Physiological Profiling of Sensorineural Hearing Loss for Predicting Speech-in-Noise Outcomes

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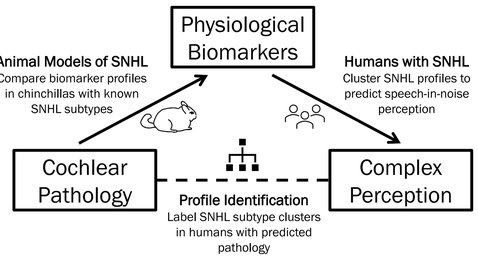
Introduction

Although the audiogram is the cornerstone of clinical hearing assessment, individuals with similar hearing thresholds often differ in their performance on suprathreshold listening tasks. This variation is likely related to underlying differences in cochlear pathologies that affect neural coding of sound but are hidden from the audiogram, such as cochlear synaptopathy [1], auditory nerve damage [2], and inner-hair-cell dysfunction [3]. Physiological biomarkers have been suggested to identify these hidden pathologies in listeners with normal hearing thresholds, but diagnosis becomes more complicated when outer-hair-cell loss is co-occurring. Given the multi-factorial nature of sensorineural hearing loss, we aim to identify subtypes of ***Complex SNHL*** based on a battery of biomarkers. Improved diagnostic precision is critical for personalizing hearing loss interventions, including emerging pharmaceutical treatments.

In this study, we assessed whether our battery of physiological biomarkers predicted individual speech-in-noise outcomes. These data, combined with our coordinated experiments in chinchillas with known cochlear pathologies, test the hypothesis that variations in the health of the periphery contribute to individual variation in suprathreshold listening.

Framework

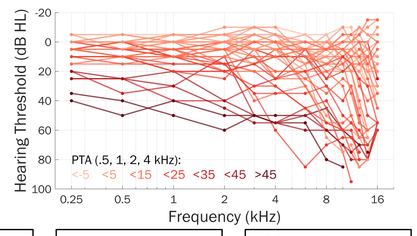
Through coordinated cross-species experiments in chinchillas with experimentally-induced cochlear pathologies and humans with a range of sensorineural hearing loss, we gain mechanistic insight into differences in cochlear pathologies and correlate diagnostics with outcomes.



Methods

Participants

- 36 participants
  - 18 female, 17 male, 1 non-binary
  - 15 with hearing loss (thresholds > 25 dB HL) in the standard clinical range (250-8000 Hz),
  - Mean age of participant: 41 years old
  - Age range: 19-68 years



Speech in Noise

- Speech was presented at 65 dB SPL. A hearing aid simulator fit to DSL v5.0 was used to increase audibility for participants with hearing loss.

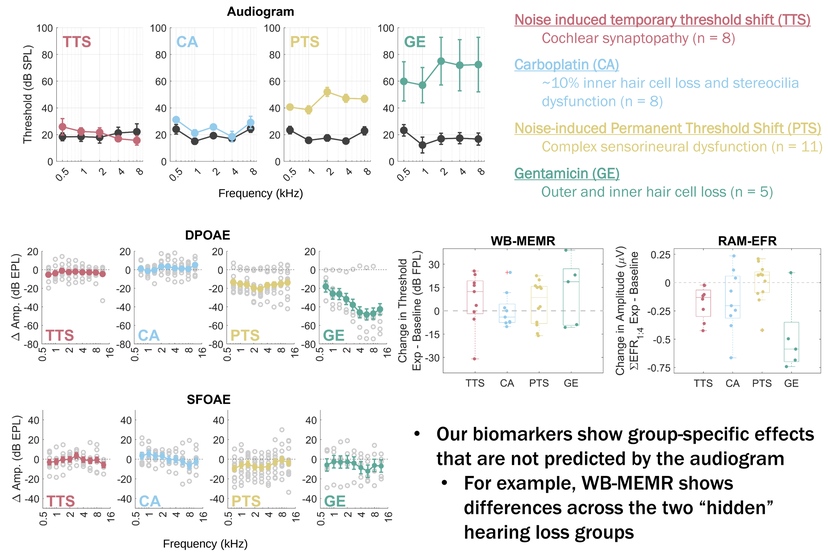
Modified Rhyme Test (MRT)	QuickSIN	Matrix Sentence Test (MST)
• Inharmonic tone complex masker [4] • Maximizes energetic masking	• Common clinical measure of speech-in-noise ability	• Maximizes informational masking [5]

Biomarkers

Measure	Sensitive to…	Chinchilla	Human
Hearing Thresholds	OHC function, limited sensitivity to IHC, neural function	Estimated via ABR thresholds at 500, 1000, 2000, 4000, 8000 Hz	Behavioral audiometry (air and bone conduction) .250-16 kHz
Swept DPOAE	OHC function	Swept 500-16000 Hz at 75/65 dB FPL	
Swept SFOAE	OHC Function, cochlear tuning	Swept 500-16000 Hz using suppressor paradigm at 40 dB FPL probe level	
Wideband Middle Ear Muscle Reflex (WB-MEMR)	Cochlear synaptopathy [6]	Wideband probe with broadband elicitors from 45 dB to 105 dB FPL	Wideband probe with broadband elicitors from 46 dB to 88 dB SPL
Envelope Following Response to RAM-stimuli (RAM-EFR)	Cochlear synaptopathy [7], IHC dysfunction	4 kHz tone with rectangular amplitude modulation at 223 Hz, vertical montage of 3 subdermal electrodes	4 kHz tone with rectangular amplitude modulation at 223 Hz, 32 channel EEG cap
Click Auditory Brainstem Response (ABR)	EHF OHC function, Cochlear synaptopathy [6]	Click at 90 dB SPL, vertical montage of 3 subdermal needle electrodes	High-pass-filtered click at 115 peSPL, 32 channel EEG cap

Cross-Species Biomarkers

Chinchillas were exposed to either noise or an ototoxic drug to create specific cochlear pathologies. Two exposures (CA, TTS) result in little to no change in hearing thresholds, while the other exposures elevate thresholds (PTS, GE).



Noise induced temporary threshold shift (TTS)
Cochlear synaptopathy (n = 8)

Carboplatin (CA)
~10% inner hair cell loss and stereocilia dysfunction (n = 8)

Noise-induced Permanent Threshold Shift (PTS)
Complex sensorineural dysfunction (n = 11)

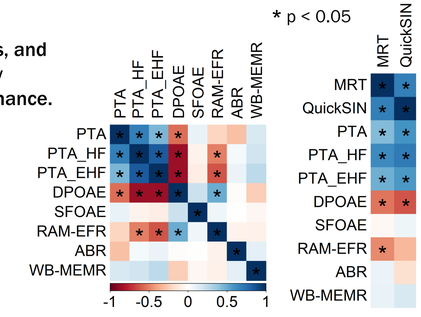
Gentamicin (GE)
Outer and inner hair cell loss (n = 5)

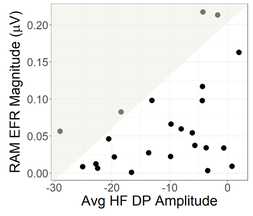
- Our biomarkers show group-specific effects that are not predicted by the audiogram
  - For example, WB-MEMR shows differences across the two "hidden" hearing loss groups

Predicting Speech-in-Noise

Biomarkers in Human Participants

- PTA, High frequency DPOAE amplitudes, and RAM EFR magnitude are all individually correlated with speech-in-noise performance.
- Though some biomarkers are correlated with each other (like the audiogram and DPOAEs), other measures may provide unique information.

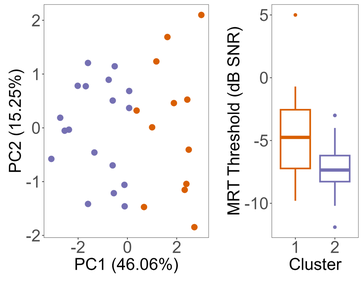




- Correlations between many variables show a triangular shape like the figure to the left.
- Participants with poor DPOAEs have poor RAM EFRs, but participants with good DPOAEs show a range of EFR magnitudes.

Cluster Analysis

- One metric was selected or calculated from each biomarker:
  - Pure tone average (PTA), 3-8 kHz,
  - Average DPOAE amplitude, 3-8 kHz,
  - Average SFOAE amplitude 3-8 kHz,
  - WB-MEMR threshold,
  - RAM-EFR amplitude,
  - ABR Wave I/V ratio
- After scaling the metrics, k-means analysis (k=2) was used to identify clusters in the data.
- Clusters from the biomarkers and PTA show differences in MRT thresholds
- In addition to PTA and DPOAE, RAM-EFR and WB-MEMR contribute to PC1



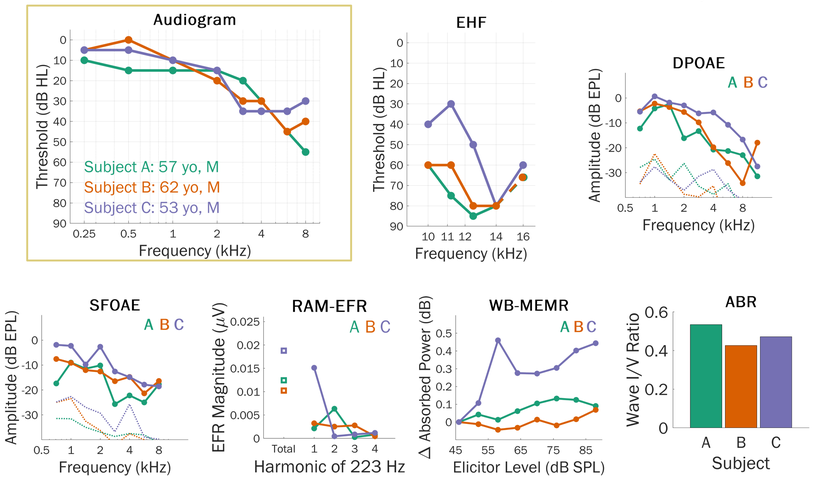
(LEFT) The first two principal components accounted for 46.06% and 15.25% of variance. (RIGHT) The clusters significantly predicted MRT threshold (p = 0.03).

Developing Biomarker Profiles

Three participants with similar audiograms differ in their ability to understand speech in noise. Subject B has the poorest speech scores and shows reduced RAM, wave I/V ratio, MEMR strength compared to Subject A and Subject C.

	A	B	C
MRT Threshold (dB SNR)	-6.1	-4.6	-8.2
QuickSIN (SNR loss)	*-1*	*9*	*3*

Better performance is indicated by a lower score



Conclusions

- The classical view of SNHL is that broadened tuning related to OHC dysfunction is the major contributor to speech-in-noise deficits, but differences between individuals with similar audiograms are highlighted by measures other than those that directly reflect OHC function (OAEs).
- Expanding the clinical test battery has potential to improve clinical decision making and prepares clinicians to individualize treatment and identify candidates for new therapeutics that target specific mechanisms of hearing loss.

Future Directions

Additional data collection and analyses

- Our statistical analyses perform better with more data, so data collection is ongoing. These biomarkers used in this study show promise and warrant future analysis to optimize useful individual and combinations of metrics.

Predicting pathology

- Cochlear histology on exposed chinchillas will provide additional insight to assist with prediction of cochlear pathologies in humans.

Correlations with hearing loss etiology and self-report of hearing ability

- Human participants each completed questionnaires regarding noise exposure history, hearing health history, and subjective report of hearing ability (e.g. SSQ)

References

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