

RESEARCH ARTICLE

Hearing loss and cognition: A protocol for ensuring speech understanding before neurocognitive assessment

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Abstract

INTRODUCTION: Many neurocognitive evaluations involve auditory stimuli, yet there are no standard testing guidelines for individuals with hearing loss. The ensuring speech understanding (ESU) test was developed to confirm speech understanding and determine whether hearing accommodations are necessary for neurocognitive testing. **METHODS:** Hearing was assessed using audiometry. The probability of ESU test failure by hearing status was estimated in 2679 participants (mean age: 81.4 ± 4.6 years) using multivariate logistic regression.

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RESULTS: Only 2.2% ($N = 58$) of participants failed the ESU test. The probability of failure increased with hearing loss severity; similar results were observed for those with and without mild cognitive impairment or dementia.

DISCUSSION: The ESU test is appropriate for individuals who have variable degrees of hearing loss and cognitive function. This test can be used prior to neurocognitive testing to help reduce the risk of hearing loss and compromised auditory access to speech stimuli causing poorer performance on neurocognitive evaluation.

KEYWORDS

aging, cognition, dementia, hearing loss, mild cognitive impairment, neurocognitive evaluation, speech understanding

1 | BACKGROUND

Neurocognitive evaluations are commonly performed in both research and clinical settings with older adults, a population in which age-related hearing loss is also highly prevalent.¹ Hearing loss has also been found to be independently associated with accelerated cognitive decline and incident cognitive impairment, which is of particular concern for the older adult population.² Administration instructions for neurocognitive testing often recommend that tests be performed face to face in a quiet environment with minimal background noise in order to optimize spoken communication. However, there are no standard guidelines by which to confirm that older adults with hearing loss have auditory access (i.e., are able to hear) the test instructions and information.³ Hearing loss is an important consideration for neurocognitive testing. Indeed, previous research demonstrated better performance by those with hearing loss when auditory components were removed,⁴ yet few studies offer accommodations for hearing loss during cognitive testing.³ The presence of hearing loss may adversely affect neurocognitive performance if the participant is unable to access spoken information that is necessary for test completion, thereby leading to neurocognitive test results that do not accurately reflect the individual's cognitive function.

The ensuring speech understanding (ESU) test was developed to address concerns related to the effects of hearing loss on the accuracy of neurocognitive evaluations, such as the effects of not having access to information necessary for testing. The objectives of this test include confirming that participants can adequately hear spoken instructions and items presented during neurocognitive assessment, as well as determining whether the use of visual aids or other accommodations are necessary. The ESU test was developed in preparation for a randomized clinical trial comparing whether hearing loss intervention reduces rates of cognitive decline in older adults compared to a control intervention providing healthy aging education.^{5,6} The current paper describes the ESU test, characterizes ESU test results after administration in a large epidemiological cohort of older adults undergoing concurrent audiological testing and neurocognitive evaluation, and provides recommendations for future applications of the ESU test.

2 | METHODS

2.1 | Participants and setting

The Atherosclerosis Risk in Communities (ARIC) study is an ongoing prospective longitudinal study of older adults from four communities across the United States.⁷ Further information regarding diversity, equity, and inclusion with respect to the ARIC study can be found in the referenced publication regarding the study design.⁸ Initial enrollment, which occurred between 1987 and 1989, included 15,792 adults aged 45 to 64 years.⁷ Field sites include Washington County, Maryland; Forsyth County, North Carolina; Jackson, Mississippi; and suburbs of Minneapolis, Minnesota. ARIC participants are independent and live in the community (i.e., are not institutionalized) and have completed subsequent study sessions for more than 30 years. This study was performed in accordance with the ethical standards in the 1964 Declaration of Helsinki as well as its subsequent amendments and was approved by the Institutional Review Boards at all participating institutions. The ESU protocol was performed prior to neurocognitive evaluation at ARIC visit 7, which occurred between February 2018 and September 2019.⁹

A total of 3589 participants completed ARIC visit 7. Individuals with missing information were excluded from the analytic sample. Excluded participants included those who did not undergo neurocognitive assessment ($N = 285$), or with incomplete ESU ($N = 46$). We further excluded participants with incomplete audiometric thresholds ($N = 559$) from ARIC visit 6 (2016 to 2017), with missing education data ($N = 3$), with self-reported race or ethnicity other than Black or White ($N = 8$), and Black participants from majority White centers ($N = 9$). The final analytic sample comprised 2679 participants.

2.2 | Hearing measures

Hearing sensitivity was assessed using pure tone audiometry and represented by the four-frequency pure tone average (PTA) for the better-hearing ear. PTA was calculated by averaging audiometric thresholds at 500, 1000, 2000, and 4000 Hz for each ear, which are indicated in

decibels hearing level (dB HL). The lower average was selected as the better-hearing ear. Any PTA less than 20 dB HL was considered within normal limits, consistent with the guidelines set forth in the 2021 World Health Organization (WHO) Report on Hearing.¹⁰ PTAs of 20 or greater were grouped into categories representing degrees of hearing loss severity according to WHO guidelines.¹⁰ The hearing loss categories used included mild (20 to 34 dB HL), moderate (35 to 49 dB HL), moderately severe (50 to 64 dB HL), severe (65 to 79 dB HL), profound (80 to 94 dB HL), and complete (≥ 95 dB HL). Severe, profound, and complete hearing loss categories were combined in statistical analyses due to the small number of individuals in these categories.

2.3 | Cognitive status

Adjudication of dementia and mild cognitive impairment (MCI) was performed by a panel of neurologists and neuropsychologists who reviewed materials, including neurocognitive examinations performed at previous visits for the ARIC study, informant interview information, neuroimaging results (when available), and neurologic and medical history.⁹ This expert committee determined diagnoses of dementia or MCI according to the National Institute on Aging-Alzheimer's Association criteria.^{11,12} More detailed information regarding the evaluations used, performance, and standardization across ARIC sites is given elsewhere.⁹

2.4 | Other variables

Demographic information, including age (continuous in years), sex (female, male), race (Black, White), and level of education (less than high school, high school or equivalent, and more than high school), was self-reported.

2.5 | ESU test

The ESU test was developed to ensure that neurocognitive testing was not unduly affected by a lack of auditory perception. The methodology for the ESU test was created by a multidisciplinary team composed of audiologists, psychologists, and gerontologists. Sentences were sourced from an established sentence corpus comprising the Hearing in Noise Test (HINT), which was developed by House Ear Institute to evaluate speech understanding in background noise, and has been widely used in the field of audiology to evaluate speech understanding among those with and without hearing loss.¹³ The benefits of using the HINT materials include sentences of equivalent length and difficulty, as well as a balance of both present and past tense verb usage. During the original development of the HINT test, Nilsson et al. (1994) observed repeated incorrect responses of articles (e.g., a, or, the) and verb tense (e.g., is/was).¹³ Therefore, verb tense (e.g., is/was), articles (e.g., the/a), and prepositions (e.g., in) were not scored on the ESU test.

RESEARCH IN CONTEXT

- 1. Systematic review:** Few studies consider how hearing may affect neurocognitive evaluation. There are also no standardized guidelines for testing individuals who have hearing loss. The ensuring speech understanding (ESU) test was created to ensure neurocognitive evaluations are not unduly influenced by hearing loss, which may decrease an individual's auditory access to test information.
- 2. Interpretation:** The ESU test is a brief measure to ensure speech understanding prior to neurocognitive assessment. Findings suggest that the ESU test can be used for individuals with various degrees of hearing loss, as well as individuals with or without mild cognitive impairment and dementia.
- 3. Future directions:** There is a need for standardized guidelines for testing individuals with hearing loss. The ESU test is recommended for use prior to neurocognitive testing to help account for the potential impacts of hearing loss on performance. Further investigation is required to establish a consensus regarding appropriate accommodations.

To be cognizant of the need for a brief assessment prior to the much lengthier neurocognitive evaluation, five sentences per trial, with each sentence containing three keywords, were established for the ESU test. This resulted in a maximum score of 15 (five sentences with three keywords) for each trial. A passing score of 13/15 was deemed appropriate by the multidisciplinary development team based on two main criteria. The first criterion is the neurocognitive test battery used, and the second was the similarity of the 86.7% score to the "excellent" score criterion traditionally used to describe speech recognition scores between 90% and 100% in audiological evaluations.^{14,15}

Prior to beginning the ESU test, the examiner ensured that the testing environment was appropriate by following standard guidelines for neurocognitive test administration: face-to-face administration in a quiet room. The examiner also confirmed that any sensory aids that the participant would normally use at home (e.g., hearing aids, glasses) were used for testing. It was expected that individuals with mild to moderate hearing loss, such as most of the participants in the study, when also using their usual sensory aids would perform well on one trial.¹⁶⁻¹⁸ The test was then explained, and the examiner checked for participant understanding; if the participant did not understand the instructions, then these were repeated, and the participant was given the opportunity to ask questions. The examiner confirmed participant understanding before beginning the test. The ESU test includes up to two trials. Each trial consists of a set of five short sentences, each containing three keywords by which the trial is scored (Figure 1). The examiner presented the sentences verbally using clear articulation and

b. The PLAYER LOST the SHOE	<input type="checkbox"/>	b. The BOOK TELLS a STORY	<input type="checkbox"/>
c. The FIRE is VERY HOT	<input type="checkbox"/>	c. The TEAM is PLAYING WELL	<input type="checkbox"/>
d. A LADY WORE a COAT	<input type="checkbox"/>	d. A BOY DID a HANDSTAND	<input type="checkbox"/>
e. The KITCHEN WINDOW was CLEAN	<input type="checkbox"/>	e. MOTHER OPENED the DRAWER	<input type="checkbox"/>
f. STRAWBERRY JAM is SWEET	<input type="checkbox"/>	f. The FISH SWAM in a POND	<input type="checkbox"/>
g. Total Score:	<input type="checkbox"/> <input type="checkbox"/>	g. Total score:	<input type="checkbox"/> <input type="checkbox"/>

FIGURE 1 HINT sentences used for ESU test keywords by which ESU test is scored are capitalized.

normal inflections. Each sentence was presented once at the pace and volume typical for neurocognitive testing.

All examiners received training in interviewing techniques, as well as administration of the ESU test and neurocognitive evaluation. Trainings reviewed the use of volume and pace commensurate with typical neurocognitive testing, and certification was approved through performance reviews by study investigators and staff with expertise in the administration and scoring of interview questionnaires and neurocognitive tests. Participants were instructed to repeat what they heard after each sentence. Keywords were scored by accuracy; words with similar phonemes were marked incorrect. ESU test scores represent the number of keywords repeated correctly by the participant. The total possible correct score for each trial of the ESU test is 15, and a score of 13 or greater is considered passing.

If the participant achieved a score of 13 or above on the first trial, the test administrator proceeded with neurocognitive testing. In the event that the participant scored less than 13, a second ESU trial was performed using a slightly louder voice to improve audibility of the test materials and increase communication efficacy. This “slightly louder voice” was demonstrated in videos shown during examiner training. The second trial also consists of five different sentences also sourced from the HINT materials (Figure 1). If the participant passed the second trial of the ESU, the test administrator proceeded using the slightly louder voice for the subsequent neurocognitive testing. If the participant failed the second trial of the ESU test, cognitive testing proceeded with the slightly louder voice and the use of additional visual prompts, such as large text representations of test questions.

2.6 | Statistical analysis

Probability of failure on the ESU test by hearing level was investigated by calculating the predictive margins from multivariable-adjusted logistic regressions. Models were adjusted for sex, race/center, education, and age. Race is closely linked with field site in ARIC. Therefore, a categorical race/center variable (Maryland White, Minnesota White, North Carolina White, North Carolina Black, Mississippi Black) is used in analyses. As very few individuals failed the ESU test, the outcome was limited to only those who failed the first ESU trial. Hearing level was represented by PTA in the better-hearing ear.

The primary analysis examined the probability of failure on the ESU test by categorical hearing loss severity. All participants with normal hearing ($N = 480$) and Black participants from North Carolina ($N = 48$) passed ESU test trial 1 and thus were excluded from this analysis as

the covariates predicted the outcome perfectly. A secondary analysis computed the probability of ESU failure in terms of hearing loss, indicated by PTA, for those with and without a diagnosis of dementia or MCI. In this secondary analysis all Black participants from North Carolina ($N = 55$) passed the ESU test trial 1 and thus were excluded from this analysis as the covariates predicted the outcome perfectly.

3 | RESULTS

Characteristics of the study population in terms of hearing loss severity are indicated in Table 1. Only 58 individuals (2.2%) did not pass the ESU on the first trial. The mean overall age was 81.4 ± 4.6 years (range: 73 to 95 years), which increased with hearing loss severity. Both the proportion of female and Black individuals decreased with increasing hearing loss severity.

Of the entire analytical sample, 2395 participants achieved a perfect score, and an additional 226 received a passing score (≥ 13 ; score = 14, $N = 182$, score = 13, $N = 44$) for the initial trial of the ESU test (Figure 2). The distribution of ESU test scores also indicated that no participant scored less than 8 on the first trial.

As the second trial of the ESU test was performed only with those who failed the first trial ($N = 58$), a brief description of performance for this subgroup is also provided. Upon comparison of ESU test scores between trials 1 and 2, a majority (63.8%; $N = 37$) of the participants who completed the second trial of the ESU test passed (Figure 3). $N = 7$ participants received the same score, $N = 5$ participants received a lower score, $N = 6$ participants improved their score but failed a second time, and $N = 3$ participants did not complete the second trial of the ESU test.

The probability of failing the first trial of the ESU test increased with increasing hearing loss severity (Figure 4). In fully adjusted models, the estimated probability of failing the ESU test was 0.003 (95% confidence interval [CI]: 0 to 0.007) for mild hearing loss, 0.023 (95% CI: 0.013 to 0.033) for moderate hearing loss, 0.081 (95% CI: 0.047 to 0.114) for moderately severe hearing loss, and 0.169 (95% CI: 0.087 to 0.251) for severe or greater hearing loss. The association was similar for both individuals with and without dementia or MCI (Figure 5).

4 | DISCUSSION

The ESU test represents a brief, objective method by which to determine whether a participant has adequate auditory access to speech or

TABLE 1 Participant characteristics by hearing loss severity.

	Hearing loss severity ^a						P value
	Total N = 2679	None N = 480	Mild N = 1137	Moderate N = 701	Moderately severe N = 290	Severe and greater N = 71	
Age (years), mean (SD)	81.4 (4.6)	79.2 (3.3)	80.7 (4.2)	82.8 (4.8)	84.1 (4.9)	83.4 (5.0)	<0.001
Female	1571 (58.6)	361 (75.2)	738 (64.9)	340 (48.5)	116 (40.0)	16 (22.5)	<0.001
Race and center							<0.001
Minneapolis, White	824 (30.8%)	132 (27.5%)	336 (29.6%)	244 (34.8%)	93 (32.1%)	19 (26.8%)	
Jackson, Black	553 (20.6%)	160 (33.3%)	277 (24.4%)	92 (13.1%)	19 (6.6%)	5 (7.0%)	
Washington, White	658 (24.6%)	105 (21.9%)	251 (22.1%)	168 (24.0%)	100 (34.5%)	34 (47.9%)	
Forsyth, Black	55 (2.1%)	13 (2.7%)	27 (2.4%)	12 (1.7%)	3 (1.0%)	0 (0.0%)	
Forsyth, White	589 (22.0%)	70 (14.6%)	246 (21.6%)	185 (26.4%)	75 (25.9%)	13 (18.3%)	
Education							<0.001
< High school	307 (11.5)	38 (7.9)	125 (11.0)	90 (12.8)	35 (12.1)	19 (26.8)	
High school or equivalent	1082 (40.4)	182 (37.9)	436 (38.3)	315 (44.9)	122 (42.1)	27 (38.0)	
More than high school	1290 (48.2)	260 (54.2)	576 (50.7)	296 (42.2)	133 (45.9)	25 (35.2)	
Hearing, ^b mean (SD)	32.6 (14.4)	15.0 (3.2)	26.6 (4.2)	41.2 (4.3)	55.1 (4.0)	73.2 (8.8)	<0.001
Hearing aid use	583 (21.8)	2 (0.4)	63 (5.5)	252 (35.9)	202 (69.7)	64 (90.1)	
Cognitive status							<0.001
Normal	2105 (78.6)	414 (86.3)	915 (80.5)	509 (72.6)	222 (76.6)	45 (63.4)	
MCI	182 (6.8)	13 (2.7)	70 (6.2)	68 (9.7)	20 (6.9)	11 (15.5)	
Dementia	392 (14.6)	53 (11.0)	152 (13.4)	124 (17.7)	48 (16.6)	15 (21.1)	
ESU test trial 1 result							<0.001
Fail	58 (2.2)	0 (0.0)	4 (0.4)	17 (2.4)	23 (7.9)	14 (19.7)	
Pass	2621 (97.8)	480 (100.0)	1133 (99.6)	684 (97.6)	267 (92.1)	57 (80.3)	

Abbreviation: MCI, mild cognitive impairment.

^aHearing loss categories defined by World Health Organization guidelines¹⁰ (mild: 20 to 34 dB HL, moderate: 35 to 49 dB HL, moderately severe: 50 to 64 dB HL, severe or greater: 65+ dB HL).

^bPure tone average (average of audiometric thresholds at 500, 1000, 2000, and 4000 Hz) of better hearing ear.

if accommodations for hearing loss should be provided prior to neurocognitive assessment. Overall, almost all participants (97.8%) passed the ESU test in this study of community-dwelling older adults (age range: 73 to 95 years). Of the 58 participants who failed trial 1, approximately 64% passed on trial 2, for which the examiner used a slightly louder voice. A marginally higher probability of failing the ESU test with increased hearing loss severity was observed, and this test performed equally well in those with and without MCI or dementia. Our results suggest that the ESU test can be routinely used prior to neurocognitive testing in older adults to guard against decreased speech understanding unduly impacting test scores and to determine when hearing accommodations need to be used.

Research comparing neurocognitive assessment performance in older adults with and without hearing loss is limited. For the neurocognitive arm of the ARIC study, hearing loss was associated with greater missingness of test scores on all auditory-only tests and two non-auditory tests in the cognitive test battery.¹⁹ Another study revealed differences in estimates of the impact of sensory impairment on cognitive test performance (e.g., differential item functioning

for tests that do not rely on hearing for administration in both ARIC and the Baltimore Longitudinal Study of Aging (BLSA).¹⁸ Additionally, results from a study examining performance on the Montreal Cognitive Assessment (MoCA), a cognitive screening, revealed that a greater proportion of individuals with normal hearing pass than those with hearing loss, a relationship that persists despite the removal of auditory test components.⁴ Another study revealed that compared to individuals with moderate to profound hearing loss, those with normal hearing or mild hearing loss performed similarly on the MoCA Hearing Impaired Version (MoCA-HI)²⁰ but significantly better on the standard MoCA.²¹

Previous literature also revealed that studies frequently use subjective participant reporting rather than measured hearing thresholds to characterize hearing ability.³ This is of concern because subjective reports of hearing have been found to underestimate hearing loss in older adults.²² Other subjective indicators of hearing loss, such as observed assistive device usage, may also not fully capture the presence of hearing loss among research participants undergoing neurocognitive testing because not all individuals who have hearing loss use amplification or other assistive devices. Previous research found

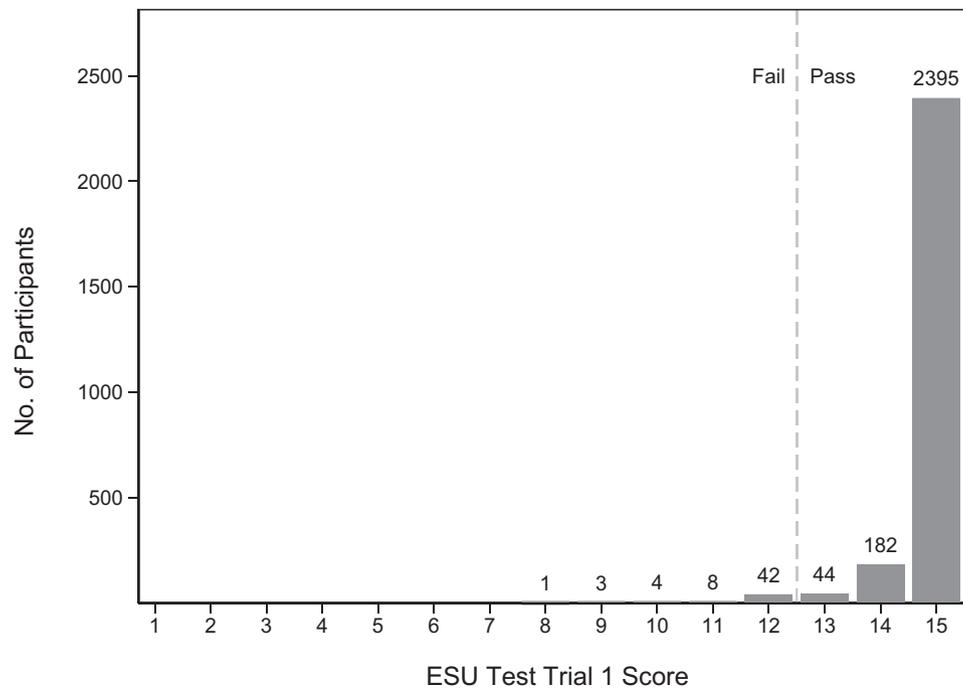


FIGURE 2 Number of participants by ESU test trial 1 score ($N = 2679$).

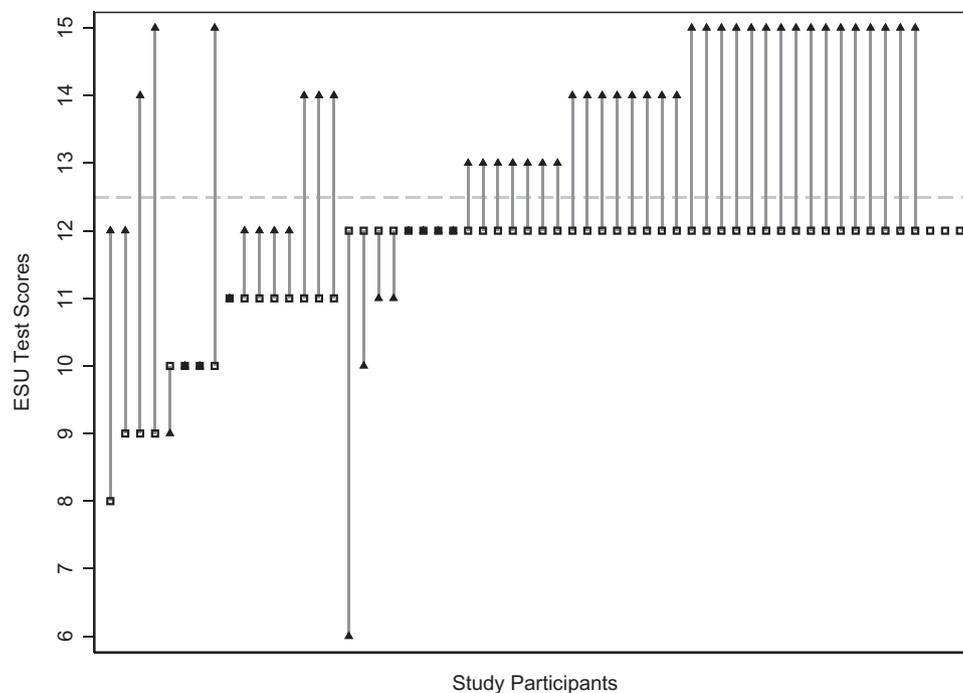


FIGURE 3 ESU test trial scores for participants completing trial 2 ($N = 58$). The score for the first trial of the ESU test is indicated by an open square, the second trial of the test by a triangle. Individuals with a filled square achieved the same score for the first and second trials of the ESU test. (ESU test trial 1 [$N = 58$], mean = 11.5, SD = 0.96; ESU test trial 2 [$N = 55$], mean = 13.22, SD = 1.90; p value: < 0.001).

that less than 20% of individuals who need hearing aids use them.²³ In the present study, participant characteristics indicate that, although hearing aid use increases with increasing hearing loss severity, only 24% of those with hearing loss report using hearing aids.

A particular strength of this study is that, to the best of the authors' knowledge, it is among the first to address the particular challenges that hearing loss poses for neurocognitive testing. The ESU test shows feasibility in a large, epidemiologic cohort of older adults that has

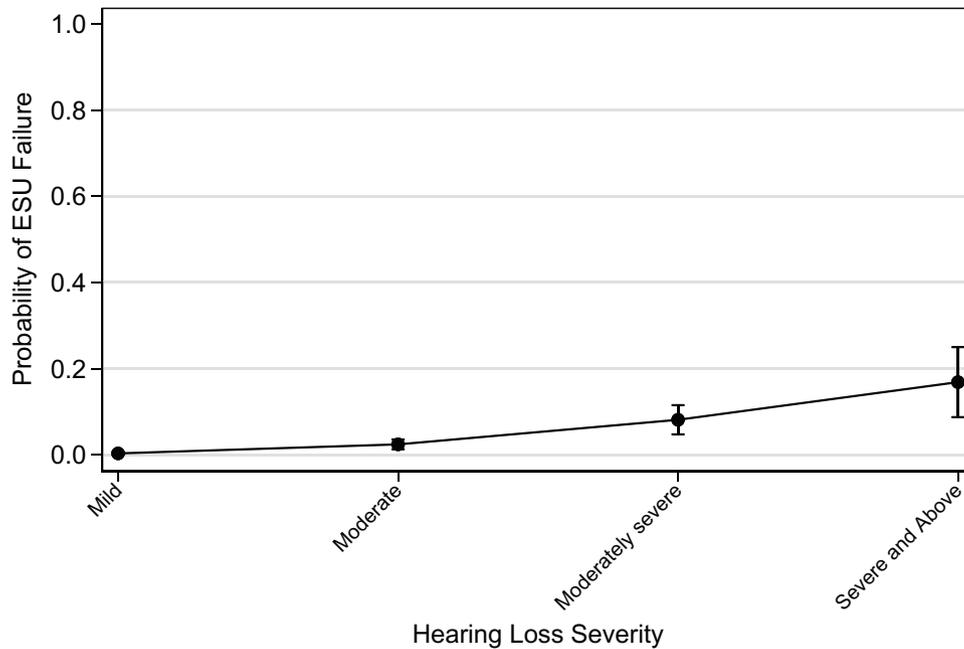


FIGURE 4 Probability of ESU failure by hearing loss severity is defined according to WHO guidelines using the better ear four-frequency (500, 1000, 2000, and 4000 Hz) pure tone average threshold as mild (20 to 34 dB HL), moderate (35 to 49 dB HL), moderately severe (50 to 64 dB HL), and severe and greater (65+ dB HL). All participants with normal hearing ($N = 480$) and all Black participants from North Carolina ($N = 42$) passed the ESU test trial 1 and thus were excluded from this analysis as the covariates for normal hearing and race center predicted the outcome perfectly, yielding a sample size of $N = 2157$ for this analysis.

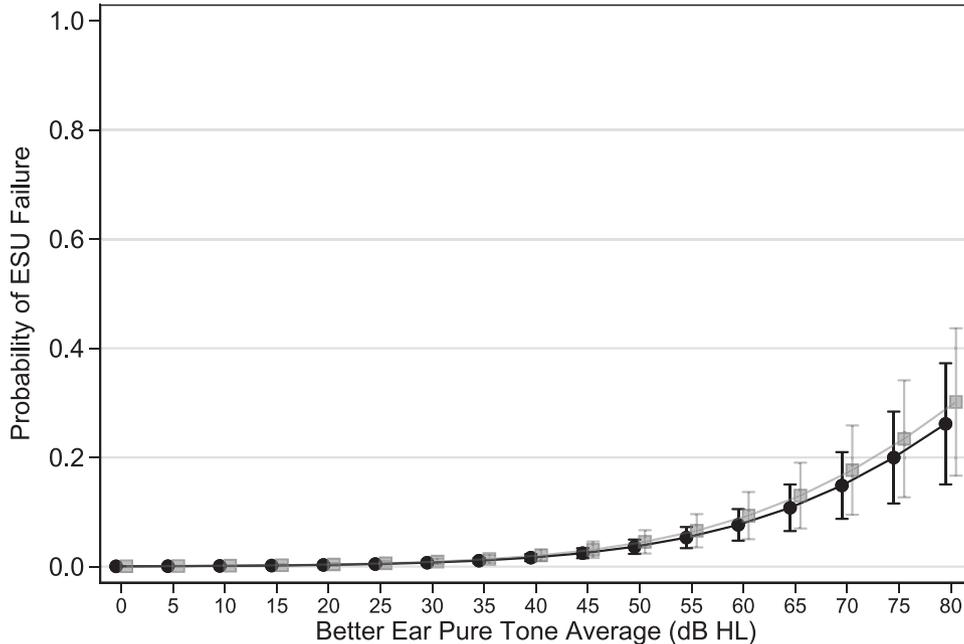


FIGURE 5 Probability of ESU failure by better ear pure tone average (PTA) for persons with and without cognitive impairment ($N = 2624$) pure tone average calculated using average of hearing thresholds at 500, 1000, 2000, and 4000 Hz. Better ear designated by lower PTA. Gray squares: individuals with dementia or mild cognitive impairment; black circles: individuals without dementia or mild cognitive impairment. All Black participants from North Carolina ($N = 55$) passed ESU test trial 1 and thus were excluded from this analysis as the covariate for race center predicted the outcome perfectly, yielding a sample size of $N = 2624$ for this analysis.

good generalizability to older adults in the U.S. Hearing loss may cause reduced speech understanding even in the quiet environments used for neurocognitive testing, adversely affecting performance. This situation is particularly relevant to the older adult population, in which hearing loss is highly prevalent. Previous research estimated that up to two thirds of adults aged 70 years and older in the United States have hearing loss.¹

The typical presentation of age-related hearing loss is decreased sensitivity beginning in the high frequencies and progressing across all frequencies over time. This hearing loss configuration creates challenges, as the high frequencies are where the consonants that impart clarity to speech signals occur. High-frequency hearing loss may result in speech becoming more difficult to understand, even in quiet settings, such as those commensurate with neurocognitive testing. A strength of the ESU test is that it is performed in a setting where neurocognitive evaluation will occur and thus incorporates information, such as speaker volume and visual facial cues (e.g., for lipreading), that will be available during testing. The administration instructions also provide accommodation recommendations that are appropriate for hearing loss, including the use of a louder voice or addition of visual prompts. An a priori cutoff score of 13 was agreed upon by the research team for the present investigation as an acceptable level of speech understanding for the neurocognitive testing in this study. However, the protocol for the ESU test allows for flexibility in setting the passing score requirement. For example, it is also possible to implement a stricter passing requirement if a perfect score is deemed necessary for the targeted neurocognitive evaluation protocol.

There are also limitations to consider for this study. Although the audiometric PTA used to define hearing provides a more reliable indicator of hearing sensitivity than subjective reporting, previous research suggests that the PTA might not fully characterize hearing functionality or account for the differences in real-world speech understanding between those with similar PTAs.²⁴ Additionally, while accommodation recommendations are included for trial 2 of the ESU test, a consensus has not yet been reached regarding the most effective approach to supporting individuals who have hearing loss during neurocognitive testing. Additional methods by which to facilitate effective communication with individuals who have hearing loss have been proposed, but some of these methods (e.g., provision of a portable amplifier) could lead to neurocognitive testing conditions (and, thus, test results) that are not reflective of a participant's daily life.²⁵ The present study included only a small number of individuals with MCI or dementia diagnoses. As such, we were unable to analyze these groups separately by hearing loss severity. Future research may investigate whether these diagnoses affect the likelihood of failure on one or both trials of the ESU test.

In conclusion, the ESU test provides a brief assessment of speech understanding to ensure, prior to neurocognitive testing, that participants have access to the instructions and test items presented verbally. It is an effective tool for use across individuals who have varying degrees of hearing loss, as well as for independent, community-dwelling individuals with MCI or dementia. It is recommended that the ESU test be used in other epidemiologic studies with neurocognitive

assessments or during clinical evaluations to protect against hearing loss and poor speech understanding adversely affecting the accuracy of such testing.

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CONFLICT OF INTEREST STATEMENT

Dr. Reed reports serving on the scientific advisory boards of Neosensory. Dr. Lin reports being a consultant to Frequency Therapeutics and Apple, and being the director of a research center funded in part by a philanthropic gift from Cochlear Ltd. to the Johns Hopkins Bloomberg School of Public Health. Dr. Lin is also a board member of the nonprofit Access HEARS. Dr. Sanchez reports industry funding related to consulting or research support from Otonomy Inc., Autifony Therapeutics Ltd., Boehringer Ingelheim, Frequency Therapeutics Ltd., Pipeline Therapeutics, Aerin Medical, Oticon Medical, Helen of Troy Ltd., Sonova Holding AG, and Phonak USA. All other authors report no relevant conflicts of interest or disclosures.

CONSENT STATEMENT

Participants of the ARIC study provided written informed consent prior to inclusion in the study, as approved the Institutional Review Boards at all participating institutions (Supporting Information).^{5, 8}

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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APPENDIX B
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