Diminished temporal coding with sensorineural hearing loss emerges in background noise

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Behavioral studies in humans suggest that sensorineural hearing loss (SNHL) decreases sensitivity to the temporal structure of sound, but neurophysiological studies in mammals provide little evidence for diminished temporal coding. We found that SNHL in chinchillas degraded peripheral temporal coding in background noise substantially more than in quiet. These results resolve discrepancies between previous studies and help to explain why perceptual difficulties in hearing-impaired listeners often emerge in noisy situations.

The physiological basis of degraded speech perception in human listeners with SNHL is a subject of active debate and investigation. Psychoacoustic studies suggest that a deficit in temporal processing may be responsible1–3, but neurophysiological studies in animals have shown little effect of SNHL on the strength of temporal coding in single neurons4–7. Neurophysiological studies of the auditory periphery have revealed relatively few changes in the degree of neural synchrony, or phase locking of spikes, to the temporal structure of acoustic stimuli, leading to speculation that temporal processing deficits might arise in the CNS1. A peripheral origin cannot be ruled out, however, as existing studies have quantified temporal coding under artificially quiet conditions only. We therefore studied the effect of SNHL on temporal coding of tones in the auditory periphery under more realistic, noisy conditions.

We induced SNHL with exposure to noise and recorded single auditory nerve fiber activity in anesthetized chinchillas using methods approved by Purdue’s Animal Care and Use Committee (Online Methods). In each auditory nerve fiber encountered, we measured a tuning curve (Fig. 1) to determine the fiber’s minimum threshold and characteristic frequency (the frequency of maximum sensitivity or, for noise-exposed fibers, the estimated frequency of maximum sensitivity before SNHL8). Next, we recorded spike trains to pure tone stimuli presented in quiet and in three levels of Gaussian background noise. We presented pure tones with frequency equal to the fiber’s characteristic frequency and level 30 dB above the fiber’s minimum threshold in quiet. We presented background noise (20-kHz bandwidth) at root-mean-square (r.m.s.) amplitudes of 10, 15 and 20 dB above that of the tone. We quantified temporal coding by calculating the vector strength of phase locking to the tone frequency from period histograms of the spike train responses (Fig. 1).

We recorded neural responses from 38 noise-exposed fibers and 42 control fibers with characteristic frequencies ranging from 0.6–2.5 kHz. Compared with control fibers of the same characteristic frequency, noise-exposed fibers had higher thresholds (mean increase ± s.d., 34.8 ± 10.6 dB) and broader tuning curve bandwidth (mean increase ± s.d., 0.88 ± 0.53 octaves; that is, nearly a factor of 2 broader), consistent with previous studies of SNHL6,7. Period histograms of auditory nerve responses to tones showed modulations in

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suggested that the stronger effect of masking in impaired fibers likely arises from broader cochlear frequency tuning.

In conclusion, our results indicate that SNHL reduces the strength of temporal coding in noise at the most peripheral level of auditory processing. Together with other mechanisms, including synaptic losses and cochlear neurodegeneration, which reduce the redundancy of neural coding and potential changes in central auditory processing, our findings help to explain why speech perception problems in the hearing impaired commonly emerge under noisy conditions. Furthermore, they underscore the benefit of conducting audiometric evaluations under less artificial conditions and highlight the promise of advancements in signal processing strategies for use in hearing aids and cochlear implants that increase the signal-to-noise ratio of speech at the output of the device.

METHODS

Methods and any associated references are available in the online version of the paper.

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AUTHOR CONTRIBUTIONS

K.S.H. and M.G.H. designed the experiments. K.S.H. collected and analyzed the data and wrote the paper with contribution from M.G.H.
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ONLINE METHODS

We collected neurophysiological data from young chinchillas using procedures approved by Purdue’s Animal Care and Use Committee. We recorded neurophysiological responses from single auditory nerve fibers using standard procedures in our laboratory\(^\text{7}\). We collected data between June and August of 2011 in two normal-hearing control animals (42 fibers) and five animals with noise-induced sensorineural hearing loss (38 fibers).

**Noise exposures.** We induced sensorineural hearing loss with a 2-h exposure to an octave-band of Gaussian noise with a center frequency of 500 Hz and SPL of 116 dB. We exposed animals to noise in a sound-attenuating booth under anesthesia using a free-field sound source (Selenium 10PW3 woofer) suspended 25–30 cm above the animal. We anesthetized the animals with xylazine (1–2 mg per kg of body weight, subcutaneous) followed several minutes later by ketamine (50–65 mg per kg, intraperitoneal). We gave atropine (0.05 mg per kg, intramuscular) to control mucous secretions and applied eye ointment to prevent drying of the eyes. We held animals in position with a stereotaxic device and maintained their body temperature at 37 °C using a feedback-controlled heating pad (Harvard Apparatus 50–7220F). We gave supplemental injections of ketamine (20–30 mg per kg, intraperitoneal) as needed to maintain an anaesthetic state. The degree of sensorineural hearing loss, as estimated from auditory brainstem response thresholds using previously published methods\(^\text{13,14}\), was 13.1 ± 2.6 dB at 500 Hz, 19.8 ± 4.4 dB at 1 kHz, 22.4 ± 7.7 dB at 2 kHz, 14.4 ± 9.4 dB at 4 kHz and 6.5 ± 5.2 dB at 8 kHz (means ± s.d.; \(n = 5\)). Elevation of auditory brain responses thresholds as a result of the noise exposure was 10–20 dB less than elevation of auditory-nerve fiber thresholds at the same frequency, consistent with previous reports\(^\text{13,14}\).

**Neurophysiological experiments.** We recorded neurophysiological data from auditory nerve fibers under anesthesia. We tested animals with sensorineural hearing loss 4–8 weeks after the noise exposure. We anesthetized the animals initially with xylazine and ketamine as described above, but maintained anesthesia with sodium pentobarbital (−15 mg per kg per 2 h, intravenous) for neurophysiological recordings. We also gave physiological saline (2–3 ml 2 h\(^{-1}\), intravenous) and lactated Ringer’s (20–30 ml 24 h\(^{-1}\), subcutaneous), and performed a tracheotomy to facilitate breathing. We positioned the animals in a stereotaxic device in a sound-attenuating booth. We transected the skin and muscles overlying the skull to expose the ear canals and bullae, and dissected both ear canals to allow insertion of hollow ear bars. We vented the right bulla through 30 cm of polyethylene tubing. We opened a craniotomy in the posterior fossa, partially aspirated the cerebellum and retracted the cerebellum medially to expose the trunk of the auditory nerve. We presented acoustic stimuli through the right ear bar with a dynamic loudspeaker (Beyerdynamic DT48) and calibrated stimuli using a probe microphone placed within a few millimeters of the tymanum (Etymotic ER7C). We made neurophysiological recordings using a 10–30-MΩ glass microelectrode advanced into the auditory nerve bundle by a hydraulic micro-drive (Kopf 640). We amplified (Dagan 2400A) and band-pass–filtered recordings from 0.03–6 kHz (Krohn-Hite 3550). We identified spikes using a time-amplitude window discriminator (BAK Electronics) and recorded their timing with 10-μs resolution.

We isolated single fibers by listening for spikes while advancing the electrode through the auditory nerve during repeated broadband-noise acoustic stimulation. When a fiber was encountered, we recorded a tuning curve using an automated algorithm that tracked, as a function of stimulus frequency, the minimum SPL of a 50-ms tone required to evoke at least one more spike than a subsequent 50-ms silent period\(^\text{15}\). Next, we recorded spike train responses to pure tone stimuli presented in quiet and in three levels of Gaussian background noise. We recorded 40 spike train responses for each condition. Pure tones were 600 ms in duration; we presented tones once per second with a frequency equal to the fiber’s characteristic frequency and level 30 dB above the fiber’s minimum threshold in quiet. We gated background noise (20-kHz bandwidth) on and off with the tones at r.m.s. levels of 10, 15 and 20 dB above the level of the tone. We quantified temporal coding under each condition by calculating the vector strength of phase locking to the tone frequency from the period histogram of the spike train response computed with 64 bins per stimulus cycle\(^\text{9}\). We computed vector strength as the ratio of the second and first coefficients of the Fourier transform of the period histogram.

**Statistical analysis.** We analyzed the effects of noise exposure and masking level on the vector strength of phase locking to tones using a repeated-measures mixed model analysis. The analysis included group (noise exposed versus control) and masking level as categorical independent variables and an interaction term between group and masking level. The analysis also included fiber identity as a categorical random effect and log-transformed characteristic frequency as a continuous random effect. We evaluated the effects of the independent variables on vector strength using F tests and pairwise comparisons of least-squares means.

We analyzed the relationship between tuning curve bandwidth and vector strength of phase locking using linear regression of characteristic frequency–normalized variables. We calculated characteristic frequency–normalized bandwidth as the octave difference between the observed bandwidth and the mean bandwidth of control fibers of the same characteristic frequency, and characteristic frequency–normalized vector strength as the observed vector strength divided by the mean vector strength of control fibers of the same characteristic frequency. We conducted separate analyses for each masking level and evaluated statistical significance using t tests of the estimated slopes.

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