

Linguistic Ability in Early Life and the Neuropathology of Alzheimer's Disease and Cerebrovascular Disease

Findings from the Nun Study

D.A. SNOWDON,^{a,b} L.H. GREINER,^a AND W.R. MARKESBERY^{a,c}

^aSanders-Brown Center on Aging, and ^bDepartment of Preventive Medicine, College of Medicine, University of Kentucky, Lexington, Kentucky 40536-0230, USA

^cDepartments of Pathology and Neurology, University of Kentucky, Lexington, Kentucky 40536-0230, USA

ABSTRACT: Findings from the Nun Study indicate that low linguistic ability in early life has a strong association with dementia and premature death in late life. In the present study, we investigated the relationship of linguistic ability in early life to the neuropathology of Alzheimer's disease and cerebrovascular disease. The analyses were done on a subset of 74 participants in the Nun Study for whom we had handwritten autobiographies completed some time between the ages of 19 and 37 (mean = 23 years). An average of 62 years after writing the autobiographies, when the participants were 78 to 97 years old, they died and their brains were removed for our neuropathologic studies. Linguistic ability in early life was measured by the idea (proposition) density of the autobiographies, i.e., a standard measure of the content of ideas in text samples. Idea density scores from early life had strong inverse correlations with the severity of Alzheimer's disease pathology in the neocortex: Correlations between idea density scores and neurofibrillary tangle counts were -0.59 for the frontal lobe, -0.48 for the temporal lobe, and -0.49 for the parietal lobe (all p values < 0.0001). Idea density scores were unrelated to the severity of atherosclerosis of the major arteries at the base of the brain and to the presence of lacunar and large brain infarcts. Low linguistic ability in early life may reflect suboptimal neurological and cognitive development, which might increase susceptibility to the development of Alzheimer's disease pathology in late life.

BACKGROUND

We have proposed that linguistic ability in early life reflects important aspects of cognitive ability, neurocognitive development, and brain reserve.¹ Our findings from the Nun Study indicate that low linguistic ability in early life has a strong relationship to poor cognitive function and the risk of dementia,¹ as well as to a reduced life expectancy.² It is not known why low linguistic ability in early life is associated with the risk of dementia and premature death in late life, although preliminary evidence suggests that Alzheimer's disease may play a role.¹

In the present study, we investigated the relationship of low linguistic ability in early life to the neuropathology of Alzheimer's disease and cerebrovascular disease. Women included in this analysis were participants in the Nun Study, a longitudinal

study of aging and Alzheimer's disease.^{1,3,4} Cognitive and physical function were assessed annually, and all participants agreed to brain donation at death. At the first exam given between 1991 and 1993, the 678 participants were 75 to 102 years old. The present analysis was conducted on a subset of 74 participants for whom we had handwritten autobiographies from early life, and all of whom had died.

LINGUISTIC MEASURES

In September 1930, the leader of the School Sisters of Notre Dame religious congregation in North America requested that each sister write a short sketch of her life and include parentage, interesting and edifying childhood events, schools attended, and influences that led her to the convent. Handwritten autobiographies were found in the archives of two convents participating in the Nun Study, that is, one in Baltimore, Maryland, and the other in Milwaukee, Wisconsin.

Two indicators of linguistic ability were derived from each autobiography: idea density^{5,6} and grammatical complexity.⁷ Our prior studies indicated that only low idea density had strong and consistent associations with the risk of dementia and premature death.^{1,2} Thus, only findings on idea density are presented in this report.

Idea density was defined as the average number of ideas expressed per ten words for the last ten sentences of each autobiography. 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. Without the linguistic coder's knowledge of the age or cognitive function of each sister during late life, each autobiography was scored for idea density. The following sentence from an autobiography illustrates the method used to compute idea density: "I was born in Eau Claire, Wis., on May 24, 1913 and was baptized in St. James Church." The ideas (propositions) expressed in this 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 idea density for that sentence was 3.9 (i.e., 7 ideas divided by 18 words and multiplied by 10, resulting in 3.9 ideas per 10 words).

NEUROPATHOLOGIC MEASURES

Gross and microscopic examination of the participants' brains was performed by a neuropathologist who was blinded to the participants' cognitive test scores. Brain infarcts were identified by examining the intact brain and 1.5 cm thick coronal sections of the cerebral hemispheres, brain stem, and cerebellum. Infarcts visible to the naked eye were classified as either lacunar infarcts (<1.5 cm) or large infarcts (≥ 1.5 cm). The neuropathologist also classified the degree of atherosclerosis of the major arteries at the base of the brain (circle of Willis), with moderate defined as atherosclerotic plaques present in 25 to 50% of the vessel wall and severe defined as greater than 50%.

Senile plaques and neurofibrillary tangles were counted in the five most severely involved microscopic fields of the middle frontal gyrus (Brodmann area 9), inferior parietal lobule (areas 39/40), and middle temporal gyrus (area 21). The number of senile plaques (both diffuse and neuritic types) per 10× microscopic field and the number of neurofibrillary tangles per 20× microscopic field were determined using Bielschowsky stained sections. As described in detail elsewhere,³ those who met our neuropathologic criteria for Alzheimer's disease had abundant senile plaques in at least one of three lobes of the neocortex (i.e., frontal, temporal, or parietal); some neuritic plaques in the neocortex; and some neurofibrillary tangles in the neocortex.

TABLE 1. Mean idea density of early life autobiographies by presence of neuropathologic conditions at autopsy for 74 participants in the Nun Study

Neuropathologic condition	Condition present at death	Unadjusted mean idea density of early life autobiographies within each convent		Adjusted mean idea density of early life autobiographies for participants in both convents combined (95% CL) ^a	Number of participants in combined analyses
		Baltimore	Milwaukee		
Met neuropathologic criteria for Alzheimer's disease	Yes	4.3**	5.5**	4.9 (4.6–5.3)***	47
	No	5.2	7.1	6.1 (5.6–6.6)	27
Neurofibrillary tangles in frontal lobe of neocortex	Yes	4.1***	5.2***	4.7 (4.3–5.1)***	40
	No	5.2	7.0	6.1 (5.7–6.5)	34
Neurofibrillary tangles in temporal lobe of neocortex	Yes	4.3**	5.4**	4.9 (4.5–5.3)***	43
	No	5.2	6.8	6.0 (5.5–6.5)	31
Neurofibrillary tangles in parietal lobe of neocortex	Yes	4.3*	5.3**	4.8 (4.4–5.3)***	37
	No	5.0	6.8	5.9 (5.4–6.3)	37
Lacunar or large brain infarct	Yes	4.6	5.8	5.2 (4.7–5.8)	28
	No	4.7	6.1	5.4 (5.0–5.8)	46
Large brain infarct	Yes	3.9*	6.0	4.9 (4.1–5.6)	14
	No	4.8	6.0	5.5 (5.1–5.8)	60
Lacunar brain infarct	Yes	4.9	5.7	5.4 (4.8–6.0)	23
	No	4.5	6.1	5.3 (5.0–5.7)	51
Moderate to severe atherosclerosis of the circle of Willis	Yes	4.5	5.7	5.2 (4.7–5.7)	36
	No	4.7	6.4	5.5 (5.1–6.0)	38

^aVariables adjusted in the analyses were age at death and location of convent (i.e., either Baltimore, Maryland or Milwaukee, Wisconsin). CL refers to confidence limits.

*** $p \leq 0.001$ for difference in mean idea density between those with and those without neuropathologic condition.

** $p \leq 0.01$ value for difference in mean idea density between those with and those without neuropathologic condition.

* $p \leq 0.05$ for difference in mean idea density between those with and those without neuropathologic condition.

RESULTS

Each of the 74 participants wrote an autobiography some time between the ages of 19 and 37 (mean = 23 years). An average of 62 years after writing the autobiographies, when the participants were 78 to 97 years old, they died and their brains were removed for our neuropathologic studies.

Findings in TABLE 1 indicate that those who met our neuropathologic criteria for Alzheimer's disease had lower idea density scores for their autobiographies from early life than those who did not meet the criteria. The presence of neurofibrillary tangles in the frontal, temporal, or parietal lobe also was strongly associated with lower idea density scores from early life (TABLE 1). Correlations between idea density scores from early life and the mean neurofibrillary tangle counts were -0.59 for the frontal lobe, -0.48 for the temporal lobe, and -0.49 for the parietal lobe. *p* Values for each of these Spearman rank correlations were less than 0.0001, and each correlation was adjusted for age at death and the location of the convent (i.e., either Baltimore, Maryland or Milwaukee, Wisconsin). When the same correlation analyses were done using mean senile plaque counts as the outcome, the correlations with idea density scores from early life were -0.34 for the frontal lobe, -0.34 for the temporal lobe, and -0.31 for the parietal lobe (all three *p* values < 0.01).

Other findings suggest that there were no consistent associations between idea density scores and lacunar brain infarcts, large brain infarcts, or moderate to severe atherosclerosis of the major arteries at the base of the brain (TABLE 1).

COMMENT

Linguistic ability, measured an average of 62 years before death, appeared to be unrelated to cerebrovascular disease pathology present at autopsy. However, a strong inverse association was found between linguistic ability and Alzheimer's disease lesions in the neocortex of the brain. Low linguistic ability in early life may reflect suboptimal neurological and cognitive development which might increase susceptibility to the development of Alzheimer's disease pathology in late life.

ACKNOWLEDGMENTS

This study was funded by grants R01AG09862 (D.A.S.), K04AG00553 (D.A.S.), and 5P50AG05144 (W.R.M.) from the National Institute on Aging, and grants from the Abercrombie Foundation and the Kleberg Foundation. More information about the Nun Study may be obtained by visiting our web page: <http://www.coa.uky.edu/nunnet>

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