

ARIC Manuscript Proposal # 3346

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1.a. Full Title: Associations between Visual and Hearing Function in an Older Adult Population

b. Abbreviated Title (Length 26 characters): Visual Hearing Function Associations

2. Writing Group:

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

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3. Timeline:

Analysis and draft will be completed in 6 months.

4.Rationale:

Prevalence of sensory loss such as hearing loss and visual impairment is high among the older adult population and the projected prevalence for both hearing and visual impairment will increase dramatically in the coming decades, consistent with population growth and longevity (Frank et al., 2011; Bourne et al.,2017). It has been estimated that 1.5 million Americans have dual sensory impairment (DSI) and the prevalence of DSI has been estimated to be over 11% for people older than 80 years old (Swenor et al., 2013).

Hearing and visual impairment alone or in combination could lead to multiple adverse outcomes and comorbidity. A recent longitudinal administrative claim study discovered that hearing loss was significantly associated with increased risk of dementia, depression, falls and myocardial infarction (Deal et al. 2018). A prospective longitudinal study also showed that visual acuity loss could adversely affect instrumental activity of daily living (IADL) levels and increase the risk of mortality (Christ et al., 2014). Literature review shows that combined hearing and visual loss could lead to a broad range of adverse outcomes among older adults including poor quality of life, impaired activities of daily living etc. (Heine & Browning, 2015).

Research from neuroscientists also demonstrated cross-modality plasticity or reorganization of polymodal association area of cortex among those sensory deprived individuals. Visual deprivation, for instance, can lead to increased recruitment of parietal cortex and superior colliculus by the auditory and somatosensory systems (Bavelier & Neville, 2002; Merabet & Pascual-Leone, 2010). Multi-sensory integration or interactive synergy among different senses have also manifested among general population including those sensory normal adults. Primary, sensory specific brain areas have shown to receive inputs from other senses to facilitate the processing of information in the native sense (Stein & Standford, 2008). The significant impact of sensory deficit and the importance of multi-sensory integration imply the value and necessity to evaluate the potential correlations between hearing and vision function, the most commonly impaired senses in order to determine whether hearing and visual function represent similar or different health domains.

The majority of existing research on hearing and visual impairment lack objective measurements with a focus on subjective sensory impairment report. Moreover, researches with objective sensory function measurements focus mainly on visual acuity, which fail to reflect the multi-domains of visual functions. Similarly, very few existing reports have investigated the relationship between visual functions and central hearing functions represented by Quick Speech in Noise (QuickSIN) test. Moreover, although a large body of literature evaluated visual or hearing impairment separately by race or sex, very few explored the sex and racial specific visual and hearing function correlation. For example, researches presented that hearing loss is more prevalent in white and in male while visual impairment is more common in female and in African American population (Lin et al., 2011 ; Muñoz et al., 2000) , leading to a natural query that whether the correlation between visual and hearing functions differs by sex and race.

In our proposal, we plan to utilize visual function measurements and Optical Coherence Tomography (OCT) based retinal parameters obtained during Eye Determinants of Cognition (EyeDOC) Study and hearing measurements including both peripheral and central hearing function indicators measured during visit 6 of ARIC study. The rich data, comprehensive and objective measurements for both hearing and visual functions provide an ideal opportunity for us to describe the visual and hearing function relationship and to explore the sex and racial specific correlation.

This project could have potential public health impact and implications for clinicians including both audiologists and ophthalmologists. The potential correlation between hearing and visual domain might suggest the value of including hearing evaluation for eye care practitioners and a brief visual assessment for audiologists. A lack of correlation, on the other hand, might indicate that visual and hearing functions represent separate health domain and multisensory loss could indicate multiple system impairment and could predict profound adverse health outcome. Thus visual and hearing impairment should be both evaluated carefully given the adverse health outcome visual and /or hearing impairment could incur.

5. Main Hypothesis/Study Questions:

Using visual function and OCT data from EyeDOC study and hearing measurement from the ARIC Study, we aim to explore the vision-hearing connection among community dwelling older adults.

Aim1: Describe the association of both visual function and OCT based retinal parameters with peripheral hearing dysfunction and hearing impairment severity.

Hypothesis: Low visual acuity or poor contrast sensitivity is moderately associated with poor peripheral hearing function (Higher Pure Tone Audiometry values). Association between contrast sensitivity and peripheral hearing function is expected to be stronger than between visual acuity and peripheral hearing. For OCT based retinal parameters, lower retinal nerve fiber layer thickness and Macular ganglion cell complex thickness are hypothesized to be associated with poor peripheral hearing functions.

Aim2: Evaluate the relationship of visual function and OCT based retinal parameters with central hearing function represented by QuickSIN.

Hypothesis: Low visual acuity, poor contrast sensitivity, lower retinal nerve fiber layer thickness and Macular ganglion cell complex thickness will be associated with poor central hearing function (Higher QuickSIN values). The strength of association between visual function indicators and QuickSIN score is expected to be stronger than association with peripheral hearing functions.

Aim3: Assess the gender and race specific relationship of visual functions and OCT based retinal parameters with peripheral and central hearing function.

Hypothesis: We expect to see stronger association between visual and hearing functions among the female and the black population compared to the male and the white population.

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

EyeDOC is an ancillary study of the Atherosclerosis Risk in Communities (ARIC) Study. We will analyze cross-sectional relationship between visual and hearing functions using visual and OCT measurements collected during the EyeDOC study and hearing measurements collected during ARIC study visit 6 (2016-2017).

Study Population & Inclusion/Exclusion Criteria

EyeDOC study will enroll around 1000 participants from two sites including Jackson Field Center with 500 participants and Washington Co. Field Center with 500 participants.

Hearing measurements were collected at ARIC visit 6 at all four study sites. 3863 participants underwent hearing tests while 3626 have complete audiometric data in order to calculate a speech-frequency PTA data in better ear.

ARIC participants recruited for the EyeDOC ancillary study with both hearing and function measured will be included in this analysis. We will exclude non-white participants from Washington Country and non-black participants from Jackson field center. We estimated that there might be 600 – 800 participants included into the analytic sample.

Primary Measurements

1. OCT based retinal parameters:
 - a. Macular ganglion cell complex (GCC) thickness
 - b. Retinal nerve fiber layer (NNFL) thickness

Four non-contact OCT angiograph volume scans were obtained via spectrometer-based Fourier-domain OCT (RTVue-XR Avanti system ; Optovue Inc.) to evaluate the specified neurodegenerative and microvascular markers. GCC thickness was determined by two macular scans and NFL thickness was evaluated by two optic nerve scan. Images were transmitted to ARIC Data Coordinating Center (DCC) where image quality will be monitored. Then specialists in Casey Eye Institute Center for Ophthalmic Optics and Lasers (COOL) extracted images via custom software and entered OCT parameters reading results including GCC and NFL thickness into the COOL web-based software.

2. Measures of Visual Function

- a. Visual Acuity, measured at distance by having participants read letters from a backlit early treatment of diabetic retinopathy study (ETDRS) chart using their normal refractive correction (if any). Eyes with a presenting visual acuity of 20/40 or worse will undergo subjective refraction with trial lenses to determine best-corrected visual acuity. In our analysis, we will use best-corrected visual acuity.
- b. Contrast Sensitivity, evaluated using the MARS chart with participants wearing their presenting correction.
- c. Near acuity/Reading speed, measured by the MNRead chart

3. Hearing function measurement

a. Peripheral hearing function: Pure Tone Audiometry (PTA) average in better ear. PTA conduction audiometry was conducted in a sound-treated booth at Visit 6 (2016-17). Air conduction thresholds in each ear were obtained at standard octaves from 0.5 kHz to 8 kHz by trained technicians using insert and an Interacoustics AD629 audiometer. All thresholds were measured in decibels of hearing level. PTA will be calculated using four frequency (0.5K Hz, 1 Hz, 2 Hz , 4 Hz) in the better hearing ear. Hearing impairment severity will be classified into three categories and defined as normal (≤ 25 decibel hearing level [dB HL]) , mild hearing loss (26 dB HL – 40 dB HL) and moderate/severe hearing loss (> 40 dB HL) .

b. Central hearing function: QuickSIN (speech in noise) test. Quicksin is a test composed of sentences recorded in four-talker babble and used to quantify participant’s ability to hear in background noise. Two sentence list (track14 and track 17) were provided for the test. Each track comprised of 6 sentences with 5 key words for each sentence. The number of words corrected recognized was recorded for each sentence ranging from 0 to 5. Signal to noise ratio variable was derived from the formula below based on QuickSIN manual.

$$\frac{(27.5 - \text{sum}(\text{words correct in the sentences for track14}) + 27.5 - \text{sum}(\text{words correct in the sentences for track17}))}{2}$$

Other Variables of Interest

Demographic variables:

- a. Age
- b. Race-center
- c. Sex

Summary of Data Analysis

Proposed Analysis

Both visual function measurements including visual acuity, contrast sensitivity and near visual acuity/reading speed and peripheral hearing function measured by average PTA will be treated as continuous variables in the primary analysis.

For aim 1 and aim 2 we will assess the distribution of hearing and visual function variables using box plot and histogram plot. We will also describe the relationship between visual acuity, contrast sensitivity, reading speed and PTA and Quicksin scores separately using scatter plot and lowess smoother. Potential outliers and high leverage observations will be identified and evaluated. We will also run separate linear regressions to estimate the Pearson correlation coefficient between visual function variables and hearing functions indicators. Models will also be adjusted for basic demographic variables including age, sex and race-center.

We will also explore the scatter plot and correlation coefficient described above by different sex and race groups in line with our aim 3. We will also run separate linear regression models using continuous visual and hearing measurements and stratify by sex and race. We also plan to compare visual functions including visual acuity, contrast sensitivity and near visual acuity/reading speed across three hearing impaired groups using ANOVA test.

Finally, to further explore the underlying visual and hearing function correlation, we will also conduct exploratory factor analysis (EFA) and check the Cronbach's alpha. EFA enables us reduce the number sensory function variables, identify underlying sensory construct and investigate the underlying relationship between different sensory domains.

The rich data of visual and hearing variables and complete measurements on visual and hearing functions provide a unique opportunity for us to investigate the relationship between visual and hearing function. Moreover, study population of biracial community dwelling older adults enable us to evaluate the sex- and race-specific visual-hearing function relationship among a community-based population.

However, it is worth noting that our study will have several limitations. OCT measurements, which require participants remain steady for a relatively long time, is susceptible to measurement error and poor imaging quality, especially for those who are in poor health. However, the imaging quality has been carefully evaluated and monitored by COOL center to minimize the imaging quality issue. Another limitation is that there might exist survival or selection bias due to the long follow-up time of more than 30 years, driving the association towards null.

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a. Will the data be used for non-CVD analysis in this manuscript? Yes 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.)

7.a. Will the DNA data be used in this manuscript? Yes 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.csc.unc.edu/ARIC/search.php>

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)

Bourne, Rupert R A, Seth R Flaxman, Tasanee Braithwaite, Maria V Cicinelli, Aditi Das, Jost B Jonas, Jill Keeffe, et al. 2017. "Magnitude, Temporal Trends, and Projections of the Global Prevalence of Blindness and Distance and near Vision Impairment: A Systematic Review and Meta-Analysis." *The Lancet. Global Health* 5 (9): e888–97. [https://doi.org/10.1016/S2214-109X\(17\)30293-0](https://doi.org/10.1016/S2214-109X(17)30293-0).

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

11.b. If yes, is the proposal

A. primarily the result of an ancillary study (list number* EyeDOC)

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 <http://www.csc.unc.edu/aric/forms/>

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 <http://www.csc.unc.edu/aric/index.php>, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.