Inner Hair Cell Damage and Cochlear Synaptopathy Differentially Impact Neural Envelope Coding of Modulations and Pitch

Andrew Sivaprakasam, Ivy Schweinzger, Hari Bharadwaj, Michael Heinz

Thursday, June 23^{th}, 2022

Introduction

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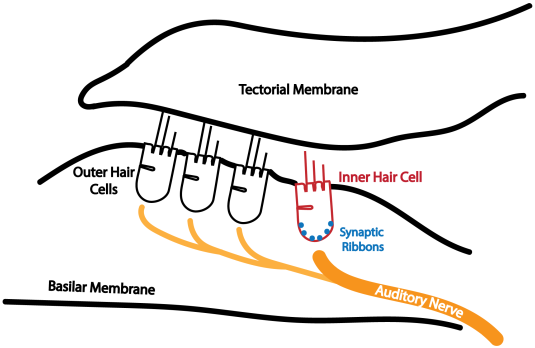
The cochlea transduces sound to neural impulses



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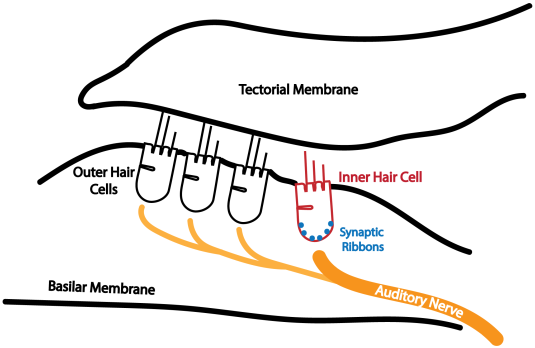

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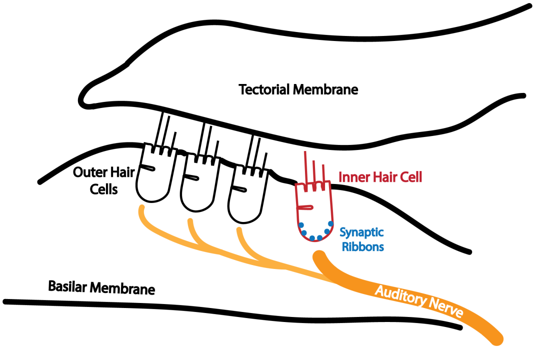

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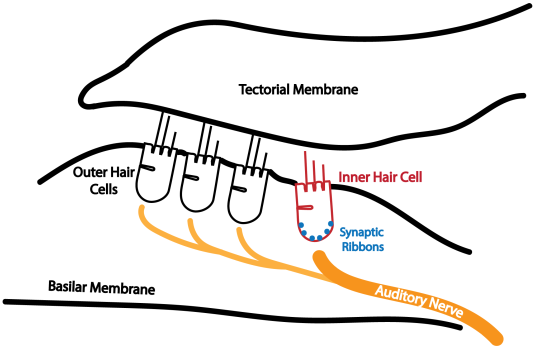


Damage to either the IHC or Synapse can alter neural firing

- Recent studies have focused on disentangling potential OHC-damage confounds from common CS assays, but have ignored possible confounds from IHC damage
- **There is a significant need to better diagnose IHC damage and differentiate its consequences from those of synaptopathy**

Chinchilla Models of IHC Damage and Synaptopathy

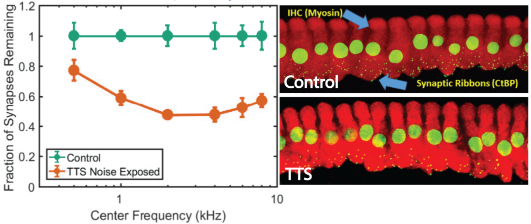
Cochlear Synaptopathy

- Noise-induced temporary threshold shifts (TTS) have been demonstrated to cause synaptopathy in chinchillas
- Band-limited noise **centered around 1kHz, at 100 dB SPL, for 2 hrs**

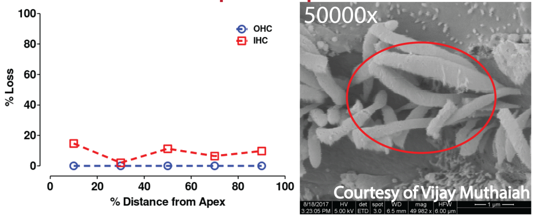
IHC Damage

- An injection of **38 mg/kg** carboplatin (CA) to chinchillas causes mild IHC loss
- Remaining IHCs have notable stereocilia damage (Axe 2017 & Wake 1994)

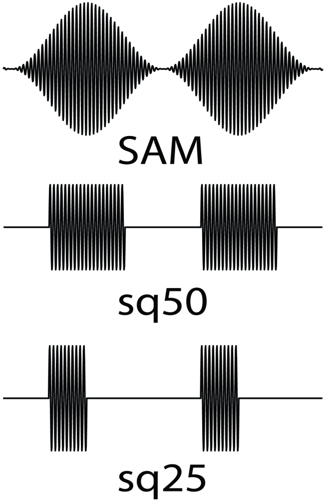
Temporary Threshold Shift



Carboplatin Exposure



Diagnostic Approaches to Synaptopathy



Envelope Following Responses to stimuli with sharp modulation envelopes may be useful in diagnosing cochlear synaptopathy in the presence of OHC damage. (Vasilkov et. al, 2021)

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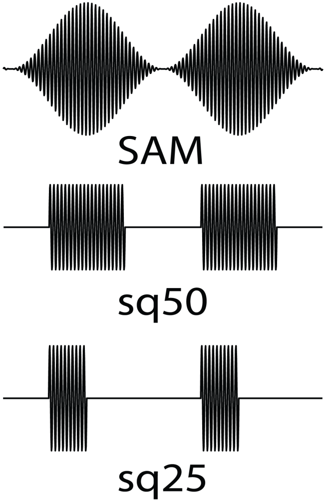

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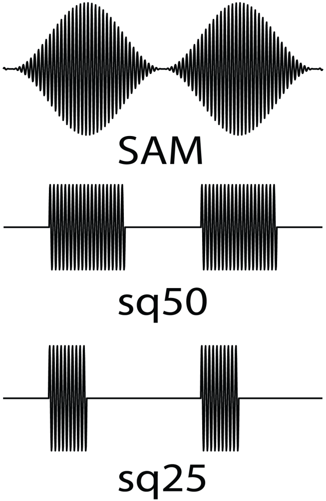

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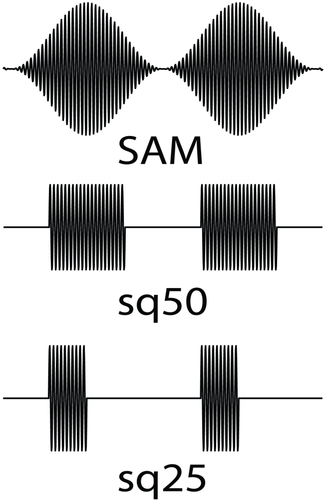

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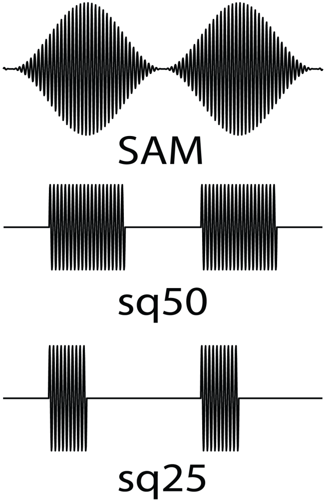

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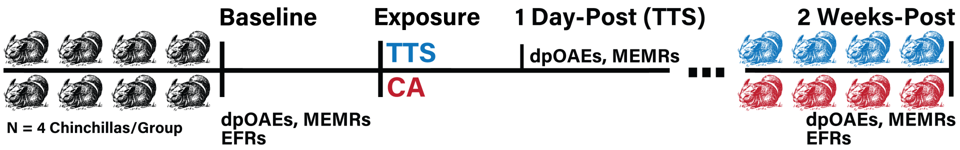
- How might IHC damage influence this measure?
- We observed some *interesting* findings in our chinchilla EFR responses to these stimuli and harmonic tone complexes.
- **Intact IHCs are important for this technique to work!**

Experimental Outline

Experiment 1 | AM Stimuli: Randomized Exposure with Baseline Measures:



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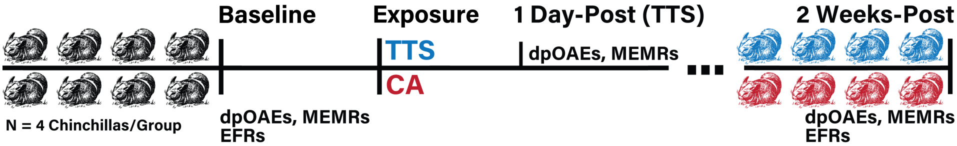
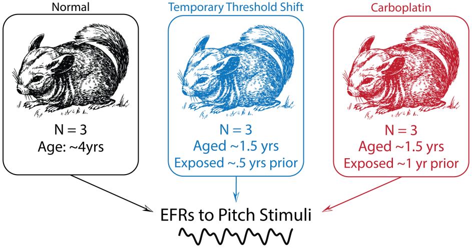


Experiment 2 | Tone Complex Stimuli: Cross-sectional Design



Hearing Assessment Post-Exposure

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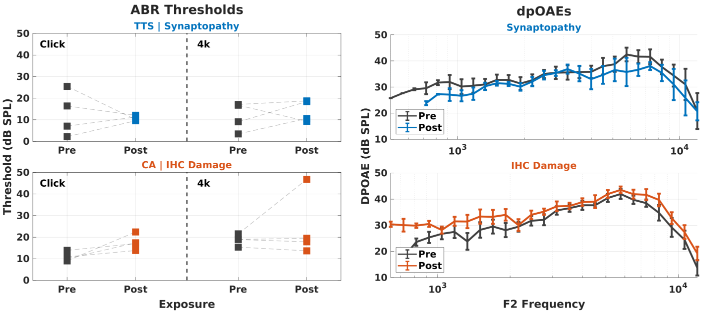
Post exposure hearing assessments did not indicate significant threshold elevation or reduced OAEs.



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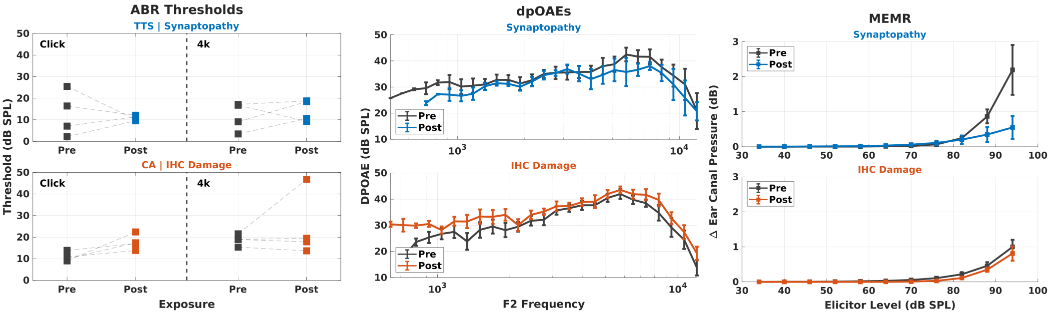
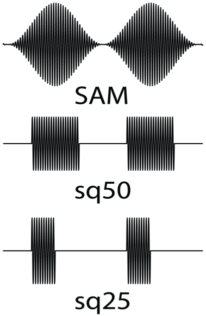


Interestingly, MEMRs strength was reduced after TTS, but not after CA exposure

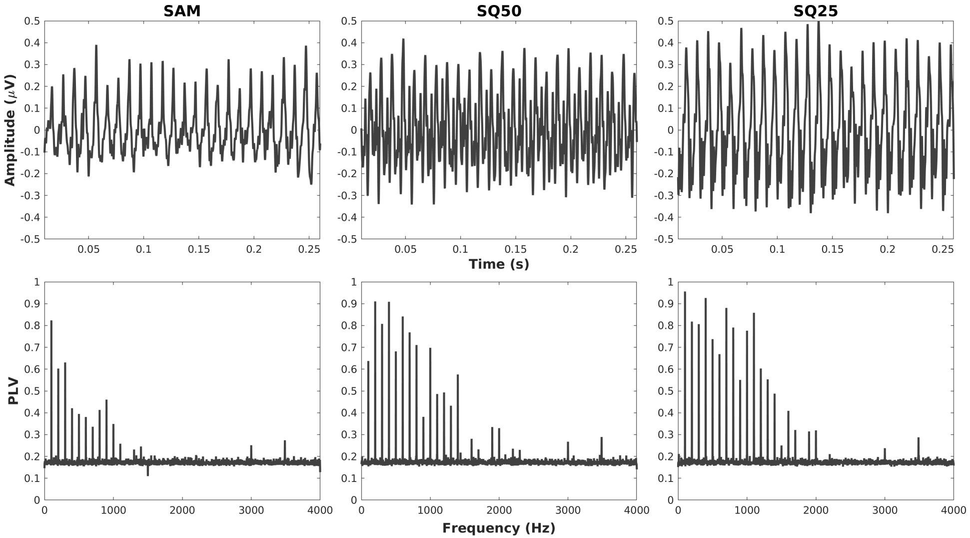
Experiment 1 | AM Envelope Following Responses

Stimuli:

- SAM, SQ50, SQ25
- $F_{mod} = 100$ Hz
- $F_{carrier} = 4$ kHz
- 78 dB SPL



Synaptopathy | Envelope Following Responses



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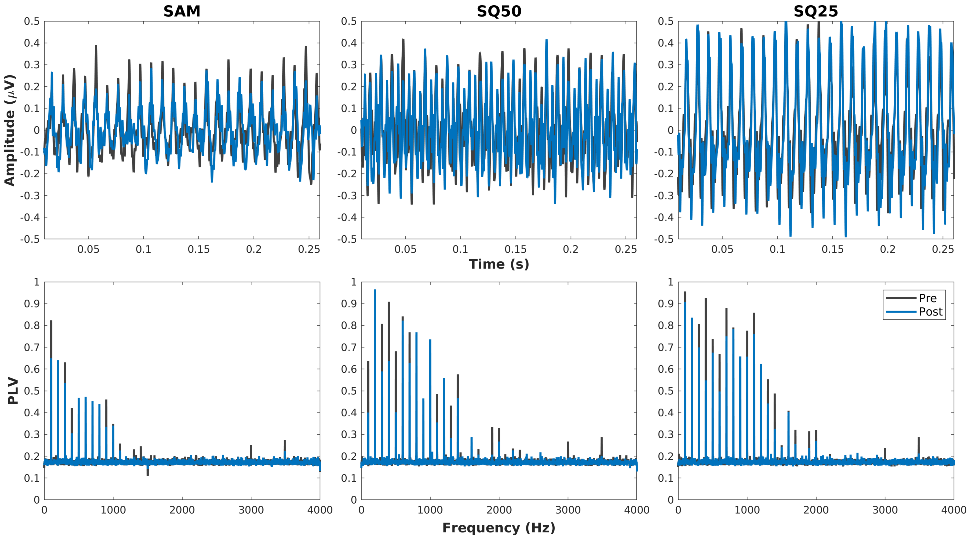
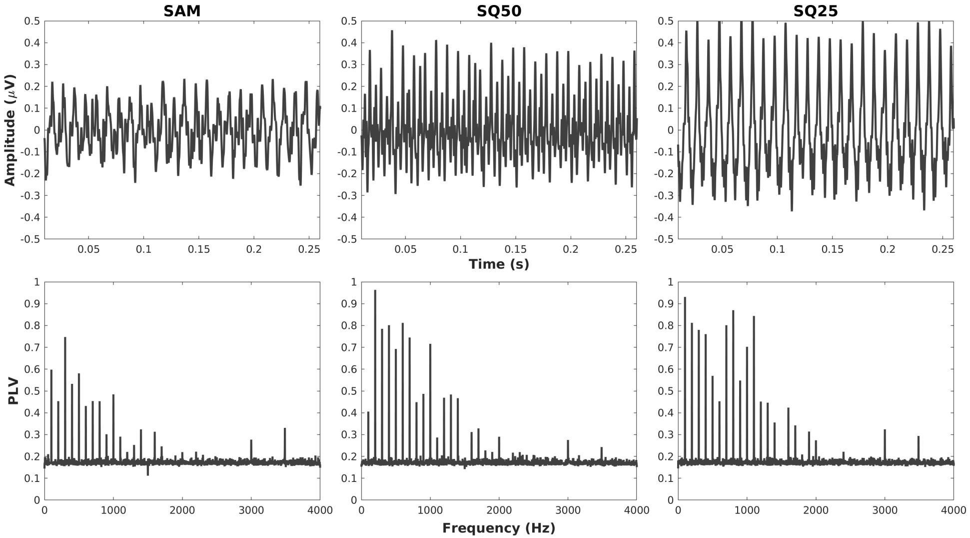


IHC Damage | Envelope Following Responses



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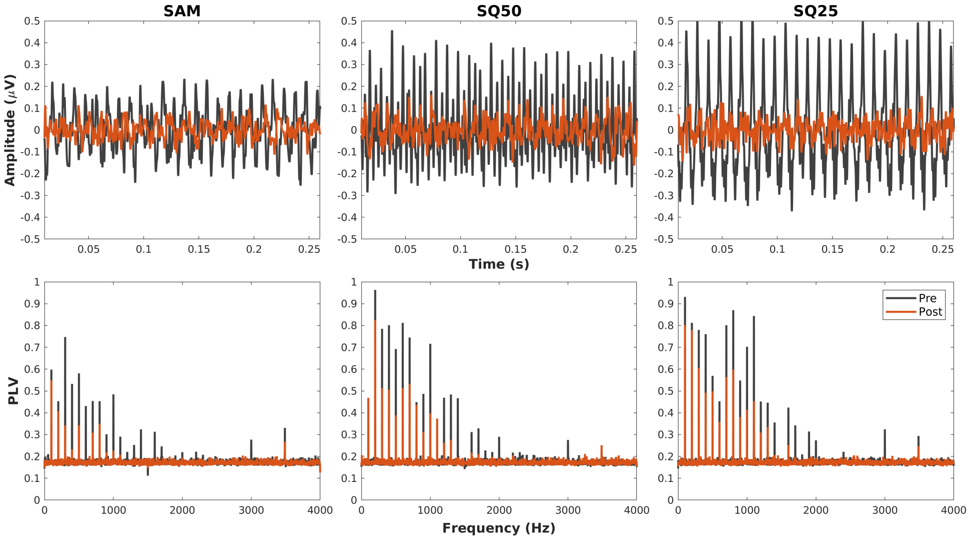
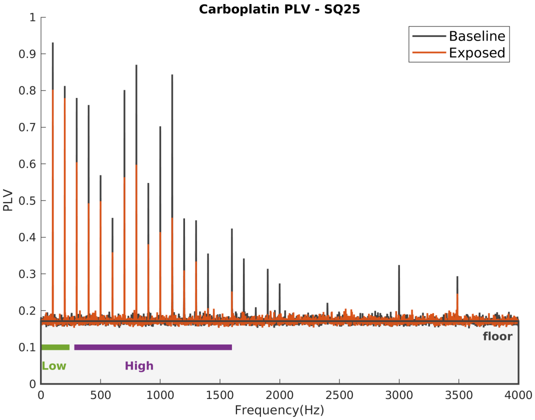


Quantifying Upper PLV Harmonic Reduction Using R_{PLV}

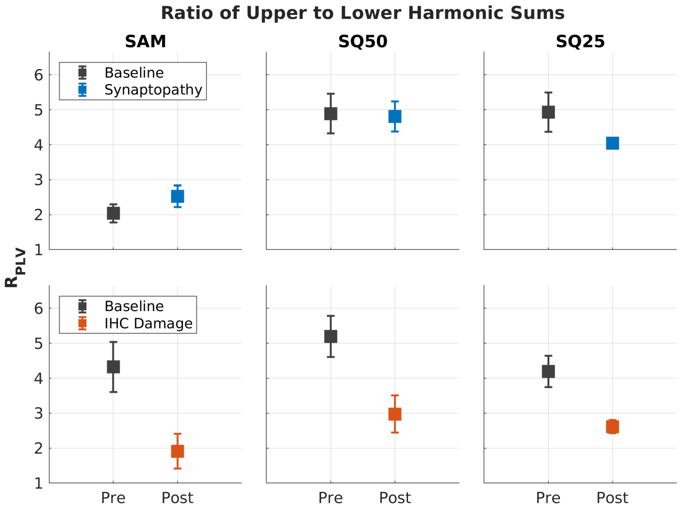


The sum of the upper harmonics (3-16) was normalized by the sum of the lower harmonics (1-2):

$$R_{PLV} = \frac{\sum_{i=3}^{16} PLV\{h(i)\} - floor}{\sum_{j=1}^{2} PLV\{h(j)\} - floor}$$

Quantifying Upper PLV Harmonic Reduction Using R_{PLV}

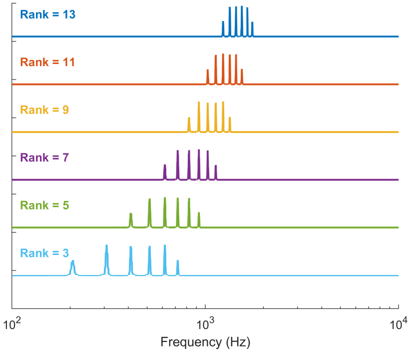
IHC damage causes a stronger and more consistent reduction in the upper harmonics than synaptopathy.



Experiment 2 | Tone Complex Envelope Following-Responses

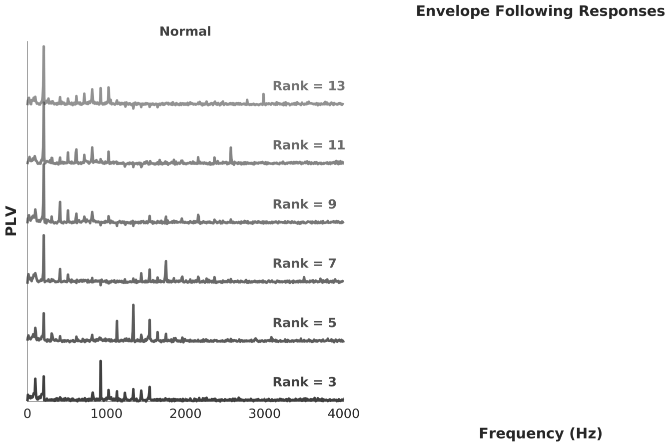
Stimuli:

- Tone Complexes
- $F_0 = 103$ Hz
- 6 Harmonics alternating in SIN/COS phase
- Harmonic Ranks: [3,5,7,9,11,13]
- 70 dB SPL



Pilot Data | Envelope Following Responses

Similar findings were also observed in the PLV spectra of pitch stimuli.



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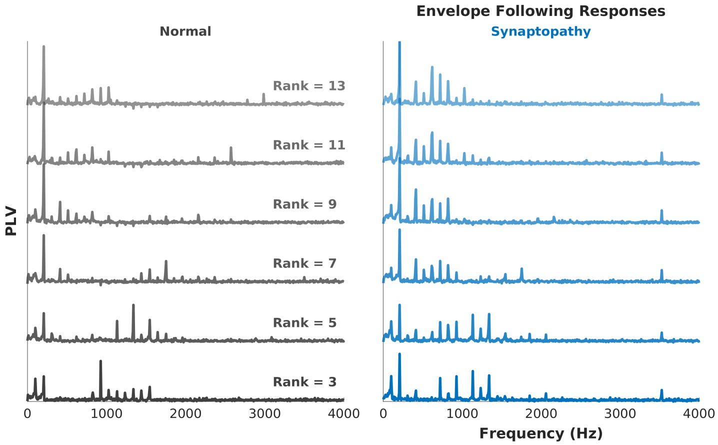

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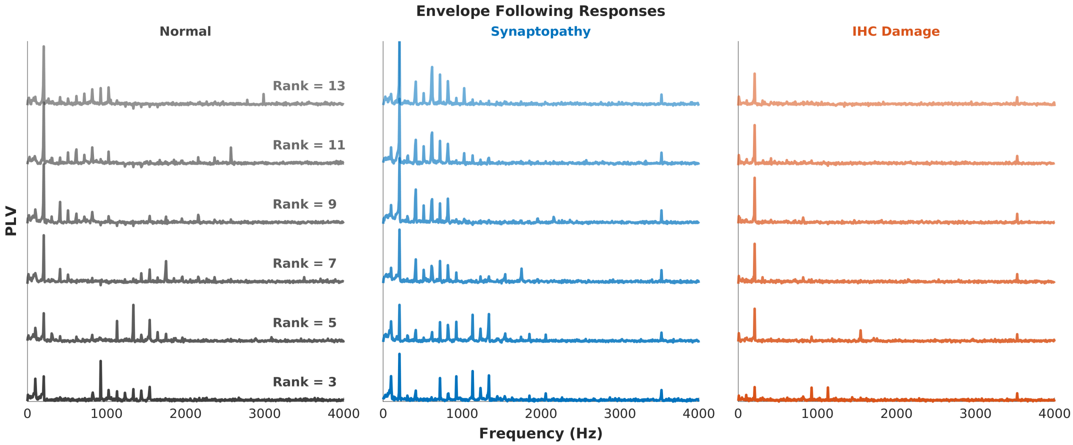

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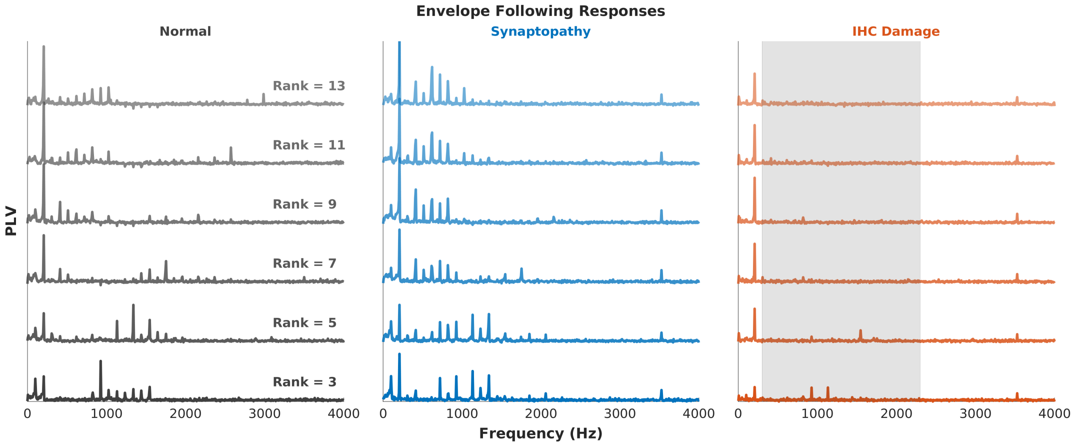
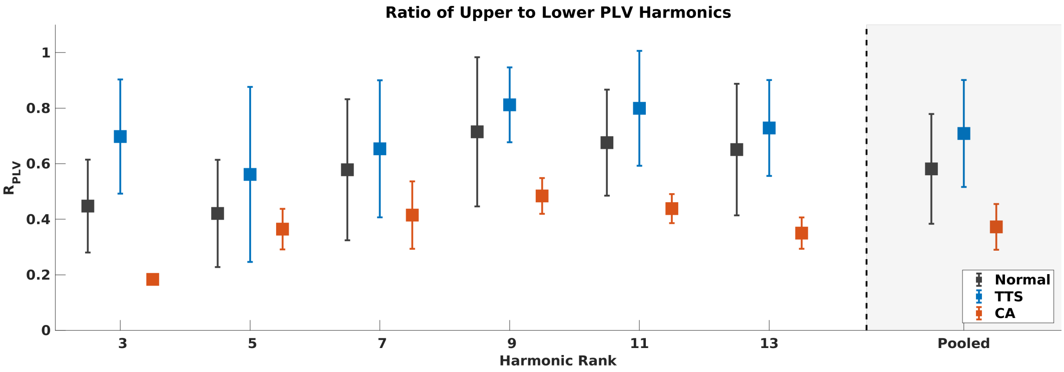


Pilot Data | Envelope Following Responses

The findings are even more apparent when using R_{PLV}:



Key Findings, Relevance, & Potential Explanations

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- The cochlea is *nonlinear*. Alterations in saturation of neural firing and other nonlinearites related to IHC transduction may result in a consistent reduction of these upper harmonics after carboplatin exposure.

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- Consistent with work from Vasilkov et. al (2021), the reduction in upper harmonic content in synaptopathy was most observable in response to the SQ25 stimulus.

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The consequences of IHC damage should not be ignored; e.g., they may confound EFR-based diagnostics aimed at isolating synaptopathy from OHC damage.

Acknowledgments

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- Michael Heinz, PhD
- Hari Bharadwaj, PhD

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- Agudemu Borjigin, PhD
- Subong Kim, PhD

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Seminars in Hearing Research at Purdue

Auditory Neuroscience Association at Purdue

Heinz Lab:

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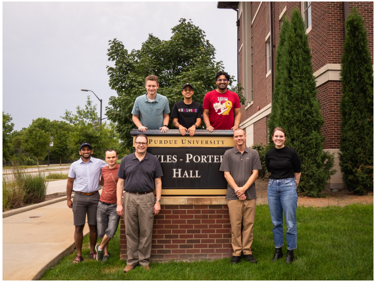
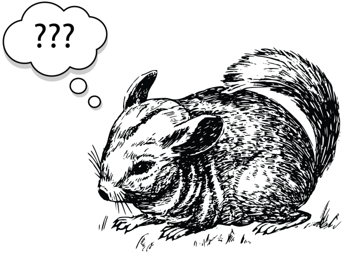
- Ivy Schweinzger, PhD
- Samantha Hauser, AuD
- Jonatan Märcher-Rørsted
- Fernando Aguilera de Alba
- Jim Bundy



Thank you!! Questions?



Appendix

Histologically Quantified IHC vs OHC Stereocilia Damage

Broader (across the cochlea) IHC stereocilia damage was a consistent finding from Liberman and Dodds (1984)
(*inconsistent with "OHCs damaged first story" of SNHL*)

Sayles and Heinz (2017)

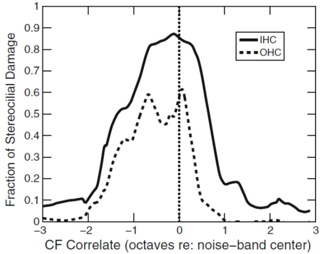
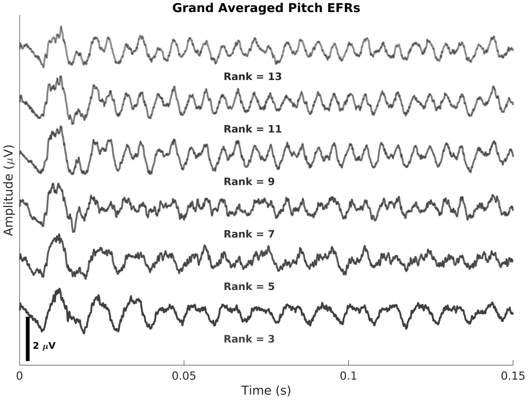
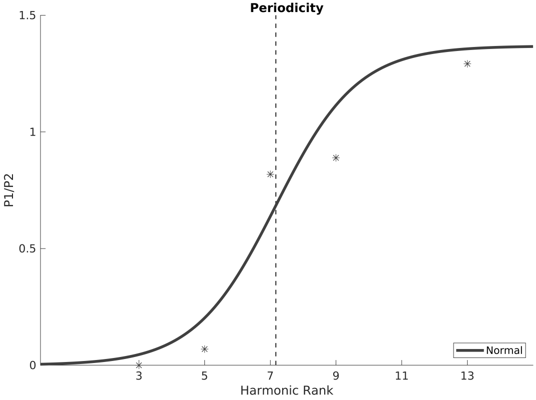


Fig. 8.2 The cochlear distribution and degree of inner hair cell (IHC) stereocilial damage from noise exposure are generally larger than they are for outer hair cells (OHCs). The fraction of IHC and OHC stereocilial damage is plotted versus the cochlear characteristic frequency (CF) associated with cochlear place (in octave difference relative to exposure-noise center frequency). Data were reanalyzed from Liberman and Dodds (1984) by averaging across animals exposed to narrowband noise with center frequencies from 1.5 to 5.5 kHz

Pilot Data | Envelope Following Responses

Normal vs Impaired Hearing EFR Findings:





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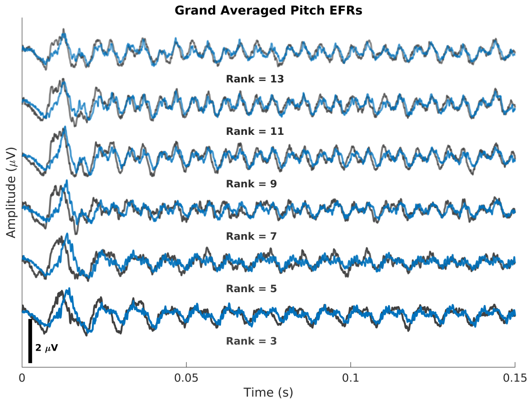

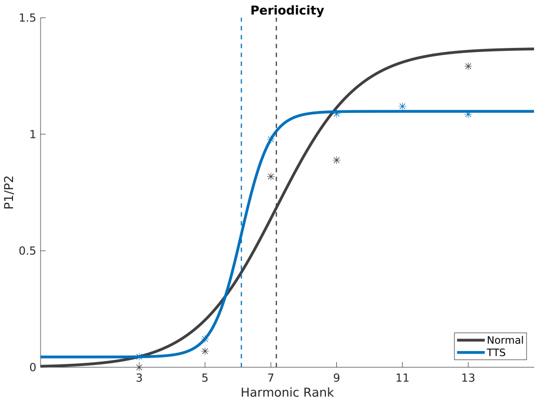

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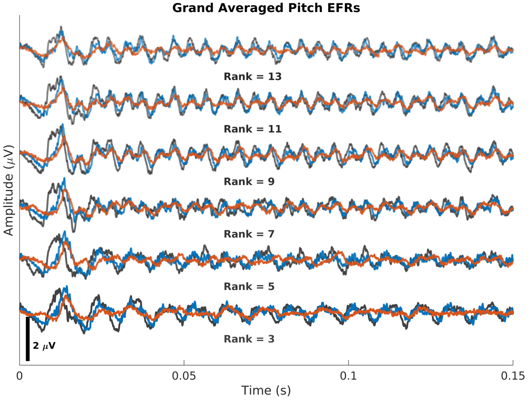
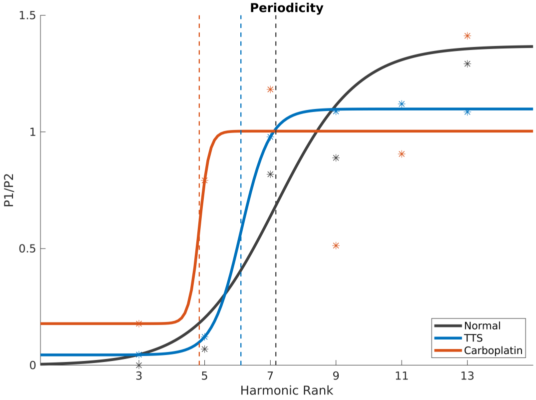




Frequency or Envelope Following Responses (FFR or EFRs)

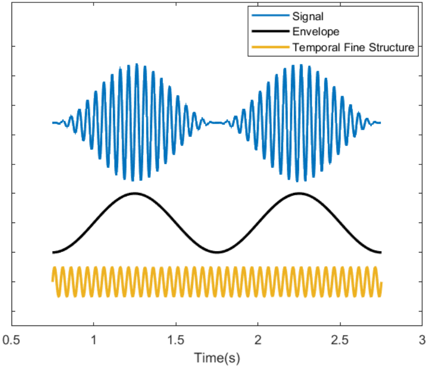
Alternating the polarity of our stimuli helps separate neural responses driven by stimulus temporal fine structure (TFS) and temporal envelope (ENV).

The TFS response (Frequency Following Response) is polarity *sensitive*, and is computed by subtraction:

$$d(t) = \frac{p(t) - n(t)}{2}$$

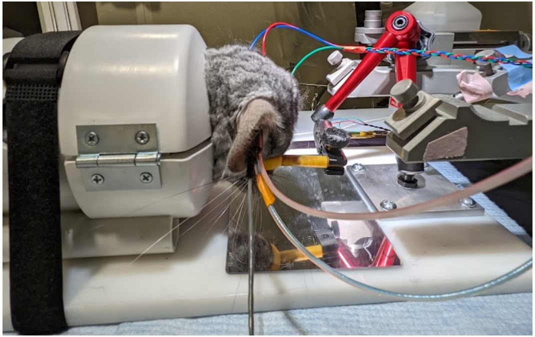
The ENV response (Envelope Following Response) is polarity *tolerant*, and is computed by addition:

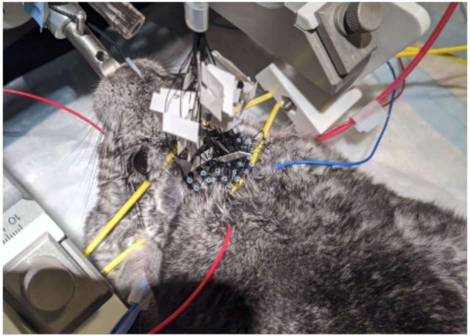
$$s(t) = \frac{p(t) + n(t)}{2}$$



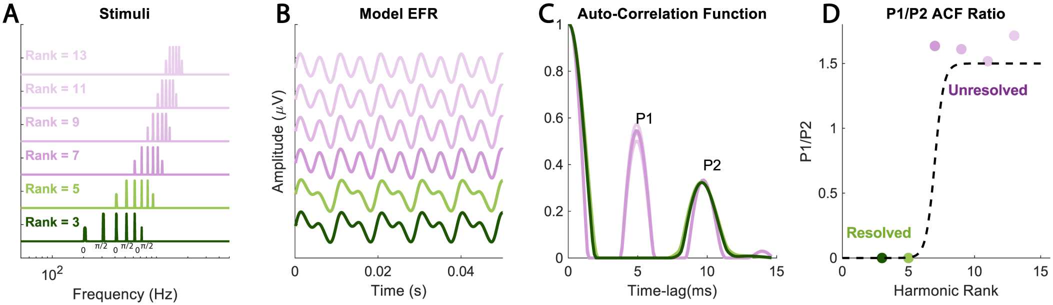
Laboratory Setup

Heinz Lab:



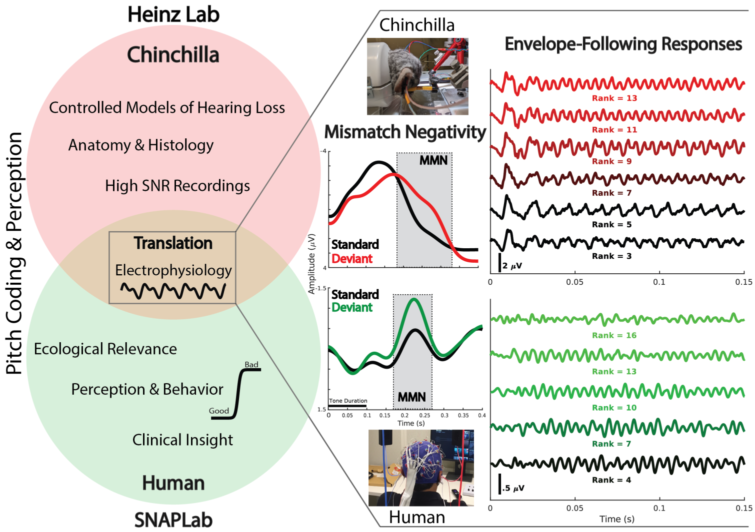


Using Phase Shifts to Change Envelope Periodicity



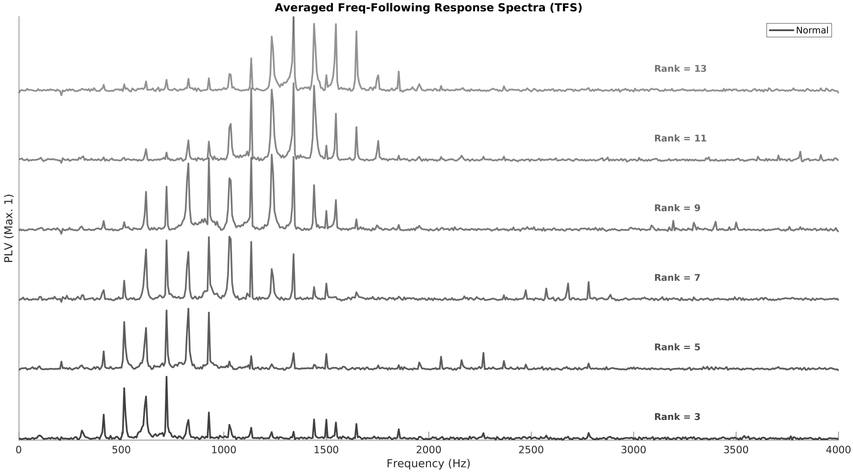
When all harmonics are resolved, the EFR has a repetition cycle of 100 Hz, but when at least 3 harmonics are unresolved, the frequency is doubled to 200 Hz.

Our Labs | My Cross-Species Approach to Studying Pitch



Pilot Data | Frequency Following Responses

These PLVs were computed by subtracting opposite polarities (polarity sensitive component)



Pilot Data | Envelope Following Responses

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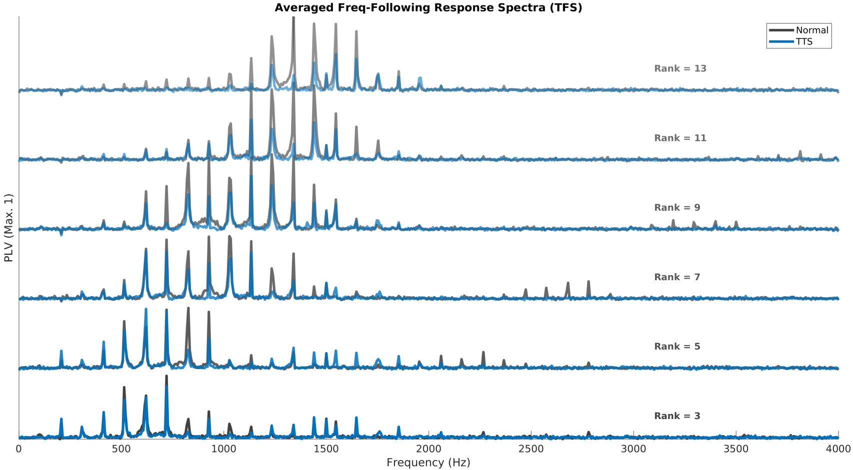

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