ARIC Manuscript Proposal #3488

PC Reviewed: 10/8/19  Status: _____  Priority: 2
SC Reviewed: _________  Status: _____  Priority: _____

1.a. Full Title: Impaired Speech in noise perception ability and Depressive Symptoms in Older Adults in the Atherosclerosis Risk in Communities (ARIC) Study

b. Abbreviated Title (Length 26 characters): Speech perception and depression

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I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. _____ [please confirm with your initials electronically or in writing]

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3. Timeline: Manuscript to be completed within 12 months
4. **Rationale:**

Recent reports suggest a lifetime prevalence of depression in individuals over the age of 65 is around 18%\(^1\), yet some studies suggest over half of reported major depressive cases are incident (late-onset) cases in older age. The presence of depressive symptoms in community-dwelling older adults has been estimated to be between 8-15% \(^{17,19}\). Depression in older adults may have severe consequences as it has been associated with increased disability, mortality, and other neuropsychological impairments\(^{17}\).

The etiology of late-life depression could be related to behavioral or neural mechanisms, including the possible influence of hearing loss. The presence of hearing loss may lead to increased social isolation and withdrawal from social activities, potentially increasing an individual’s risk of developing depression or depressive symptoms\(^{17,20}\). Additionally, hearing loss may create reduced activation of central auditory pathways leading to compensatory activation in the cognitive control network, and atrophy in specific brain regions\(^{29}\). These changes are known to decrease cognitive performance and thereby increase depression risk\(^{30}\).

However, hearing is a complex process. Two physiologic processes are required for hearing and listening: peripheral transduction and encoding of sound in the cochlea followed by central processing of the auditory signal in the brain. Pure tone audiometry (PTA) is considered a measure of peripheral hearing and focuses on the ability of the auditory system to access sound. Speech in noise measures, such as the QuickSIN\(^{28}\), are thought to reflect central auditory processing and capture the ability of the auditory system to separate and recognize speech signals from noise.

The role of peripheral vs. central auditory processing with depressive symptoms has not been well-described. Prior research on the association between hearing loss and late-life depression has been mixed but suggests impaired peripheral hearing increases risk of depression and depressive symptoms in older adults.\(^{17,20-23}\) A recent systematic review meta-analysis of hearing loss and depression\(^{24}\) reports greater odds of depression in hearing impaired compared to normal hearing in both cross-sectional and cohort studies (OR= 1.47 and 1.54, respectively).

To date, very few studies have investigated the influence of depressive symptoms on speech in noise perception ability\(^{25-26}\), to our knowledge only one study\(^{27}\) has assessed the influence of speech in noise perception ability on depression or depressive symptoms in older adults, finding no reported association with depression. Individuals with impaired speech in noise performance and decreased central auditory processing may find it much harder to engage with their surrounding environment and become frustrated with their inability to communicate effectively. Prior work and neuroimaging studies have found individual’s with hearing impairment demonstrate decreased emotional reactivity\(^{28}\) and decreased amygdala and parahippocampal responses to emotional sounds\(^{30}\), yet study on the influence of central auditory processing impairment as measured via speech in noise performance has not been investigated.

To address this research gap, we will quantify how speech in noise perception ability, measured using the QuickSIN assessment, is independently associated with depressive symptoms as measured through the Center for Epidemiologic Studies Depression Scale in ARIC participants who attended visit 6. This work is both novel to the ARIC cohort as well as to the current larger evidence base on hearing impairment and depression by including measures of speech in noise perception as representative of central auditory processing. Prior proposals on hearing impairment and depression in the ARIC cohort assessed the cross-sectional association of peripheral hearing measures and depression.
5. **Main Hypothesis/Study Questions**: To quantify the relationship of speech in noise perception, measured by the QuickSIN test, and depressive symptoms independent of peripheral hearing impairment. We hypothesize that:

- Poorer speech in noise perception ability is cross-sectionally associated with increased presence of depressive symptoms, after adjustment for peripheral hearing loss and other clinical and demographic factors.
- Poorer speech in noise perception ability is associated with a change in depressive symptoms, after adjustment for peripheral hearing loss and other clinical and demographic factors.

6. **Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).**

**Study Design**: The primary analysis is cross-sectional at Visit 6. A secondary analysis includes a longitudinal assessment of visit 6 speech in noise perception measures and change in depressive symptoms from visit 5 to 6.

**Study Population**: Our study sample originates from the full cohort of 15,792 participants who attended visit 6. Participants in the primary analysis include those with complete QuickSIN measures, audiometry, and CES-D assessment at visit 6, leading to an analytic sample of 3,346. In a secondary analysis on change in depressive symptoms, our study sample includes individuals with QuickSIN measured at visit 6 and CES-D assessment at both visit 5 and 6, with a final analytic sample of 3,206 participants.

**Exposure**: The QuickSIN is a measure of speech understanding in the presence of progressively increasing background noise. It is a widely used clinical measure to estimate the impact of hearing loss on speech understanding in a realistic setting and can be used as an estimate of functional difficulty on hearing in noise. QuickSIN measures were completed on all participants who attended visit 6. We will evaluate QuickSIN as continuous using number of correct responses. The method for testing is as follows:

In two trials, participants were presented with six sentences (different for each trial), in the presence of multi-talker babble such as might be experienced in a noisy restaurant, under successively more difficult listening conditions. The sentences were presented binaurally with a fixed presentation level for speech (70 dB HL), and with 5 dB incremental increases in noise level for each sentence, ranging from 25 dB quieter for the first sentence to no difference in volume between speech and noise for the final sentence. After each sentence, participants were instructed to repeat the sentence and to guess if unsure. Scoring for each sentence was on a scale of 0-5 based on correct identification of five target words. For analysis, scores from the two trials will be averaged to give the mean number of words correctly identified, with a possible range from 0 to 30 (higher scores are better).
**Outcome:** Depressive symptoms were assessed via Center for Epidemiologic Studies Depression Scale (CES-D) at visits 5 and 6. Depression as measured via the scale will be modeled continuously as well as explored via a statistical distribution such as tertiles. The CES-D questionnaire is a 20 item scale. Scores range from 0 to 60, with higher scores suggesting greater depressive symptoms.

**Additional Independent variables:** Basic demographic information was collected at Visit 1, including birthdate for calculating age at study visit, sex, education, race, and study site. Education will be categorized according to standardized ARIC algorithms as less than high school, high school, or greater than high school. Additional covariates include smoking status (ever vs. never), hypertension, diabetes, cognitive factor score to account for cognitive status, and self-reported health compared to other persons of the same age (excellent, good, fair, or poor) as measured on the annual follow-up calls. Hypertension is defined as diastolic blood pressure 90 mmHg, systolic blood pressure 140 mmHg, or antihypertensive medication use. The presence of diabetes is defined as fasting blood glucose level 126 mg/dL, nonfasting glucose 200 mg/dL, self-reported diabetes (as diagnosed by a physician), or use of diabetes medication.

**Statistical Analysis:** We will explore differences in demographics by speech in noise perception ability using chi square and t-tests as appropriate. Prevalence of depressive symptoms by QuickSIN score will be estimated using multiple linear regression, adjusting for age, sex, race, study site, education, smoking, hypertension, diabetes, cognitive status, and self-reported health. All models will be adjusted for pure tone average (PTA) to account for the influence of impaired ability to detect sound on speech in noise perception. In a sensitivity analysis, we will consider adjustment for peripheral hearing level by restricting our analysis to persons without severe hearing loss as measured by PTA with multiple levels of restriction representing various degrees of hearing loss (PTA <40 dB HL, < 55 dB HL, and <70 dB HL). We will further explore for possible statistical interactions of age, sex, and cognitive factor score with QuickSIN score by stratification. Imputation will be used to address missing covariates. For our secondary analysis, we will investigate change in depressive symptoms over time between visit 5 and visit 6 by QuickSIN score (from visit 6) using multinomial logistic regression, with change in depressive symptom score (difference in score between visit 5 and visit 6) categorized as stable depressive symptoms (referent), increasing depressive symptoms, or decreasing depressive symptoms. In secondary analyses, we will use multivariable-adjusted linear regression to model change in depressive symptoms continuously.

We will use a multi-model approach for adjustment in both our primary and secondary analysis:

- Model 1: PTA alone
- Model 2: Model 1 + demographics
- Model 3: Model 2 + hypertension + diabetes + smoking
- Model 4: Model 3 + cognitive factor score

**7.a. Will the data be used for non-CVD analysis in this manuscript?**  [ ] Yes  [X] No
b. If Yes, is the author aware that the file ICTDER03 must be used to exclude persons with a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used? ____ Yes  ____ No
(This file ICTDER has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? ____ Yes  _X_ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER03 must be used to exclude those with value RES_DNA = “No use/storage DNA”? ____ Yes  ____ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at:  http://www.cscc.unc.edu/aric/mantrack/maintain/search/dtSearch.html

  _X___ Yes  _______ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

  #3204 Association between hearing loss and depression: A cross-sectional analysis from the Atherosclerosis Risk in Communities (ARIC) Study.

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? ____ Yes  _X_ No

11.b. If yes, is the proposal

  ___  A. primarily the result of an ancillary study (list number* _________)
  ___  B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* __________ __________ __________)

  *ancillary studies are listed by number at https://www2.cscc.unc.edu/aric/approved-ancillary-studies

12a. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is your responsibility to upload manuscripts to PubMed Central whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in
REFERENCES


