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Noise-induced hearing loss alters the temporal dynamics of auditory-nerve responses

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Abstract

Auditory-nerve fibers demonstrate dynamic response properties in that they adapt to rapid changes in sound level, both at the onset and offset of a sound. These dynamic response properties affect temporal coding of stimulus modulations that are perceptually relevant for many sounds such as speech and music. Temporal dynamics have been well characterized in auditory-nerve fibers from normal-hearing animals, but little is known about the effects of sensorineural hearing loss on these dynamics. This study examined the effects of noise-induced hearing loss on the temporal dynamics in auditory-nerve fiber responses from anesthetized chinchillas. Post-stimulus time histograms were computed from responses to 50-ms tones presented at characteristic frequency and 30 dB above fiber threshold. Several response metrics related to temporal dynamics were computed from post-stimulus-time histograms and were compared between normal-hearing and noise-exposed animals. Results indicate that noise-exposed auditory-nerve fibers show significantly reduced response latency, increased onset response and percent adaptation, faster adaptation after onset, and slower recovery after offset. The decrease in response latency only occurred in noise-exposed fibers with significantly reduced frequency selectivity. These changes in temporal dynamics have important implications for temporal envelope coding in hearing-impaired ears, as well as for the design of dynamic compression algorithms for hearing aids.

Keywords

Auditory nerve; adaptation; recovery; latency; acoustic trauma; chinchilla

1. Introduction

Neural spike rate adaptation is a feature of virtually all sensory systems and has been hypothesized to have a variety of functional roles for processing time varying signals (Benda et al., 2005; French et al., 2001; Hildebrandt et al., 2009). In the auditory system, neural responses adapt to rapid changes in sound level that provide important information for behaviorally relevant sounds, e.g., speech or music. The temporal dynamics of neural responses have been well characterized for auditory-nerve (AN) fibers in terms of response latency, relative onset to steady-state responses, and the time course of adaptation and recovery from adaptation (Heil and Irvine, 1997; Westerman and Smith, 1984). These dynamic properties have each been shown to have important implications for encoding complex sounds. Thus, a

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thorough understanding of the effects of sensorineural hearing loss (SNHL) on the temporal dynamics of AN responses would provide valuable insight into the deficits faced by hearing-impaired (HI) listeners as well as the ongoing clinical debate regarding the optimal time scales for dynamic control of hearing-aid amplification (Moore, 2008; Moore et al., 1999).

Traveling-wave delays contribute significantly to AN-fiber response latency and create robust spatiotemporal patterns that have been hypothesized to be important for pitch and speech coding (Carney, 1994; Cedolin and Delgutte, 2007; Loeb et al., 1983; Shamma, 1985). Reductions in traveling-wave delays due to reduced frequency selectivity contribute to a degradation in spatiotemporal patterns following SNHL (Heinz et al., 2010). These results are potentially consistent with shorter-than-normal AN response latencies in HI animals at equal sensation levels (Dallos and Harris, 1978; Salvi et al., 1979; Wang and Dallos, 1972); however, previous studies did not correlate reduced latencies with AN-fiber frequency selectivity. A more thorough characterization may provide better insight for novel hearing-aid strategies that attempt to restore normal spatiotemporal patterns by compensating for reduced response latencies, which have had limited success to date (Calandruccio et al., 2007; Shi et al., 2006).

AN-fiber adaptation produces large onset responses, which result in greater sensitivity to transient stimuli than to steady-state stimuli (Westerman and Smith, 1984). This dynamic property is thought to help in the perception of speech-like sounds with rapid changes, e.g., consonants (Delgutte and Kiang, 1984), and to contribute to the coding of amplitude modulated sounds (Smith and Brachman, 1980). It has been hypothesized that AN-fiber onset responses could be smaller in impaired ears due to outer-hair-cell (OHC) loss and that this would degrade the perception of transient speech sounds, such as consonants (Allen et al., 2009). Although the effects of SNHL on onset responses have not been well characterized in mammals, evidence from chicks indicates that onset responses are enhanced, rather than reduced, following acoustic trauma (Crumling and Saunders, 2007).

The time courses of adaptation and recovery from adaptation have often been estimated in terms of single- or double-exponential curves, with rapid and short-term adaptation time constants on the order of 5–10 ms and 60 ms, respectively, and recovery time constants of ~40 ms (Chimento and Schreiner, 1991; Smith, 1977; Westerman and Smith, 1984). Although the effects of SNHL on the time courses of adaptation and recovery in the auditory nerve have not been well characterized in mammals, there are several reasons that a thorough characterization would be useful. Because slower post-stimulus recovery from adaptation enhances envelope coding (Zilany et al., 2009), this could be a contributing factor to enhanced envelope coding following SNHL (Kale and Heinz, in press; Moore et al., 1996). Consistent with this possibility, recovery from forward masking has been reported to be significantly longer following SNHL in a number of central responses (Arehole et al., 1987; Walton et al., 1995). Although this longer recovery from forward masking can be (at least partially) explained by reduced cochlear compression, as highlighted in psychophysical studies (e.g., Plack et al., 2004), it is important to test whether neural recovery from adaptation is similar between normal and impaired hearing.

The primary goal of the present study was to characterize the effects of noise-induced hearing loss on the temporal dynamics of AN-fiber responses. A population of post-stimulus-time (PST) histograms from normal-hearing and HI chinchillas (Heinz et al., 2010; Kale and Heinz, in press) were comprehensively analyzed in terms of response latency, onset rate, adapted rate, percent adaptation, and adaptation and recovery time constants. Several effects of SNHL were found, which have important implications for temporal encoding of complex stimuli and for amplification strategies to restore normal coding in impaired ears.

2. Materials and methods

Single-fiber AN recordings were made from 10 normal-hearing (NH) and 12 noise-induced HI chinchillas, all males 8–12 months old and weighing between 400–650 grams. The Purdue University Animal Care and Use Committee (PACUC) approved the care and use of all animals in this study.

2.1. Acoustic trauma

SNHL was induced with the same noise-exposure protocol used previously in cats (Heinz and Young, 2004; Miller et al., 1997), and for which anatomical/physiological correlates of acoustic trauma have been characterized (Lieberman, 1984; Liberman and Dodds, 1984a,b; Liberman and Kiang, 1984). Animals were first anesthetized by xylazine (1–1.5 mg/kg im) followed by ketamine (50–65 mg/kg im). Atropine (0.1 mg/kg im) was given to control mucus secretions, and eye ointment was used to prevent drying of the eyes. Prior to each exposure, auditory brainstem responses (ABRs) were measured using tone pips at 1, 2, 4 and 8 kHz to verify NH thresholds. A noise 50 Hz wide and centered at 2 kHz was then presented to each animal uninterrupted for four hours in a free field environment. Noise levels were calibrated at the entrance to the ear canal to be between 114 and 115 dB SPL. Animals were then allowed to recover for at least 4 weeks, after which ABRs were again measured to determine the threshold shifts. An ABR threshold shift of at least 20 dB at 2 kHz was considered as an indication of sufficient SNHL (Ngan and May, 2001).

2.2. Surgical procedures

The animals were initially anesthetized with xylazine (1 – 1.5 mg/kg im) and ketamine (50 – 65 mg/kg im). Supplemental doses of barbiturate anesthetic (sodium pentobarbital, ~7.5 mg/kg/h iv) were given to maintain an areflexic state. In 4 animals, the supplementary doses of sodium pentobarbital were given in the intra-peritoneal cavity. Physiological saline (2–5 ml/h iv) and lactated Ringer's solution (20–30 ml/24h) were given to prevent dehydration. Core body temperature was maintained between 37°C and 38°C, monitored using a rectal probe. A tracheotomy was performed to facilitate breathing and the skin and muscles overlying the skull were retracted to expose the ear canals and bulla. The bulla was vented with a 30-cm long polyethylene tube to maintain the middle ear pressure (Guinan and Peake, 1967).

2.3. Neurophysiological recordings

For neurophysiological recordings, the head of each animal was secured using stereotaxic equipment (Kopf, Tujunga, CA). Extra-cellular nerve action potentials were recorded with 10 – 30 MΩ glass micropipettes filled with 3 M NaCl. The electrode signal was amplified using a cellular amplifier (Dagan, Minneapolis, MN) and filtered prior to timing the action potentials (10 μs resolution) based on a time amplitude window discriminator (Bak Electronics, Mount Airy, MD). Synchronous presentation of acoustic stimuli and data recording was controlled by custom software running in MATLAB (The Mathworks, Natick, MA) integrated with custom and commercial hardware (Tucker-Davis Technologies, Alachua, FL; National Instruments, Austin, TX). A broadband noise search stimulus (20 dB re 20 μPa/√Hz for normal experiments, and higher as needed in impaired experiments), was used to isolate AN fibers. The state of the cochlea was monitored by tracking fiber thresholds as a function of CF over time and looking for abrupt increases above the minimum thresholds as collected early in the experiment. Only one NH experiment showed elevated thresholds (and broadened tuning) over time. All data collected after the threshold elevation were excluded from data analysis.

2.4. Acoustic stimuli

Isolated fibers were characterized initially by an automated tuning curve algorithm, which tracked the minimum sound level required for a 50 ms tone to elicit at least one more spike than a subsequent 50 ms silence (Chintanpalli and Heinz, 2007; Kiang et al., 1970). Each fiber's characteristic frequency (CF), threshold, and Q_{10} (ratio of CF to tuning-curve bandwidth 10 dB above threshold) were estimated from the tuning curve. For impaired fibers with broad tuning, CF was chosen to correspond to the bottom of the steep high-frequency tuning-curve slope, which estimates the pre-exposure cochlear CF (Lieberman, 1984). A few impaired fibers had 'w-shaped' tuning curves with a sharp tip and a sensitive tail responding to a broad range of frequencies (Lieberman and Dodds, 1984a). For such fibers, the broad bandwidth across the entire "w" shape was used to compute Q_{10} values.

PST histograms were created from responses to pure tones of 50 ms duration (2 ms cosine squared onset-offset ramps). Tones were presented at CF and 30 dB above each fiber's threshold (i.e., 30 dB sensation level). Each stimulus was repeated every 250 ms and ~300 repetitions of each stimulus were presented. AN fibers were also characterized based on spontaneous rate (SR), which was computed as the mean spike rate across the last 50 ms of silence from the PST histogram. Fibers were classified as high-SR if $SR \geq 18$ spikes/s, medium-SR if $1 \leq SR < 18$ spikes/s, and low-SR if $SR < 1$ spike/s (Temchin et al., 2008).

2.5. Data analysis

PST histograms were computed with a bin width equal to 100 μ s for response latency measures. Such a small bin width provided the fine temporal resolution necessary for latency measures. To quantify the time course of neural adaptation and stimulus off-time recovery, a bin width of 1 ms was used (Westerman and Smith, 1984).

Response Latency—Response latency was quantified using three different metrics. The *first peak latency* metric computed the latency to the first peak in the PST histogram, which corresponded to maximum onset response peak for fibers with CFs ≥ 1 kHz. For fibers with CFs < 1 kHz, PST histograms showed multiple peaks due to strong phase locking at these low frequencies. In such cases, the first prominent peak, defined as the first peak having a discharge rate $\geq 70\%$ of the maximum response peak, was selected. The second response latency metric, *driven response latency*, was computed from the time instant (PST bin) at which discharge rate exceeded the maximum spontaneous activity by 2 standard deviations (s.d.) for the first time after stimulus onset. The maximum and s.d. of spontaneous activity were computed from the PST bins corresponding to the last 50 ms of the stimulus off-time. For several fibers, this metric yielded unrealistically low latency values (< 2 ms for $CF \leq 4$ kHz) due to spurious jumps in spontaneous activity preceding the driven response. For these few fibers, the second time to exceed maximum SR + 2 s.d. was taken as the driven response latency. A third latency metric was the *first spike latency* metric (e.g., Heil, 1997), which showed results consistent with those from the other latency metrics. However, first spike latency data were noisier due to the influence of spontaneous rate. In all analyses, none of the latency measures were corrected for acoustic delays.

Onset and adapted rate responses—*Onset rate* was quantified as the maximum discharge rate corresponding to the onset response peak in the PST histogram. The *adapted rate* response was computed as the average discharge rate during the last 10 ms of the stimulus on-time (i.e., 40–50 ms post stimulus onset). *Percent adaptation* (Crumling and Saunders, 2007) measured the percent change from the peak onset rate to adapted rate over the stimulus duration, i.e., $[(r_{\text{onset}} - r_{\text{adapted}}) / r_{\text{onset}}] \times 100\%$.

Time constants for adaptation and recovery—The rate of decay from maximum onset response to adapted rate (i.e., time course of adaptation) was quantified by fitting individual AN fiber PST histograms. Least-squares fits were made with an equation that included an exponential decay term and a DC component ($Ae^{-t/\tau} + B$), where τ is the *adaptation time constant* and A and B are amplitude terms. No lower or upper bounds were used in the fitting procedure. However, a handful of AN fibers ($n = 21 / 305$, mostly with CFs < 750 Hz) had fits with time constants below 1 ms. These values were below the PST bin width as well as the lower limits of adaptation time constants previously reported in the literature (e.g., Westerman and Smith, 1987). Typically when longer duration stimuli have been used, rapid time constants on the order of 3–4 ms and short term time constants on the order of 60 ms have been reported. Thus, the single time constant fit to the shorter tone responses in the present study should fall between these two values and hence, values of $\tau < 1$ ms were discarded on the basis of not being biophysically accurate. Two exponential fits were not used in the present analyses because these fits were under-constrained due to the short duration of the stimuli used here (Yates et al., 1985), and were thus much less consistent than the single time-constant fits. Single-exponential adaptation fits were also made to *average PST histograms* for each of the SR groups.

The rate of post-stimulus offset recovery to spontaneous rate was measured by least-squares fits to the PST histograms with an equation that included an exponential rise and a DC term [$A(1 - e^{-t/\tau}) + B$]. Individual-fiber PST histograms starting from the absolute minimum after stimulus offset and extending to 250 ms were used for fitting. No lower or upper bounds were included in the fitting procedures. *Recovery time constants* were computed only for high-SR fibers for which the recovery time course is well defined (i.e., the recovery time course was more difficult to assess with low or medium SR). A total of $n = 34 / 190$ recovery time constants were discarded due to poor fits or poorly defined recovery (e.g., due to extended ringing for low-CF fibers or PST histograms that never dropped below 50% of SR post offset). Very few fibers within the CF region of interest (1 – 4 kHz) were discarded (NH: 4 / 58; HI: 3 / 45).

Adaptation and recovery time constants, maximum onset response rate, and percent adaptation were also computed from PST histograms constructed with three different bin widths (0.2 ms, 0.25 ms, and 0.5 ms). Since the trends between the NH and noise-exposed populations were the same for all bin widths, only results based on a 1-ms bin width are presented.

3. Results

3.1. Characterization of hearing loss

Fig. 1 shows pure tone thresholds and Q_{10} values computed from the tuning curves of AN fibers obtained from NH animals (crosses) and from animals with noise-induced hearing loss (NIHL, circles). Q_{10} is the measure of a fiber's frequency selectivity and is defined as the ratio of CF to 10-dB tuning-curve bandwidth. Many fibers from the NIHL population showed threshold elevation (Fig. 1A) and broadened tuning (Fig. 1B). Trend lines in Fig. 1A indicate average thresholds for NH fibers (thin black line) and for fibers from the NIHL population (thick gray line). Solid lines in Fig. 1B indicate 5th and 95th percentile confidence intervals for NH chinchilla Q_{10} values (Kale and Heinz, in press). Maximum threshold elevation and broadening of tuning was observed for NIHL fibers with $1 \leq \text{CF} \leq 4$ kHz. Average threshold elevation for HI fibers ranged from ~20 dB to 50 dB in the CF range of 1–4 kHz with most of these fibers showing significantly broadened tuning. Tuning is considered to be significantly broadened in NIHL fibers when the Q_{10} is below the 5th percentile NH confidence interval (Fig. 1B). All statistical tests of the effects of NIHL presented in this study compare the trends between NH fibers ($n=77$) and HI fibers ($n=81$) from the CF region of maximum impairment (1–4 kHz). This region of maximum impairment was consistent with our noise-exposure protocol, which used narrowband (50 Hz) noise centered at 2 kHz to induce acoustic trauma.

Another consequence of NIHL was an overall reduction in SR (Fig. 2), which produced a shift in the distribution of AN fibers across the three SR groups for CFs between 1–4 kHz. A greater proportion of HI fibers (19%) were classified as low SR than were NH fibers (5%), whereas the proportion of high-SR fibers was greater in the NH population (75%) than in the HI population (55%). The proportion of medium-SR fibers was fairly similar between the NH (20%) and HI (26%) populations. The reduction in SR following NIHL is consistent with previous data (Heinz and Young, 2004; Liberman and Dodds, 1984a).

Threshold elevation following NIHL was similar across the three SR groups. The NH thresholds (in dB SPL) for high-, medium-, and low-SR fibers were 17.7 ± 4.7 dB, 24.4 ± 7.2 dB, and 31.8 ± 5.7 dB, respectively, consistent with previous AN data from chinchillas (Temchin et al., 2008). In contrast, the HI thresholds for high-, medium-, and low-SR fibers were 52.4 ± 13.9 dB, 60.6 ± 14.8 dB, and 69.9 ± 11.7 dB, respectively, corresponding to average threshold elevations between 34–38 dB across CFs from 1–4 kHz.

3.2. Response latency was reduced following noise-induced hearing loss

Fig. 3 shows response latency measured with both the *first peak latency* metric (Fig. 3A) and the *driven response latency* metric (Fig. 3B) as a function of CF. For both metrics, response latency decreased as CF increased for both NH and HI populations, as expected from the cochlear traveling wave moving from base to apex. Noise-exposed fibers showed reduced response latencies within and above the CF region of maximum impairment, with consistent results from both metrics. This reduction in latency was roughly constant across all fibers with CF above ~1.5 kHz and was on the order of 0.5 ms. The reduction in response latencies following NIHL was significant for the total population of AN fibers, as confirmed by unpaired (independent samples) t-tests (Table 1). Similar results were found for the first-spike latency metric (Table 1); however, more variability was present in the first-spike latency estimates than for the metrics shown in Fig. 3. For this reason, and the strong dependence of first-spike latency on SR for NH fibers (discussed further in Section 4.1), only the first peak latency and driven response latency metrics are considered further.

Because there were more low-SR fibers following NIHL (Fig. 2) and mean first-peak and driven-response latencies were generally shorter for lower SRs (Table 1, all cases except NH first peak latency), it is important to evaluate whether the overall reduction in response latency could be accounted for by the reduction in SR. This explanation appears unlikely because the observed differences between SR groups within a population were *not* statistically significant ($p > 0.05$) for either first peak latency or driven response latency (except for HI first peak latency low-SR vs. high-SR, $p < 0.035$). Furthermore, the reduction in latency was observed in each of the individual SR groups, with all SR groups showing a significant or nearly significant difference (even with the reduced number of fibers after grouping by SR). Thus, these results suggest that the reduced response latency observed in NIHL fibers was not due to the reduction in SR in HI fibers.

A more likely explanation is that reduced latency may have resulted from broadened tuning in AN fibers following NIHL. Fig. 4 shows response latencies computed from both the first peak latency metric (Fig. 4A) and the driven response latency metric (Fig. 4B) as a function of *normalized- Q_{10}* . Since Q_{10} is CF-dependent (Fig. 1B), Q_{10} values were normalized with reference to the 5th percentile confidence interval of the NH data. Normalized- Q_{10} values < 1 indicate fibers with significantly broadened tuning. HI fibers with normalized- $Q_{10} < 1$ ($n=54/81$) showed reduced response latency for both first peak latency (4.29 ± 0.55 ms) and driven response latency (3.69 ± 0.41 ms). For both metrics, the difference between response latencies for noise-exposed fibers with broadened tuning and NH fibers with CFs between 1–4 kHz was statistically significant ($p < 0.0001$). Furthermore, statistical tests showed that the difference in response latencies between NH fibers and HI fibers without significantly

broadened tuning (normalized- $Q_{10} \geq 1$, $n=27/81$) was *not* statistically significant for either the first-peak latency (4.74 ± 0.83 ms, $p=0.41$) or the driven response latency (4.05 ± 0.60 ms, $p=0.15$) metric. Finally, the difference in latencies between HI fibers with broadened tuning (normalized- $Q_{10} < 1$) and HI fibers without broadened tuning (normalized- $Q_{10} \geq 1$) was statistically significant for both first peak latency ($p = 0.005$) and driven response latency ($p < 0.003$). Thus, these results suggest that the observed reduction in response latency was associated with reduced frequency selectivity; HI fibers with elevated thresholds but without significantly broadened tuning did not show significant reductions in latency.

3.3. AN fibers with SNHL showed enhanced onset responses and increased percent adaptation

Noise-exposure affected both onset and adapted responses in PST histograms, although these effects differed somewhat across the three SR groups. Fig. 5 shows averaged PST histograms for both NH and HI fibers from within the CF region of maximum impairment (1 – 4 kHz). The three panels illustrate averaged PST histograms for each of the three different SR groups. For both low and medium SR fibers (panels A and B), the averaged onset rate was ~1.9 times greater for HI fibers than for NH fibers, whereas the adapted rate was only ~1.5 times greater for HI fibers than for NH fibers. For high SR fibers (panel C), the averaged onset response in HI fibers was ~1.2 times greater than in NH fibers, while the averaged adapted rate was virtually identical between NH and HI populations. These averaged PST histograms illustrate that onset responses were higher in HI fibers for all SR groups, whereas adapted rates were only higher in low and medium-SR groups. Thus, although the degree to which SNHL affected onset and adapted rates differed across SR groups, an enhancement in the onset response relative to the adapted response was apparent in all fibers.

The increase in the onset-response salience observed in the averaged-PST histograms was also apparent when onset and adapted rates were computed from individual AN fibers. Fig. 6 compares onset rate, adapted rate, and percent adaptation computed from individual NH and HI fibers as a function of CF. Onset rate (Fig. 6A) was on average higher in HI fibers than in NH fibers within the entire CF region of maximum impairment (1–4 kHz). These differences between NH and HI onset rates were significant for the total populations as well as for each SR group individually (Table 2). In contrast to onset rates, adapted rates (Fig. 6B) were only higher on average in the impaired population for the upper half of the CF region of maximum impairment. Thus, the overall difference in adapted rates between NH and HI fibers did not reach significance (Table 2), although this difference was significant for the medium SR group. There also was a large difference in adapted rates for low-SR fibers (increasing from 92 to 138 spikes/s following SNHL), although this difference was not significant (likely due to the small number of low-SR fibers). In contrast to low- and medium-SR fibers, the adapted rates for high-SR fibers were the same between NH and HI fibers, consistent with the averaged-PST results from Fig. 5. The overall salience of the onset response relative to the adapted response was quantified in each AN fiber in terms of percent adaptation (Fig. 6C). HI fibers showed higher percent adaptation than NH fibers within most of the CF region of maximum impairment, consistent with the CF distribution of SNHL effects on onset (Fig. 6A) and adapted (Fig. 6B) rates. This difference between NH and HI percent adaptation was significant for the total population of AN fibers, but only reached significance for the high-SR group (Table 2). Thus, these data from 30-dB SL PST histograms suggest that SNHL produces a more salient onset response that results from a greater increase in onset rate than adapted rate.

3.4. AN fibers showed faster adaptation and slower recovery following noise-induced hearing loss

Single-exponential adaptation and recovery time constants are shown in Fig. 7 for NH (crosses) and HI fibers (circles). Hearing impaired fibers showed lower adaptation time constants (faster

adaptation) than NH fibers within the CF region of maximum impairment (Fig. 7A). This reduction in adaptation time constant was significant when all fibers were considered (Table 3). The mean adaptation time constants within each SR group were also lower for HI fibers, as compared to NH fibers, with significant differences for low- and medium-SR fibers. Single adaptation time constants derived from fits to the average PST histograms (Fig. 6) were also lower following NIHL, both for all fibers (6.35 vs 5.45 ms) and for low- (7.73 vs 6.26 ms), medium- (8.52 vs. 5.82 ms) and high-SR (5.95 vs 5.07 ms) fibers. The reduction in adaptation time constants with NIHL was largest for the low- and medium-SR groups, and less for the high-SR group (both for the individual-fiber fits in Fig. 7 and the average-PST fits). Consistent with this observation, differences in adaptation time constants across SR groups (low vs. high, low vs. medium, and medium vs. high) were significant for NH fibers, but *not* for HI fibers. These results suggest that low-SR fibers have a slower rate of adaptation than high-SR fibers in cases of NH (consistent with previous reports on recovery rates, Relkin and Doucet, 1991), but that this difference between low- and high-SR adaptation rate is reduced (or eliminated) following NIHL.

A significant effect of SNHL was also observed in the rate of recovery to spontaneous rate after stimulus offset (Figs. 5C and 7B). The mean time constant for recovery to SR after stimulus offset was found to be 30.7 ms for NH fibers (Table 3), consistent with previous estimates from guinea-pig AN fibers (Yates et al., 1985). Recovery time constants for high-SR fibers were higher in HI fibers (41.2 ms) than in NH fibers within the CF region of maximum impairment, indicating a slower rate of recovery following SNHL. This increase in the average rate of recovery for individual fibers was significant (Table 3), and was consistent with recovery fits to the average PST histograms for high SR fibers (Fig. 5C), which yielded the following time constants: 26.9 ms (NH; $R^2 > 0.961$), and 34.1 ms (HI; $R^2 > 0.954$). Thus, SNHL had significant (but opposite) effects on the rate of adaptation following stimulus onset and the rate of recovery following stimulus offset.

4. Discussion

4.1. Response latency was reduced following SNHL when frequency selectivity was reduced

Noise-induced hearing loss typically produces a reduction in SR (Fig. 2; also see Liberman and Dodds, 1984a), and thus it is particularly important that latency metrics for quantifying the effects of SNHL are not influenced by SR. For example, although average first-spike latency has been used at numerous levels of the auditory system (Heil, 1997; Heil et al., 2008; Kitzes et al., 1978), this metric can be strongly affected by SR because the first spike that occurs after stimulus onset may be spontaneous and not actually stimulus driven (Heil, 2004; Krishna, 2002). In fact, AN-fiber first-spike latency has been shown to decrease with increasing SR for NH fibers (Heil and Irvine, 1997). Thus, response latency was computed with several metrics in the present study, including first-spike latency, first-peak latency, and driven-response latency (Table 1). Although consistent and statistically significant results were obtained across all metrics, first-spike latency was more variable and had a strong dependence on SR for NH fibers. Because first-peak latency (Fig. 3A) relies on the first significant peak in the PST histogram, it is much less susceptible to spontaneous spikes; however, this metric may somewhat overestimate the true instantaneous “response” latency in that it ignores spike times just before the peak response that are clearly non-spontaneous. Thus, the driven-response latency metric (Fig. 3B) was developed to reliably estimate the first non-spontaneous response as the time to exceed maximum spontaneous activity plus two standard deviations. Driven-response latency was the most robust of all metrics used, i.e., it showed the least variability in latency across fibers with similar CFs. Overall, neither of the two primary metrics used (Fig. 3, Table 1) showed significant differences in latencies between SR groups for either the NH or HI populations (unlike NH first-spike latencies, Table 1), suggesting that SR does not affect

cochlear response latency. This finding, combined with reduced latencies following SNHL in each SR group for all metrics, suggests that reduced SR does not contribute to the overall reduction in latency following SNHL.

The present data suggest that reduced frequency selectivity was a primary factor responsible for the reduction in AN-fiber response latencies, which were measured for CF-tone PST histograms at 30-dB SL. The decrease in response latency by ~0.5 ms for HI fibers (Fig. 3, Table 1) at equal SL was consistent with first-peak latencies in click responses of noise-exposed chinchillas (Salvi et al., 1979), and whole-nerve action potential latencies to tones measured in kanamycin-treated guinea pigs (Wang and Dallos, 1972). However, differences in AN latencies have not been found when measured at equal SPLs, suggesting that reduced response latencies in HI ears may result solely from the higher SPLs used in HI ears (Salvi et al., 1979; Wang and Dallos, 1972). The present results clarify this issue by demonstrating that higher SPLs alone do not account for reduced latencies. Within the CF region of maximal hearing impairment (CFs=1–4 kHz), noise-exposed fibers without significantly broadened tuning had permanent threshold shifts of 25–45 dB (Fig. 1), yet did not have significantly different response latencies at higher sound levels (Fig. 4). These results also suggest that hair-cell synaptic effects (e.g., reduced exocytosis delays from increased Ca^{2+} concentration; Beutner et al., 2001; Fridberger et al., 1998) are unlikely to be the primary factor in reduced latencies, because synaptic effects would be expected to influence both broad and narrowly tuned AN fibers. Rather, the primary effect is likely to relate to cochlear effects due to reduced OHC function, which is typically associated with reduced frequency selectivity following NIHL (Liberman and Dodds, 1984b). Recent cross-fiber correlogram data showed decreased AN-fiber characteristic delays between nearby CFs at equal SL when frequency selectivity was degraded (Heinz et al., 2010). Thus, reduced AN-fiber latencies are likely to result from reduced traveling-wave delays on the basilar membrane due to degraded tuning associated with OHC damage.

4.2. The salience of onset responses was increased following SNHL

The increase in onset rates in the HI population was considerably larger than for adapted rates, which resulted in significant increases in percent adaptation following SNHL (Fig. 6, Table 2). The increase in onset rates and percent adaptation was consistent with equal-SL tone responses from acoustically overexposed chicks (Crumling and Saunders, 2007). The present results provide additional insight into this finding in that the degree of this effect was found to vary across SR groups. Onset rates in HI fibers were enhanced for all SR groups (Fig. 5, Table 2). In contrast, HI adapted rates were only enhanced for low- and medium-SR groups, with only the medium-SR group reaching statistical significance. It is noteworthy that even though the high-SR responses for HI fibers were quite similar to NH responses, there were differences that included a small (but significant) increase in onset rate, slower recovery (discussed below), and lower SR (Fig. 5C). Thus, equal-SL tone responses were generally enhanced upon hearing impairment, but more so for low- and medium-SR fibers. Interestingly, this enhancement varied with time through the response (i.e., the enhancement in onset responses was greater than for adapted responses).

The differences in enhancement between onset and adapted responses and across SR groups may provide some insight into the biophysical bases for the increased salience of onset responses following SNHL. It is possible that the NH low- and medium-SR fibers were less saturated at 30-dB SL than were the high-SR fibers due to the influence of cochlear compression (Sachs and Abbas, 1974). The loss of cochlear compression with SNHL could have led to increased discharge rates and brought the low- and medium-SR fibers closer to saturation. This effect, combined with the observation that the ratio of onset to adapted rates increases in NH fibers with increasing level above 20–25 dB SL, presumably due to saturation effects (Smith

and Zwislocki, 1975; Westerman and Smith, 1984), could account for the increase in percent adaptation observed for low- and medium-SR fibers following SNHL. However, the fact that percent adaptation was similar across SR groups in NH fibers, but differed in HI fibers appears to be inconsistent with this effective sound-level based explanation.

The unequal increases in onset and adapted responses could be due to structural and/or synaptic (pre or post) changes occurring following SNHL, which have been shown to occur at the AN/cochlear-nucleus synapse in response to decreased peripheral activity (Ryugo et al., 1997). Post-synaptic effects are not likely to account for the observed changes, because they would be expected to affect both onset and adapted responses equally. Intracellular hair-cell Ca^{2+} has been shown to increase following noise exposure (Fridberger et al., 1998; Maurer et al., 1999) and could differentially affect mechanisms that contribute to the onset and adapted responses. For example, it has been hypothesized that onset responses may depend on rapidly inactivating Ca^{2+} channels, whereas adapted responses may depend on noninactivating voltage-gated Ca^{2+} channels (Heil and Irvine, 1997). Furthermore, augmentation of the readily releasable vesicle pool in relation to increased intracellular Ca^{2+} has been hypothesized to provide a compensatory mechanism to overcome reduced transduction activity and would likely contribute to larger increases in onset than adapted responses following SNHL (Crumling and Saunders, 2007).

4.3. The time courses of adaptation and recovery from adaptation were altered following SNHL

Adaptation time constants were reduced following SNHL, whereas time constants quantifying the recovery to spontaneous activity after stimulus offset were increased. More rapid adaptation in HI fibers was observed for all SR groups, but was only significantly different than normal hearing in low- and medium-SR fibers (Table 3). Thus, the differences in adaptation rates across SR groups observed in NH fibers (low-SR fibers being significantly slower than high-SR fibers) were not observed in the HI population. In contrast to the present results, similar AN-fiber adaptation time constants were found in unexposed and noise-exposed chicks (Crumling and Saunders, 2007); however, results were not separated by SR group.

One limitation of the present results was the short duration of the PST histograms used to quantify the time course of adaptation after stimulus onset. Many PST histograms did not reach an asymptotic discharge rate within the 50-ms duration, consistent with previous findings that both rapid (~3–10 ms) and short-term adaptation (~60–100 ms) exist when longer-duration stimuli were used (Chimento and Schreiner, 1991; Westerman and Smith, 1984). The 50-ms PST histograms analyzed here did not permit fitting of two-exponential curves, as discussed in previous studies (Meddis, 1986; Smith, 1985; Yates, 1986; Yates et al., 1985). Thus, the single-time-constant fits used in the present study likely represent a combination of both rapid and short-term components, although their mean values (4.7 – 10.4 ms) suggest they were most influenced by rapid adaptation. Despite these limitations in the present data, clear differences in both adaptation and recovery from adaptation were observed between the NH and HI populations. Future studies with longer stimuli are needed to characterize the effects of SNHL on the individual adaptation processes.

The biophysical bases for faster adaptation and slower recovery following SNHL are unknown; however, both pre- and post-synaptic effects could contribute given suggestions that AN-fiber adaptation cannot be fully explained based on pre-synaptic mechanisms (Chimento and Schreiner, 1991; Zhang et al., 2007). In fact, a recently developed AN model (Zilany et al., 2009) required two separate mechanisms to describe onset adaptation (largely governed in the model by exponential adaptation) and recovery dynamics (largely dominated by slow power-law dynamics). The faster adaptation time course following SNHL may be somewhat influenced by level effects, as rapid (but not short-term) adaptation time constants have been

reported to decrease with increasing sensation level (Westerman and Smith, 1984; but also see Chimento and Schreiner 1991). The larger decreases in adaptation time constants for low- and medium-SR fibers (Table 3) are consistent with the idea that loss of cochlear compression could increase the effective sound level at 30-dB SL for low- and medium-SR fibers, but not high-SR fibers. Whether or not sound-level effects contributed to the observed changes, cellular mechanisms related to elevated intracellular Ca^{2+} levels in hair cells following noise exposure may underlie these changes in the time course of adaptation and recovery (Fridberger et al., 1998; Maurer et al., 1999). For example, slower AN recovery following NIHL is consistent with recent data suggesting that recovery at endbulb of Held synapses in the cochlear nucleus depends on the rate of activity and accumulation of intracellular Ca^{2+} at the presynaptic terminal, with slower recovery corresponding to elevated Ca^{2+} (Wang and Manis, 2008).

4.4. Potential implications of altered temporal dynamics following SNHL

The finding that SNHL affects several aspects of the temporal dynamics of AN-fiber responses may have important implications for physiological correlates of perception in HI listeners as well as for translational aspects of diagnostic and rehabilitative audiology. Onset responses have been hypothesized to be important for coding regions of rapid spectral change that contribute significantly to speech perception (Delgutte and Kiang, 1984), and to benefit the encoding of amplitude modulated sounds (Smith and Brachman, 1980). The salience of AN onset responses has been hypothesized to be reduced following OHC damage and to contribute to poor consonant recognition in HI listeners (Allen et al., 2009). Surprisingly, the present results along with those of Crumling and Saunders (2007) suggest that onset responses are actually enhanced, rather than diminished, following NIHL. These data thus suggest that synaptic effects of SNHL on onset responses may be stronger than cochlear effects. The effect of SNHL on onset responses would be expected to be perceptually significant based on computational modeling that used spectral-temporal clustering of onset cues to predict the effects of hearing aids on speech intelligibility (Bondy et al., 2004).

Larger onset responses and the slower recovery from adaptation following NIHL may also have important perceptual implications for speech perception in noise. Slower recovery enhances amplitude-modulation coding in model AN responses (Zilany et al., 2009), and thus may be a contributing factor to enhanced envelope coding in AN fibers following NIHL (Kale and Heinz, in press). Although envelope coding is *enhanced* following SNHL, this effect may in fact *degrade* speech perception in noise by magnifying amplitude fluctuations in temporally varying background sounds (Moore et al., 1995).

The finding of slower recovery from adaptation following SNHL may have important implications for the use of temporal-masking curves (TMCs) to compare cochlear nonlinearity in NH and HI listeners. In this technique, differences in the decay of forward masking between NH and HI listeners are thought to originate primarily from differences in cochlear compression, with all other factors being unaffected by impairment. Thus, a surprising finding has been that HI listeners often show shallower off-frequency TMCs than NH listeners despite the belief that off-frequency cochlear responses are linear for both NH and HI ears (Plack et al., 2004). The present data suggest that differences in the time course of recovery from adaptation due to SNHL may contribute to differences in TMCs between NH and HI listeners. Thus, these results are important to consider when interpreting results from existing psychoacoustic techniques for estimating cochlear compression in HI listeners, as well as for the development of new techniques that aim to avoid limitations in the assumptions underlying these approaches (Wojtczak and Oxenham, 2009).

The findings of altered adaptation and recovery time courses and reduced latencies may have important implications for hearing-aid amplification strategies. Hearing-aid compression time constants can affect user comfort and satisfaction, with fast time constants often producing

better speech understanding in noise and slower time constants producing increased comfort but at the expense of reduced speech understanding (Gatehouse et al., 2006; Moore, 2008). The present data suggest that changes occur in AN adaptation and recovery rates and that these effects may need to be considered in the active clinical debate regarding the optimal time course for dynamically adjusting hearing-aid compression (e.g., attack and release times). The finding that reduced latencies occur with degraded frequency selectivity supports novel model-based hearing-aid strategies to restore normal spatiotemporal patterns by compensating for reduced cochlear delays (Shi et al., 2006). However, the finding that latencies were not reduced in HI fibers without broadened tuning suggests the need to consider the frequency resolution of individual patients in such strategies and may explain their limited success to date (Calandruccio et al., 2007).

Finally, recently extended computational models of AN responses that accurately describe many of the physiological effects of inner-hair-cell (IHC) and OHC dysfunction have been used in a number of applications related to SNHL (Heinz, 2010). However, the present data suggest that these models may need to be extended to include synaptic effects that may contribute to altered temporal dynamics following SNHL. A recent model extension that added power-law dynamics to the commonly used exponential adaptation improved a number of response properties, including amplitude-modulation coding, long-term adaptation, forward masking, and increment and decrement coding (Zilany et al., 2009). The importance of both rapid and short-term exponential and power-law adaptation demonstrated by this model suggests that more detailed data is needed to better quantify the effects of SNHL on each of these types of adaptation.

Abbreviations

ABR	auditory brainstem response
AN	auditory nerve
CF	characteristic frequency
HI	hearing impaired
IHC	inner hair cell
NH	normal hearing
NIHL	noise-induced hearing loss
OHC	outer hair cell
PST	post-stimulus time
SNHL	sensorineural hearing loss
SL	sensation level
SPL	sound pressure level
SR	spontaneous rate
s.d.	standard deviation
TMC	temporal masking curve

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References

- Allen, JB.; Regnier, M.; Phatak, S.; Li, FP. Nonlinear cochlear signal processing and phoneme perception. In: Cooper, NP.; Kemp, DT., editors. *Concepts and Challenges in the Biophysics of Hearing*. Singapore: World Scientific Publ Co Pte Ltd; 2009. p. 93-105.
- Arehole S, Salvi RJ, Saunders SS, Henderson D. Evoked response 'forward masking' patterns in chinchillas with temporary hearing loss. *Hear. Res* 1987;27:193–205. [PubMed: 3610848]
- Benda J, Longtin A, Maler L. Spike-frequency adaptation separates transient communication signals from background oscillations. *J. Neurosci* 2005;25:2312–2321. [PubMed: 15745957]
- Beutner D, Voets T, Neher E, Moser T. Calcium dependence of exocytosis and endocytosis at the cochlear inner hair cell afferent synapse. *Neuron* 2001;29:681–690. [PubMed: 11301027]
- Bondy, J.; Bruce, IC.; Becker, S.; Haykin, S. Predicting speech intelligibility from a population of neurons. In: Thrun, S.; Saul, L.; Scholkopf, B., editors. *NIPS 2003 Conference Proceedings: Advances in Neural Information Processing Systems*; Cambridge, MA: MIT Press; 2004. p. 1409-1416.
- Calandruccio L, Doherty KA, Carney LH, Kikkeri HN. Perception of temporally processed speech by listeners with hearing impairment. *Ear. Hear* 2007;28:512–523. [PubMed: 17609613]
- Carney LH. Spatiotemporal encoding of sound level: Models for normal encoding and recruitment of loudness. *Hear. Res* 1994;76:31–44. [PubMed: 7928712]
- Cedolin, L.; Delgutte, B. Spatio-temporal representation of the pitch of complex tones in the auditory nerve. In: Kollmeier, B.; Klump, G.; Hohmann, V.; Langemann, U.; Mauermann, M.; Uppenkamp, S.; Verhey, J., editors. *Hearing – From Sensory Processing to Perception*. Berlin: Springer-Verlag; 2007. p. 61-70.
- Chimento TC, Schreiner CE. Adaptation and recovery from adaptation in single fiber responses of the cat auditory nerve. *J. Acoust. Soc. Am* 1991;90:263–273. [PubMed: 1652600]
- Chintanpalli A, Heinz MG. The effect of auditory-nerve response variability on estimates of tuning curves. *J. Acoust. Soc. Am* 2007;122:EL203–EL209. [PubMed: 18247642]
- Crumling MA, Saunders JC. Tonotopic distribution of short-term adaptation properties in the cochlear nerve of normal and acoustically overexposed chicks. *J. Assoc. Res. Otolaryngol* 2007;8:54–68. [PubMed: 17200911]
- Dallos P, Harris D. Properties of auditory nerve responses in absence of outer hair cells. *J. Neurophysiol* 1978;41:365–383. [PubMed: 650272]
- Delgutte B, Kiang NYS. Speech coding in the auditory nerve: IV. Sounds with consonant-like dynamic characteristics. *J. Acoust. Soc. Am* 1984;75:897–907. [PubMed: 6707319]
- French AS, Hoyer U, Sekizawa S, Torkkeli PH. Frequency response functions and information capacities of paired spider mechanoreceptor neurons. *Biol. Cybern* 2001;85:293–300. [PubMed: 11592626]
- Fridberger A, Flock A, Ulfendahl M, Flock B. Acoustic overstimulation increases outer hair cell Ca^{2+} concentrations and causes dynamic contractions of the hearing organ. *Proc. Natl. Acad. Sci. USA* 1998;95:7127–7132. [PubMed: 9618550]
- Gatehouse S, Naylor G, Elberling C. Linear and nonlinear hearing aid fittings - I. Patterns of benefit. *Int. J. Audiol* 2006;45:130–152. [PubMed: 16579490]
- Guinan JJ Jr, Peake WT. Middle-ear characteristics of anesthetized cats. *J. Acoust. Soc. Am* 1967;41:1237–1261. [PubMed: 6074788]
- Heil P. Auditory cortical onset responses revisited. I. First-spike timing. *J. Neurophysiol* 1997;77:2616–2641. [PubMed: 9163380]
- Heil P. First-spike latency of auditory neurons revisited. *Curr. Opin. Neurobiol* 2004;14:461–467. [PubMed: 15321067]
- Heil P, Irvine DR. First-spike timing of auditory-nerve fibers and comparison with auditory cortex. *J. Neurophysiol* 1997;78:2438–2454. [PubMed: 9356395]
- Heil P, Neubauer H, Brown M, Irvine DRF. Towards a unifying basis of auditory thresholds: distributions of the first-spike latencies of auditory-nerve fibers. *Hear. Res* 2008;238:25–38. [PubMed: 18077116]

- Heinz, MG. Computational Modeling of Sensorineural Hearing Loss. In: Meddis, R.; Lopez-Poveda, EA.; Popper, AN.; Fay, RR., editors. *Computational Models of the Auditory System*. New York: Springer; 2010. p. 177-202.
- Heinz MG, Young ED. Response growth with sound level in auditory-nerve fibers after noise-induced hearing loss. *J. Neurophysiol* 2004;91:784–795. [PubMed: 14534289]
- Heinz, MG.; Swaminathan, J.; Boley, JD.; Kale, S. Across-fiber coding of temporal fine-structure: Effects of noise-induced hearing loss on auditory-nerve responses. In: Lopez-Poveda, EA.; Palmer, AR.; Meddis, R., editors. *The Neurophysiological Bases of Auditory Perception*. New York: Springer; 2010. p. 621-630.
- Hildebrandt KJ, Benda J, Hennig RM. The origin of adaptation in the auditory pathway of locusts is specific to cell type and function. *J. Neurosci* 2009;29:2626–2636. [PubMed: 19244538]
- Kale S, Heinz MG. Envelope coding in auditory-nerve fibers following noise-induced hearing loss. *J. Assoc. Res. Otolaryngol.* in press DOI: 10.1007/s10162-010-0223-6.
- Kiang, NYS.; Moxon, EC.; Levine, RA. Auditory-nerve activity in cats with normal and abnormal cochleas. In: Wolstenholme, GEW.; Knight, T., editors. *Sensorineural Hearing Loss*. London: Churchill; 1970. p. 241-273.
- Kitzes LM, Gibson MM, Rose JE, Hind JE. Initial discharge latency and threshold considerations for some neurons in cochlear nuclear complex of cat. *J. Neurophysiol* 1978;41:1165–1182. [PubMed: 212537]
- Krishna BS. A unified mechanism for spontaneous-rate and first-spike timing in the auditory nerve. *J. Comput. Neurosci* 2002;13:71–91. [PubMed: 12215723]
- Liberman MC. Single-neuron labeling and chronic cochlear pathology. I. Threshold shift and characteristic-frequency shift. *Hear. Res* 1984;16:33–41. [PubMed: 6096345]
- Liberman MC, Dodds LW. Single-neuron labeling and chronic cochlear pathology. II. Stereocilia damage and alterations of spontaneous discharge rates. *Hear. Res* 1984a;16:43–53. [PubMed: 6511672]
- Liberman MC, Kiang NYS. Single-neuron labeling and chronic cochlear pathology. IV. Stereocilia damage and alterations in rate- and phase-level functions. *Hear. Res* 1984;16:75–90. [PubMed: 6511674]
- Liberman MC, Dodds LW. Single-neuron labeling and chronic cochlear pathology. III. Stereocilia damage and alterations of threshold tuning curves. *Hear. Res* 1984b;16:55–74. [PubMed: 6511673]
- Loeb GE, White MW, Merzenich MM. Spatial cross-correlation - a proposed mechanism for acoustic pitch perception. *Biol. Cybern* 1983;47:149–163. [PubMed: 6615914]
- Maurer J, Heinrich UR, Hinni M, Mann W. Alteration of the calcium content in inner hair cells of the cochlea of the guinea pig after acute noise trauma with and without application of the organic calcium channel blocker diltiazem. *ORL J Otorhinolaryngol Relat Spec* 1999;61:328–333. [PubMed: 10545806]
- Meddis R. Very rapid adaptation in the guinea-pig auditory-nerve - Comment. *Hear. Res* 1986;23:287–288. [PubMed: 3745028]
- Miller RL, Schilling JR, Franck KR, Young ED. Effects of acoustic trauma on the representation of the vowel /e/ in cat auditory nerve fibers. *J Acoust Soc Am* 1997;101:3602–3616. [PubMed: 9193048]
- Moore BC. The choice of compression speed in hearing aids: theoretical and practical considerations and the role of individual differences. *Trends Amplif* 2008;12:103–112. [PubMed: 18567591]
- Moore BC, Glasberg BR, Vickers DA. Simulation of the effects of loudness recruitment on the intelligibility of speech in noise. *Br. J. Audiol* 1995;29:131–143. [PubMed: 8574199]
- Moore BCJ, Wojtczak M, Vickers DA. Effect of loudness recruitment on the perception of amplitude modulation. *J. Acoust. Soc. Am* 1996;100:481–489.
- Moore BCJ, Peters RW, Stone MA. Benefits of linear amplification and multichannel compression for speech comprehension in backgrounds with spectral and temporal dips. *J. Acoust. Soc. Am* 1999;105:400–411. [PubMed: 9921666]
- Ngan EM, May BJ. Relationship between the auditory brainstem response and auditory nerve thresholds in cats with hearing loss. *Hear. Res* 2001;156:44–52. [PubMed: 11377881]
- Plack CJ, Drga V, Lopez-Poveda EA. Inferred basilar-membrane response functions for listeners with mild to moderate sensorineural hearing loss. *J. Acoust. Soc. Am* 2004;115:1684–1695. [PubMed: 15101647]

- Relkin EM, Doucet JR. Recovery from prior stimulation. I: Relationship to spontaneous firing rates of primary auditory neurons. *Hear Res* 1991;55:215–222. [PubMed: 1757289]
- Ryugo DK, Pongstaporn T, Huchton DM, Niparko JK. Ultrastructural analysis of primary endings in deaf white cats: morphologic alterations in endbulbs of Held. *J. Comp. Neurol* 1997;385:230–244. [PubMed: 9268125]
- Sachs MB, Abbas PJ. Rate versus level functions for auditory-nerve fibers in cats: Tone-burst stimuli. *J. Acoust. Soc. Am* 1974;56:1835–1847. [PubMed: 4443483]
- Salvi RJ, Henderson D, Hamernik RP. Single auditory-nerve fiber and action potential latencies in normal and noise-treated chinchillas. *Hear. Res* 1979;1:237–251.
- Shamma SA. Speech processing in the auditory system. I: The representation of speech sounds in the responses of the auditory nerve. *J. Acoust. Soc. Am* 1985;78:1612–1621. [PubMed: 4067077]
- Shi LF, Carney LH, Doherty KA. Correction of the peripheral spatiotemporal response pattern: A potential new signal-processing strategy. *J. Speech. Lang. Hear. Res* 2006;49:848–855. [PubMed: 16908879]
- Smith RL. Short-term adaptation in single auditory nerve fibers: Some poststimulatory effects. *J. Neurophysiol* 1977;40:1098–1112. [PubMed: 903799]
- Smith RL. Very rapid adaptation in the guinea-pig auditory-nerve - Comments. *Hear. Res* 1985;19:89–92. [PubMed: 4066517]
- Smith RL, Zwislocki JJ. Short-term adaptation and incremental responses of single auditory-nerve fibers. *Biol. Cybern* 1975;17:169–182. [PubMed: 1125344]
- Smith RL, Brachman ML. Response modulation of auditory-nerve fibers by AM stimuli: effects of average intensity. *Hear. Res* 1980;2:123–133. [PubMed: 7364668]
- Temchin AN, Rich NC, Ruggero MA. Threshold tuning curves of chinchilla auditory nerve fibers. II. Dependence on spontaneous activity and relation to cochlear nonlinearity. *J. Neurophysiol* 2008;100:2899–2906. [PubMed: 18753325]
- Walton JP, Frisina RD, Meierhans LR. Sensorineural hearing loss alters recovery from short-term adaptation in the C57BL/6 mouse. *Hear. Res* 1995;88:19–26. [PubMed: 8575994]
- Wang CY, Dallos P. Latency of whole-nerve action potentials: influence of hair-cell normalcy. *J. Acoust. Soc. Am* 1972;52:1678–1686. [PubMed: 4641372]
- Wang Y, Manis PB. Short-term synaptic depression and recovery at the mature mammalian endbulb of Held synapse in mice. *J. Neurophysiol* 2008;100:1255–1264. [PubMed: 18632895]
- Westerman LA, Smith RL. Rapid and short-term adaptation in auditory nerve responses. *Hear. Res* 1984;15:249–260. [PubMed: 6501113]
- Westerman LA, Smith RL. Conservation of adapting components in auditory-nerve responses. *J. Acoust. Soc. Am* 1987;81:680–691. [PubMed: 3584675]
- Wojtczak M, Oxenham AJ. Pitfalls in behavioral estimates of basilar-membrane compression in humans. *J. Acoust. Soc. Am* 2009;125:270–281. [PubMed: 19173414]
- Yates GK. Very rapid adaptation in the guinea-pig auditory-nerve - Reply. *Hear. Res* 1986;23:288–290.
- Yates GK, Robertson D, Johnstone BM. Very rapid adaptation in the guinea-pig auditory-nerve. *Hear. Res* 1985;17:1–12. [PubMed: 3997676]
- Zhang F, Miller CA, Robinson BK, Abbas PJ, Hu N. Changes across time in spike rate and spike amplitude of auditory nerve fibers stimulated by electric pulse trains. *J. Assoc. Res. Otolaryngol* 2007;8:356–372. [PubMed: 17562109]
- Zilany MS, Bruce IC, Nelson PC, Carney LH. A phenomenological model of the synapse between the inner hair cell and auditory nerve: long-term adaptation with power-law dynamics. *J. Acoust. Soc. Am* 2009;126:2390–2412. [PubMed: 19894822]

FIG. 1.

AN fibers from noise-exposed animals exhibited increased thresholds and broader tuning. Circles represent all NIHL data ($n=128$ fibers) while crosses represent all NH data ($n=177$). (A) Plot of thresholds versus fiber CF. The thick dark gray and thin black lines represent trend lines for NIHL and NH populations, respectively, computed with a 0.7-octave wide triangular window with 0.35-octave steps and a minimum of 3 data points per window. The gray CF region (1–4 kHz) indicates the region of maximum hearing impairment over which all statistical comparisons were made in this study. (B) Plot of Q_{10} versus CF. The two parallel black lines represent the 5th and 95th percentile fits taken from a larger NH population of chinchilla AN

fibers (Kale and Heinz, in press). NIHL data below the 5th percentile line corresponds to fibers with significantly degraded frequency selectivity (normalized- $Q_{10} < 1.0$, see text).

FIG. 2.

AN fibers from noise-exposed animals exhibited reduced spontaneous rates. Thick gray line represents HI fibers (CF=1–4 kHz; n=81) while the thinner black line represents NH data (CF=1–4 kHz; n=77). Bin width is 5 spikes/s.

FIG. 3.

AN fibers from noise-exposed animals exhibited reduced response latencies. (A) Plot of *first peak latency* (see text) versus fiber CF. (B) Plot of *driven response latency* (see text) versus CF. Circles represent NIHL data ($n=128$) while crosses represent NH data ($n=177$). The thick dark gray (NIHL) and thin black (NH) lines represent trend lines (0.7-octave wide triangular window, 0.35-octave steps, minimum of 3 data points per window). Gray CF region (1–4 kHz) indicates the region of maximum hearing impairment.

FIG. 4.

AN-fiber latencies from NIHL animals were only reduced with broader tuning. (A) Plot of *first peak latency* (see text) versus normalized-Q₁₀. Normalized-Q₁₀'s are CF-independent, where values below 1 (gray region) represent Q₁₀ values below the 5th percentile for NH Q₁₀ data. (B) Plot of *driven response latency* (see text) versus normalized-Q₁₀. Circles represent NIHL data (n=81) while crosses represent NH data (n=77). The thick dark gray (NIHL) and thin black (NH) lines represent trend lines (1.0-octave wide triangular window, 0.5-octave steps, minimum of 4 data points per window). All data is for CFs between 1–4 kHz.

FIG. 5.

AN fibers from noise-exposed animals exhibited enhanced onset (all SR) and adapted responses (low and medium SR), as well as slower recovery (high SR). Averaged PST histograms are shown for (A) low-SR fibers (NH: $n=4$; HI: $n=15$), (B) medium-SR fibers (NH: $n=15$; HI: $n=21$), and (C) high-SR fibers (NH: $n=58$; HI: $n=45$). The inset in panel C shows a magnified view of the onset region for the high-SR PST histogram. Gray and black lines represent HI and NH responses, respectively, averaged across the CF region of maximum impairment (1–4 kHz).

FIG. 6.

AN fibers from noise-exposed animals exhibited enhanced onset rates and increased percent adaptation. Plots show onset rate (A), adapted rate (B), and percent adaptation (C) versus fiber CF. Circles represent NIHL data ($n=128$) while crosses represent NH data ($n=177$). The thick dark gray (NIHL) and thin black (NH) lines represent trend lines (0.7-octave wide triangular window, 0.35-octave steps, minimum of 3 data points per window). Gray CF region (1–4 kHz) indicates the region of maximum hearing impairment.

FIG. 7.

AN fibers from noise-exposed animals exhibited faster adaptation and slower recovery. (A) Adaptation time constants versus fiber CF for all SR groups (NH: $n=162$; HI: $n=122$). (B) Recovery time constants versus CF for high SR fibers (NH: $n=95$; HI: $n=61$). Circles represent NIHL data while crosses represent NH data. The thick dark gray (NIHL) and thin black (NH) lines represent trend lines (0.7-octave wide triangular window, 0.35-octave steps, minimum of 3 data points per window). Gray CF region (1–4 kHz) indicates the region of maximum hearing impairment.

Response latencies were reduced in AN fibers from noise-exposed animals. Mean latencies ($\pm$ s.d.) and unpaired (independent samples) t-test p-values were computed based on all normal-hearing (NH) and hearing-impaired (HI) fibers within the CF region of maximum impairment (1–4 kHz). Statistics are shown for all fibers as well as for the three SR groups individually (number of fibers, n, in each group is shown in the first column).

Table 1

Population	First Peak Latency (ms)			Driven Response Latency (ms)			First Spike Latency (ms)		
	NH	HI	p	NH	HI	p	NH	HI	p
<i>All fibers</i> (NH: 77; HI: 81)	4.86 $\pm$ 0.61	4.44 $\pm$ 0.68	<0.0001	4.21 $\pm$ 0.46	3.81 $\pm$ 0.51	<0.0001	5.31 $\pm$ 1.74	4.56 $\pm$ 0.88	<0.001
<i>High SR</i> (NH: 58; HI: 45)	4.87 $\pm$ 0.58	4.61 $\pm$ 0.78	<0.06	4.27 $\pm$ 0.46	3.90 $\pm$ 0.59	<0.001	4.76 $\pm$ 0.78	4.51 $\pm$ 0.89	0.13
<i>Med SR</i> (NH: 15; HI: 21)	4.81 $\pm$ 0.70	4.29 $\pm$ 0.56	<0.02	4.04 $\pm$ 0.46	3.76 $\pm$ 0.40	<0.06	6.35 $\pm$ 1.41	4.58 $\pm$ 0.82	<0.0001
<i>Low SR</i> (NH: 4; HI: 15)	4.90 $\pm$ 0.80	4.15 $\pm$ 0.29	<0.01	3.95 $\pm$ 0.29	3.62 $\pm$ 0.29	<0.06	9.43 $\pm$ 4.73	4.68 $\pm$ 0.97	<0.002

AN fibers from noise-exposed animals showed enhanced onset rates and increased percent adaptation. Adapted rate was only enhanced significantly in the medium SR group. Statistics and number of fibers (as in Table 1) based on CFs between 1–4 kHz.

Table 2

Population	Onset Rate (spikes/s)			Adapted Rate (spikes/s)			Percent Adaptation		
	NH	HI	p	NH	HI	p	NH	HI	p
<i>All fibers</i>	477±138	595±135	< 0.0001	145±39	154±35	0.13	68.6±6.7	73.3±6.2	< 0.0001
<i>High SR</i>	498±111	567±125	< 0.01	155±27	156±33	0.89	68.0±6.3	71.8±5.9	< 0.01
<i>Med SR</i>	432±173	655±147	< 0.001	123±47	163±33	< 0.01	70.7±6.9	74.1±6.4	0.13
<i>Low SR</i>	331±243	593±125	< 0.01	92±76	138±41	0.11	69.6±11.3	76.6±5.5	0.09

AN fibers from noise-exposed animals showed a faster rate of adaptation and a slower rate of recovery. Recovery was only characterized for high SR fibers, see text. Statistics based on fibers with CFs between 1–4 kHz.

Table 3

Population	Adaptation Time Constant (ms)			Recovery Time Constant (ms)		
	NH	HI	p	NH	HI	p
<i>All fibers</i>	6.04±2.94	4.89±1.99	< 0.005			
<i>High SR</i>	5.30±2.02	4.88±1.80	0.29	30.7±16.3	41.2±13.9	< 0.002
<i>Med SR</i>	7.74±3.27	4.69±2.21	< 0.005			
<i>Low SR</i>	10.38±6.31	5.18±2.27	< 0.02			