Overzealous Tail: Distorted Tonotopy Degrades Suprathreshold Sound Coding in Sensorineural Hearing Loss

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Abstract. Patients with similar audiograms often experience varying levels of difficulty with understanding speech in noisy environments, despite using state-of-the-art hearing aids. With audibility largely restored by amplification, these divergent suprathreshold outcomes are often attributed to reduced frequency selectivity (i.e., broadening of the so-called "tip" of cochlear frequency tuning curves) associated with sensorineural hearing loss (SNHL), and to non-peripheral factors such as attention, and working memory. However, our ongoing cross-species studies on neural coding in SNHL suggest that distorted tonotopy—a phenomenon where hypersensitive tails of cochlear tuning curves dominate and commandeer the temporal response in the basal half of the cochlea—can significantly contribute to the degraded neural coding of sounds. This effect is particularly pronounced with naturalistic stimuli, such as speech, which contain intense low-frequency components alongside softer but highly informative high-frequency content. Going from bad to worse, this effect is further exacerbated in noisy backgrounds with pink-like spectral characteristics (e.g., background talkers, environmental noises). Specifically, in a chinchilla model of SNHL with noise-induced permanent threshold shifts, auditory-nerve single-unit measurements revealed that hypersensitive tuning-curve tails were the primary contributor to the severe degradation of speech-envelope coding through the masking effects of low-frequency energy on basal responses, manifesting both as impaired representation of higher vowel formants and near erasure of transient responses to high-frequency consonants. In parallel human studies of individuals with mild or moderate SNHL, we utilized behavioral measures, otoacoustic emissions, and electroencephalography (EEG) to characterize distorted tonotopy. Results indicate that humans with SNHL also exhibit hypersensitive tuning-curve tails, even with mild-moderate SNHL. Furthermore, EEG measurements revealed that these hypersensitive tails are linked to impaired tracking of speech envelopes. Importantly, variations in the estimated degree of distorted tonotopy were also predictive of the large individual differences in speech-in-noise outcomes that persist despite prescriptive amplification. Taken together, our results suggest that distorted tonotopy is a prominent contributor to suprathreshold deficits in SNHL in both laboratory animals and in human listeners. Additionally, in both species, non-invasive assays offer promise towards providing useful indices of distorted tonotopy that may, in the long run, be developed and leveraged for clinical use.

INTRODUCTION

Threshold audiometry and restoration of speech audibility through amplification are the cornerstones of current audiological practice. Yet, patients with sensorineural hearing loss (SNHL) often struggle to understand *audible* speech, particularly in complex everyday environments with background noise [1], [2]. These *suprathreshold* challenges persist even among hearing-aid users, who experience widely varying listening outcomes, with many abandoning their hearing aids [3], [4], [5]. Successful listening in complex environments with multiple sound sources relies on a collaborative heterarchy (Fig. 1), encompassing precise bottom-up encoding of spectrotemporal sound features [6], temporal analysis of these coded representations by the central auditory system to segregate target sounds from the background [7], [8], and attentive selection of the segregated target stream [9].

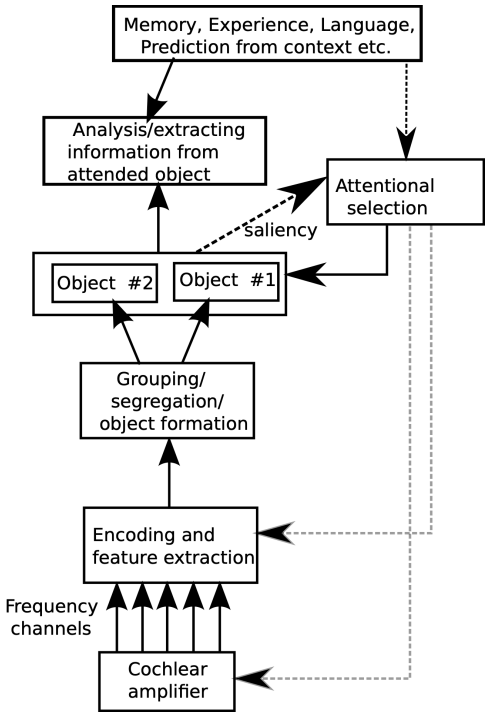

FIGURE 1. A schematic illustration, adapted from [9], of the collaborative heterarchy of processes underlying suprathreshold hearing in complex everyday environments with multiple sound sources. Successful listening in such settings relies on precise bottom-up encoding of spectrotemporal detail, auditory scene analysis to segregate the sound mixture into individual sources, and selective attention to process one source while ignoring others.

Although it is well-recognized that cochlear hearing loss can reduce the fidelity of bottom-up sound coding [10], emerging evidence suggests that SNHL can also disrupt other elements of this heterarchy. For instance, the degraded representation of spectrotemporal or interaural cues can reduce the perceived salience of pitch, location, and timbre cues that listeners use to focus selective attention to pick out the target sound amidst competition [11], [12]. Furthermore, reduced peripheral input from SNHL can instigate maladaptive central neural "gain" detrimental to our ability to analyze the encoded acoustic mixture to discern target sounds from background noise [13], [14]. Characterizing these diverse suprathreshold sequelae of SNHL and how they each impact listening outcomes for individual patients is paramount for developing targeted, personalized treatments. Here, we focus on the mechanisms through which SNHL degrades the bottom-up coding of speech in early portions of the auditory pathway, and how they relate to suprathreshold speech perception in noise (SPIN).

CANDIDATE MECHANISMS OF DEGRADED BOTTOM-UP SPEECH CODING

Conventionally, suprathreshold peripheral alterations in SNHL that are hypothesized to contribute to SPIN deficits include reduced frequency selectivity, degraded fidelity of temporal coding, and cochlear deafferentation. Reduced frequency selectivity is observed in individuals with SNHL with psychophysical tuning curves getting up to five times as broad in individuals with moderate threshold elevation compared to those with normal hearing sensitivity [10]. This broadening of the "tip" of threshold tuning curves is mirrored in single-unit auditory-nerve fiber recordings in animals with damage to cochlear outer hair cells [15], suggesting that altered cochlear responses may directly contribute to our ability to resolve frequency differences between target and background sounds. Furthermore, altered cochlear tuning can also directly impact temporal coding in the auditory nerve. Specifically, while the increased bandwidth of response of any given cochlear section can enhance the representation of sound envelopes in quiet [16], the same mechanism can degrade envelope coding in the presence of background noise by allowing more noise energy to excite that section [17]. Perceptual studies in humans using subband-vocoded speech suggest that temporal-coding deficits in SNHL may also extend to the representation of temporal fine structure, i.e., the cycle-by-cycle fluctuation in the phase of sound-driven cochlear vibrations [18]. However, surviving single-unit auditory-nerve fibers in animal models of SNHL do not exhibit a parallel deficit in phase locking [19], suggesting that deficits in fine-structure coding, if present, must emerge either as a consequence of tuning changes that make noise masking more potent, or at the neural population level as a consequence of reduced auditory nerve firing rates (i.e., fewer neural spikes) producing a weaker volley effect that would typically sharpen temporal coding at downstream sites [20]. Finally, seminal work by Kujawa and Liberman [21] demonstrated that afferent synapses and nerve terminals, rather than hair cells, are the most vulnerable structures in the cochlea to damage from acoustic overexposure, aging, and ototoxic agents. Cross-species evidence suggests that this purely neural form of SNHL is widespread [22], occurring even in individuals with normal hearing sensitivity. This cochlear deafferentation has also been hypothesized to degrade temporal-coding precision both by reducing the number of number of auditory nerve fibers phase-locked to the temporal fine structure, and by reducing the dynamic range of sound levels over which temporal envelopes are robustly coded [23], [24].

Off-frequency Coding in the Auditory Periphery is Understudied

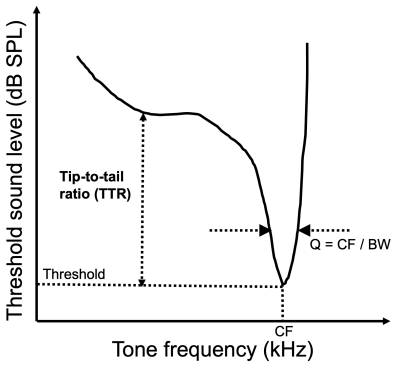

FIGURE 2. A schematic illustration of the characteristic shape and parameters of auditory-nerve threshold tuning curves in the healthy cochlea. Beyond the characteristic frequency (CF) that the fiber is most sensitive to, frequency selectivity is calculated as the quality factor (Q) of the tuning-curve tip around CF, and the low-frequency sensitivity is calculated as a tip-to-tail ratio (TTR).

Beyond the conventionally hypothesized mechanisms of reduced frequency selectivity, degraded phase-locking precision, and cochlear deafferentation, another mechanism that can also distort speech coding is the off-frequency response of the cochlear base to low-frequency sounds. It is well-known that auditory-nerve threshold tuning curves in a healthy cochlea are asymmetric (see Fig. 2), with the curve exhibiting a sharp edge on the high-frequency side and both shallower slopes and a flatter "tail" on the low-frequency side. This is mirrored in both psychophysical tuning curves (PTCs) and distortion-product otoacoustic emission (DPOAE) suppression tuning curves in human listeners [25], [26]. In animals with outer hair-cell injury, not only is the tuning curve tip broader (lower quality factor or Q), but there is also a marked reduction in the tip-to-tail ratio (TTR) [15] both from the elevation of the tuning-curve tip and a dropping (i.e., hypersensitivity) of the low-frequency tail. The reduced TTR is thought to contribute to the well-known "upward spread of masking" effect where increasing levels of narrowband noise can induce rapid and supralinear increases in detection thresholds for tones with frequencies well-above the noise band [27], [28]. Although the effects of reduced TTR are well-studied in the realm of tuning curves and with simple tonal and narrowband noise stimuli, little is known about how this off-frequency sensitivity of the cochlear base to low-frequency sounds affects the coding of complex sounds like speech, and SPIN outcomes. This is particularly important because naturalistic sounds like speech have pink-noise-like spectra with substantial low-frequency energy. The following sections summarize our ongoing efforts to address this gap through coordinated cross-species investigations in human participants with SNHL and multiple preclinical chinchilla models. Our findings across chinchillas and humans suggest that distorted tonotopic coding from off-frequency responses of the cochlear base is the dominant factor contributing to degraded suprathreshold coding of speech and SPIN outcomes.

CROSS-SPECIES EVIDENCE OF DISTORTED TONOTOPY IN SNHL

Insights from Chinchilla Models

Chinchillas are a particularly valuable model for auditory science in general, and studies of neural coding in SNHL in particular [29]. Chinchillas have a similar frequency range of sensitivity as humans, allowing for study of neural coding of both low and high-frequency sounds [30]. Pre-clinical chinchilla models of isolated cochlear pathologies, such as outer vs. inner hair cell injury, cochlear synaptopathy, and loss of endocochlear potentials from the stria vascularis, are described in the literature. Each of these pathologies can contribute to the overall clinical umbrella category of SNHL [31]. Our ongoing cross-species work takes advantage of these factors to obtain integrative insight into how neural coding in the periphery, directly measurable in chinchillas, is ultimately related to suprathreshold listening outcomes in human participants. Common non-invasive acoustic and electrophysiological measures possible in both species provide a translational bridge [22].

Although frequency tuning is well-characterized near threshold, direct recordings of suprathreshold auditory nerve responses are scarce, especially for complex sounds like broadband noise and speech. To understand the contribution of off-frequency coding to complex sounds, it is necessary to identify which spectrotemporal features in the input sound drive the response of each auditory nerve fiber. This can be accomplished by leveraging system identification approaches such as reverse correlations, Wiener kernels, and their nonlinear generalizations [32].

Accordingly, [33], [34] applied Wiener-kernel analysis to single-unit auditory-nerve responses to suprathreshold broadband noise measured from two pre-clinical chinchilla models of SNHL: (1) a noise-induced hearing loss (NIHL) model created by exposing animals to low-frequency noise for 2-4 hours at 115-116 dB SPL, and (2) a model of

metabolic hearing loss (MHL) produced by intravenous administration of furosemide, an ototoxic loop diuretic. While both models can result in similar elevation of auditory-nerve thresholds, the effects of NIHL are produced by diffuse trauma to the stereocilia of both inner and outer hair cells, whereas the effects of MHL are produced by a reduction in the electrochemical gradient (i.e., the endocochlear potential) powering active hair-cell transduction, which has been shown to be reduced in aged animal models [35]. These models mirror two common etiologies and phenotypes of SNHL observed in humans [36]. First- and second-order Wiener-kernels derived by comparing auditory nerve spike times to the fluctuations in specific realizations of the input broadband noise provide a direct quantification of temporal fine-structure and envelope coding properties, respectively. Figure 3 shows prototypical examples of threshold tuning curves (Fig. 3a) and suprathreshold envelope coding (Fig. 3b) for both the NIHL and MHL models. Despite similar levels of threshold elevation at CF, NIHL is associated with substantially larger reductions in the tuning-curve TTR and severely distorted tonotopic coding of suprathreshold sounds (shifts of well over an octave). Strikingly, whereas auditory-nerve responses in MHL did not exhibit distorted tonotopic coding until threshold elevation reached a moderately severe degree (thresholds > 65 dB SPL), distorted tonotopic coding of both envelope and temporal fine-structure was observed even with mild threshold elevation (threshold > 30 dB SPL) in NIHL demonstrating that SNHL can produces markedly divergent neural coding deficits depending on the underlying cochlear pathology.

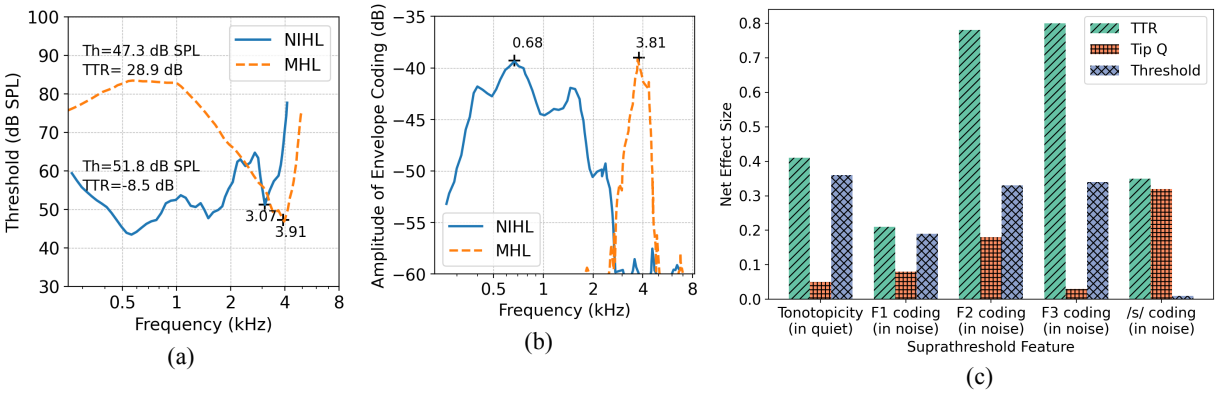

Figure 3. Examples of (a) auditory-nerve threshold tuning curves, and (b) Wiener-kernel metrics of suprathreshold envelope coding from chinchilla models of noise-induced hearing (NIHL) and metabolic hearing loss (MHL) from [33]. Despite similar elevation of the threshold at CF, correct tonotopy is maintained in MHL, but NIHL is associated with reduced TTR and markedly distorted tonotopic coding of suprathreshold sounds. (c) Statistical quantification of the impact of distorted tonotopy (TTR), broadened tuning at the "tip" (Tip Q), and hearing sensitivity (Threshold) on suprathreshold coding of important speech features. The net effect size attributable to each factor was estimated from a type II analysis of variance across single-unit auditory-nerve fibers. Across all speech features studied, the effects of TTR were dominant and outweighed the effects of reduced frequency selectivity near CF and elevated thresholds. Data from [37].

To examine the effects of distorted tonotopy on the SPIN coding, for the first time in the literature, [37] recorded single-unit auditory nerve responses to connected speech from a similar chinchilla model of NIHL as in [33], [34]. A spectrally specific temporal analysis of the single-unit spike trains was performed to characterize coding of vowels and consonants by examining the representation of vowel formants, stop consonants, and fricatives using [32]. Audibility compensation was applied in line with loudness models in SNHL [38] to mirror hearing-aid amplification provided in human patients. Across all speech features analyzed, distorted tonotopy severely degraded suprathreshold coding despite audibility compensation. Specifically, the responses of auditory-nerve fibers with higher CFs were commandeered by low-frequency energy at the expense of tonotopically "correct" high-frequency information important for speech identification. Crucially, contrary to the conventional view that broadened tuning near CF is a major factor, an analysis of variance of the auditory-nerve fiber responses revealed instead that distorted tonotopy was the dominant factor contributing to neural coding deficits (Fig. 3c).

Insights from Psychophysical and Electroencephalographic (EEG) studies in Human Listeners

To examine whether distorted tonotopy is a substantial contributor to neural coding and perceptual deficits in human listeners, we measured psychophysical tuning curves (PTCs) and EEG response to connected speech [39]. Specifically, PTCs were measured using a rapid Bekesy-tracking procedure as the narrowband noise level needed to mask a pulsing 4 kHz tone presented at a constant sensation level of 20 dB SL [40]. Figure 4a shows the PTCs obtained from participants with SNHL and controls with normal hearing, grouped by audiometric pure-tone average thresholds up to 6 kHz. Both broadening of the tip near 4 kHz and reduced TTR are apparent in participants with SNHL, mirroring the effects seen in chinchilla auditory-nerve tuning curves. To test whether the reduced TTR is associated with distorted tonotopy we quantified neural envelope coding using measures of phase coherence between the input speech envelopes and the EEG response [41]. This was done across three conditions; a reference condition with the speech presented in quiet (Q), and with added low frequency noise (LFN; 840 – 2378 Hz), or high-frequency noise (HFN; > 2378 Hz). The noise spectrum was matched to that of the speech. For participants with normal hearing, addition of HFN resulted in a significant reduction in the strength of speech envelope coding compared to the quiet condition (Fig. 4b). In contrast, for participants with hearing loss, addition of HFN had no measurable effect. Instead, a reduction in envelope-coding fidelity was only observed with the addition of LFN (Fig. 4b). These EEG findings suggest that in SNHL, the response of the cochlear base is driven by low-frequency stimulus components at the expense of tonotopically "correct" high-frequency information – a markedly distorted tonotopic coding paralleling the auditory nerve responses in chinchillas.

To examine how distorted tonotopy relates to listening outcomes with hearing aids, SPIN scores were measured using the modified rhyme test (single target word with a carrier phrase) materials [42] presented in LFN. Amplification was provided using a clinically realistic wide-dynamic-range compression hearing-aid simulator [43] fit to DSLv5 prescriptive targets. Despite all participants having audibility restored (speech intelligibility index > 90%), individual performance varied widely (Fig. 4c). Crucially, these individual variations in "aided" SPIN performance were predicted by individual variations in TTR, suggesting that distorted tonotopic coding is a major factor limiting suprathreshold SPIN outcomes with hearing aids. Furthermore, a type II analysis of variance applied to SPIN performance revealed that TTR is the dominant contributor (net effect size of 1.48) to outcomes, outweighing broadening of tuning-curve tip (net effect size of 0.47) and the small residual variations in speech audibility (net effect size = 0.48).

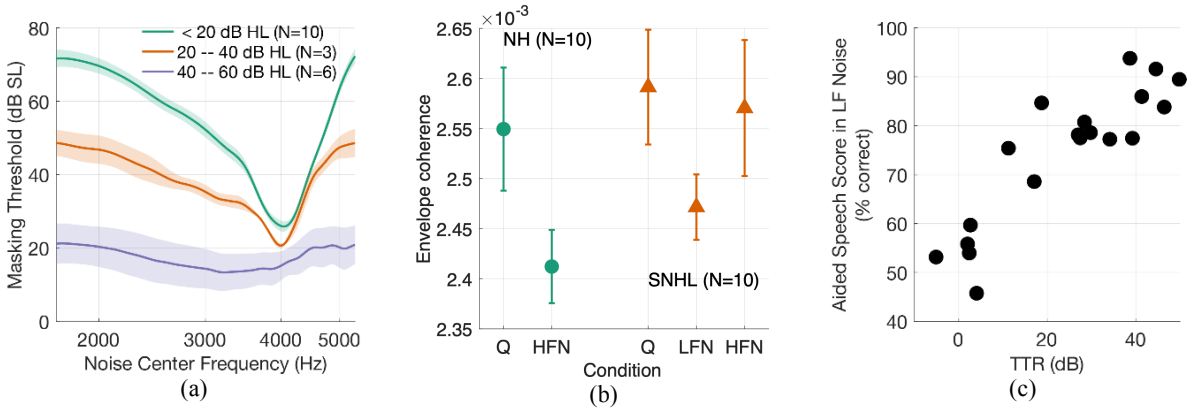

Figure 4. (a) Psychophysical tuning curves (PTCs) using simultaneous masking of a 20 dB SL 4-kHz probe tone by narrowband noise masker from human subjects with different audiometric thresholds (legend) at 4 kHz. Results suggest that distorted tonotopy may be prevalent in humans with mild/moderate SNHL. (b) Electrophysiological measures of envelope coding in participants with audiometric normal hearing (NH) or SNHL in quiet (Q), speech-shaped low-frequency noise (LFN; <2.4 kHz), or high-frequency noise (HFN; > 2.4 kHz) are consistent with distorted tonotopy. (c) Relationship between aided (DSLv5 prescription) word identification scores in a background of low-frequency speech-shaped noise and PTC TTR suggests that distorted tonotopy is a major contributor to individual variations in aided listening outcomes.

CONCLUSIONS

Taken together, our coordinated cross-species data from chinchilla models and human listeners demonstrate that distorted tonotopy is a major contributor to degraded bottom-up speech coding in SNHL. Given that the degree of distorted tonotopy varies widely across human listeners and is dependent on precise etiology of the hearing loss, these off-frequency effects must be considered in the individualization of clinical management of hearing loss.

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COMMENTS AND DISCUSSION

[Karolina Charaziak]: Hi Hari! I enjoyed your talk, and your manuscript nicely outlines the current efforts towards understanding how hearing loss could contribute to degraded speech perception. I was wondering if you could comment more on your PTC results and the effect of stimulus SPL rather than SL. Broadening of the PTC at higher intensities (required in hearing impaired subjects to compensate for audibility loss) is a common feature even in normally hearing subjects. Also, PTCs are iso-response curves that may artificially "sharpen" the tuning in nonlinear systems -- if hearing loss degrades nonlinear gain then it could further contribute to the broadening of PTC. Have you considered using iso-input tests instead? Finally, I am curious about the mechanisms behind the hypersensitive tails -- we talked a little bit about that during the discussion, but I was wondering if you think the cause is preneural (i.e. in the mechanics) and if so, should you see it in OAE responses.

[Hari Bharadwaj]: Hi Karolina, Thank you for the comments! The Wiener-kernel analysis for suprathreshold broadband noise is essentially an iso-input curve for auditory nerve responses in the chinchillas. Specifically, the second-order kernels used get the envelope component (i.e., not just the phase-locked part like with traditional revcor analysis). Indeed, these analyses are an important test of checking that the dramatic overrepresentation of low-frequency information in high-frequency auditory nerve fibers happens at typical suprathreshold levels and is not just an artifact of threshold tuning curves. In humans, we look at masking of EEG responses, but the responses that are analyzed there are from much more downstream than the periphery, so it could have non-peripheral effects mixed in. Our current thinking is that the distorted tonotopy effect is pre-neural. John Guinan's comments about how OHC-stereocilia damage might increase IHC fluid drive in the tail seems like a good candidate mechanism, but remains to be explored. As you suggest, running something like DPOAE suppression tuning curves in our human participants and comparing to the EEG data would be great. The DP-suppression data from Gorga's group (e.g., Gruhlke et al., 2012) does show greatly reduced tip-to-tail ratios in human participants with hearing loss. Thank you!

[**Geoffrey Manley**]: I am curious why you show an example of 4 kHz when (a) low-frequency tuning curves as far as I remember in mammals below 3 kHz don't have tails anyway, and (b) the vast majority of the energy in speech is well below 4 kHz. So how is this relevant to the topic?

[Hari Bharadwaj]: The vast majority of speech energy being below 3 kHz is part of what is going to exacerbate this distorted tonotopy effect. The high-frequency content in speech has a lot of information although it doesn't have as much energy. If you take a fricative for example, that Satya [Parida] did with auditory nerve recordings in chinchilla with background noise, the low-frequency energy ends up driving the balance response. The reason we picked 4 kHz is somewhat arbitrary, but measurements at different frequencies tend to be highly correlated and the 4 kHz data is an indicator of the degree of distorted tonotopicity in the individual overall. In the chinchilla nerve population data that I showed from Mike's [Heinz] lab, we see that the distorted tonotopy effect is not just a high-frequency phenomenon but extends all the way down to a bit under 1 kHz.

[Bastian Epp]: Dear Hari and co-authors! Thanks for a great study. It is really an impressive an innovative approach that for sure will be of great value! I mainly have some thoughts that might be interesting to discuss regarding specific details, but also underlying assumptions. (a) Great to see that you are looking into tonotopy. You are using this argument throughout the paper. Because you are making an interesting point, it might be beneficial to actually provide a definition of what you understand under "tonotopy" in this study. (b) Even though not your argument: "...deficits in SNHL may also extend to... of sound-driven cochlear vibrations". Here I might question if the assumption in psychophysics that you can conclude about cochlear function based on a listening experiment can so easily be transferred without being more explicit. The results you are showing might actually offer a different view - and you actually provide physiological data. Sticking too close to the interpretations from classical psychophysics that frequency selectivity is solely based on cochlear function might be detrimental here. (c) The data in Fig 3 - at which levels did you measure here? (d) Can you lay out your assumptions underlying the interpretation of your EEG data? This might be helpful for the reader to navigate through the different domains you are using. (e) I am curious to hear what you mean with "...these individual variations in "aided"...were predicted by individual variations in TTR". Is this in the sense of a correlation (Fig 4c?) or did you do some more specific prediction that also hold 1-1? (f) As a peripheral note: We have found something related in a modeling study when looking at cochlear synaptopathy. Basically we found that (even for a NH system), that the envelope is not encoded "on-frequency", but pretty remote from what is considered the corresponding "place" when talking tonotopy as assumed in psychophysics. Hence, your definition of tonotopy becomes relevant here. Based on the modeling results, I would argue that ANY stimulus at higher levels is NOT encoded at the place identified by tonotopic mapping through low-intensity tones. What do you think? I would even argue that psychophysics is not in danger at all if one assumes that the brain (the thing that keeps the cochlea warm) actually utilizes not strictly a place. This is supported by the fact that IHC are not per-se overly frequency-selective. And another work we did (unpublished), we even found that "compression" as measured psychoacustically might also not really be overly "local".

[**Hari Bharadwaj**]: Hi Bastian, thank you for your interesting comments! As we continue this work, we will keep the issues you are raised in mind. Just a few thoughts in response below. (a) The sense in which we are using "tonotopy" and "distorted tonotopy" is that in normal hearing, when we play broadband noise at suprathreshold levels, chinchilla auditory nerve fibers do in fact pick out the same frequencies in suprathreshold sounds as the CF of threshold tuning curve (good tonotopy), whereas in NIHL, basal fibers appear to pick out low-frequency sounds to the exclusion of tonotopically "correct" content. While there is spread of excitation towards the base for narrowband sounds regardless of hearing loss, normal-hearing chinchilla nerve fibers don't appear to lose tonotopy in this sense even at high/suprathreshold levels. (b) I agree that the vocoding studies are merely consistent with certain cochlear effects rather than direct indicators of cochlear issues. (c) For the data in Fig. 3, suprathreshold responses were measured 20 dB above the noise threshold of each fiber. (d) For human speech EEG data, we are not assuming much about how different bands of speech are encoded, but asking if low-pass and high-pass noise has distinct effects in SNHL vs. NH, and if so, are the differences consistent with overzealous tails. We do observe that highpass noise has a larger effect in NH but not in SNHL. Instead, it is lowpass noise that seems to have the larger effect is SNHL. While the measured EEG is well downstream of cochlear mechanics, this observation is exactly what we would predict from distorted tonotopy. (e) For Fig. 4c, we are just measuring speech-in-noise outcomes with hearing aids (i.e., "aided")

and asking if the remaining individual variations are predicted from the estimated degree of distorted tonotopy for each individual (i.e., overzealous tuning-curve tails). Indeed, we find that they are highly correlated. As I mentioned in the talk, the TTR is a better a predictor than audiograms or the estimated audibility (via the speech intelligibility index)! (f) I completely agree that coding of modulations or responses to narrowband sounds in general can have strong off-frequency contributions, especially for high stimulus levels and for fast modulations (both typical of EFR measurements). However, when you are using broadband sounds like speech or white noise and considering modulations in the speech range (rather than pitch range where the AM rate is often too fast for the side bands of low-frequency cochlear places), normal-hearing chinchilla nerve fibers appear to show good tonotopic coding. In NIHL however, that seems to be dramatically degraded by overzealous tails!