ORIGINAL CONTRIBUTION

Hearing Loss and Incident Dementia

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Objective: To determine whether hearing loss is associated with incident all-cause dementia and Alzheimer disease (AD).

Design: Prospective study of 639 individuals who underwent audiometric testing and were dementia free in 1990 to 1994. Hearing loss was defined by a pure-tone average of hearing thresholds at 0.5, 1, 2, and 4 kHz in the better-hearing ear (normal, <25 dB [n=455]; mild loss, 25-40 dB [n=125]; moderate loss, 41-70 dB [n=53]; and severe loss, >70 dB [n=6]). Diagnosis of incident dementia was made by consensus diagnostic conference. Cox proportional hazards models were used to model time to incident dementia according to severity of hearing loss and were adjusted for age, sex, race, education, diabetes mellitus, smoking, and hypertension.

Setting: Baltimore Longitudinal Study of Aging.

Participants: Six hundred thirty-nine individuals aged 36 to 90 years.

Main Outcome Measure: Incident caces of all-cause dementia and AD until May 31, 2008.

Results: During a median follow-up of 11.9 years, 58 cases of incident all-cause dementia were diagnosed, of which 37 cases were AD. The risk of incident all-cause dementia increased log linearly with the severity of baseline hearing loss (1.27 per 10-dB loss; 95% confidence interval, 1.06-1.50). Compared with normal hearing, the hazard ratio (95% confidence interval) for incident all-cause dementia was 1.89 (1.00-3.58) for mild hearing loss, 3.00 (1.43-6.30) for moderate hearing loss, and 4.94 (1.09-22.40) for severe hearing loss. The risk of incident AD also increased with baseline hearing loss (1.20 per 10 dB of hearing loss) but with a wider confidence interval (0.94-1.53).

Conclusions: Hearing loss is independently associated with incident all-cause dementia. Whether hearing loss is a marker for early-stage dementia or is actually a modifiable risk factor for dementia deserves further study.

Arch Neurol. 2011;68(2):214-220

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THE PREVALENCE OF DEMENTIA is projected to double every 20 years such that by 2050, more than 100 million people or nearly 1 in 85 persons will be affected worldwide.[1,2] The devastating impact of dementia on affected individuals and the burden imposed on their families and society has made the prevention and treatment of dementia a public health priority. Interventions that could merely delay the onset of dementia by 1 year would lead to a more than 10% decrease in the global prevalence of dementia in 2050.[3] Unfortunately, there are no known interventions that currently have such effectiveness.

Epidemiologic approaches have focused on the identification of putative risk factors that could be targeted for prevention based on the assumption that dementia is easier to prevent than to reverse. Candidate factors include low involvement in leisure activities and social interactions, sedentary state, diabetes mellitus, and hypertension.[4] Some researchers have also suggested that hearing loss, by reducing stimulatory input and hampering social interaction, may be associated with dementia,[5,6] but, to our knowledge, this hypothesis has never been prospectively studied. Given the growing number of people with hearing loss[7] and the array of technological interventions currently available for aural rehabilitation, understanding whether hearing loss is a risk factor for dementia is important. We performed the present study to investigate the prospective association of hearing loss with incident dementia within the cohort of the Baltimore Longitudinal Study of Aging (BLSA).

METHODS

SUBJECTS

Subjects were participants in the BLSA, an ongoing prospective study of the effects of aging that was initiated in 1958 by the National Institute on Aging.[8] The BLSA cohort consists of

community-dwelling volunteers who travel to the National Institute on Aging in Baltimore biennially for 2½ days of intensive testing. From 1990 through 1994, 1305 participants completed at least 1 study visit, of whom 976 underwent audiometry and 749 had both audiometry and cognitive testing. Some participants had missing audiometry or cognitive testing data because of inadequate time for testing or tester unavailability during study visits. After excluding individuals with prevalent dementia (n=58), those with more than 3 errors on the Blessed Information Memory Concentration Test (n=39), and those with suspected dementia (n=13), our baseline cohort consisted of 639 participants who were followed up until May 31, 2008 (median participant follow-up of 11.9 years) (**Figure 1**). For participants with more than 1 visit during this period, data from the first assessment were used. All participants provided written informed consent, and the BLSA study protocol was approved by the institutional review board.

COGNITIVE TESTING AND DIAGNOSIS OF DEMENTIA

The protocol for adjudication of dementia in the BLSA has been used continuously since 1986 and has been described previously.[9] Participants 65 years or older underwent a complete neurological and neuropsychological examination using a standard battery of tests. Participants younger than 65 years first underwent screening with the Blessed Information Memory Concentration Test and underwent further examination if they made 3 or more errors. Dementia diagnosis was established during a multidisciplinary consensus diagnostic conference using the *Diagnostic and Statistical Manual of Mental Disorders* (Third Edition Revised) for diagnosis of dementia[10] and the National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer Disease and Related Disorders Association criteria for diagnosis of Alzheimer disease (AD).[11] If participants were determined to have clinically significant cognitive decline (typically memory) but did not meet criteria for dementia, they were classified as having suspected dementia, which corresponds to the current diagnosis of mild cognitive impairment.[12] Participants initially underwent evaluation for dementia every 2 years during their routine BLSA follow-up visits. In 1997, follow-up was shifted to a sliding-scale schedule to reduce participant burden and improve data collection. Participants older than 80 years were examined annually; those aged 60 to 80 years, biennially; and those younger than 60 years, every 4 years.

AUDIOMETRY

Audiometry was performed in the BLSA from 1958 to 1994. During the entire period from 1990 through 1994, when the baseline evaluation for this analysis was performed, hearing thresholds were measured using an automated testing device (Audiometer Model 320; Virtual Equipment Co, Portland, Oregon) in a soundproof chamber under unaided conditions. A pure-tone average (PTA) of air conduction thresholds at 0.5, 1, 2, and 4 kHz was calculated for each ear, and the PTA in the better-hearing ear was used for subsequent analyses because that ear would be the principal determinant of hearing and speech perception ability on an everyday basis. We used the PTA in decibels as both a continuous variable and a categorical variable defined by the following commonly used levels of hearing loss: normal (<25 dB), mild loss (25-40 dB), moderate loss (41-70 dB), and severe loss (>70 dB). Before 1990, audiometric testing was performed using a Bekesy audiometer (GSI 1701; Grason Stadler, Littleton, Massachusetts), and these data were used in analyses of prebaseline hearing trajectories.

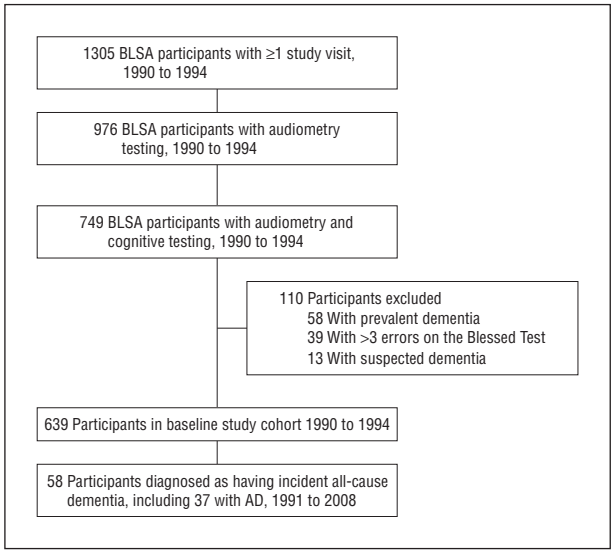

Figure 1. Selection of participants for study inclusion. AD indicates Alzheimer disease; Blessed Test, Blessed Information Memory Concentration Test; and BLSA, Baltimore Longitudinal Study of Aging.

OTHER COVARIATES

A diagnosis of diabetes mellitus was based on a fasting glucose level of more than 125 mg/dL (to convert to millimoles per liter, multiply by 0.0555), a pathologic oral glucose tolerance test result, or history of a physician diagnosis plus treatment with oral antidiabetic drugs or insulin. The diagnosis of hypertension was based on a systolic blood pressure of greater than 140 mm Hg and/or diastolic blood pressure of at least 90 mm Hg or treatment with antihypertensive medications. Race (white/black/other), education (in years), smoking status (current/former/never), and hearing aid use were based on self-report.

STATISTICAL ANALYSES

Baseline characteristics of cohort members were compared using 1-way analysis of variance for continuous variables and χ^2 or Fisher exact test for categorical variables. Cox proportional hazards models were used to study time to incident all-cause dementia or AD. Participants not diagnosed as having dementia were censored at the time of their last negative cognitive evaluation finding. Time-on-study (ie, time of entry into the baseline study cohort) was used as the time scale with the exception of 1 model that used age as the time scale.

All Cox models included covariates of sex, age, race, education, diabetes, smoking, and hypertension. Diabetes and hypertension were included as covariates in the analysis because they have been found to be risk factors for dementia.[4] Additional models included baseline Blessed scores (residual variability in cognition after definition of the baseline cohort) and hearing aid use. All covariates were treated as time-constant variables. Cox model proportionality assumptions and the linear association between hearing loss and dementia were tested using the Schoenfeld residuals method.[13] To examine the graphical association between hearing threshold and dementia, we used a smoothing spline for the hearing threshold and age in the Cox proportional hazards model.[14] A locally weighted scatterplot smoother (loess smoother) was then applied to the exponential of the partial residuals derived from the hazards model against the hearing threshold. A bootstrap procedure was used to generate 10 000 data sets that were then used to estimate the 95% confidence interval (CI) for the loess smoother. Analysis of hearing loss trajectories before baseline was performed using a ran-

Table 1. Demographic and Clinical Characteristics of Baseline Study Cohort by Hearing Loss Status

	Hearing Loss Status[a]				
	Normal (n=455)	Mild (n=125)	Moderate (n=53)	Severe (n=6)	*P* Value
Male sex	225 (49.5)	94 (75.2)	36 (67.9)	5 (83.3)	<.001
Age, mean (SD), y	59.9 (12.2)	71.1 (8.6)	77.0 (8.4)	77.7 (4.8)	<.001
Race					
White	404 (88.8)	121 (96.8)	49 (92.5)	6 (100.0)	.17
Black	44 (9.7)	4 (3.2)	4 (7.5)	0	
Other	7 (1.5)	0	0	0	
Education, mean (SD), y	16.6 (2.8)	16.2 (3.0)	16.7 (3.6)	16.2 (4.0)	.74
Diabetes mellitus	62 (13.6)	20 (16.0)	12 (22.6)	1 (16.7)	.27
Smoking					
Current	19 (4.2)	1 (0.8)	1 (1.9)	0	.05
Former	244 (53.6)	85 (68.0)	35 (66.0)	3 (50.0)	
Never	192 (42.2)	39 (31.2)	17 (32.1)	3 (50.0)	
Hypertension	204 (44.8)	79 (63.2)	38 (71.7)	6 (100.0)	<.001
Hearing aid use[b]	6 (1.5)	14 (11.9)	39 (78.0)	4 (66.7)	<.001
Blessed Information Memory Concentration Test score					
0	265 (58.2)	65 (52.0)	31 (58.5)	0	.08
1	112 (24.6)	32 (25.6)	13 (24.5)	2 (33.3)	
2	49 (10.8)	19 (15.2)	6 (11.3)	3 (50.0)	
3	29 (6.4)	9 (7.2)	3 (5.7)	1 (16.7)	
Development of all-cause dementia during follow-up	20 (4.4)	21 (16.8)	15 (28.3)	2 (33.3)	<.001

[a] Hearing loss is defined by the pure-tone average (PTA) of 0.5, 1, 2, and 4 kHz, with tones presented by air conduction in the better-hearing ear. A PTA of less than 25 dB indicates normal hearing; 25 to 40 dB, mild loss; 41 to 70 dB, moderate loss; and greater than 70 dB, severe loss. Unless otherwise indicated, data are expressed as number (percentage) of participants. Percentages have been rounded and might not total 100.

[b] Data on hearing aid use were missing for 72 individuals. Participants with hearing aid use data per hearing loss category included 393 with normal hearing, 118 with mild loss, 50 with moderate loss, and 6 with severe loss.

dom effects analysis and adjusted for age. Population-attributable risk (PAR) was calculated using the following equation[15]:

$$\mathrm{PAR} = (P_{\mathrm{exposed}}([R-1])/(1 + P_{\mathrm{exposed}}[RR-1]),$$

where P_{exposed} was the prevalence of baseline hearing loss of at least 25 dB and *RR* was the rate ratio (hazard ratio [HR]) of dementia risk associated with hearing loss. Participants with missing data were excluded from analyses; this represented less than 0.2% of the study sample (1 participant) for all analyses except for analyses incorporating hearing aid use, in which there were more extensive missing data (typically among normal-hearing participants who did not respond). Significance testing for all analyses was 2 sided with a type I error of .05. The statistical software used was a free available software environment (R, version 2.9.1; http://www.r-project.org).

RESULTS

Baseline demographic characteristics of participants by hearing loss category are presented in **Table 1**. In general, participants with greater hearing loss were more likely to be older, male, and hypertensive. Blessed scores did not differ by hearing loss category ($P=.08$), although the range of errors was narrow (0-3) because participants with more than 3 errors were excluded from the study cohort at baseline.

Baseline covariates associated with an increased risk of incident all-cause dementia are hearing loss, age, hypertension, hearing aid use, and Blessed score (**Table 2**). Independent of age, in the 15 years before baseline assessment (520 participants with 2678 observations), participants who later developed incident dementia experienced an average PTA loss of 0.52 dB/y (95% CI, 0.34-0.70 dB/y) compared with 0.27 dB/y (0.21-0.33 dB/y) in those who did not develop dementia.

In Cox proportional hazards models adjusted for sex, age, race, education, diabetes, smoking, and hypertension (base model), the excess risk of incident dementia per 10 dB of hearing loss was 1.27 (95% CI, 1.06-1.50) (**Table 3**). The risk of incident dementia became evident for hearing loss of greater than 25 dB and thereafter increased log linearly with more severe loss (**Figure 2**). This association remained significant after censoring participants who developed dementia within a 2-, 4-, or 6-year washout period from baseline ($P=.008$, $P=.003$, and $P=.04$, respectively).

Confirmatory analyses from models including baseline Blessed error score (to account for baseline cognitive function) or models using age as the time scale rather than time-on-study (to account for residual confounding between age and hearing loss) produced virtually unchanged findings (cf Table 3). Restricting the analytical cohort to participants 65 years or older at baseline (n=315) or excluding participants at baseline with a history of stroke or transient ischemic attack (n=19) also did not substantially change the main findings (Table 3). There was no evidence to suggest that self-reported hearing aid use was associated with a reduction in dementia risk (HR, 0.97; $P=.92$).

Table 2. Demographic and Clinical Characteristics of Baseline Study Cohort by Incident Dementia[a]

	No Dementia (n=581)	Dementia (n=58)	Univariate HR (95% CI)
Hearing loss, mean (SD), PTA[b]	18.8 (13.9)	32.6 (17.0)	1.1 (1.0-1.1)[c]
Hearing loss[d]			
Normal	435 (74.9)	20 (34.5)	1 [Reference]
Mild	104 (17.9)	21 (36.2)	4.9 (2.6-8.8)
Moderate	38 (6.5)	15 (25.9)	12.1 (6.2-23.9)
Severe	4 (0.7)	2 (3.4)	21.9 (5.1-94.2)
Male sex	327 (56.3)	33 (56.9)	1.1 (0.6-1.8)
Age, mean (SD), y	62.2 (12.3)	78.3 (6.4)	1.2 (1.2-1.2)
Race			
White	523 (90.0)	57 (98.3)	1 [Reference]
Black	51 (8.8)	1 (1.7)	0.2 (0.02-1.2)
Other	7 (1.2)	0	
Education, mean (SD), y	16.5 (3.0)	16.6 (3.0)	1.0 (0.9-1.1)
Diabetes mellitus	84 (14.5)	11 (19.0)	1.6 (0.9-3.0)
Smoking			
Current	20 (3.4)	1 (1.7)	1 [Reference]
Former	333 (57.3)	34 (58.6)	2.3 (0.3-17.0)
Never	228 (39.2)	23 (39.7)	2.1 (0.3-15.3)
Hypertension	286 (49.2)	41 (70.7)	2.9 (1.7-5.2)
Hearing aid use[e]	47 (9.2)	16 (30.2)	5.3 (2.9-9.6)
Blessed Information Memory Concentration Test score			
0	338 (58.2)	23 (39.7)	1 [Reference]
1	140 (24.1)	19 (32.8)	2.1 (1.2-3.9)
2	64 (11.0)	13 (22.4)	2.8 (1.4-5.6)
3	39 (6.7)	3 (5.2)	1.2 (0.4-4.1)

Abbreviations: CI, confidence interval; HR, hazard ratio; PTA, pure-tone average.

[a] Unless otherwise indicated, data are expressed as number (percentage) of participants. Percentages have been rounded and might not total 100.

[b] Hearing loss is defined by the PTA of hearing thresholds at 0.5, 1, 2, and 4 kHz, with tones presented by air conduction to the better-hearing ear.

[c] Indicates hazard per 1 dB of PTA.

[d] A PTA of less than 25 dB indicates normal hearing; 25 to 40 dB, mild loss; 41 to 70 dB, moderate loss; and greater than 70 dB, severe loss.

[e] Data on hearing aid use were missing for 72 individuals. Participants with hearing aid use data include 514 with no dementia and 53 with dementia.

Table 3. Cox Proportional Hazards Models for Incident All-Cause Dementia per 10 dB of Hearing Loss

Model	No. of Participants	HR (95% CI)[a]	*P* Value
Base[b]	638	1.27 (1.06-1.50)	.008
Base and Blessed Information Memory Concentration Test score	638	1.24 (1.04-1.48)	.01
Base with age as time scale	638	1.29 (1.08-1.53)	.005
Base and hearing aid use	566	1.33 (1.07-1.64)	.008

Abbreviations: CI, confidence interval; HR, hazard ratio.

[a] Hearing loss is defined by the pure-tone average of hearing thresholds at 0.5, 1, 2, and 4 kHz, with tones presented by air conduction in the better-hearing ear.

[b] Base model covariates include sex, age, race, education, diabetes mellitus, smoking, and hypertension.

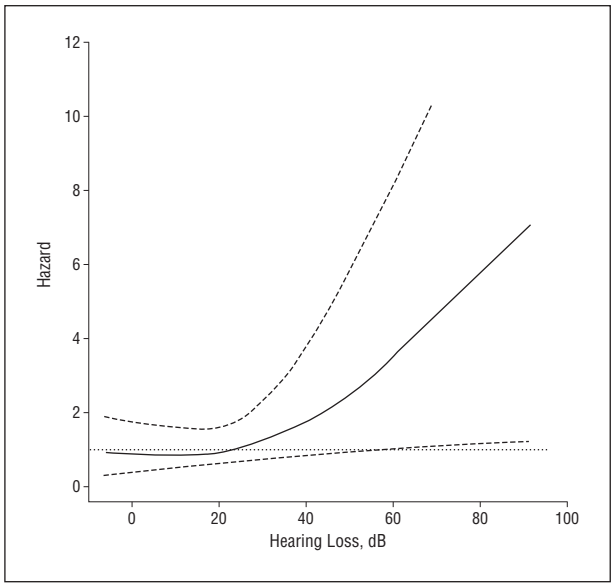

Figure 2. Risk of incident all-cause dementia by baseline hearing loss after adjustment for age, sex, race, education, diabetes mellitus, smoking, and hypertension. Hearing loss is defined by the pure-tone average of thresholds at 0.5, 1, 2, and 4 kHz in the better-hearing ear. Upper and lower dashed lines correspond to the 95% confidence interval.

In subsequent analyses, we categorized hearing loss according to commonly accepted levels of hearing loss severity. Compared with those with normal hearing, participants with mild hearing loss had an HR for incident dementia of 1.89 (95% CI, 1.00-3.58; *P*=.049), those with moderate hearing loss had an HR of 3.00 (1.43-6.30; *P*=.004), and those with severe hearing loss (n=6) had an HR of 4.94 (1.09-22.40; *P*=.04).

When the outcome of the analysis was restricted to incident AD (37 of the 58 cases of dementia), hearing loss was associated with an excess risk of 1.20 per 10 dB of hearing loss (95% CI, 0.94-1.53). This result is comparable to the risk seen for all-cause dementia (Table 3) but with a wider CI, possibly owing to the smaller sample size.

We estimated the proportion of incident all-cause dementia risk that was attributable to hearing loss for participants older than 60 years in our cohort, assuming that hearing loss could be causally associated with dementia. Hearing loss of at least 25 dB in the better-hearing ear was present in 43% of this subcohort, and the relative risk (HR) of dementia associated with hearing loss was 2.32 (95% CI, 1.32- 4.07). Thus, the attributable risk of dementia associated with hearing loss in this subcohort was 36.4% (95% CI, 12.8%-58.6%).

COMMENT

In this study, hearing loss was independently associated with incident all-cause dementia after adjustment for sex, age, race, education, diabetes, smoking, and hypertension, and our findings were robust to multiple sensitivity analyses. The risk of all-cause dementia increased log linearly with hearing loss severity, and for individuals older than 60 years in our cohort, more than one-third of the risk of incident all-cause dementia was associated with hearing loss.

Our findings contribute significantly to the discussion in the literature on whether hearing loss is a risk factor for

dementia. Previous studies suggested that individuals with hearing loss are more likely to have a diagnosis of dementia[5,6] and poorer cognitive function.[16] Supporting this hypothesis, smaller prospective studies have observed that hearing loss is associated with accelerated cognitive decline in individuals with prevalent dementia.[17,18] Although a prospective study[19] of cognitively normal elderly volunteers failed to find any meaningful association between hearing loss at study entry and later cognitive function, the results of that study are questionable because of the short (5-year) follow-up and a 50% dropout rate. In our study, hearing loss, a condition that is highly prevalent in older adults and that often remains untreated,[20] was strongly and prospectively associated with incident dementia.

A number of mechanisms may be theoretically implicated in the observed association between hearing loss and incident dementia. There may be an overdiagnosis of dementia in individuals affected by hearing loss or, vice versa, an overdiagnosis of hearing loss in individuals with cognitive impairment at baseline. An overdiagnosis of dementia in our study is unlikely because the diagnostic protocol for incident dementia relied on a consensus conference that examined information from multiple sources. We also conducted sensitivity analyses censoring individuals diagnosed as having dementia during a 6-year washout period from baseline that did not affect our results. In such an analysis, individuals would already have had normal findings on several cognitive examinations with hearing loss before being diagnosed as having dementia, likely indicating that the dementia diagnosis was not confounded by poor communication. Hearing loss (short of profound deafness) also minimally impairs face-to-face communication in quiet environments (ie, during cognitive testing), particularly in the setting of testing by experienced examiners who are accustomed to working with older adults.[21]

An overdiagnosis of hearing loss is also unlikely because no evidence suggests that mild cognitive impairment would affect the reliability of audiometric testing. Pure-tone audiometry has been performed in children as young as 5 years. We also excluded any individuals with recognized cognitive impairment at baseline (mild cognitive impairment or Blessed score >3), and our results were robust to models controlling for baseline Blessed scores.

Another possibility is that hearing loss and progressive cognitive impairment are caused by a common neuropathologic process, possibly the same that leads to AD. However, pure-tone audiometry is typically considered a measure of the auditory periphery because detection of pure tones relies solely on cochlear transduction and neuronal afferents to brainstem nuclei and the primary auditory cortex. Perception of pure tones does not require higher levels of auditory cortical processing,[22] and results of auditory brainstem response testing of these pathways are usually normal in patients with AD.[23] In contrast, central auditory nuclei required for higher-order auditory processing can be affected by AD neuropathology,[24-26] and tests of central auditory function have been found to be associated with AD.[27]

The likelihood of another neurobiological process such as vascular disease or factors related to family history (eg, apolipoprotein E [ApoE] status) causing hearing loss and dementia also cannot be fully excluded. However, risk factors for vascular disease such as diabetes, smoking, and hypertension were adjusted for in our models, and a preliminary study has not found a positive association between ApoE status and hearing loss.[28] Other variables, such as mental and leisure activities, were not included as covariates in our models because these variables would not be expected to cause hearing loss and act as meaningful confounders in our models. Our results were also robust to excluding individuals at baseline who had a history of stroke or transient ischemic attack.

Finally, hearing loss may be causally related to dementia, possibly through exhaustion of cognitive reserve, social isolation, environmental deafferentation, or a combination of these pathways. Cognitive reserve reflects interindividual differences in neurocognitive processing that allow some individuals to cope better with neuropathology than others.[29] Functional magnetic resonance imaging studies showing interindividual variation in efficiency of task-related neural processing provide some evidence of this concept.[30,31] Cognitive reserve has also been used to explain discrepancies between the extent of neuropathology seen at autopsy and clinical expression of dementia.[32] The potential effect of hearing loss on cognitive reserve is suggested by studies demonstrating that, under conditions in which auditory perception is difficult (ie, hearing loss), greater cognitive resources are dedicated to auditory perceptual processing to the detriment of other cognitive processes such as working memory.[33,34] This reallocation of neural resources to auditory processing could deplete the cognitive reserve available to other cognitive processes and possibly lead to the earlier clinical expression of dementia.[35]

Communication impairments caused by hearing loss can also lead to social isolation in older adults,[36,37] and epidemiologic[38,39] and neuroanatomic studies[40] have demonstrated associations between poor social networks and dementia. Our results also seem to support this possible pathway because the risk of dementia associated with hearing loss appeared to only increase at hearing thresholds of greater than 25 dB, which is considered the threshold at which hearing loss begins to impair verbal communication.[41] Finally, a hypothetical mechanism by which hearing loss could directly affect AD neuropathology is suggested by animal studies demonstrating that environmental enrichment (possibly analogous in humans to having access to auditory and environmental stimuli) can reduce β-amyloid levels in transgenic mouse models.[42] This hypothesis is also supported by studies showing that individuals who remain engaged in leisure activities have a lower risk of dementia.[43]

In the present study, self-reported hearing aid use was not associated with a significant reduction in dementia risk, but data on other key variables (eg, type of hearing aid used, hours worn per day, number of years used, characteristics of participants choosing to use hearing aids, use of other communicative strategies, and adequacy of rehabilitation) that would affect the success of aural rehabilitation and affect any observed association were not gathered. Consequently, whether hearing devices and aural rehabilitative strategies could affect cognitive decline and dementia remains unknown and will require further study.

Our study has limitations. First, only the severity of hearing loss at baseline was considered in the analysis, and information was not available on the trajectory of hearing loss after baseline assessment or on the possible etiology of the hearing loss. However, it is unlikely that this limitation substantially biased our findings given that reversible hearing loss is rare, and hearing loss tends to only worsen with time. Residual confounding by other environmental, genetic, or neuropathologic processes is also plausible but speculative based on our current knowledge of established risk factors for hearing loss and dementia. Given the very close association between age and both hearing loss and dementia, there is a possibility of unaccounted residual confounding. However, this is unlikely because we also confirmed our findings in a statistical model using age rather than time-on-study as the time scale to account for nonlinear effects of age on hearing and cognition.[44] Our findings were also unchanged after restricting our cohort to participants 65 years or older at baseline.

Finally, caution must be applied when generalizing the results of our current study because the BLSA is a volunteer cohort of individuals of high socioeconomic status. Further confirmation of our results will need to be performed in larger studies using more representative, community-based samples. However, this potential limitation to broad generalizability could strengthen the internal validity of our findings given the relative homogeneity of the study cohort in observed and likely unobservable characteristics.

If confirmed in other independent cohorts, the findings of our study could have substantial implications for individuals and public health. Hearing loss in older adults may be preventable[45] and can be practically addressed with current technology (eg, digital hearing aids and cochlear implants) and with other rehabilitative interventions focused on optimizing social and environmental conditions for hearing. With the increasing number of people with hearing loss, research into the mechanistic pathways linking hearing loss with dementia and the potential of rehabilitative strategies to moderate this association are critically needed.

Accepted for Publication: April 29, 2010.
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Author Contributions: Drs Metter and Ferrucci had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design*: Lin, Metter, and Ferrucci. *Acquisition of data:* Metter, O'Brien, Resnick, Zonderman, and Ferrucci. *Analysis and interpretation of data*: Lin, Metter, O'Brien, Resnick, Zonderman, and Ferrucci. *Drafting of the manuscript*: Lin and Metter. *Critical revision of the manuscript for important intellectual content*: Lin, O'Brien, Resnick, Zonderman, and Ferrucci. *Statistical analysis*: Lin, Metter, Zonderman, and Ferrucci. *Obtained funding*: O'Brien and Resnick. *Administrative, technical, or material support:* O'Brien and Zonderman. *Study supervision*: Resnick and Ferrucci.
Financial Disclosure: None reported.
Funding/Support: This work was supported by the Intramural Research Program of the National Institute on Aging and grant 1K23DC011279-01 from the National Institute on Deafness and Other Communication Disorders (Dr Lin).
Role of the Sponsor: The National Institute on Aging funded the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation and review of the manuscript. The sponsor was not involved in manuscript approval.

REFERENCES

1. Ferri CP, Prince M, Brayne C, et al; Alzheimer's Disease International. Global prevalence of dementia: a Delphi consensus study. *Lancet*. 2005;366(9503):2112-2117.
2. Alzheimer's Disease International. *World Alzheimer Report 2009*. In: Prince M, Jackson J, eds. London, England: Alzheimer's Disease International; 2009.
3. Brookmeyer R, Johnson E, Ziegler-Graham K, Arrighi HM. Forecasting the global burden of Alzheimer's disease. *Alzheimers Dement*. 2007;3(3):186-191.
4. Coley N, Andrieu S, Gardette V, et al. Dementia prevention: methodological explanations for inconsistent results. *Epidemiol Rev*. 2008;30:35-66.
5. Uhlmann RF, Larson EB, Rees TS, Koepsell TD, Duckert LG. Relationship of hearing impairment to dementia and cognitive dysfunction in older adults. *JAMA*. 1989;261(13):1916-1919.
6. Ives DG, Bonino P, Traven ND, Kuller LH. Characteristics and comorbidities of rural older adults with hearing impairment. *J Am Geriatr Soc*. 1995;43(7):803-806.
7. Agrawal Y, Platz EA, Niparko JK. Prevalence of hearing loss and differences by demographic characteristics among US adults: data from the National Health and Nutrition Examination Survey, 1999-2004. *Arch Intern Med*. 2008;168(14):1522-1530.
8. Shock N, Greulich R, Andres R, et al. *Normal Human Aging: The Baltimore Longitudinal Study of Aging* . Washington, DC: National Institutes of Health; 1984. NIH publication 84-2450.
9. Kawas C, Gray S, Brookmeyer R, Fozard J, Zonderman A. Age-specific incidence rates of Alzheimer's disease: the Baltimore Longitudinal Study of Aging. *Neurology*. 2000;54(11):2072-2077.
10. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised*. Washington, DC: American Psychiatric Association; 1987.
11. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology*. 1984;34(7):939-944.
12. Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: clinical characterization and outcome. *Arch Neurol*. 1999;56(3):303-308.
13. Schoenfeld D. Partial residuals for the proportional hazards regression model. *Biometrika*. 1982;69(1):239-241.
14. Therneau T, Grambsch P. *Modeling Survival Data: Extending the Cox Model*. New York, NY: Springer Publishing Co Inc; 2000.
15. Northridge ME. Public health methods: attributable risk as a link between causality and public health action. *Am J Public Health*. 1995;85(9):1202-1204.
16. Cacciatore F, Napoli C, Abete P, Marciano E, Triassi M, Rengo F. Quality of life determinants and hearing function in an elderly population: Osservatorio Geriatrico Campano Study Group. *Gerontology*. 1999;45(6):323-328.
17. Peters CA, Potter JF, Scholer SG. Hearing impairment as a predictor of cognitive decline in dementia. *J Am Geriatr Soc*. 1988;36(11):981-986.
18. Uhlmann RF, Larson EB, Koepsell TD. Hearing impairment and cognitive decline in senile dementia of the Alzheimer's type. *J Am Geriatr Soc*. 1986;34(3):207-210.
19. Gennis V, Garry PJ, Haaland KY, Yeo RA, Goodwin JS. Hearing and cognition in the elderly: new findings and a review of the literature. *Arch Intern Med*. 1991;151(11):2259-2264.
20. Popelka MM, Cruickshanks KJ, Wiley TL, Tweed TS, Klein BE, Klein R. Low prevalence of hearing aid use among older adults with hearing loss: the Epidemiology of Hearing Loss Study. *J Am Geriatr Soc*. 1998;46(9):1075-1078.
21. Gordon-Salant S. Hearing loss and aging: new research findings and clinical implications. *J Rehabil Res Dev*. 2005;42(4)(suppl 2):9-24.
22. Pickles JO. *An Introduction to the Physiology of Hearing*. Bingley, England: Emerald Group Publishing; 2008.
23. Grimes AM, Grady CL, Pikus A. Auditory evoked potentials in patients with dementia of the Alzheimer type. *Ear Hear*. 1987;8(3):157-161.

24. Sinha UK, Hollen KM, Rodriguez R, Miller CA. Auditory system degeneration in Alzheimer's disease. *Neurology*. 1993;43(4):779-785.
25. Parvizi J, Van Hoesen GW, Damasio A. The selective vulnerability of brainstem nuclei to Alzheimer's disease. *Ann Neurol*. 2001;49(1):53-66.
26. Baloyannis SJ, Mauroudis I, Manolides SL, Manolides LS. Synaptic alterations in the medial geniculate bodies and the inferior colliculi in Alzheimer's disease: a Golgi and electron microscope study. *Acta Otolaryngol*. 2009;129(4):416-418.
27. Gates GA, Beiser A, Rees TS, D'Agostino RB, Wolf PA. Central auditory dysfunction may precede the onset of clinical dementia in people with probable Alzheimer's disease. *J Am Geriatr Soc*. 2002;50(3):482-488.
28. O'Grady G, Boyles AL, Speer M, DeRuyter F, Strittmatter W, Worley G. Apolipoprotein E alleles and sensorineural hearing loss. *Int J Audiol*. 2007;46(4):183-186.
29. Stern Y. Cognitive reserve. *Neuropsychologia*. 2009;47(10):2015-2028.
30. Holtzer R, Rakitin BC, Steffener J, Flynn J, Kumar A, Stern Y. Age effects on load-dependent brain activations in working memory for novel material. *Brain Res*. 2009;1249:148-161.
31. Zarahn E, Rakitin B, Abela D, Flynn J, Stern Y. Age-related changes in brain activation during a delayed item recognition task. *Neurobiol Aging*. 2007;28(5):784-798.
32. Savva GM, Wharton SB, Ince PG, Forster G, Matthews FE, Brayne C; Medical Research Council Cognitive Function and Ageing Study. Age, neuropathology, and dementia. *N Engl J Med*. 2009;360(22):2302-2309.
33. Tun PA, McCoy S, Wingfield A. Aging, hearing acuity, and the attentional costs of effortful listening. *Psychol Aging*. 2009;24(3):761-766.
34. Pichora-Fuller MK, Schneider BA, Daneman M. How young and old adults listen to and remember speech in noise. *J Acoust Soc Am*. 1995;97(1):593-608.
35. Boyle PA, Wilson RS, Schneider JA, Bienias JL, Bennett DA. Processing resources reduce the effect of Alzheimer pathology on other cognitive systems. *Neurology*. 2008;70(17):1534-1542.
36. Strawbridge WJ, Wallhagen MI, Shema SJ, Kaplan GA. Negative consequences of hearing impairment in old age: a longitudinal analysis. *Gerontologist*. 2000;40(3):320-326.
37. Weinstein BE, Ventry IM. Hearing impairment and social isolation in the elderly. *J Speech Hear Res*. 1982;25(4):593-599.
38. Fratiglioni L, Wang HX, Ericsson K, Maytan M, Winblad B. Influence of social network on occurrence of dementia: a community-based longitudinal study. *Lancet*. 2000;355(9212):1315-1319.
39. Barnes LL, Mendes de Leon CF, Wilson RS, Bienias JL, Evans DA. Social resources and cognitive decline in a population of older African Americans and whites. *Neurology*. 2004;63(12):2322-2326.
40. Bennett DA, Schneider JA, Tang Y, Arnold SE, Wilson RS. The effect of social networks on the relation between Alzheimer's disease pathology and level of cognitive function in old people: a longitudinal cohort study. *Lancet Neurol*. 2006;5(5):406-412.
41. Dalton DS, Cruickshanks KJ, Klein BE, Klein R, Wiley TL, Nondahl DM. The impact of hearing loss on quality of life in older adults. *Gerontologist*. 2003;43(5):661-668.
42. Lazarov O, Robinson J, Tang YP, et al. Environmental enrichment reduces Aβ levels and amyloid deposition in transgenic mice. *Cell*. 2005;120(5):701-713.
43. Verghese J, Lipton RB, Katz MJ, et al. Leisure activities and the risk of dementia in the elderly. *N Engl J Med*. 2003;348(25):2508-2516.
44. Korn EL, Graubard BI, Midthune D. Time-to-event analysis of longitudinal follow-up of a survey: choice of the time-scale. *Am J Epidemiol*. 1997;145(1):72-80.
45. Zhan W, Cruickshanks KJ, Klein BE, et al. Generational differences in the prevalence of hearing impairment in older adults. *Am J Epidemiol*. 2010;171(2):260-266.

Announcement

"What is Your Diagnosis?" is a new quarterly online feature of the *Archives of Neurology* edited by Lawrence S. Honig, MD, PhD, of Columbia University. A case history including an image will be presented, followed by the request for your diagnosis from a list of 4 possible choices. The correct diagnosis will then be presented with a commentary as to why it is correct. We believe it will become a popular and anticipated new feature and welcome your comments and suggestions.