

## Introduction

Age-related hearing loss is challenging to study, because genetic risks and environmental exposures can affect cochlear function and vary across the lifespan<sup>[1,2]</sup>.

Cochlear pathologies including stria vascularis degeneration and outer hair cell (OHC) damage are each hypothesized to affect active cochlear amplification with differential effects across frequencies.

- Strial declines (metabolic) lower the endocochlear potential, which weakens OHC responses across low and high frequencies.
- OHC damage or loss (sensory) is typically more extensive near the cochlear base, which affects high frequency thresholds.

Otoacoustic emission (OAE) measures are used to assess the energy added to the traveling wave in cochlear amplification, which weaken as pure-tone thresholds increase.

OAEs can involve different generation mechanisms (nonlinear distortion and reflectance), which could provide complementary information on hearing loss etiologies.

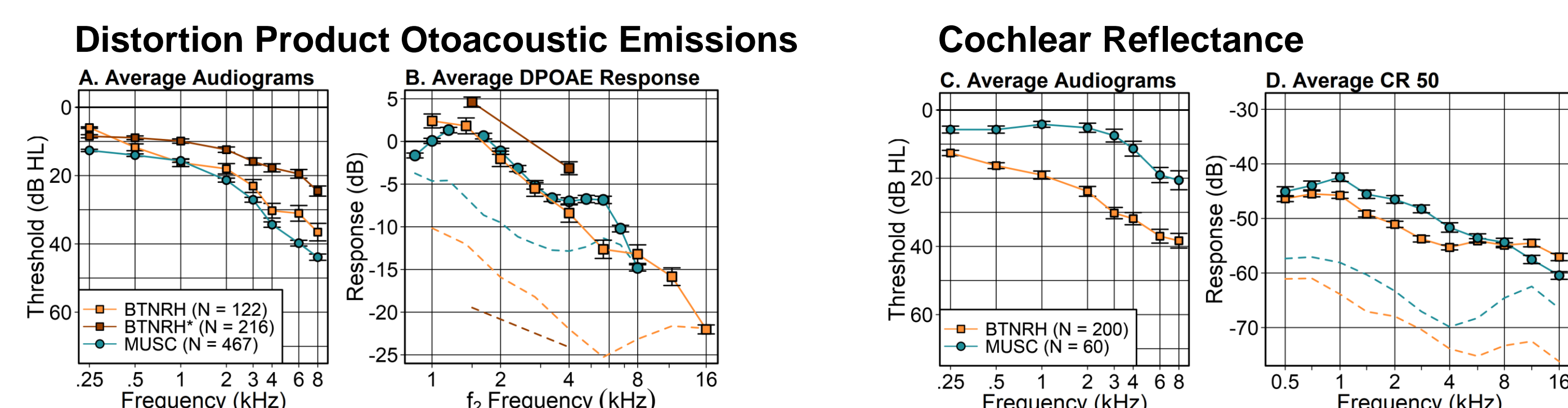
**The current study compared OAE measures and characterized their associations with estimates of metabolic and sensory hearing loss.**

## Methods: Retrospective Data Sets

Retrospective data sets from the Medical University of South Carolina (MUSC) and Boys Town National Research Hospital (BTNRH) were used for statistical power and replication.

- MUSC: N = 539 [59% female; ages 19-89+ years; 26% non-White]
- BTNRH: N = 429 [55% female; ages 18-86 years; 10% non-White]

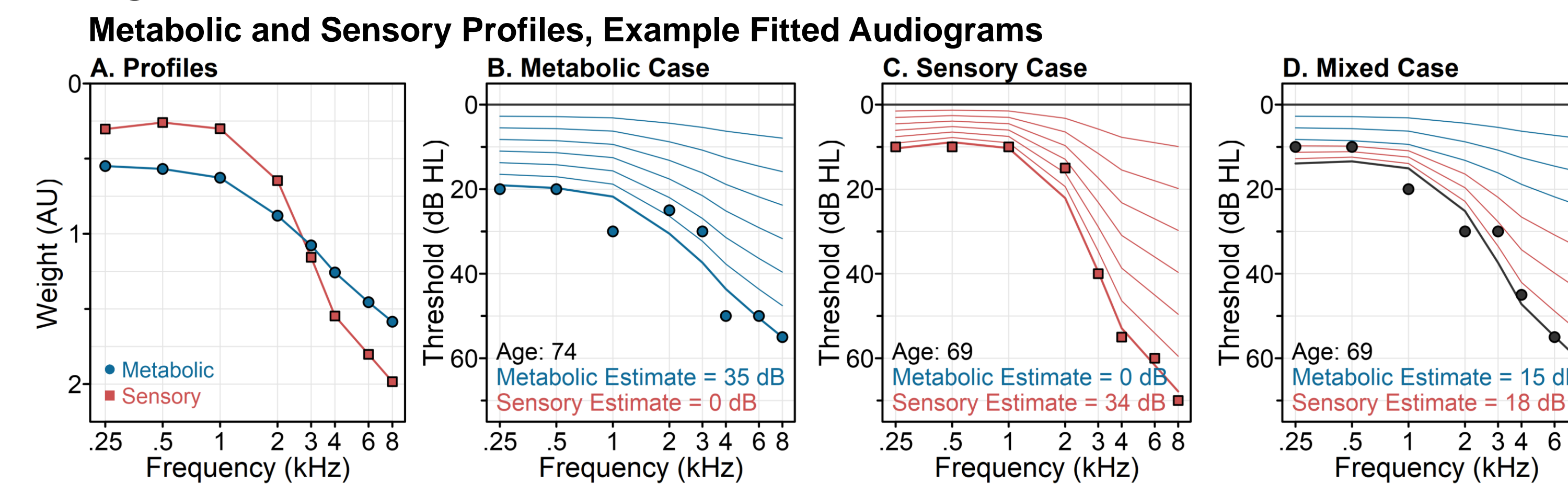
Data included age, sex, race, self-reported noise history, distortion-product otoacoustic emissions (DPOAE), and cochlear reflectance (CR) responses to wideband noise.



**Above.** Average audiograms for participants with DPOAE (A) or CR measurements (C). The DPOAE and CR response magnitudes are plotted as filled symbols and solid lines, and the dashed lines indicate the noise floors (B, D). Site differences in the measurements likely resulted from different recruitment strategies.

## Methods: Analyses

Metabolic and sensory components of age-related hearing loss were estimated for each audiogram in the two datasets.



**Above.** A) Metabolic and sensory profiles are shown with weights in arbitrary units (AU) that sum to one<sup>[3]</sup>. Both profiles were fitted to an audiogram by minimizing the difference between pure-tone thresholds and the summed profiles, after each profile was multiplied by a constant term (component estimates). Representative audiograms with distinct configurations, shown above (B-D), were selected based on pure metabolic loss (B), pure sensory loss (C), or a mixed metabolic and sensory loss (D) according to the estimates. Despite a similar magnitude of hearing loss, the audiograms show different patterns of pure-tone thresholds.

We examined how the across-frequency configuration of DPOAE and CR vary with respect to metabolic or sensory estimates from each participant.

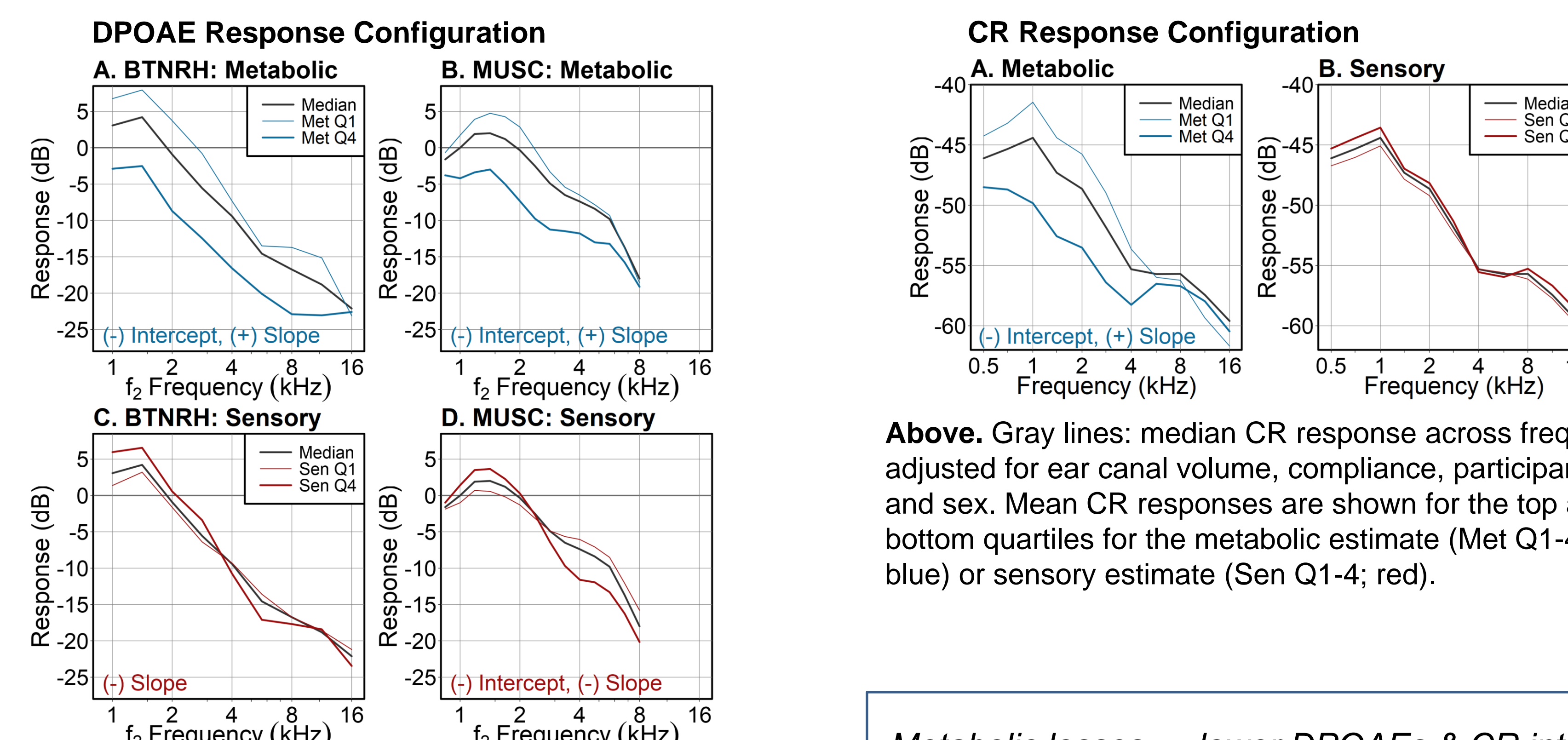
- Predictions:** 1) higher metabolic estimates relate to lower intercepts  
2) higher sensory estimates relate to more negative slopes

## Results

Metabolic estimates were significantly higher for older participants and were significantly associated with lower fitted OAE intercepts (plots below).

Sensory estimates also significantly increased with participant age, with larger age-related differences for males than females, and with positive noise history.

Sensory estimates significantly increased with steeper, more negative slopes for DPOAE but not CR (plots below).

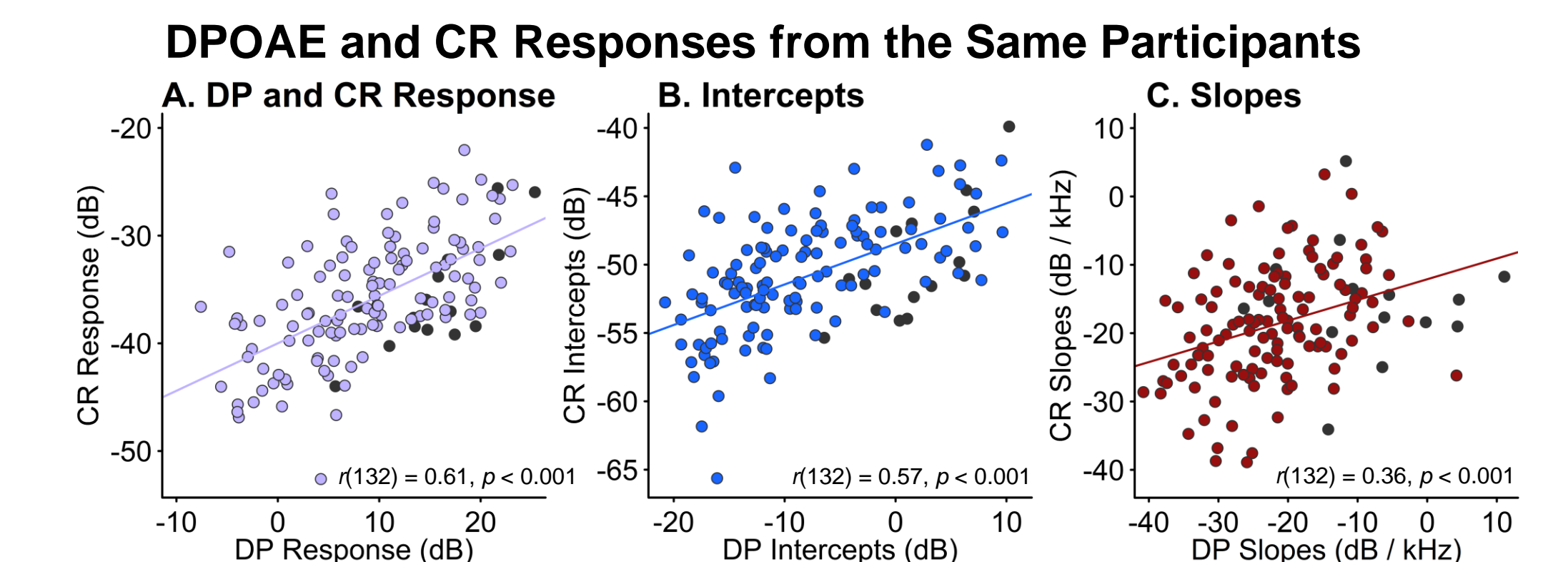


**Above.** Gray lines represent the median DPOAE response, adjusted for ear canal volume, compliance, participant age, and sex. Mean DPOAEs are shown for the top and bottom quartiles for the metabolic estimate (A-B; Met Q1-4; blue) or sensory estimate (C-D; Sen Q1-4, red).

*Metabolic losses ↔ lower DPOAEs & CR intercepts*  
*Sensory losses ↔ steeper, negative DPOAE slopes*

## Comparing DPOAE and CR Responses

For participants with both measures collected, the DPOAE and CR responses shared significant variance in dB-summed magnitudes, fitted intercepts, and fitted slopes.



**Left.** Significant associations between the magnitudes (A), fitted intercepts (B), and slopes (C) for the DPOAE (x-axes) and CR responses (y-axes).

While the DPOAE and CR responses were significantly related, the two OAE measures were largely independent.

We examined the extent to which component estimates were uniquely predicted by DPOAE and CR configuration.

When DPOAE and CR were modelled together, only metabolic associations with DPOAE shape parameters were significant and not CR shape parameters.

*This suggests that DPOAEs explain unique variance for the metabolic estimates.*

## Conclusions

Both the DPOAE and CR responses were related to component estimates of age-related hearing loss. However, distortion-based measures (e.g., DPOAE) may provide more sensitivity than reflection-based measures (e.g., CR).

Determining cochlear pathologies associated with hearing loss for individual older adults could be important for supporting targeted therapeutics<sup>[4]</sup>.

**References:** [1] Dubno, Eckert, Lee, Matthews, Schmiedt (2013). Classifying human audiometric phenotypes of age-related hearing loss from animal models. *JARO*, 14(5), 687–701. [2] Schmiedt (2010). The physiology of cochlear presbycusis. In Gordon-Salant S, Frisina RD, Popper AN, Fay R (Eds), *The Aging Auditory System* (pp. 9–38). New York: Springer. [3] Vaden, Eckert, Matthews, Schmiedt, Dubno (2022). Metabolic and sensory components of age-related hearing loss. *JARO*, 23(2), 253-272. [4] Eckert, Harris, Lang, Lewis, Schmiedt, Schulte, Steel, Vaden, Dubno (2021). Translational and interdisciplinary insights into presbycusis: a multidimensional disease. *Hearing Research*, 402: 108109.

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