Subtypes of Sensorineural Hearing Loss Variably Alter the Neural Encoding of Fundamental Frequency

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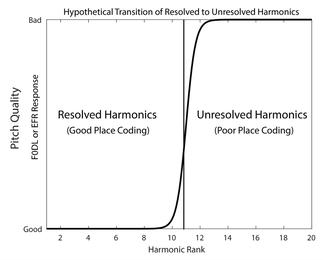
Introduction

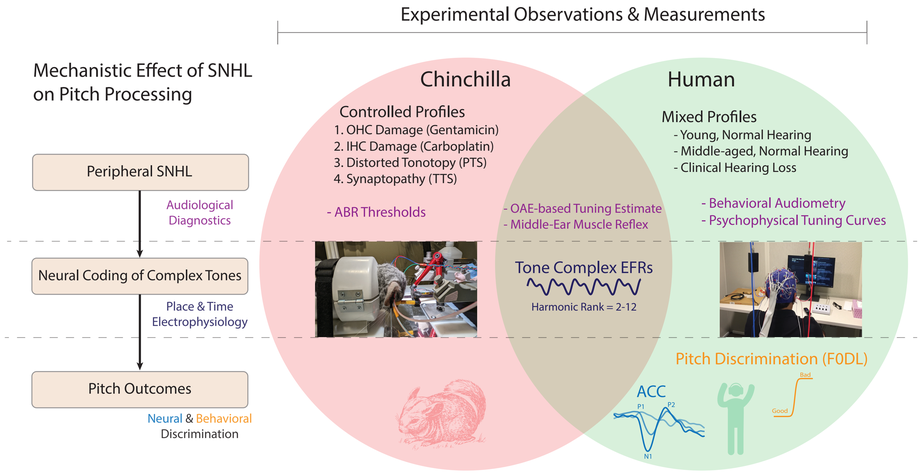
An intact sense of pitch is critical to not only discriminate notes in a musical scale, but also perceive vowels and emotion.

- Longstanding pitch theories weigh the importance of **tonotopy (place)** vs **temporal coding (time).**
- The precise mechanisms by which SNHL affects pitch coding and perception are yet to be resolved.
- **Cochlear Synaptopathy**, **Inner Hair Cell** (IHC), and **Outer Hair Cell** (OHC) **damage** may differentially impact place and time cues useful for pitch perception, despite often being indifferentiable through non-specific standard clinical assays.

Band-limited tone complexes have been used to probe the fidelity of cochlear time and place cues through both physiological (Envelope Following Responses, EFRs) and behavioral (Fundamental Frequency Difference Limens, F0DLs) measures.



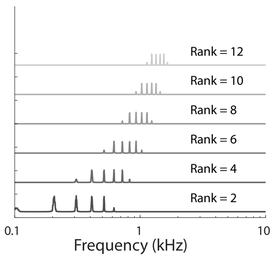
Methods



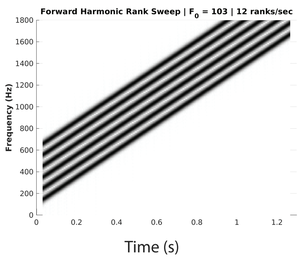
EFRs to tone complex stimuli and controlled models of hearing loss in chinchillas are being leveraged to better understand the mixed profiles of hearing loss that appear in a broad population of human subjects. This will facilitate mechanistic explanations for the variability seen in pitch outcomes like Acoustic Change Complex (ACC), and F0DLs

Stimulus Design

Discrete Tone Complex Stimuli



Swept Tone Complex Stimulus



EFRs to discrete and swept tone complex stimuli were selected to investigate neural coding across cochlear place.

The harmonics in each tone complex were presented in alternating (ALT) phase. This results in a temporal envelope modulation of 2*F0, while place cues are spaced 1*F0 apart.

This elicits an EFR with energy at F0 when all harmonics in the complex are resolved, but 2*F0 when harmonics are unresolved[1].

The change in envelope coding with increasing harmonic rank was quantified through spectral (Phase Locking Value, PLV) and temporal (AutoCorrelation Function, ACF) analyses.

Chinchilla Exposure Paradigms

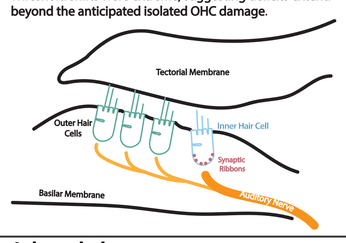
Four exposure paradigms were chosen, each causing a different profile of SNHL.

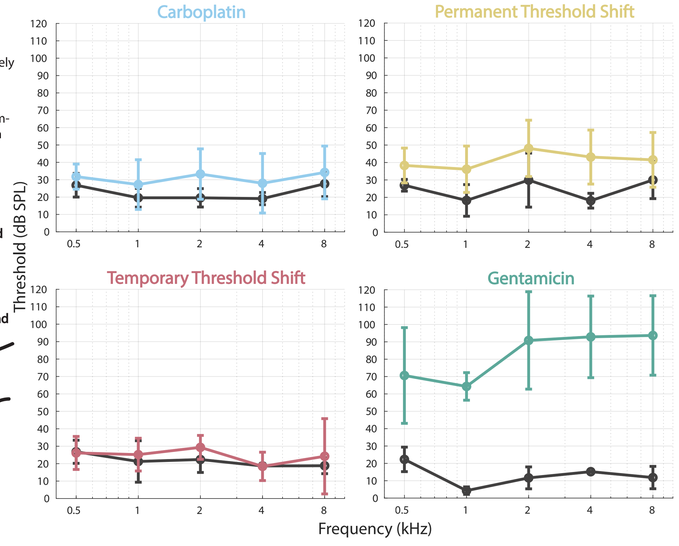
IHC Damage:
Carboplatin (38 mg/kg, IP). Data collected 2 weeks post exposure. Results in **minimal threshold shift**, with relatively uniform **IHC stereocilial damage, ~15% loss of IHCs[2]**

Synaptopathy:
1kHz Octave-Band Noise, 100 dB SPL, 2hrs. Results in temporary hearing loss 1 day post exposure (confirmed with middle ear muscle reflex, dpOAEs), with **recovery and normal thresholds 2 weeks after exposure, despite substantial loss of synapses[3].**

Complex SNHL:
.5 kHz Octave-Band Noise, 116 dB SPL, 2hrs. Results in **permanent hearing loss** (20-30 dB elevation), with **mixed IHC stereocilial damage and OHC loss.**

Gentamicin:
Gentamicin (10 mg/kg, IM) followed by Ethacrynic Acid (40 mg/kg, IV). Data collected 1 week after exposure. **Threshold shifts were extreme, suggesting deficits extend beyond the anticipated isolated OHC damage.**





Results

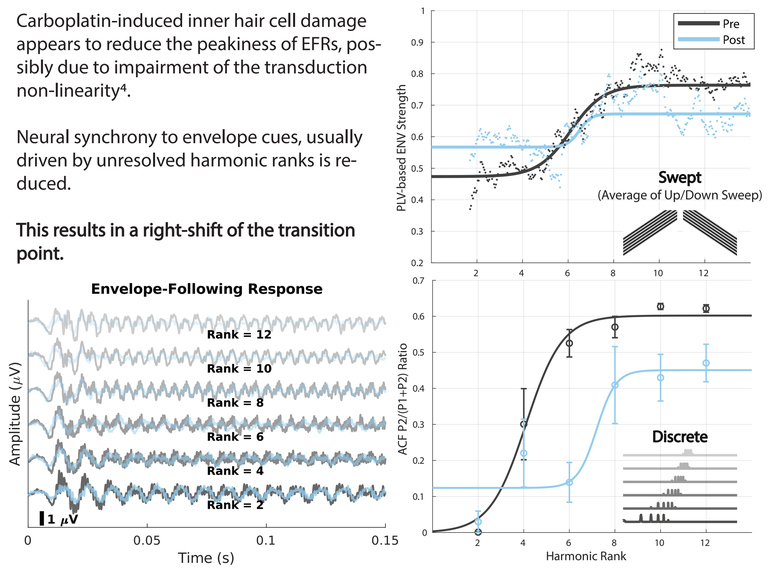
Deficits in the neural coding of complex tones and fundamental frequency depend on the type of cochlear damage.

Carboplatin (N=6)

Carboplatin-induced inner hair cell damage appears to reduce the peakiness of EFRs, possibly due to impairment of the transduction non-linearity[4].

Neural synchrony to envelope cues, usually driven by unresolved harmonic ranks is reduced.

This results in a right-shift of the transition point.

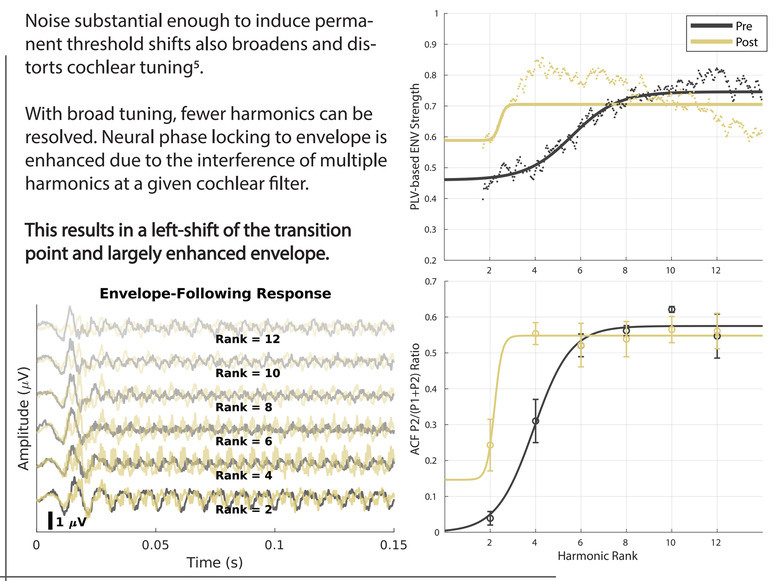


Permanent Threshold Shift (N=6)

Noise substantial enough to induce permanent threshold shifts also broadens and distorts cochlear tuning[5].

With broad tuning, fewer harmonics can be resolved. Neural phase locking to envelope is enhanced due to the interference of multiple harmonics at a given cochlear filter.

This results in a left-shift of the transition point and largely enhanced envelope.

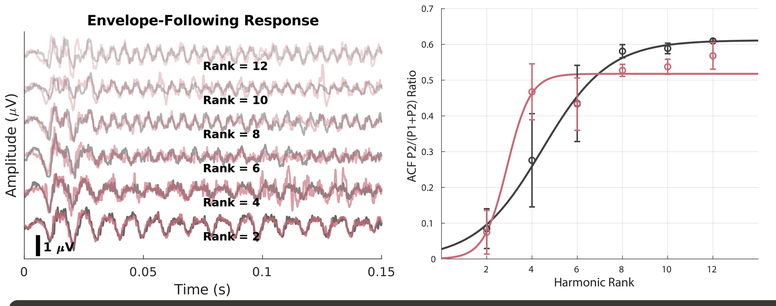


Temporary Threshold Shift (N=5)

We expected more similarities to the carboplatin model, given that synaptopathy should alter IHC output to the auditory nerve.

However, TTS induced EFR deficits appear similar to those explained by broader tuning in the PTS group-- though more subtle.

We observe a slight left-shift of the transition point, with moderately enhanced envelope at lower harmonic ranks.

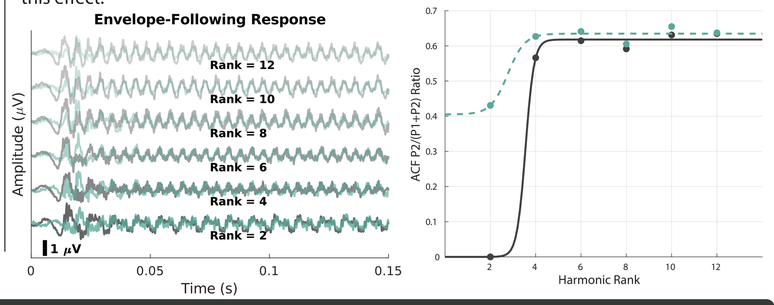


Gentamicin (N=2)

ABR thresholds after gentamicin exposure were severely elevated, necessitating a higher stimulus level (80 dB SPL, dashed).

The swept tone complex was useful for efficiently probing the transition point at multiple levels with limited time and an unpredictable severity of hearing loss.

We observe a left-shift similar to that in the PTS group, though more data is needed to confirm this effect.



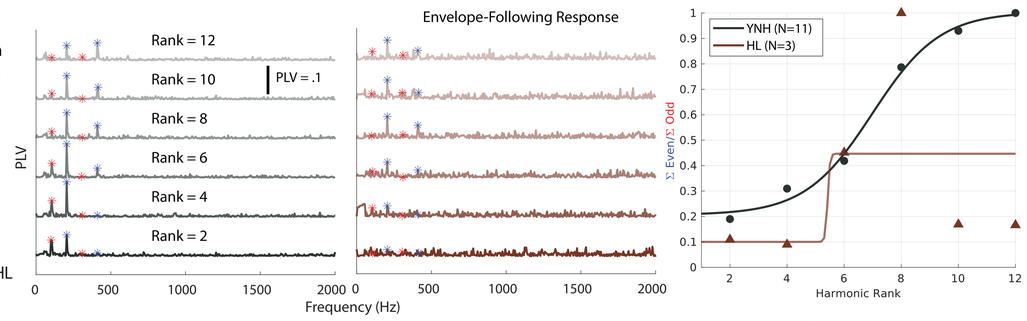
Pitch Perceptual Implications

The EFR reveals that the fidelity of cochlear place and timing cues are differentially impacted based on the subtype of hearing loss. We are investigating how pitch discrimination (F0DL) is affected by deficits in place and time coding and frequency selectivity.

Human EFR Data

Preliminary data indicate robust EFRs to discrete harmonic rank stimuli in young, normal-hearing, (YNH) subjects. A resolved-unresolved transition point is evident around a harmonic rank between 6 and 8.

Subjects with hearing loss (HL, defined as audiometric thresholds > 25 dB HL below or at 8 kHz) have reduced EFR amplitudes, and poorer phase locking to the F0. Phase locking to envelope (2*F0) appears stronger at lower harmonic ranks.

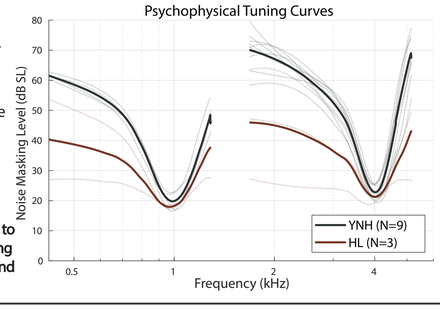


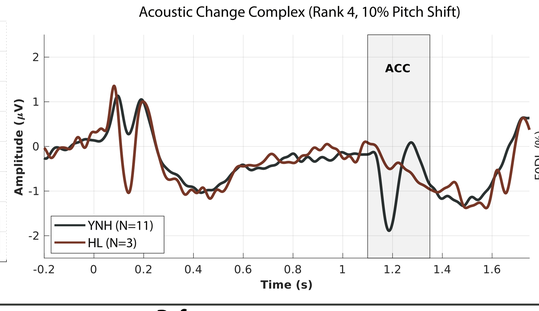
Linking Physiology to Perception

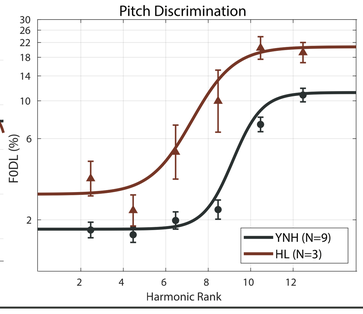
Beyond the audiogram, other measures also differ between YNH and HL listeners, perhaps explaining deficits in pitch perception.

- Broader tuning in HL subjects may help explain envelope-dominant coding and disrupted place cues observed in the EFR
- Both neural (ACC) and perceptual (F0DL) pitch discrimination are worse in subjects with hearing loss.
- F0DL performance shifts at a lower harmonic rank, which may suggest disrupted place cues

Combining these approaches allows us to rigorously explore place and time coding deficits that present with hearing loss and link them to pitch perception.







Acknowledgements:

We would like to thank the Purdue Interdisciplinary Training Program in Auditory Neuroscience (TPAN; 1T32DC016853), NIDCD F30DC020916 (A.S.), F32DC021345 (S.H.), R01DC009838 (M.H.), and R01DC015989 (H.B.) for funding and Dr. Andrew Oxenham for helpful feedback and discussion related to this experimental approach.

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