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Research Article

Audiometric Age-Related Hearing Loss and Cognition in the Hispanic Community Health Study

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Abstract

Background: Age-related hearing loss (HL), a common and treatable condition, has been associated with other age-related conditions. Late life cognitive impairment is a major public health concern that is rarely treatable. Studies examining the relationship between HL and cognition have been limited by non-Hispanic cohorts, small samples, or limited confounding control. We overcome these limitations in a large Hispanic cohort.

Methods: This was a multisite cross-sectional study of 5,277 subjects at least 50 years old (Hispanic Community Health Study, HCHS). The main exposure was audiometric HL. The main outcome measure was neurocognitive performance ascertained by the Digit Symbol Substitution Test (DSST), Word Frequency Test, Spanish-English Verbal Learning Test (SEVLT), and Six-Item Screener.

Results: The mean age was 58.4 years (SD = 6.2). A 20-dB (equivalent to a one-category worsening) increase in HL was associated with a −1.53 (95% CI, −2.11, −0.94) raw score point difference in the DSST, adjusting for demographics, hearing aid use, and cardiovascular disease. Similarly, a 20-dB increase in HL was associated with a −0.86 (−1.23, −0.49) point difference on the Word Frequency Test, −0.76 (−1.04, −0.47) on the SEVLT 3 trials, −0.45 (−0.60, −0.29) on the SELVT recall, and −0.07 (−0.12, −0.02) on the Six-Item Screener.

Conclusions: In the largest study of formal, audiometric HL and cognition to date, HL was independently associated with worse performance in a range of neurocognitive measures. Because HL is common and potentially treatable, it should be investigated as a modifiable risk factor for neurocognitive decline and dementia.

Keywords: Cognitive impairment, Aging, Presbycusis, Audiometry.

Age-related hearing loss (HL), defined as age-dependent degeneration of the auditory system, has recently emerged as a potentially modifiable risk factor for several conditions of aging, including impaired cognition and dementia (1–4). This possibility has elevated HL from an inconvenience to a critical public health issue of national concern (5,6).

The health and socioeconomic impact of dementia is staggering, estimated to reach $2 trillion globally by 2030 (4). Despite

considerable research, no disease-modifying treatments currently exist. Substantial efforts are thus underway to identify modifiable risk factors of cognitive impairment. Given its high prevalence, HL was recently suggested as the greatest potentially modifiable dementia risk factor (4).

Prior studies on HL and cognition have been limited for several reasons. First, the study population has been largely white (7–10).

Inclusion of African Americans is uncommon (11) and inclusion of Hispanics is rare (3). A recent report on hearing health care from the U.S. National Academy of Sciences recommended studying diverse populations, which would allow generalizability (6). Second, many studies have been limited in sample size, which reduces the ability for sub-analyses. Third, studies have typically controlled for only hearing aid use as well as demographic and cardiovascular covariates (10). Fourth, many prior studies have used self-reported/non-audiometric (3,12) or central auditory tests (13–16), neither of which are the clinical standard for behavioral measurement of hearing thresholds (17,18).

We previously reported an association between observed (non-audiometric) HL and incident dementia in an urban multiethnic elderly cohort (3). In the current study, we examine cross-sectional associations between audiometrically defined HL and cognitive performance in tests of psychomotor speed, attention, verbal functioning and memory, learning, and global cognition in more than 5,000 middle and late-age adults enrolled in the Hispanic Community Health Study (HCHS). We hypothesize that dose-dependent associations will exist, which will be robust to a variety of potential confounders. To the best of our knowledge, this is the largest study of formal, audiometric HL and cognition to date (10).

Methods

Cohort and Participants

The Hispanic Community Health Study/Study of Latinos (HCHS) is a longitudinal, multicenter community-based cohort study. It incorporates interviews, physical examinations, and specialized testing such as neuropsychological evaluations. All participants undergo audiometry. Assessments were conducted in English or Spanish, as preferred by the subject. Only the 2008–2011 wave of data is currently available; thus, cross-sectional analysis was performed.

Inclusion is illustrated in Figure 1. There were 14,155 total participants in the original data set. To restrict the analysis to people at risk for age-related HL, subjects under 50 years of age (*n* = 7,980) and those with self-reported early-onset HL (*n* = 212) were excluded.
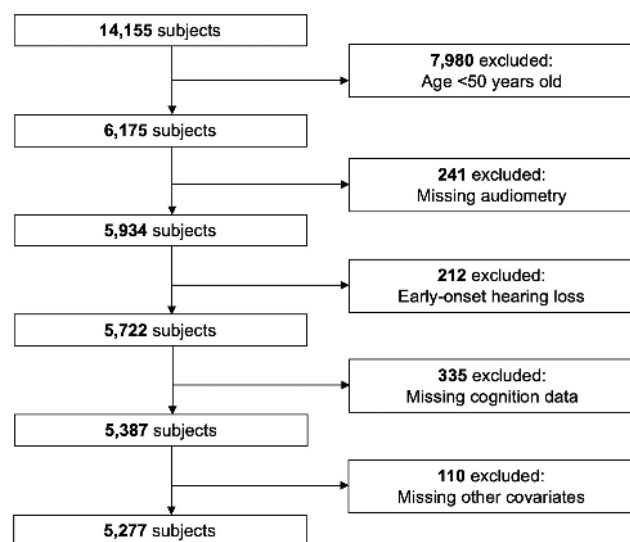
Figure 1. Flowchart of enrollment and inclusion for analysis. Cognition data include the Digit Symbol Substitution Test, Word Fluency Test, Spanish-English Verbal Learning Test (SEVLT), and Six-Item Screener.

Participants who were missing data for audiometry, any of the five primary outcomes, or covariate data were further excluded. In the final analysis 5,277 subjects remained.

Hearing

Hearing, measured using pure tone audiometry, was the exposure of interest. Hearing thresholds (in dB HL, decibel hearing level) were collected from frequencies 500–8,000 Hz. The four-frequency pure tone average was computed as the mean threshold (dB) at 500, 1000, 2000, and 4000 Hz. Hearing level was based on the pure tone average in the better hearing ear, consistent with prior epidemiologic studies of age-related HL (1,11). Hearing was primarily analyzed continuously. The severity of HL was categorized as follows: normal hearing (0–25 dB), mild (26–40 dB), moderate (41–55 dB), moderately-severe-or-worse (≥56 dB) (19).

Outcomes

We examined as outcomes the five core cognitive measures collected in the HCHS. These measures included tests of global cognitive function, verbal memory, and frontal-executive abilities. For all tests, higher scores indicate better cognitive performance. All tests were analyzed continuously.

Attention and speed were measured with the Digit Symbol Substitution Test (DSST) of the Wechsler Adult Intelligence Scale-Revised and the Word Frequency Test (letter fluency test). The *DSST* measures psychomotor speed and attention. Subjects are asked to fill in a series of symbols corresponding to specific digits within 90 seconds (20). It is a widely used measured of cognitive function in epidemiologic studies (21). The observed score range was 0 (worst) to 80 (best). The *Word Frequency Test* is a measure of verbal fluency. Subjects are asked to state words that begin with certain letters as quickly as possible during two 60-second trials (22). The observed score range was 0 (worst) to 49 (best).

Verbal learning and memory were measured with the *Spanish-English Verbal Learning Test* (SEVLT). The subject is read a list of common words over three separate trials and asked to recall the list after each learning trial (23). The sum of the number of words across the three trials is recorded (SEVLT 3 trials), with a possible score ranging from 0 (worst) to 45 (best). A distracting word list is then presented and repeated back. Immediately after, the subject is asked to recall the initial word list (SEVLT recall), with a possible score ranging from 0 (worst) to 15 (best).

Global cognitive function was measured by the *Six-Item Screener* (24). This is a brief, six-item screen for cognitive impairment. The score ranges from 0 (worst) to 6 (best).

Covariates

Covariates that might confound the relationship between HL and cognition were included in the multivariable model. Demographics covariates included age, gender, and years of education. Gender was assessed by the examiner asking the participant what his/her gender was. Hearing aid use was coded as yes/no depending on whether subjects self-reported any use in the past 12 months. Cardiovascular disease was treated as a confounder because it may cause both HL and cognitive impairment. A composite cardiovascular disease variable aggregating multiple risk factors was created to avoid multicollinearity. Multicollinearity, which occurs if related individual predictors are independently included in a model, can result in overadjustment (25) and erratic model behavior (26). A point was assigned for each of three risk factors that were present:

coronary artery disease, hypertension, and/or self-reported stroke/transient ischemic attack. Additional points were added for diabetes based on fasting serum glucose and, if available, oral glucose tolerance test, and HbA1C (1 point for impaired glucose tolerance, 2 points of diabetes) (27). Depressive symptoms, which could act as both a confounder and/or a mediator (28), were assessed with the Center for Epidemiologic Studies Depression Scale-10 (CESD-10) (29). Anxiety was assessed with the State-Trait Anxiety Inventory-10 (30,31). Cognitive testing was performed in English or Spanish based on the participant's preference. Bilingualism was assessed by whether the subject spoke English, Spanish, or both at home.

Statistical Analysis

One-way analysis of variance was used to compare means of continuous variables of interest between subjects across four levels of hearing categories (normal, mild, moderate, moderately-severe-or-worse). The dependent variable was the variable of interest (age, education, etc.). The chi-squared and Fisher's Exact Tests were used to compare categorical variables across hearing categories.

Regression was used to examine associations between hearing performance examined continuously and the cognitive outcomes. Univariable regression was performed first, followed by multivariable regression adjusting for possible confounders. Linear regression was used as outcomes were continuous (DSST, SEVLT, and word frequency, Six-Item Screener). We additionally looked for interaction between hearing × gender and hearing × age

To allow comparisons across different cognitive tests, z-scores were computed. Ordinal logistic regression (proportional odds model) was used for the Six-Item Screener in a sensitivity analysis where it was treated as an ordinal categorical variable (since the score only ranged from 0 to 6). In another sensitivity analysis, a quadratic term for age was added to the main multivariable models to attempt to better control for the confounding effect of age.

For the interpretation of models, we report HL changes in 20-dB increments. This is because 20 dB is approximately equivalent to a 1-category worsening (i.e. across standard clinical categories of normal, mild, moderate, moderately-severe, severe, and profound). (Some studies in the literature have used 10-dB increments. Because we used linear regression, our effect sizes and confidence intervals for 20-dB increments can be converted to those of 10-dB increments simply by dividing by 2.)

We estimated the approximate years of aging corresponding to the cognitive score reduction seen with a 20-dB increase in HL. This was obtained by dividing the cognitive score reduction per 20-dB HL in the fully adjusted model (Table 1) by the cognitive score reduction per 1 year of aging (Supplementary Table 1, Supplementary Figure 1).

Statistical significance was considered at the $p < .05$ level. Data analysis was performed from March 2018 to February 2019 using R 3.5.1 (R Foundation for Statistical Computing) with RStudio 1.2.1009 (RStudio, Inc., Boston, MA).

Results

Baseline Characteristics

Baseline respondent characteristics, categorized by hearing level, are reported in Table 2. The mean age was 58.4 years (SD = 6.2). Of 5,277 subjects, 2,023 were men (38.3%). Across hearing categories, there was a significant difference for age, gender, education, hearing aid use, cardiovascular disease score, and all cognitive tests.

Table 1. Regression Models for Cognitive Outcomes Based on Hearing Loss in Those 50 Years and Older; Hispanic Community Health Study (HCHS; $n = 5,277$)

Model (Predictors)	Digit Symbol Substitution Test Score Difference Per 20 dB of HL (95% CI)*	p	Word Frequency Test Score Difference Per 20 dB of HL (95% CI)*	p	SEVLT 3 Trials Score Difference Per 20 dB of HL (95% CI)*	p	SEVLT Recall Score Difference Per 20 dB of HL (95% CI)*	p	Six-Item Screener Score Difference Per 20 dB of HL (95% CI)*	p
1. Hearing loss† (univariable model)	-5.17 (-5.82, -4.53)	<.001	-1.52 (-1.88, -1.15)	<.001	-1.97 (-2.25, -1.70)	<.001	-0.97 (-1.11, -0.83)	<.001	-0.18 (-0.23, -0.14)	<.001
2. Above + demographics‡	-1.51 (-2.08, -0.94)	<.001	-0.87 (-1.23, -0.50)	<.001	-0.80 (-1.08, -0.52)	<.001	-0.44 (-0.59, -0.29)	<.001	-0.07 (-0.11, -0.02)	<.01
3. Above + hearing aid§	-1.61 (-2.19, -1.02)	<.001	-0.90 (-1.27, -0.53)	<.001	-0.78 (-1.06, -0.49)	<.001	-0.46 (-0.61, -0.30)	<.001	-0.07 (-0.12, -0.02)	<.01
4. Above + cardiovascular risk factors‖ (fully adjusted model)	-1.53 (-2.11, -0.94)	<.001	-0.86 (-1.23, -0.49)	<.001	-0.76 (-1.04, -0.47)	<.001	-0.45 (-0.60, -0.29)	<.001	-0.07 (-0.12, -0.02)	<.01

Notes: Linear regression was used for all cognitive outcomes. SEVLT = Spanish-English Verbal Learning Test.
*A 20-dB increase in hearing loss is approximately equivalent to a 1-category worsening (categories are: normal, mild, moderate, moderately-severe, severe, profound).
†Hearing loss, based on magnitude of pure tone average in better hearing ear.
‡Demographics include age, gender, education.
§Hearing aid is yes/no (used in past year).
‖Cardiovascular risk factors include coronary artery disease (test-defined), hypertension (measured), stroke/transient ischemic attack (self-reported), diabetes (lab-defined).

Table 2. Subject Characteristics Stratified by Hearing Loss Category in Those 50 Years and Older; Hispanic Community Health Study (HCHS; $n = 5,277$)

	Total	No HL (0–25 dB)	Mild HL (26–40 dB)	Moderate HL (41–55 dB)	Moderately-Severe-or-Worse HL (>55 dB)	Test Statistic*	p-value
No. (%)	5277	4347	746	136	48		
Age, mean ± SD (Range)	58.4 ± 6.2 (50–76)	57.6 ± 5.9 (50–75)	61.7 ± 6.6 (50–76)	63.3 ± 7.3 (50–74)	63.4 ± 6.0 (50–74)	$F = 118$	<.001
Men, no. (%)	2023 (38.3)	1528 (35.2)	403 (54.0)	69 (50.7)	23 (47.9)	$\chi^2 = 107$	<.001
Education, years, mean ± SD	10.5 ± 4.6	10.7 ± 4.6	9.5 ± 4.6	8.8 ± 4.4	8.5 ± 4.4	$F = 25$	<.001
Hearing aid use, no. (%)	46 (0.9)	9 (0.2)	8 (1.1)	18 (13.2)	11 (22.9)	N/A†	<.001
Cardiovascular disease score, mean ± SD	1.7 ± 1.1	1.6 ± 1.1	1.9 ± 1.1	2.0 ± 1.1	2.1 ± 1.1	$F = 20$	<.001
Cardiovascular disease score components, no. (%)							
Coronary artery disease	595 (11.3)	449 (10.3)	109 (14.6)	23 (16.9)	14 (29.2)	$\chi^2 = 32$	<.001
Hypertension	2480 (47.0)	1969 (45.3)	404 (54.2)	79 (58.1)	28 (58.3)	$\chi^2 = 30$	<.001
Stroke or transient ischemic attack	129 (2.4)	96 (2.2)	26 (3.5)	4 (2.9)	3 (6.3)	N/A†	<.05
Diabetes							
Impaired glucose tolerance	2633 (49.9)	2184 (50.2)	364 (48.8)	63 (46.3)	22 (45.8)	$\chi^2 = 30$	<.001
Diabetes	1438 (27.3)	1125 (25.9)	246 (33.0)	50 (36.8)	17 (35.4)	$F = 51$	<.001
Digit Symbol Substitution Test score, mean ± SD	32.1 ± 13.0	33.0 ± 12.9	28.3 ± 12.4	26.4 ± 11.7	23.4 ± 10.1	$F = 51$	<.001
Word Frequency Test score, mean ± SD	18.1 ± 7.2	18.3 ± 7.2	17.1 ± 6.9	15.8 ± 7.4	14.3 ± 5.7	$F = 18$	<.001
SEVLT 3 trials score, mean ± SD	22.4 ± 5.5	22.8 ± 5.4	20.9 ± 5.5	19.7 ± 5.6	19.5 ± 4.5	$F = 12$	<.001
SEVLT recall score, mean ± SD	8.1 ± 2.9	8.2 ± 2.8	7.3 ± 2.9	7.2 ± 2.8	6.3 ± 2.7	$F = 42$	<.001
Six-Item Screener score, mean ± SD	5.3 ± 0.9	5.3 ± 0.8	5.1 ± 1.0	5.3 ± 0.8	4.9 ± 1.0	$F = 34$	<.001

Notes: Test statistic and p-value refer to comparison of a particular subject characteristic across the four hearing categories. HL, hearing loss; SEVLT = Spanish-English Verbal Learning Test.

*Degrees of freedom = 3 for all test statistics.

†Fisher's Exact Test used, which does not generate a test statistic.

Univariable Analysis

Scatterplots showing the unadjusted relationships between hearing (pure tone average, dB HL) and the cognitive outcomes appears in Figure 2. There was a significant inverse relationship between HL and all outcomes (p <.001, r_s range –0.21 to –0.10). The corresponding regressions for these univariable analyses are discussed below. The univariable relationships between demographic variables (age, gender, education) and cognitive outcomes appear in Supplementary Table 1.

Multivariable Analysis

The summary for linear regression models appears in Table 1. In the univariable model (model 1), HL was significantly associated with a lower score on all five cognitive outcomes. Covariates were added to the models to adjust for potential confounding. Adding demographic factors (model 2; age, gender, education) attenuated the relationship between hearing and all cognitive outcomes. Adding hearing aids (model 3) had a small effect. Finally, adding cardiovascular risk factors (model 4) also had a small effect. Scatterplots of this fully adjusted model appear in Figure 2. For all models, p < .001.
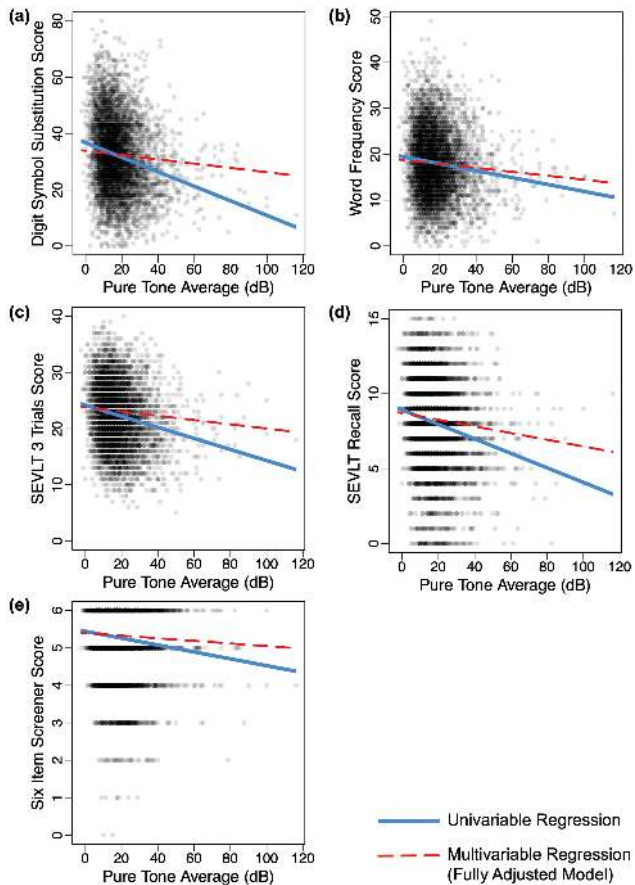
Figure 2. Scatterplot illustrating the relationship between hearing (pure tone average in dB) and cognitive outcomes. The solid blue line indicates the univariable relationship. The dashed red line indicates the multivariable relationship from the fully adjusted model that includes demographics (age, gender, education), hearing aid use, and cardiovascular risk factors (**a**) Digit Symbol Substitution Test score, (**b**) Word Frequency Test score, (**c**) Spanish-English Verbal Learning Test (SEVLT) 3 trials score, (**d**) SEVLT recall score, and (**e**) Six-Item Screener score. Lines of best fit are from univariable regression. Darker points indicate overlapping of points.

In the fully adjusted model (model 4), a 20-dB increase (equivalent to a 1-category worsening) in HL was associated with a –1.53 point raw score (95% CI, –2.11, –0.94) difference in DSST score, a –0.86 (95% CI, –1.23, –0.49) point difference on Word Frequency Test score, a –0.76 (95% CI, –1.04, –0.47) point difference in SEVLT 3 trials, a –0.45 (95% CI, –0.60, –0.29) point difference in SEVLT recall, and a –0.07 (95% CI, –0.12, –0.02) point difference in the Six-Item Screener. For all multivariable models, p < .001 (except p < .01 where Six-Item Screener is the outcome).

A 20-dB increase in HL (controlling for confounders) was equivalent to an aging effect (i.e. the model-predicted pure effect of aging) of 2.2 years for the DSST, 9.8 years for the Word Frequency Test, 3.9 years for the SEVLT 3 trials, 4.8 years for the SEVLT recall, and 0.7 years for the Six-Item Screener.

We additionally computed z-scores to compare the association across cognitive outcomes. The strength of association between hearing and cognition showed similar results across outcomes. (Supplementary Table 2)

The fully adjusted model was then used to calculate the difference in cognitive outcomes for each HL category (the median within-category value was chosen) compared to normal (0 dB) hearing (Table 3). Compared to normal hearing, the difference in DSST score was –2.48 (95% CI, –3.43, –1.53) for mild HL or –6.11 (95% CI, –8.45, –3.78) for severe HL. Likewise, the difference in the Word Frequency Test score was –1.40 (95% CI, –2.00, –0.80) for mild HL or –3.45 (95% CI, –4.93, –1.96) for severe HL. For SEVLT 3 trials, the difference was –1.23 (95% CI, –1.69, –0.76) for mild HL and –3.02 (95% CI, –4.17, –1.88) for severe HL. For SEVLT recall, the difference was –0.73 (95% CI, –0.98, –0.47) for mild HL and –1.79 (95% CI, –2.40, –1.17) for severe HL. Finally, for the Six-Item Screener, the difference was –0.11 (95% CI, –0.19, –0.04) for mild HL and –0.28 (95% CI, –0.47, –0.09) for severe HL.

Finally, we looked for effect modification (interaction) by gender and age. Significant effect modification was noted in only a few instances, including the DSST (hearing × gender, interaction term coefficient p < .01 and hearing × age, p < .05) and the Six-Item Screener (hearing × gender, p < .05). In the DSST, scores differed by –1.88 points (95% CI, –2.66, –1.09) per 20 dB in women compared with only –1.11 points (95% CI, –1.98, –0.25) in men. In the Six-Item Screener, scores differed by –0.13 points (95% CI, –0.19, –0.06) per 20 dB in women compared with only –0.01 points (95% CI, –0.10, 0.08) in men. Finally, in the DSST scores difference was –2.23 points (95% CI, –3.10, –1.36) in 50–60 year olds, –1.33 (95% CI, –2.20, –0.47) in 60–70 year olds, and –2.52 (95% CI, –4.23, –0.81) in 70–80 year olds. The age-stratified analysis appears in Table 4.

In a sensitivity analysis, depressive symptoms assessed by the CESD-10 was added as a covariate because depression may be either a confounder or a mediator of the relationship between hearing and cognition (28,32–34). When added to the fully adjusted model, the relationship between hearing and all cognitive outcomes was modestly attenuated but remained significant. (Supplementary Table 3) Similar findings were noted if anxiety assessed by the State-Trait Anxiety Inventory was added as a covariate. (Supplementary Table3) We also added preferred language during cognitive testing as well as bilingualism as covariates. When added to the fully adjusted model, the relationship between hearing and all cognitive outcomes was minimally attenuated. (Supplementary Table 3) The fully adjusted model was also restricted to only subjects with no or mild HL or, separately, to those who did not use hearing aids. In both scenarios, the hearing-cognitive outcome relationships were not attenuated. (Supplementary Table 3).

Table 3. Absolute Differences in Cognitive Outcome Scores for Categories of Hearing Loss in Those 50 Years and Older; Hispanic Community Health Study (HCHS; n = 5,277)

Hearing Loss Category (median dB)	Digit Symbol Substitution Test*	Word Frequency Test*	SEVLT 3 Trials*	SEVLT Recall*	Six-Item Screener**
Mild (32.5 dB)	−2.48 (−3.43, −1.53)	−1.40 (−2.00, −0.80)	−1.23 (−1.69, −0.76)	−0.73 (−0.98, −0.47)	−0.11 (−0.19, −0.04)
Moderate (47.5 dB)	−3.63 (−5.02, −2.24)	−2.05 (−2.93, −1.17)	−1.79 (−2.47, −1.11)	−1.06 (−1.43, −0.69)	−0.17 (−0.28, −0.05)
Moderately-severe (62.5 dB)	−4.78 (−6.60, −2.95)	−2.69 (−3.85, −1.53)	−2.36 (−3.26, −1.47)	−1.40 (−1.88, −0.91)	−0.22 (−0.37, −0.07)
Severe (80 dB)	−6.11 (−8.45, −3.78)	−3.45 (−4.93, −1.96)	−3.02 (−4.17, −1.88)	−1.79 (−2.40, −1.17)	−0.28 (−0.47, −0.09)

Notes: Score differences are compared to normal hearing (0 dB HL). Score differences are followed by 95% CI. Results are for the fully adjusted model, which adjusts for demographics, hearing aid use, and cardiovascular risk factors. SEVLT = Spanish-English Verbal Learning Test.

*p< .001.
**p < .01.

Table 4. Age-Stratified Fully Adjusted Regression Models for Cognitive Outcomes Based on Hearing Loss; Hispanic Community Health Study (HCHS; n = 5,277).

Age Stratum	No.	Digit Symbol Substitution Test		Word Frequency Test		SEVLT 3 Trials		SEVLT Recall		Six-Item Screener	
		Score Difference Per 20 dB of HL (95% CI)a	p	Score Difference Per 20 dB of HL (95% CI)a	p	Score Difference Per 20 dB of HL (95% CI)a	p	Score Difference Per 20 dB of HL (95% CI)a	p	Score Difference Per 20 dB of HL (95% CI)a	p
50-59 Years	3,245	−2.23 (−3.10, −1.36)	<0.001	−0.93 (−1.46, −0.40)	<0.01	−1.22 (−1.63, −0.80)	<0.001	−0.63 (−0.85, −0.41)	<0.001	−0.08 (−0.14, −0.02)	<0.05
60-69 Years	1,676	−1.33 (−2.20, −0.47)	<0.01	−0.80 (−1.37, −0.23)	<0.01	−0.54 (−0.97, −0.11)	<0.05	−0.37 (−0.60, −0.13)	<0.01	−0.09 (−0.17, −0.01)	<0.5
70-79 Years	356	−2.52 (−4.23, −0.81)	<0.01	−0.94 (−2.13, 0.24)	0.12	−0.43 (−1.41, 0.56)	0.39	−0.33 (−0.85, 0.19)	0.22	−0.07 (−0.26, 0.13)	0.51

Notes: Linear regression was used for all cognitive outcomes. Results are for the fully adjusted model, which adjusts for demographics, hearing aid use, and cardiovascular risk factors. HL, hearing loss; SEVLT = Spanish-English Verbal Learning Test.

* A 20-dB increase in HL is approximately equivalent to a 1-category worsening (categories are: normal, mild, moderate, moderately-severe, severe, profound).

Adding a quadratic term for age to the fully adjusted linear models to attempt to better control for the confounding effect of age did not change the relationship between hearing and cognition (Supplementary Table 3). In addition, it did not appreciably decrease the Akaike information criteria, indicating no improvement in model fit (<0.02% change for all models).

We also used ordinal logistic regression to analyze the Six-Item Screener since the score only ranges from 0 to 6. This modeling technique provides the odds of a lower score category (i.e. lower whole number score) versus a higher score category. In the fully adjusted model (model 4), the odds being in a lower score category increased 1.14 times (95% CI, 1.02, 1.27; $p < .05$) for every 20-dB increase in HL.

Discussion

We found that age-related HL, defined audiometrically, was associated with lower cognitive performance in all tests and domains, including tests that can be taken independent of hearing ability. A dose–response relationship was observed. Furthermore, this association was present even at mild levels of hearing impairment.

We found robust and significant associations between HL and all five cognitive outcomes, spanning domains of psychomotor speed, attention, verbal functioning, learning, verbal memory, and global cognition. In the fully adjusted models, HL was associated with decreased scores in the DSST, Word Frequency Test, SEVLT3 trials, SEVLT recall, and Six-Item Screener. The strength of association between hearing and cognition was similar and statistically equivalent across these outcomes. These models controlled for a wide variety of confounders including demographics (age, gender, and education), hearing aid use, and cardiovascular risk factors.

Our data extend findings of prior primarily educated/white (7–10) cohorts to Hispanics, the fastest growing ethnicity in the United States. Although it is difficult to compare studies because of heterogeneity of outcomes and covariates, the hearing–cognition relationship apparently holds across numerous racial/ethnic groups (3,11). Interestingly, controlling for bilingualism or testing language had no effect.

There is growing medical and policy interest in the association between age-related HL and cognition (1–3). This stems from the high burden of untreatable dementia (4), high prevalence of HL (80% of those over 80 years (35)), and low prevalence of hearing aid use (under 25% of those over 80 years (36)).

The observed association between HL and cognition is clinically meaningful. To put the findings in context, the reduction in cognition associated with a modest 1-category hearing drop in the fully adjusted models was equivalent to an additional 0.7 (Six-Item Screener) to 10 (Word Frequency Test) years of aging.

Even with mild HL, there was a measurable difference in cognitive outcomes compared to normal hearing individuals. This finding is meaningful because mild HL is very common and begins around age 50 (35). Large differences were noted for the most severely hearing-impaired category.

We examined whether the relationship between HL and cognition varied by gender or by age. Despite a few instances of significant interaction, there was no meaningful pattern observed.

The association between hearing and cognition remained significant after adjusting for depressive symptoms. Depression could act as a confounder, causing poorer hearing test and cognitive test performance due to lack of motivation (i.e. measurement error of both the exposure and outcome.) Depression could also act as a mediator,

whereby HL causes depression, which, through additional steps such as social withdrawal, results in poorer cognition. Although there is inadequate evidence to state that HL causes depression, they have been associated in cross-sectional and longitudinal studies (4,28,32–34). Prior studies of audiometric (9,37) or non-audiometric (38) HL have rarely taken comorbid depressive symptoms into account.

Cognitive dysfunction has many different risk factors. As a result, only a small fraction of the overall variability in cognition is explained by HL. However, any relationship between HL and cognition is noteworthy because of the high prevalence of HL (80% in people over 80 years) and poor treatment levels (under 20% use hearing aids or cochlear implants). Thus, a relatively high proportion of cognitive dysfunction could be attributable to HL. A recent review predicted that preventing or treating HL could result in the single largest percentage reduction in dementia of any known risk factor (4).

A methodologic concern is that HL could result in lower performance on cognitive tests because subjects could not hear the instructions or the oral presentation of test stimuli. In this scenario, hearing-impaired subjects would be misclassified as having worse cognition, creating a false-association. This seems unlikely because neuropsychological testing in HCHS was conducted in a quiet, well-lit setting with a single trained examiner (39). In this environment, HL should not interfere with clearly spoken instructions except when profound. Fewer than 0.1% of subjects had profound HL and fewer than 0.4% had severe or profound HL. Furthermore, we found a strong inverse association between HL and cognition even when we restricted the analysis to subjects with normal hearing or mild HL, or to only subjects who did not use hearing aids. Finally, strong associations were seen in the DSST, which is a non-verbal test. Although initial instructions are spoken, the subject repeats non-scored trials until he/she clearly understands the task. After this point, the entire test is performed in silence with pen and pencil.

This study had limitations. Our analyses were cross-sectional and limited to the only available wave of HCHS. Thus, our inferences about temporality and causality are limited at this time. Although findings remained significant after controlling for numerous confounders, residual confounding remains a possibility. For example, as-yet unidentified factors could cause both HL and impaired cognition. We used linear regression, which is easy to interpret and apply to clinical scenarios. Future studies should also explore non-linear regression techniques.

However, this study has important strengths. With more than 5,000 included subjects this is the largest study to date examining the association of formally tested audiometric hearing and cognition. The large sample size provided power to examine for interaction. We also performed unique sensitivity analyses, including adding bilingualism or testing language as a covariate, adding depressive symptoms as a covariate, restricting to subjects with no more than mild HL, and restricting to subjects without hearing aids. These sensitivity analyses had no or little effect on the hearing–cognition relationship.

Finally, prior studies, including some with larger sample sizes (16), have relied on self-reported (3,12) or central auditory tests (14–16) instead of audiometrically measured peripheral hearing tests. Self-reported HL can be subject to bias (17) since it does not always correlate to true, audiometric hearing levels. Central auditory tests, while often affected by peripheral auditory function, do not ideally measure age-related changes of the peripheral auditory system. Neurodegeneration underlying cognitive impairment and dementia may cause central auditory dysfunction, but should not cause peripheral age-related HL (40,41).

Our study is the largest study to date to examine the association of objectively and formally ascertained hearing and cognitive performance in middle and late age, and establishes that even mild HL is associated with worse cognitive performance. It also extends prior findings to the U.S. Hispanic population. Future studies should explore the mechanisms that underlie the association and whether HL coexists with cognitive decline (having common origins) or causes cognitive decline.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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Conflict of Interest

J.S.G. (travel expenses for industry-sponsored meetings, Cochlear, Advanced Bionics, Oticon Medical; consulting fees, Oticon Medical, Auditory Insight; educational grants to department, Storz, Stryker, Acclarent).

References

1. Lin FR, Metter EJ, O'Brien RJ, Resnick SM, Zonderman AB, Ferrucci L. Hearing loss and incident dementia. *Arch Neurol.* 2011;68:214–220. doi:10.1001/archneurol.2010.362

2. Gallacher J, Ilubaera V, Ben-Shlomo Y, et al. Auditory threshold, phonologic demand, and incident dementia. *Neurology.* 2012;79:1583–1590. doi:10.1212/WNL.0b013e31826e263d

3. Golub JS, Luchsinger JA, Manly JJ, Stern Y, Mayeux R, Schupf N. Observed hearing loss and incident dementia in a multiethnic cohort. *J Am Geriatr Soc.* 2017;65:1691–1697. doi:10.1111/jgs.14848

4. Livingston G, Sommerlad A, Orgeta V, Costafreda SG, Huntley J, Ames D, et al. Dementia prevention, intervention, and care. *Lancet.* 2017; 390:2673–2734. doi:10.1016/s0140-6736(17)31363-6

5. Lin FR, Hazzard WR, Blazer DG. Priorities for improving hearing health care for adults: a report from the national academies of sciences, engineering, and medicine. *JAMA.* 2016;316:819–820. doi:10.1001/jama.2016.7916

6. Blazer DG, Domnitz S, Liverman CT. *Hearing Heatlh Care for Adults: Priorities for Improving Access and Affordability.* Washington, DC: The National Academies of Sciences, Engineering, Medicine; 2016.

7. Lin FR, Ferrucci L, Metter EJ, An Y, Zonderman AB, Resnick SM. Hearing loss and cognition in the Baltimore Longitudinal Study of Aging. *Neuropsychology.* 2011;25:763–770. doi:10.1037/a0024238

8. Ray J, Popli G, Fell G. Association of cognition and age-related hearing impairment in the english longitudinal study of ageing. *JAMA Otolaryngol Head Neck Surg.* 2018;144:876–882. doi:10.1001/jamaoto.2018.1656

9. Harrison Bush AL, Lister JJ, Lin FR, Betz J, Edwards JD. Peripheral hearing and cognition: evidence from the Staying Keen in Later Life (SKILL) Study. *Ear Hear.* 2015;36:395–407. doi:10.1097/AUD.0000000000000142

10. Loughrey DG, Kelly ME, Kelley GA, Brennan S, Lawlor BA. Association of age-related hearing loss with cognitive function, cognitive impairment, and dementia: a systematic review and meta-analysis. *JAMA Otolaryngol Head Neck Surg.* 2018;144:115–126. doi:10.1001/jamaoto.2017.2513

11. Deal JA, Betz J, Yaffe K, et al.; Health ABC Study Group. Hearing impairment and incident dementia and cognitive decline in older adults: the health ABC study. *J Gerontol A Biol Sci Med Sci.* 2017;72:703–709. doi:10.1093/gerona/glw069

12. Gurgel RK, Ward PD, Schwartz S, Norton MC, Foster NL, Tschanz JT. Relationship of hearing loss and dementia: a prospective,

13. Zheng Y, Fan S, Liao W, Fang W, Xiao S, Liu J. Hearing impairment and risk of Alzheimer's disease: a meta-analysis of prospective cohort studies. *Neurol Sci.* 2017;38:233–239. doi:10.1007/s10072-016-2779-3

14. Gates GA, Anderson ML, McCurry SM, Feeney MP, Larson EB. Central auditory dysfunction as a harbinger of Alzheimer dementia. *Arch Otolaryngol Head Neck Surg.* 2011;137:390–395. doi:10.1001/archoto.2011.28

15. 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;50:482–488.

16. Rönnberg J, Hygge S, Keidser G, Rudner M. The effect of functional hearing loss and age on long- and short-term visuospatial memory: evidence from the UK biobank resource. *Front Aging Neurosci.* 2014;6:326. doi:10.3389/fnagi.2014.00326

17. Choi JS, Betz J, Deal J, et al. A comparison of self-report and audiometric measures of hearing and their associations with functional outcomes in older adults. *J Aging Health.* 2016;28:890–910. doi:10.1177/0898264315614006

18. Gates GA, Anderson ML, Feeney MP, McCurry SM, Larson EB. Central auditory dysfunction in older persons with memory impairment or Alzheimer dementia. *Arch Otolaryngol Head Neck Surg.* 2008;134:771–777. doi:10.1001/archotol.134.7.771

19. ASHA. *Degrees of Hearing Loss.* https://www.asha.org/public/hearing/degree-of-hearing-loss/. Accessed January 14, 2019.

20. Wechsler D. *WAIS-R Manual: Wechsler Adult Intelligence Scale—Revised.* New York, NY: Harcourt Brace Jovanovich for Psychological Corp; 1981.

21. Venkatraman VK, Aizenstein HJ, Newman AB, et al. Lower digit symbol substitution score in the oldest old is related to magnetization transfer and diffusion tensor imaging of the white matter. *Front Aging Neurosci.* 2011;3:11. doi:10.3389/fnagi.2011.00011

22. Spreen O, Strauss E. *A Compendium of Neuropscyhological Tests,* 2nd ed. New York, NY: Oxford University Press; 1998.

23. González HM, Mungas D, Reed BR, Marshall S, Haan MN. A new verbal learning and memory test for English- and Spanish-speaking older people. *J Int Neuropsychol Soc.* 2001;7:544–555.

24. Callahan CM, Unverzagt FW, Hui SL, Perkins AJ, Hendrie HC. Six-item screener to identify cognitive impairment among potential subjects for clinical research. *Med Care.* 2002;40:771–781. doi:10.1097/01.MLR.0000024610.33213.C8

25. Luchsinger JA, Reitz C, Honig LS, Tang MX, Shea S, Mayeux R. Aggregation of vascular risk factors and risk of incident Alzheimer disease. *Neurology.* 2005;65:545–551. doi:10.1212/01.wnl.0000172914.08967.dc

26. Vatcheva KP, Lee M, McCormick JB, Rahbar MH. Multicollinearity in regression analyses conducted in epidemiologic studies. *Epidemiology (Sunnyvale).* 2016;6. doi:10.4172/2161-1165.1000227

27. HCHS/SOL. *Derived Variable Dictionary.* 2014:68.

28. Rutherford BR, Brewster K, Golub JS, Kim AH, Roose SP. Sensation and psychiatry: linking age-related hearing loss to late-life depression and cognitive decline. *Am J Psychiatry.* 2018;175:215–224. doi:10.1176/appi.ajp.2017.17040423

29. Brown PJ, Roose SP, Fieo R, et al. Frailty and depression in older adults: a high-risk clinical population. *Am J Geriatr Psychiatry.* 2014;22:1083–1095. doi:10.1016/j.jagp.2013.04.010

30. González P, Nuñez A, Merz E, et al. Measurement properties of the Center for Epidemiologic Studies Depression Scale (CES-D 10): findings from HCHS/SOL. *Psychol Assess.* 2017;29:372–381. doi:10.1037/pas0000330

31. Spielberger CD, Gorsuch RL, Lushene RE. *The State-Trait Anxiety Inventory: Test Manual.* Palo Alto, CA: Consulting Psychological Press; 1970.

32. Golub JS, Brewster K, Brickman AM, Ciarleglio A, Kim AH, Luchsinger J, et al. *Audiometric Age-Related Hearing Loss Is Associated with Depressive Symptoms in Hispanics.* 2019. In press.

33. Brewster KK, Ciarleglio A, Brown PJ, et al. Age-related hearing loss and its association with depression in later life. *Am J Geriatr Psychiatry.* 2018;26:788–796. doi:10.1016/j.jagp.2018.04.003

34. Lee AT, Tong MC, Yuen KC, Tang PS, Vanhasselt CA. Hearing impairment and depressive symptoms in an older chinese population. *J Otolaryngol Head Neck Surg*. 2010;39:498–503. doi:10.2310/7070.2010.090265

35. Goman AM, Lin FR. Prevalence of hearing loss by severity in the United States. *Am J Public Health*. 2016;106:1820–1822. doi:10.2105/AJPH.2016.303299

36. Chien W, Lin FR. Prevalence of hearing aid use among older adults in the United States. *Arch Intern Med*. 2012;172:292–293. doi:10.1001/archinternmed.2011.1408

37. Deal JA, Sharrett AR, Albert MS, et al. Hearing impairment and cognitive decline: a pilot study conducted within the atherosclerosis risk in communities neurocognitive study. *Am J Epidemiol*. 2015;181:680–690. doi:10.1093/aje/kwu333

38. Amieva H, Ouvrard C, Giulioli C, Meillon C, Rullier L, Dartigues JF. Self-reported hearing loss, hearing aids, and cognitive decline in elderly adults: a 25-year study. *J Am Geriatr Soc*. 2015;63:2099–2104. doi:10.1111/jgs.13649

39. HCHS/SOL. *Hispanic Community Health Study: Study of Latinos. Manual 9: Neurocognitive Function Summary*. January 23, 2008–Version 1.0.; 2008.

40. Lin FR. Hearing loss and cognition among older adults in the United States. *J Gerontol A Biol Sci Med Sci*. 2011;66:1131–1136. doi:10.1093/gerona/glr115

41. Sinha UK, Hollen KM, Rodriguez R, Miller CA. Auditory system degeneration in Alzheimer's disease. *Neurology*. 1993;43:779–785.