray H, Royce J, Snipper A. *Lasting Effects of Early Education: A Report From the Consortium for Longitudinal Studies.* Chicago, Ill: University of Chicago Press; 1982.
14. Sternberg RJ, Powell JS. Comprehending verbal comprehension. *Am Psychol.* 1983;38:878-893.
15. McKeown MG, Curtis ME, eds. *The Nature of Vocabulary Acquisition.* Hillsdale, NJ: Lawrence Erlbaum Associates Inc Publishers; 1987.
16. Kemper S, Rash S, Kynette D, Norman S. Telling stories: the structure of adults' narratives. *Eur J Cognitive Psych.* 1990;2:205-228.
17. Kemper S, LaBarge E, Ferraro FR, Cheung H, Cheung H, Storandt M. On the preservation of syntax in Alzheimer's disease: evidence from written sentences. *Arch Neurol.* 1993;50:81-86.
18. Cheung H, Kemper S. Competing complexity metrics and adults' production of complex sentences. *Appl Psycholinguist.* 1992;13:53-76.
19. Kintsch W, Keenan J. Reading rate and retention as a function of the number of the propositions in the base structure of sentences. *Cog Psych.* 1973; 5:257-274.
20. Turner A, Greene E. *The Construction and Use of a Propositional Text Base.* Boulder: University of Colorado Psychology Dept; 1977.
21. Kemper S. Adults' diaries: changes made to written narratives across the life-span. *Discourse Processes.* 1990;13:207-223.
22. Kemper S, Kynette D, Norman S. Age differences in spoken language. In: West R, Sinnott JD, eds. *Everyday Memory and Aging: Current Research and Methodology.* New York, NY: Springer-Verlag NY Inc; 1992:138-152.
23. Kemper S, Kynette D, Rash S, O'Brien K, Sprott R. Life-span changes to adults' language. *Appl Psycholinguist.* 1989;10:49-66.
24. Lyons K, Kemper S, LaBarge E, Ferraro F, Balota D, Storandt M. Language and Alzheimer's disease: a reduction in syntactic complexity. *Aging Cogn.* 1993;50:81-86.
25. Rosenberg S, Abbeduto L. Indicators of linguistic competence in the peer group conversational behavior of mildly retarded adults. *Appl Psycholinguist.* 1987;8:19-32.
26. Morris JC, Heyman A, Mohs RC, et al. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD), I: clinical and neuropsychological assessment of Alzheimer's disease. *Neurology.* 1989;39:1159-1165.
27. Welsh KA, Butters N, Mohs RC, et al. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD), V: a normative study of the neuropsychological battery. *Neurology.* 1994;44:609-614.
28. Kuriansky J, Gurland B. The Performance Test of Activities of Daily Living. *Int J Aging Hum Dev.* 1976;7:343-352.
29. Potvin AR, Tourtellotte WW, Dailey JS, et al. Simulated Activities of Daily Living Examination. *Arch Phys Med Rehabil.* 1972;53:476-486,498.
30. Bouras C, Hof PR, Giannakopoulos P, Michel J-P, Morrison JH. Regional distribution of neurofibrillary tangles and senile plaques in the cerebral cortex of elderly patients: a quantitative evaluation of a one-year autopsy population from a geriatric hospital. *Cereb Cortex.* 1994;4:138-150.
31. Bierer LM, Hof PR, Purohit DP, et al. Neocortical neurofibrillary tangles correlate with dementia severity in Alzheimer's disease. *Arch Neurol.* 1995;52:81-88.
32. Nagy ZS, Esiri MM, Jobst KA, et al. Relative roles of plaques and tangles in the dementia of Alzheimer's disease: correlations using three sets of neuropathological criteria. *Dementia.* 1995;6: 21-31.
33. Khachaturian ZS. Diagnosis of Alzheimer's disease. *Arch Neurol.* 1985;42:1097-1105.
34. Snedecor GW, Cochran WG. *Statistical Methods.* 6th ed. Ames: Iowa State University Press; 1967.
35. Woolf B. On estimating the relationship between blood group and disease. *Ann Hum Genet.* 1955;19:251-253.
36. SAS Institute Inc. *SAS Users Guide: Statistics, Version 5 Edition.* Cary, NC: SAS Institute Inc; 1985.
37. Ohm T, Muller H, Braak H, Bohl J. Close-meshed prevalence rates of different stages as a tool to uncover the rate of Alzheimer's disease-related neurofibrillary changes. *Neuroscience.* 1995;64:209-217.