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Beyond Audibility – Diverse Cochlear Pathophysiology Profiles in SNHL

Hari Bharadwaj, PhD, University of Pittsburgh

Samantha Hauser, AuD, Purdue University

Hari Bharadwaj, PhD

Hari Bharadwaj is assistant professor in the Department of Communication Science and Disorders at University of Pittsburgh. His laboratory investigates how sound information is encoded and analyzed by our ears and brains in complex/noisy environments. By understanding not only successful hearing in these settings, but also how it can be disrupted in diverse forms of hearing loss and in individuals with neuropsychiatric disorders, his lab seeks to advance precision diagnostics for hearing problems, and improve assistive devices such hearing aids, cochlear implants, and brain-machine interfaces.

Samantha Hauser, AuD

Samantha Hauser is a PhD student in the Department of Speech, Language, and Hearing Sciences at Purdue University. She is co-mentored by Drs. Hari Bharadwaj and Michael Heinz. Her current research explores diagnostic tools sensitive to the individual differences in cochlear pathology that underlie sensorineural hearing loss. Samantha received her AuD from Vanderbilt University in 2018 and worked as a clinical audiologist in Connecticut before beginning her PhD.

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- **Content Disclosure:** This learning event does not focus exclusively on any specific product or service.
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Learning Outcomes

After this course, participants will be able to:

- Identify key factors besides audibility that are important for successful listening in noisy environments.
- Describe the suprathreshold functional consequences of noise and age-related cochlear synaptopathy and distorted tonotopy from noise-induced outer hair cell damage.
- Describe the need for precision diagnostic tools based on different cochlear components of sensorineural hearing loss.

Listening in a noisy world – “Cocktail-party” problem

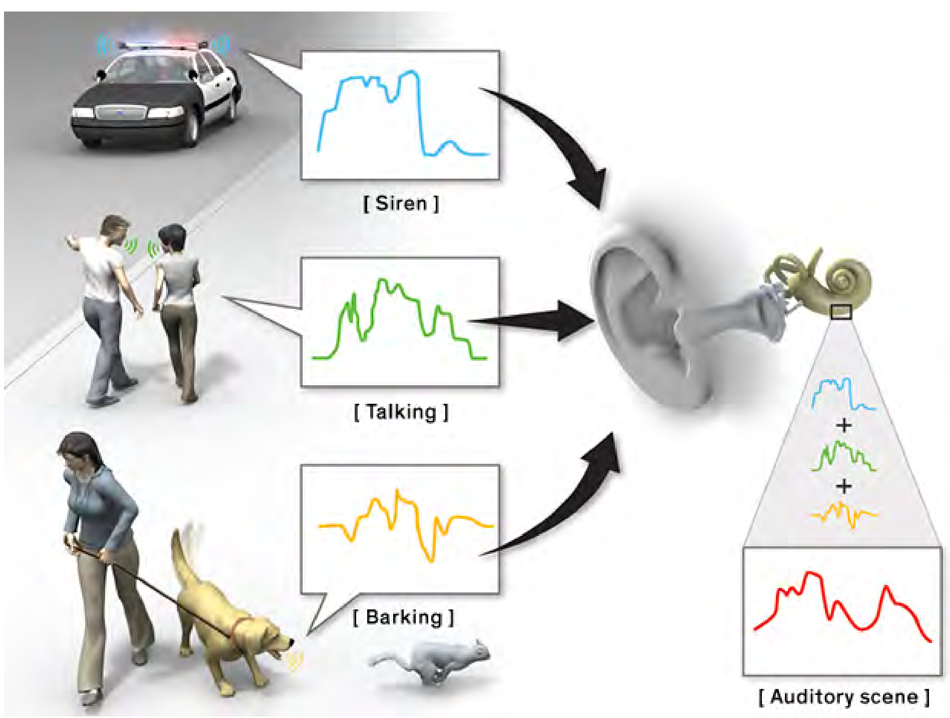


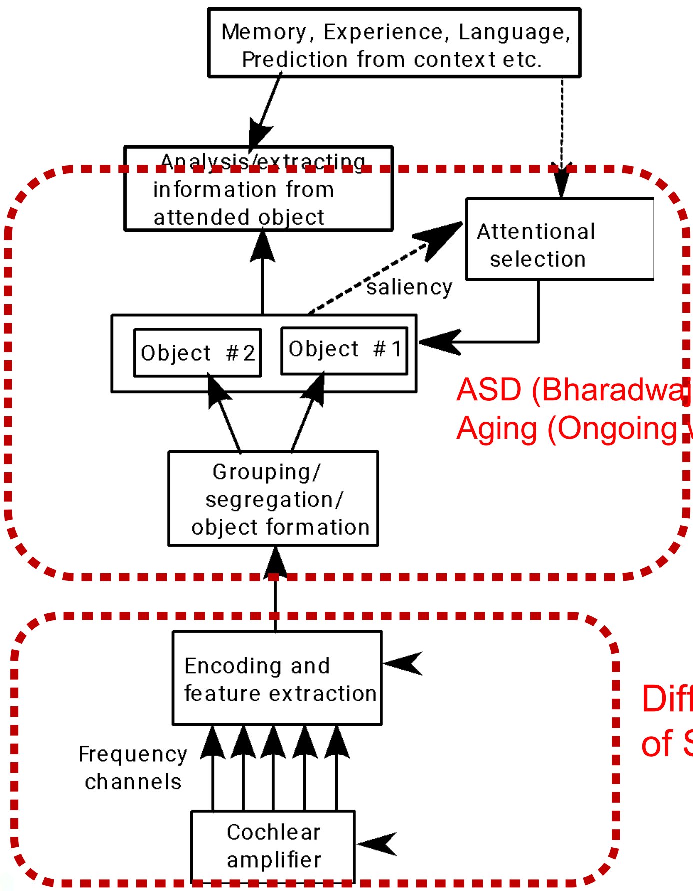
Illustration courtesy of IEEE (Deliang Wang)

- Amazing feat of “engineering” realized by animal brains. Machines can’t do this yet!

---But fragile---

- Listening difficulties in cocktail-party settings is the third most common chronic complaint among 50+ adults (CDC)
- Challenging for many groups of people (e.g., hearing loss, neurodivergent groups, elderly, those with neurotrauma)

Listening in a noisy world – “Cocktail-party” problem



ASD (Kenet et al., 2012)
TBI (Bressler et al., 2014 J Neurotrauma)

ASD (Bharadwaj et al., 2022 PLoS Biol),
Aging (Ongoing work)

Different forms of SNHL

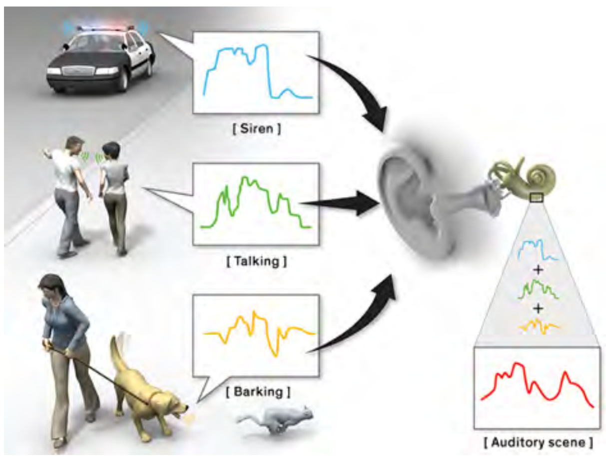
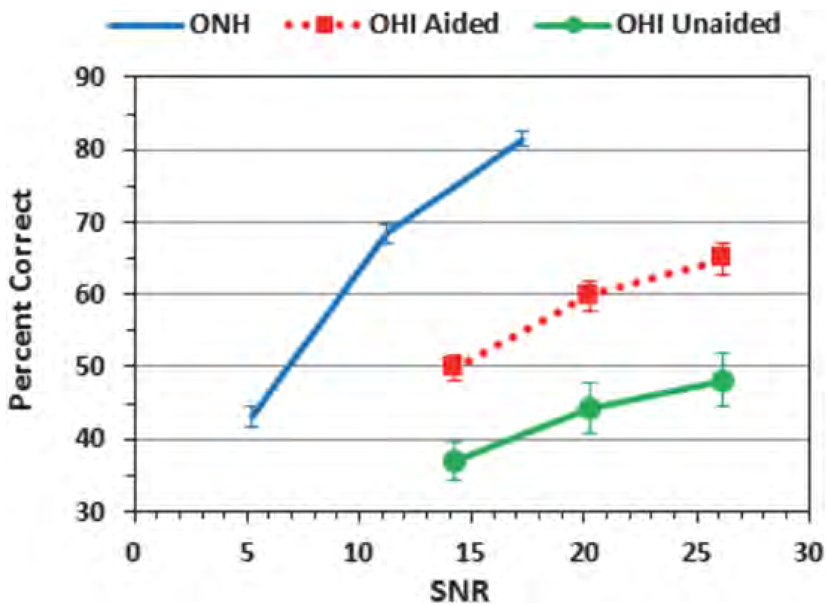


Illustration courtesy of IEEE (Deliang Wang);
Shinn-Cunningham, Trends Cogn Sci 2008

Hearing deficits in SNHL go well beyond reduced audibility

Speech recognition in noise lags well behind NH even when sounds are amplified to be audible

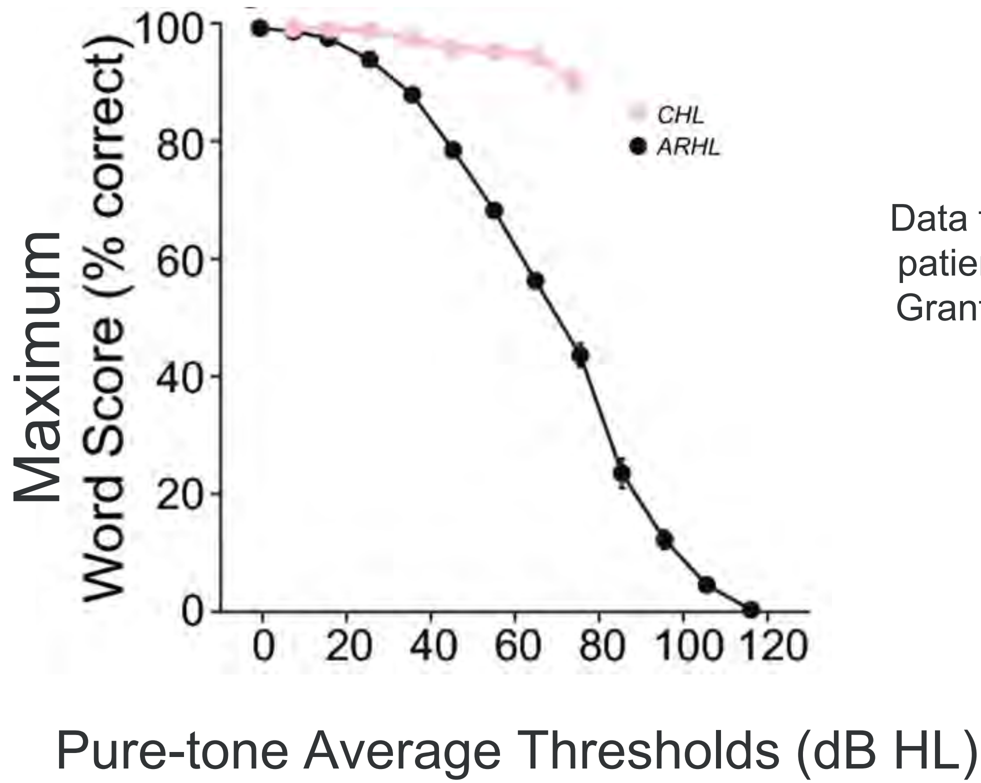


Consonant identification in noise: Woods et al., 2015

Only about 30% of hearing-aid users are satisfied with their instruments in “cocktail-party” environments. Drops further if asked about large-group settings (Kochkin, 2002).

QuickSIN “SNR Loss” averages 4.6 dB with appropriately fit amplification (Walden & Walden 2004). Less than 10% get below 3 dB (Leavitt et al., 2020).

Some indications even from speech-in-quiet data that there are deficits in SNHL beyond audibility



Data from ~94000 patients at MEEI.
Grant et al., 2022

SNHL is complex and has many components!

Sensory and neural components of the organ of Corti

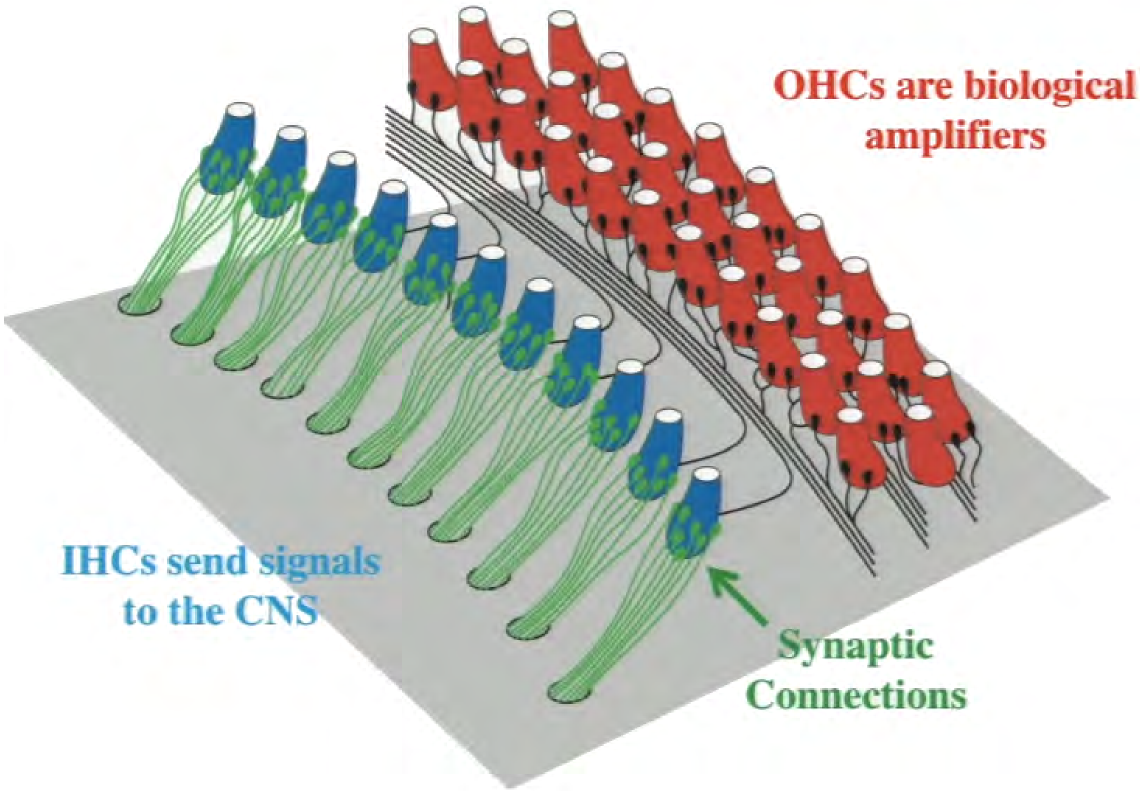


Illustration courtesy of Liberman M. C.

Conventional view of sensorineural hearing loss

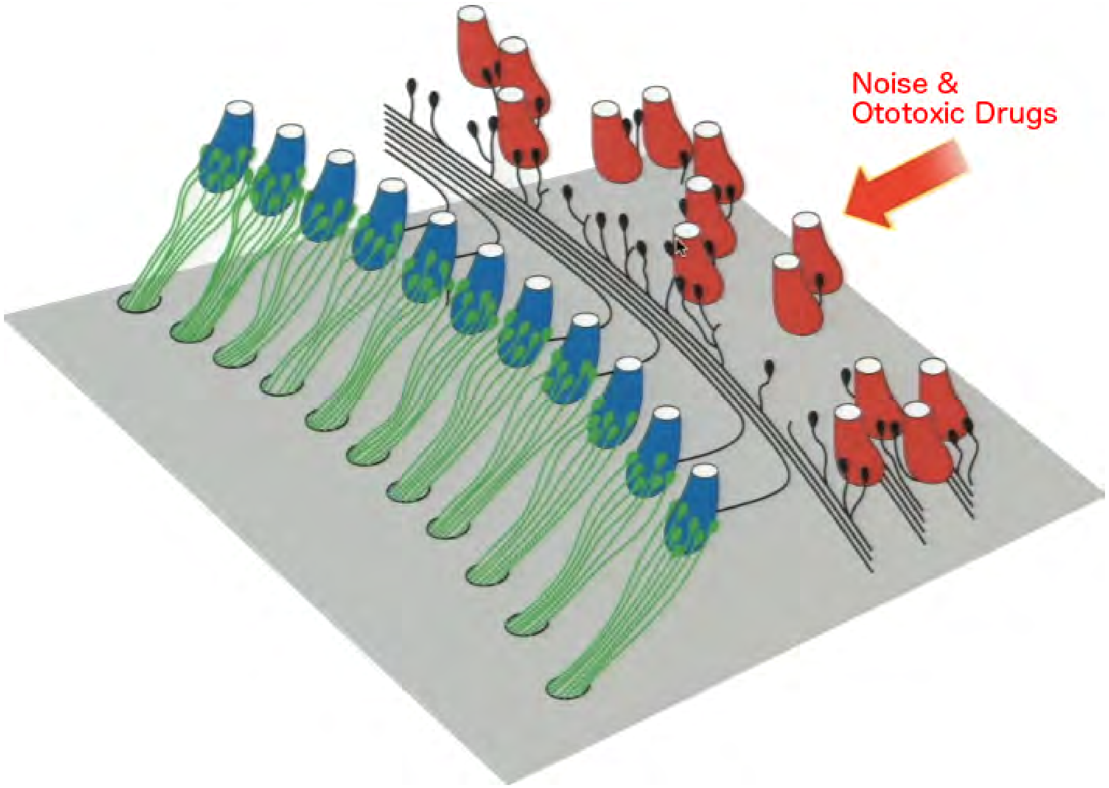


Illustration courtesy of Liberman M. C.

Conventional view of sensorineural hearing loss

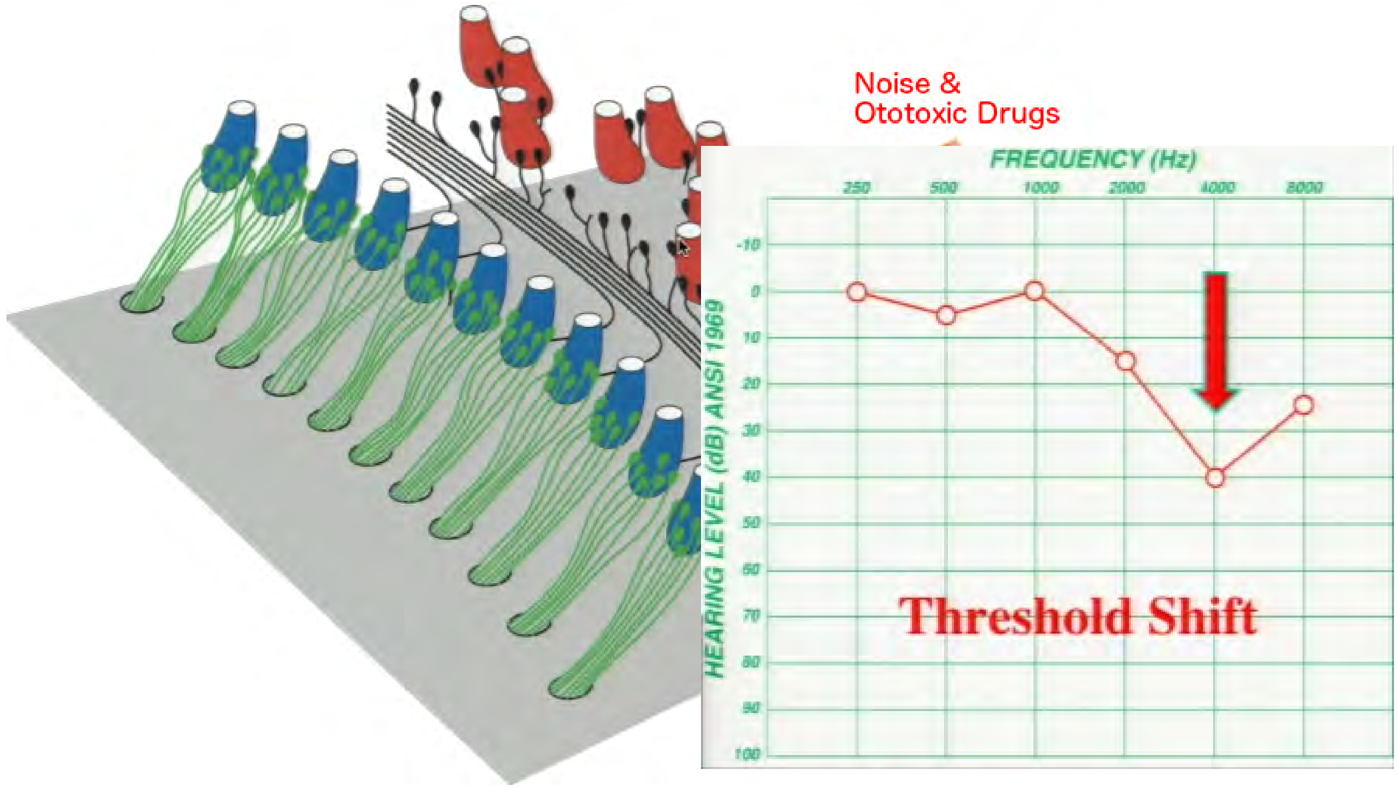


Illustration courtesy of Liberman M. C.

Recently recognized: Primary neural degeneration

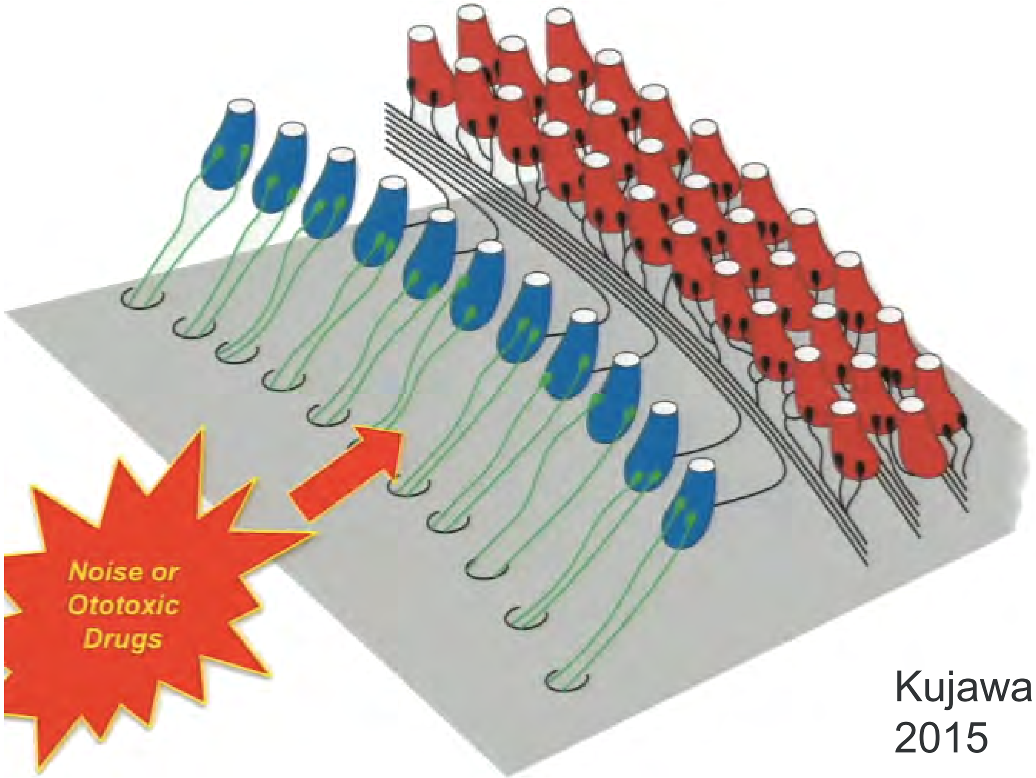
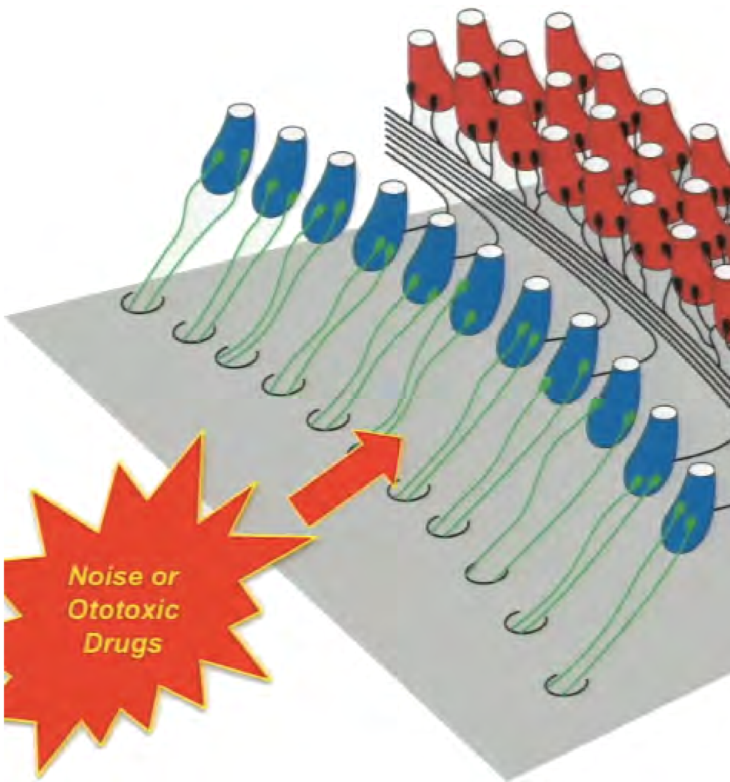


Illustration courtesy of Liberman M. C.

Kujawa & Liberman, 2009; 2015

Recently recognized: Primary neural degeneration



Kujawa & Liberman, 2009; 2015

Illustration courtesy of Liberman M. C.

Synapses and unmyelinated terminals degenerate first

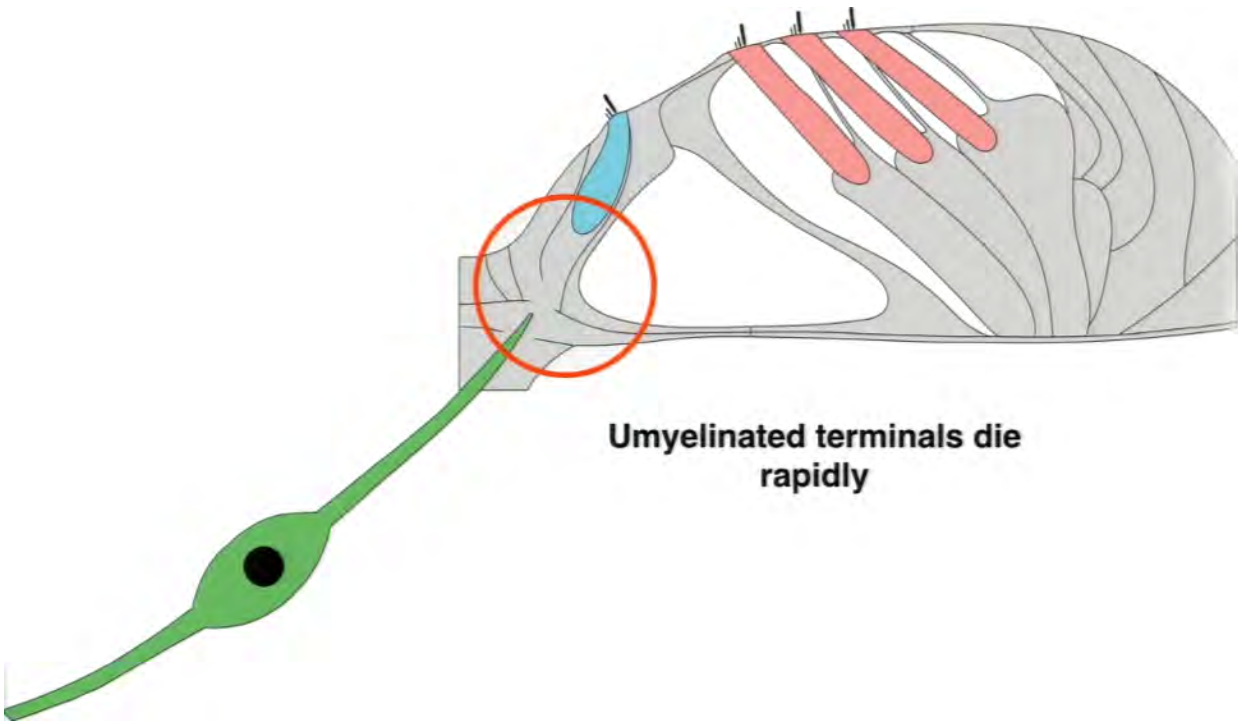
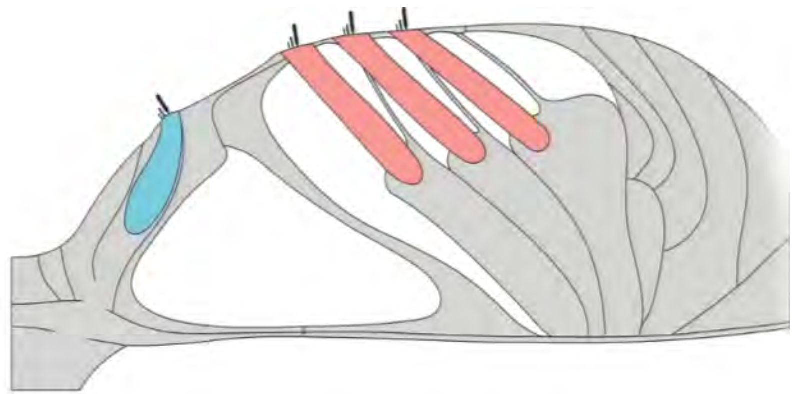


Illustration courtesy of Liberman M. C.

Spiral ganglion cell bodies stick around for much longer!



Peripheral axons survive for weeks

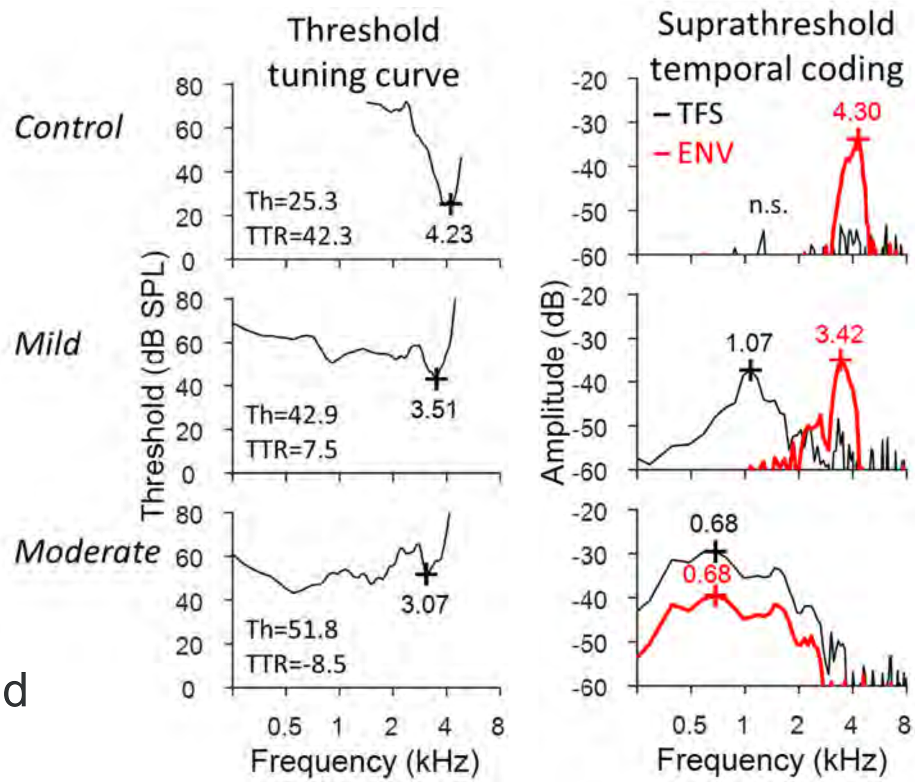
Cell body and central axons survive for years/decades

Illustration courtesy of Liberman M. C.

Recently recognized: Distorted tonotopy after OHC loss!

Threshold tuning curves in SNHL:
- Loss of gain/amplification (elevation of "tip")
- Broadened tuning of the "tip"
- Hypersensitive "tails"

What about suprathreshold responses to broadband stimuli?



Henry et al., 2019 J Neurosci

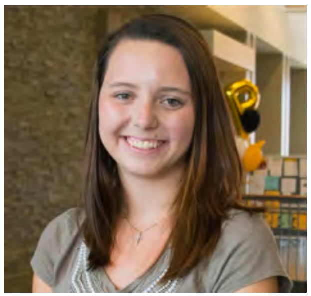
Distorted tonotopy associated with low tip-to-tail ratios (TTRs)

Complex SNHL: Why care?

- Amplification strategies that are responsive to "suprathreshold" alterations in each individual – Beyond audibility and loudness

- Emerging pharmacological therapies target specific components of cochlear pathology
  - Selecting the right candidates for treatments
  - Sensitive end points for evaluating efficacy in clinical trials

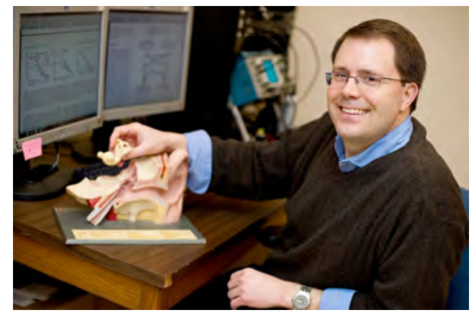
Acknowledgements


Alexandra Hustedt-Mai


Homeira Kafi


Vijay Muthaiah


Satya Parida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Anna Hagedorn


Kelsey Dougherty

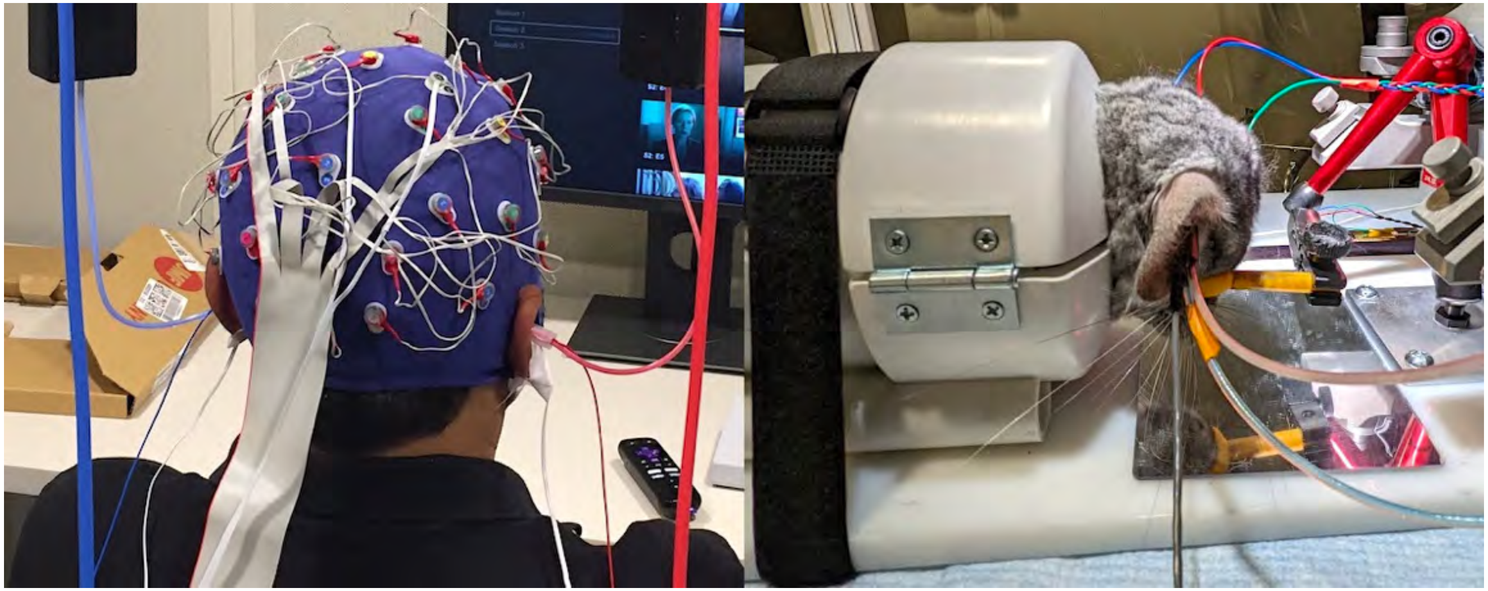

Hannah Ginsberg


Jennifer Simpson

NIH National Institute on Deafness and Other Communication Disorders (NIDCD)

R01 DC015989,
R01DC009838

Cross-species (humans + chinchillas) studies on different forms of SNHL



Bharadwaj & Heinz lab ongoing collaboration.

Cochlear Synaptopathy

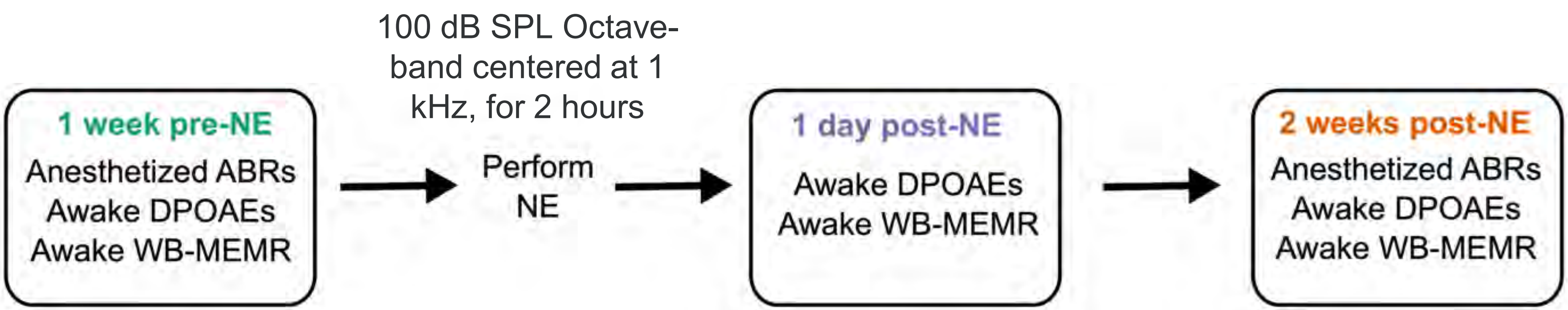
Human subjects – One control & two “at risk” groups tightly matched in audiograms

- Young controls (YCtrl) individuals with nominal sound exposures (aged 18—35 years, N=55)

- Young individuals with regular and substantial exposure to intense sounds (YExp) from Purdue marching band and gun clubs (18—35 years, N=53)
  - Audiometrically matched (within 5 dB) to YCtrl up to 16 kHz in mean & median thresholds

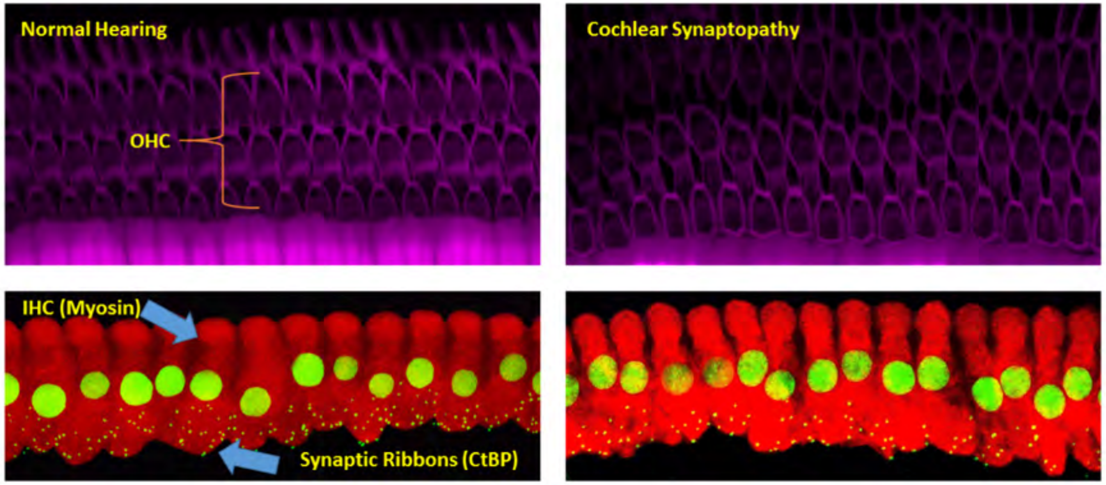
- Middle-aged individuals (MA; 36 – 60 years, N=58)
  - Audiometrically matched to YCtrl (within 5 dB) up to 8 kHz in mean & median

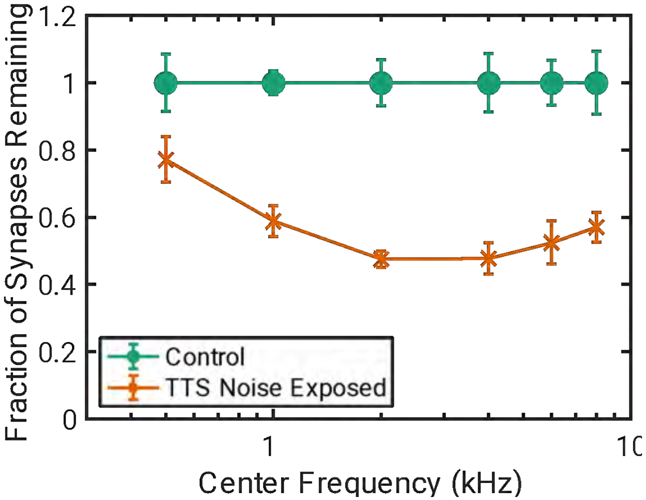
One chinchilla group: Studied pre- and post- noise exposure



Bharadwaj et al., 2022 Commun Biol

Histology confirms IHC synaptopathy without hair-cell loss

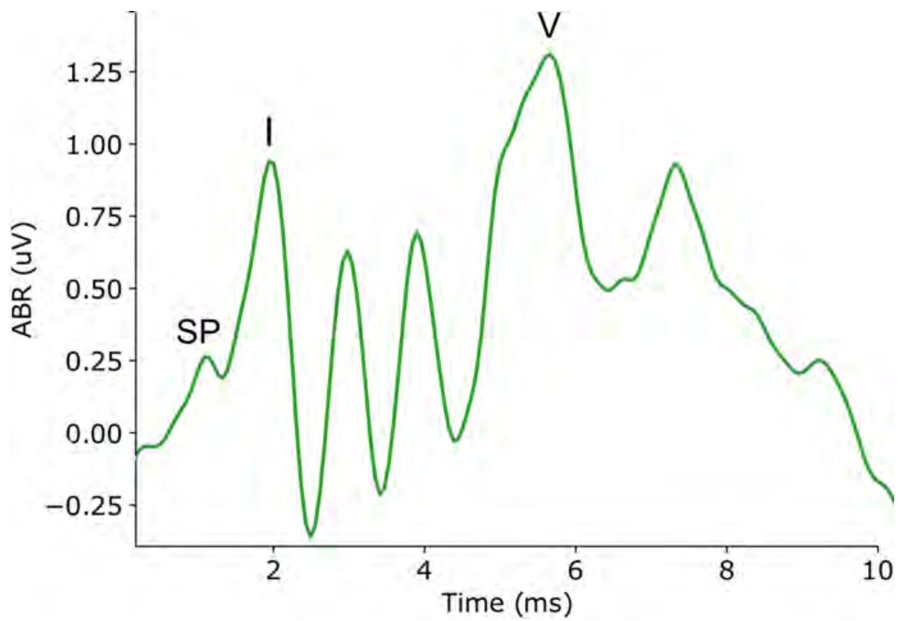




Bharadwaj et al., 2022 Commun Biol

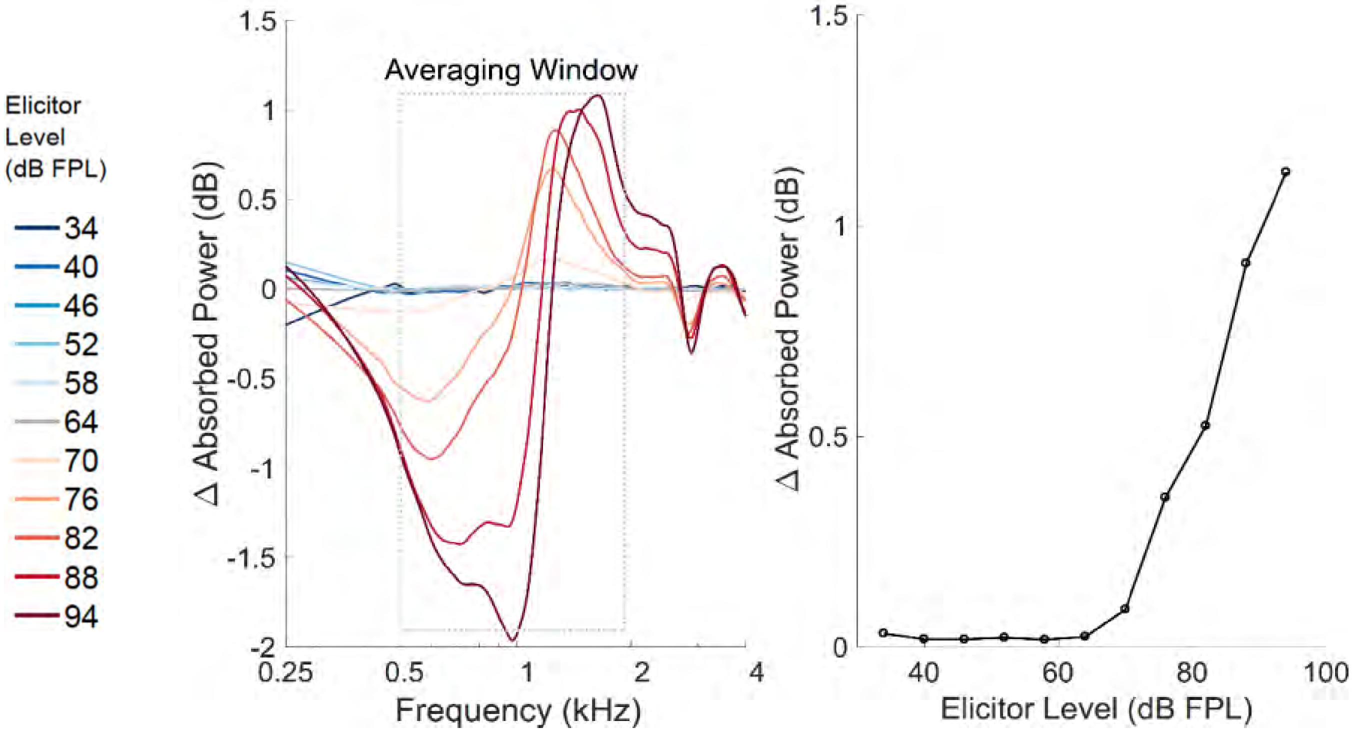
Candidate Assay #1: ABR wave I amplitude, suitably normalized

The ABR wave I amplitudes are a reliable correlate of synaptopathy in mice [Furman et al., 2012; Sergeyenko et al., 2013].



Tiptrode measurement of human ABR in response to high-pass (3 – 8 kHz) click

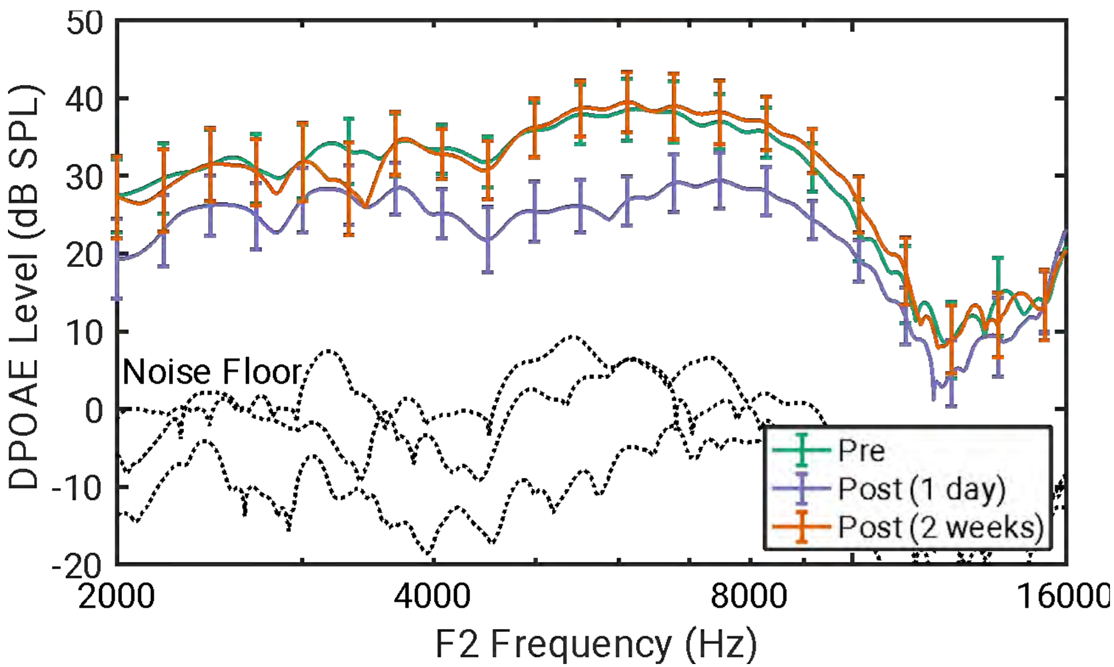
Candidate Assay #2: “Wideband” middle-ear muscle reflex (WBMEMR)



The MEMR can be thought of as being driven by the integrated output of cochlear afferents, possibly with greater weighting of low-SR fibers

Bharadwaj et al., Neurosci 2019; Valero et al., Hear Res 2018

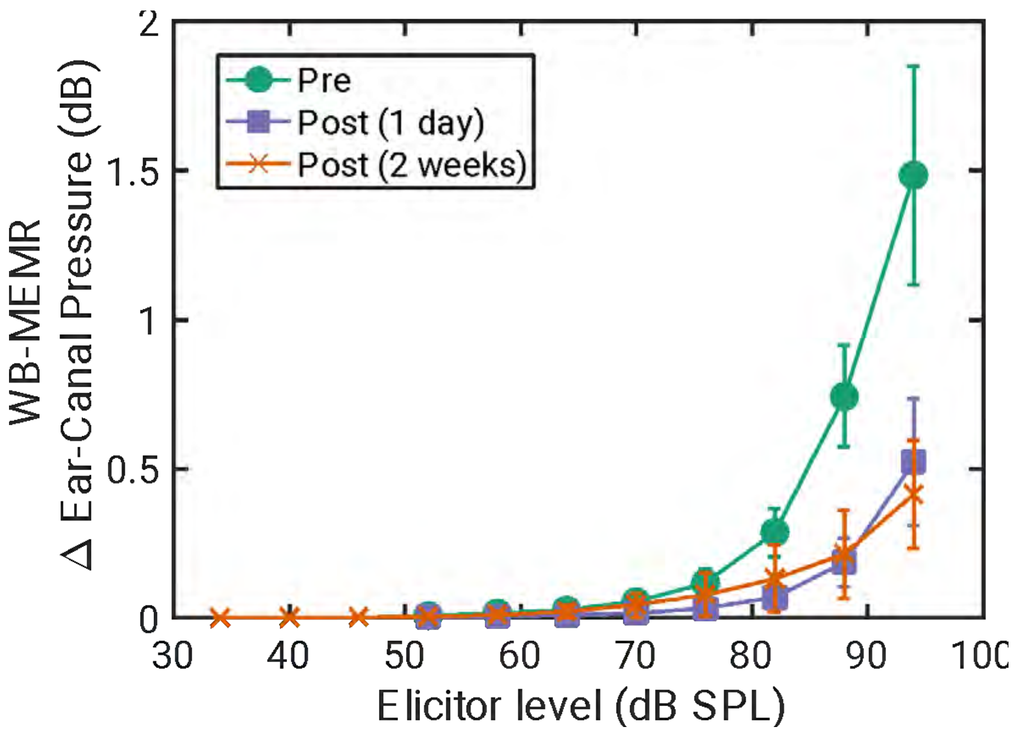
Chinchilla DPOAEs confirm temporary shifts in OHC function



ABR threshold shifts were < 5 dB at 2 weeks, not shown

Bharadwaj et al., 2022 Commun Biol

Unlike DPOAEs, WBMEMRs don't recover (>50% reduction)



Bharadwaj et al., 2022 Commun Biol

Human: WB-MEMR suggests broad synaptopathy in middle-aged individuals

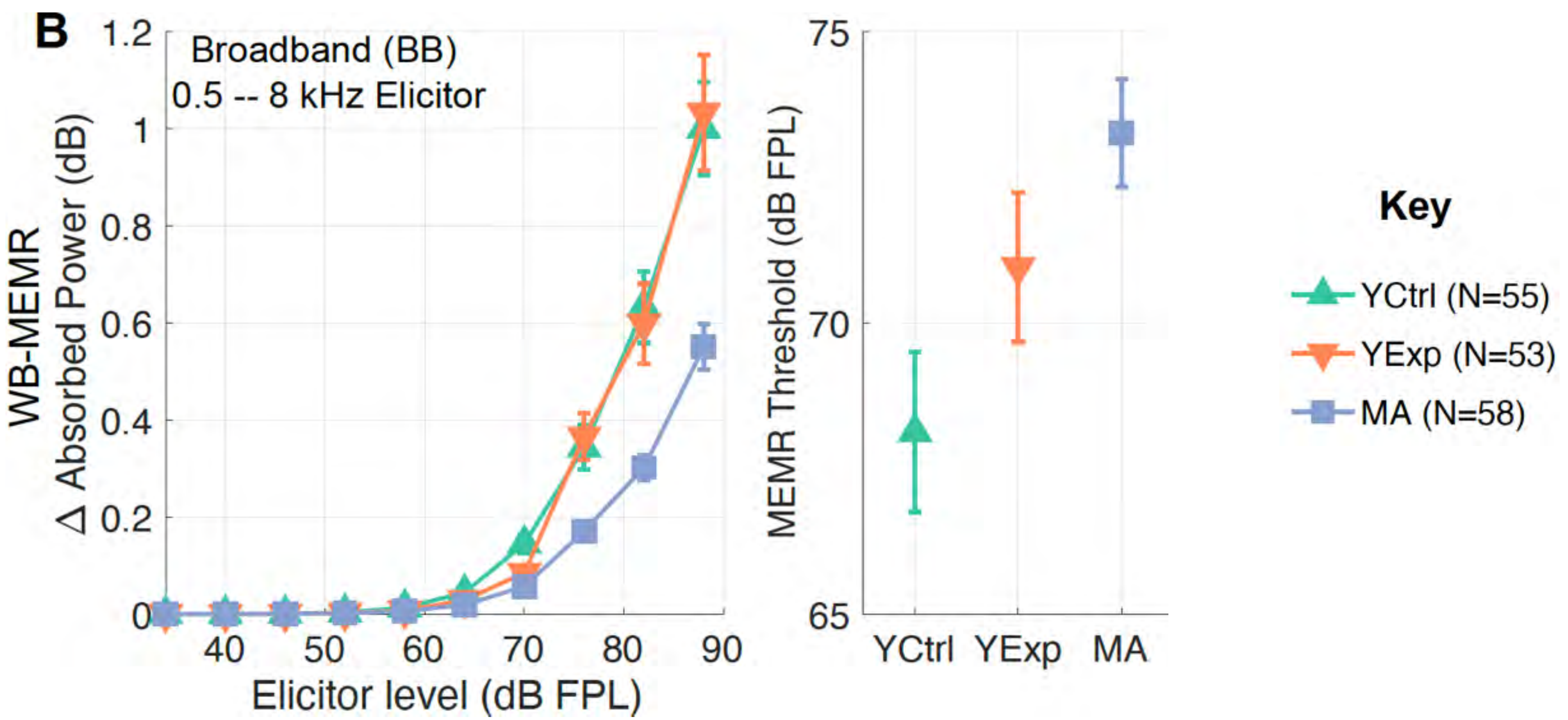
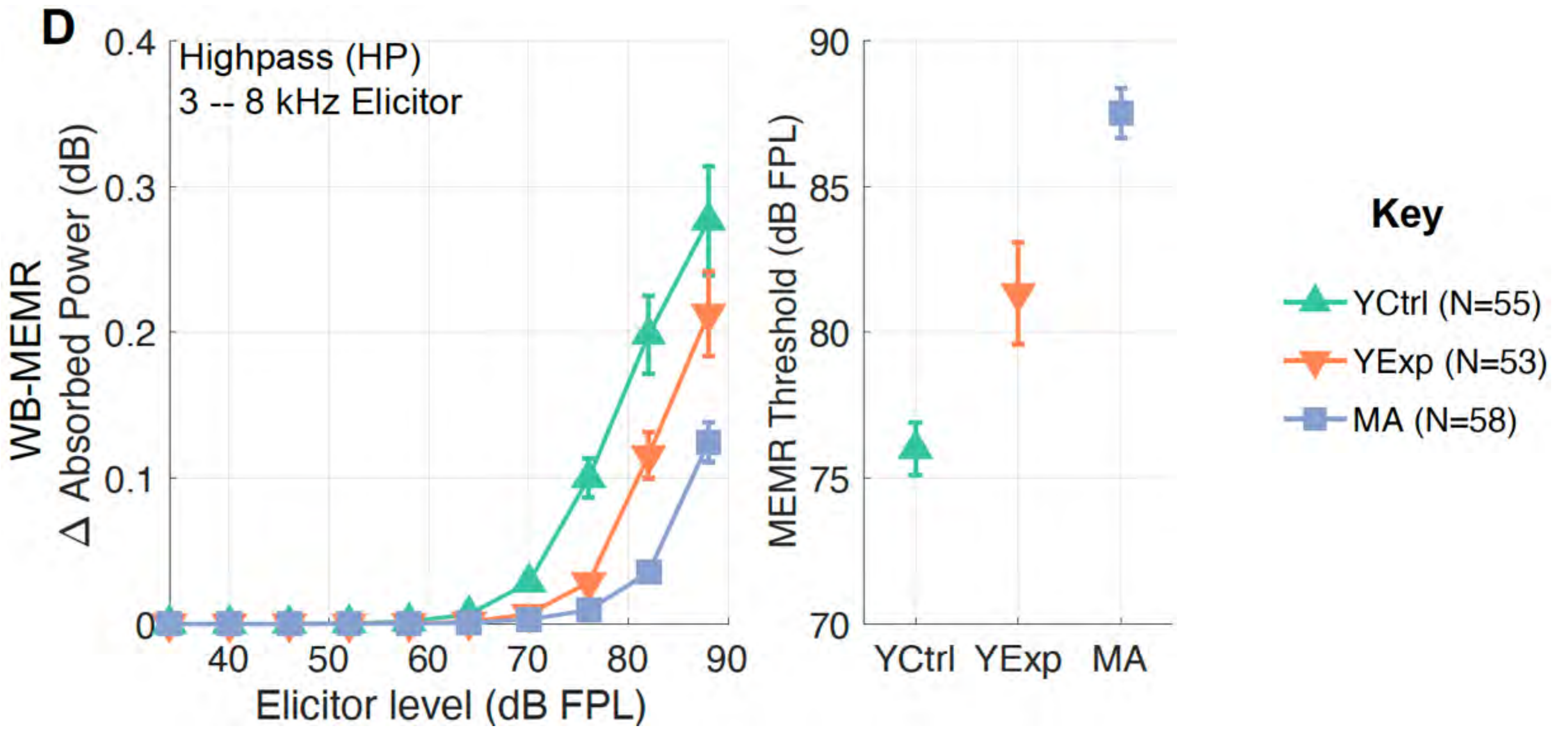


Fig. 2B Bharadwaj et al., 2022 Commun Biol

Human: WB-MEMR suggests synaptopathy in the 3-8 kHz region attributable to acoustic overexposure



Bharadwaj et al., 2022 Commun Biol

Human: ABR wave I goes down relative to wave V in both at-risk groups, more so in middle-age

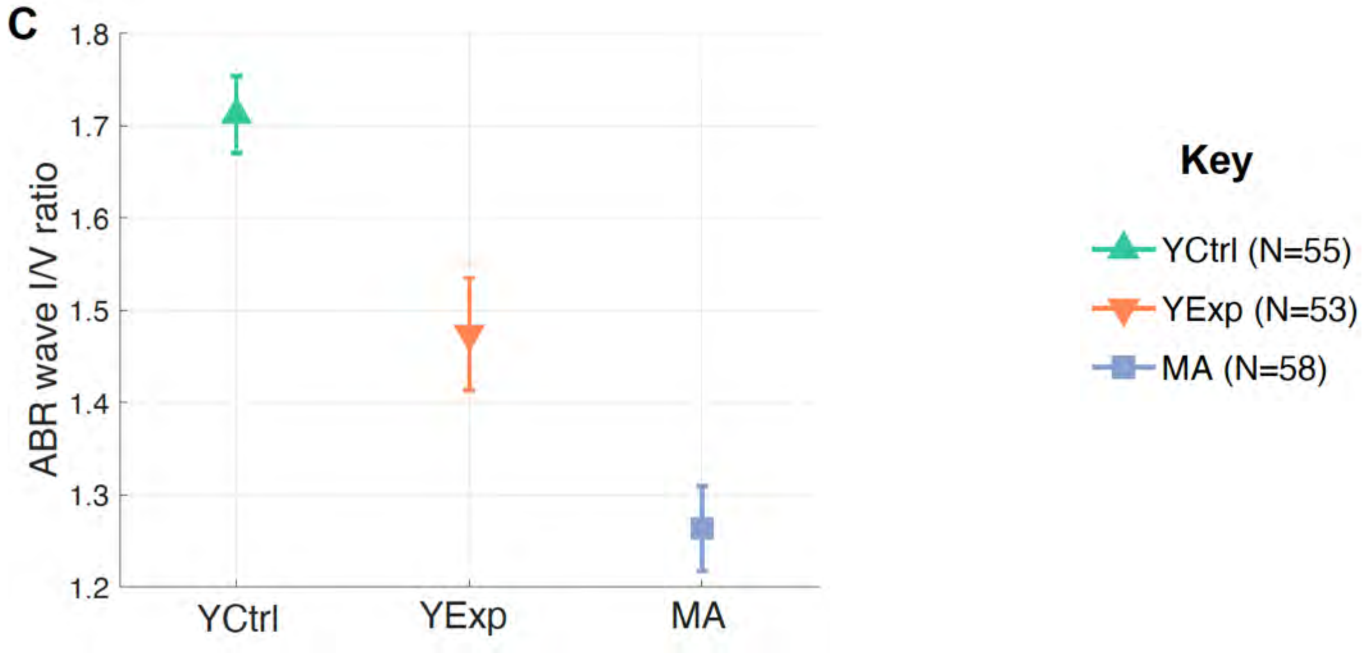


Fig. 2C Bharadwaj et al., 2022 Commun Biol

“Big Data” (NHANES 2012 repository) reveal similar effects robustly despite lower sensitivity

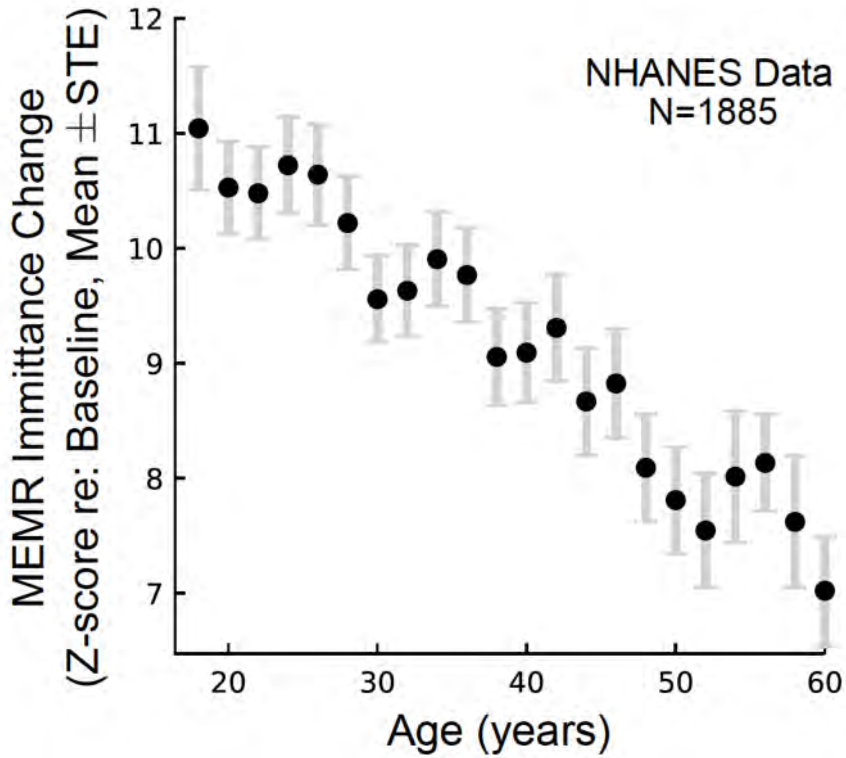


Fig. 3D Bharadwaj et al., 2022 Commun Biol

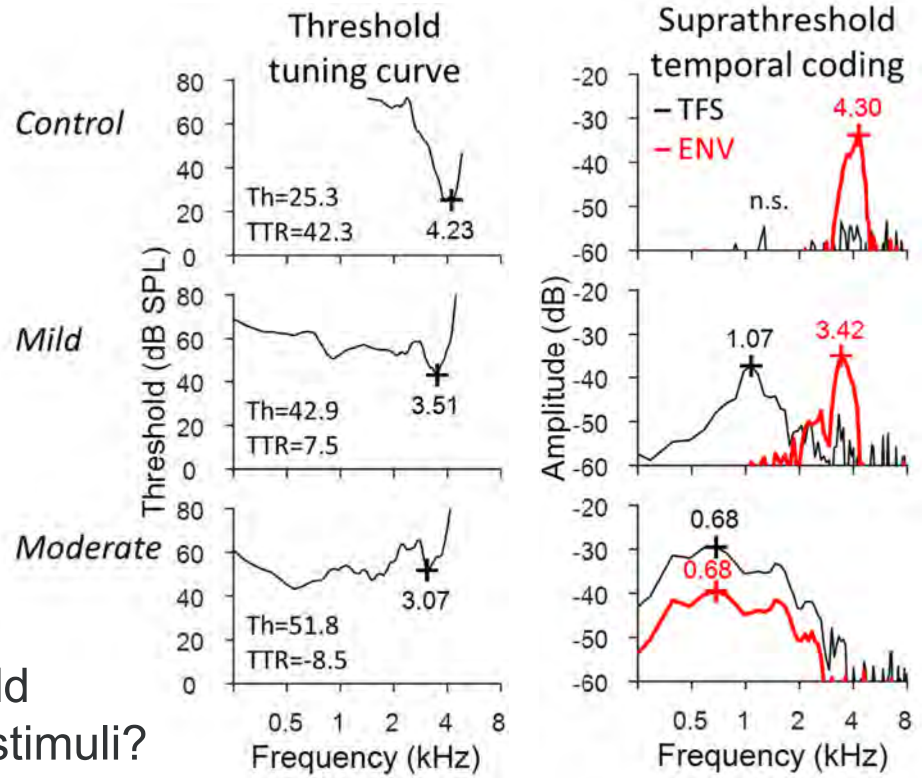
Clinic-style MEMR with a 2 kHz tone elicitor at 105 dB HL

All subjects here have 20 dB HL or better up to 8 kHz

Distorted tonotopy in outer-hair cell damage

Insights from chinchilla auditory nerve recordings

Threshold tuning curves in SNHL:
- Loss of gain/amplification (elevation of "tip")
- Broadened tuning of the "tip"
- Hypersensitive "tails"

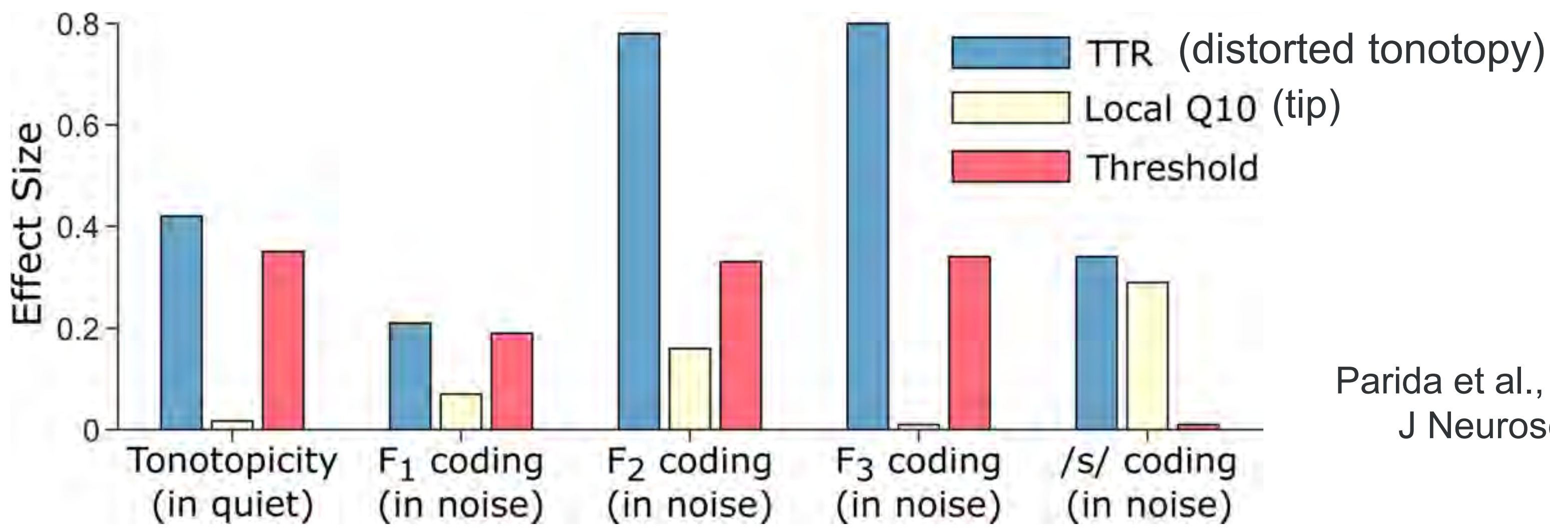


Distorted tonotopy associated with low tip-to-tail ratios (TTRs)

What about suprathreshold responses to broadband stimuli?

Henry et al., 2019 J Neurosci

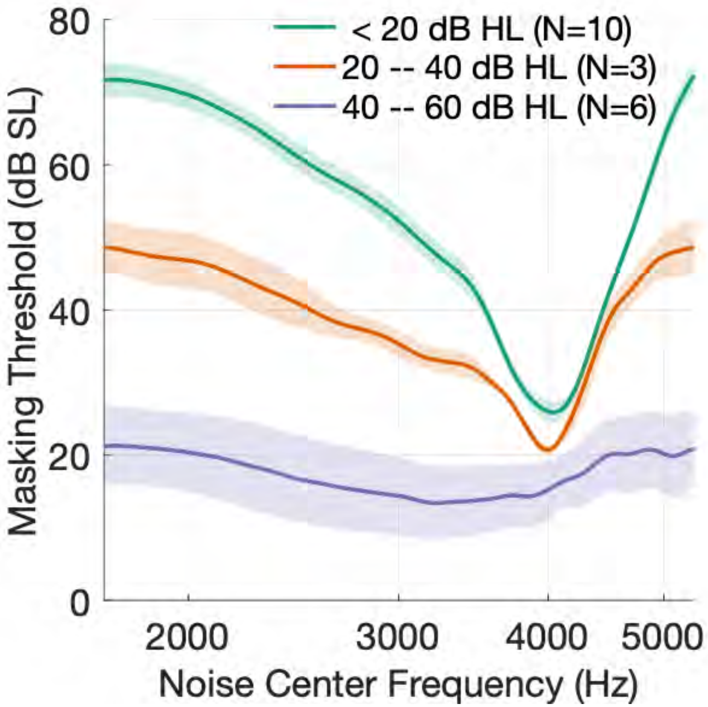
Altered suprathreshold auditory nerve responses to speech-in-noise are dominated by the effects of distorted tonotopy!



Parida et al., 2022
J Neurosci

Does this happen in humans?

Human psychophysical tuning curves @ 4 kHz, 20 dB SL

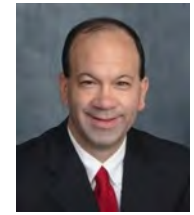


Reduced tip-to-tail ratio (TTR) apparent!

Kafi et al., In preparation

Does distorted tonotopy contribute to speech-in-noise deficits despite amplification?

Hearing-aid simulation

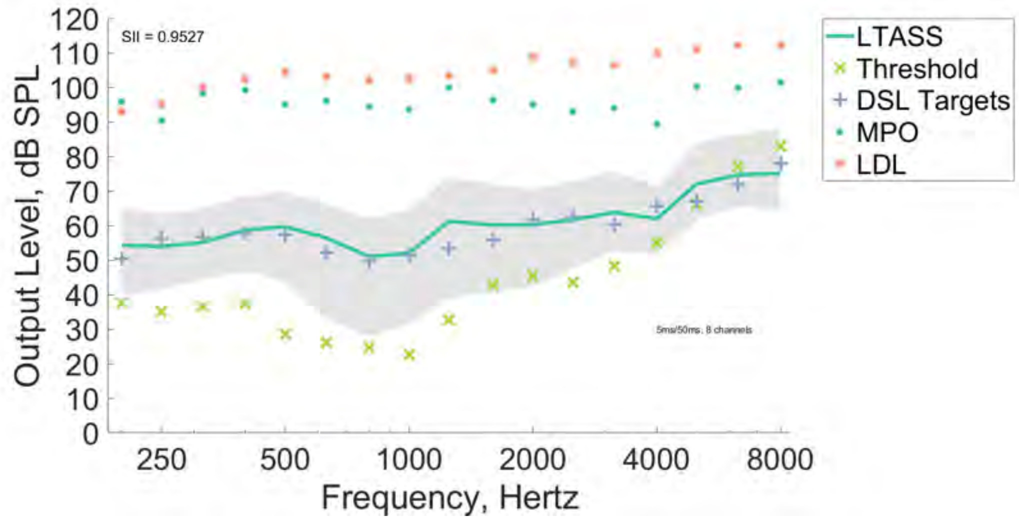


Joshua Alexander

Wide dynamic-range compressive (WDRC) 8-channel hearing aid (Alexander & Masterson, 2015) initially programmed to meet DSLv5 prescriptive targets.

“Speech mapping” and fine-tuning were performed while playing the “carrot” passage to ensure that the simulator yielded sufficient audibility in the individual (real) ear (SII =0.902 ± 0.036) for 65 dB SPL.

Speech-in-noise (low-frequency noise) task with 70 dB SPL stimuli.

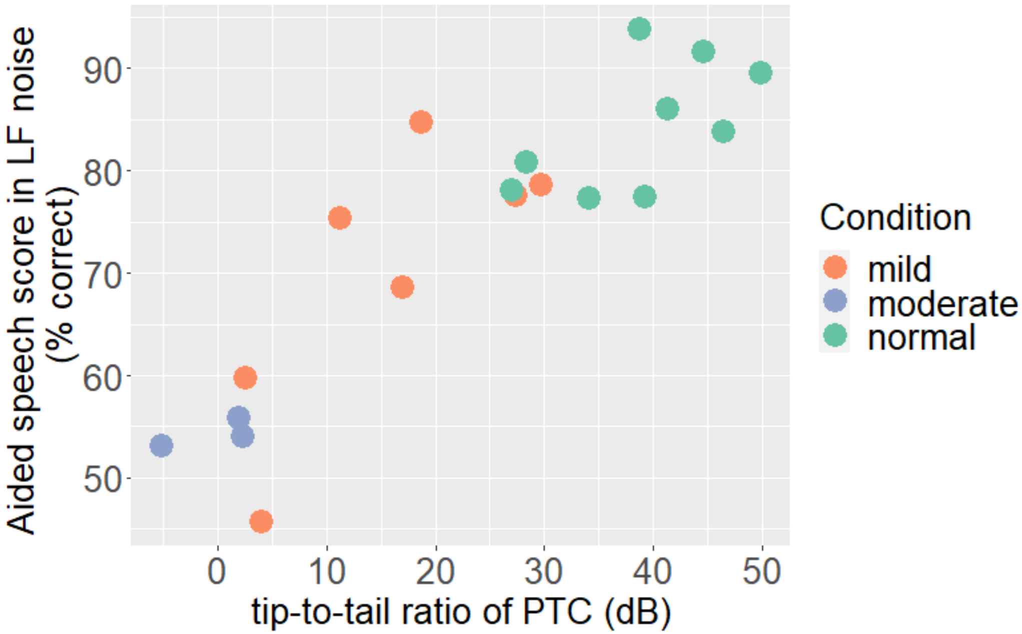


Kafi et al., In preparation

Speech-in-noise outcomes vary for low SNRs, but predicted by distorted tonotopy metric!

All subjects were at ceiling for SNRs of 6 and 12 dB, confirming audibility in low-noise conditions.

For SNRs of -12 and -6 dB, large variations in outcome correlated with psychophysical tuning curve tip-to-tail ratio.



Kafi et al., In preparation

Speech-in-noise outcomes better predicted by distorted tonotopy metrics than audiograms or DPOAEs!

variables	sum of sq. errors	Df	F value	Pr>f
PTC-TTR	386.30	1	10.2206	0.006001**
DPOAE-SNR	192.34	1	5.0889	0.039442*
Audiogram	75.71	1	2.0031	0.177404
Residuals	566.94	15		

Type II ANOVA table from linear model.

Audiogram = 1 -- 6 kHz pulsed-tone average thresholds

DPOAE-SNR = average SNR for L2 of 40-70 dB SPL at 4 kHz

Kafi et al., In preparation

Summary

- SNHL is complex with different possible underlying profiles of cochlear pathophysiology
- Different underlying profiles of damage lead to distinct suprathreshold outcomes
- Precision diagnostics that can disentangle different underlying profiles of pathophysiology can help with
  - Individualized amplification strategies that go beyond restoring audibility
  - Candidacy and outcome measures for emerging pharmaceuticals