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The effects of interrupted noise exposures on the noise-damaged cochlea

William A. Ahroon, Roger P. Hamernik *

Auditory Research Laboratory, Plattsburgh State University of New York, 107 Beaumont Hall, 101 Broad Street, Plattsburgh, NY 12901-2681, USA

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Abstract

A variety of interrupted noise exposure paradigms will produce a toughening effect in the mammalian auditory system. That is, the threshold shift will gradually become smaller with each successive daily exposure. The ability of the system to be toughened has not been explored in subjects with a pre-existing noise-induced hearing loss. Using the chinchilla as the experimental animal, evoked potential audiometry to obtain thresholds, and surface preparation histology to quantify the sensory cell population, the issue of toughening was examined in the noise-damaged auditory system. Toughening was produced by a 1.0 kHz, narrow-band impact at 115 dB peak SPL for 10 days, 6 h/day, and trauma was produced by a 1.0 kHz, narrow-band impact at 121 dB peak SPL for 5 days, 24 h/day. Four groups of animals were used. Group 1: traumatic exposure followed 30 days later by the toughening exposure. Group 2: toughening exposure followed 30 days later by the traumatic exposure. Group 3: a trauma-only control. Group 4: a toughening-only control. Group 2 that received the toughening exposure 30 days prior to the traumatic exposure showed a 10 to more than 20 dB toughening effect between the 0.5 and 4.0 kHz test frequencies, while Group 1 that received the traumatic exposure followed 30 days later by the toughening exposure showed no toughening. The permanent changes in the evoked response audiograms and sensory cell populations were the same in Groups 1, 2 and 3 that were exposed to the traumatic noise, regardless of whether or not the animals were ever subjected to the toughening noise or whether the toughening noise preceded or followed the traumatic noise.

Key words: Toughening; Hearing loss; Interrupted noise; Asymptotic threshold

1. Introduction

Miller et al. (1963) showed that threshold shifts (TS) following a daily interrupted noise exposure can decrease over time despite the continuing daily noise exposure. This effect, often referred to as toughening, has been replicated a number of times with a rather varied set of stimuli (Clark et al., 1987; Subramaniam et al., 1991; McFadden et al., 1997; Hamernik et al., 1994). While the outer hair cells and components of the efferent system are considered to be the major contributors to this phenomenon the underlying physiological processes are not yet fully understood.

The amount of toughening, TS_R, defined as the difference in TS measured following the first and last exposures, was shown by Hamernik et al. (1994) to be dependent on the level of the interrupted noise. Using levels of impact noise that varied between 115 and 127 dB peak SPL, they showed large toughening effects at the lowest levels and little or no toughening at the highest. Each of the toughening stimuli used produced some sensory cell loss. Boettcher et al. (1992) and Hamernik and Ahroon (1998) also reported significant sensory cell loss in the toughened cochlea as a result of the toughening stimulus.

The auditory system, toughened by an interrupted noise exposure, has been shown in a number of studies (see McFadden et al. (1997) for a comprehensive review) to be protected to some extent from a subsequent traumatic exposure. There are, however, several reports that show either no protective effects (e.g. Miller et al., 1963) or a protective effect only on the temporary threshold shift (TTS) component of a TS (Ahroon and Hamernik, 1999; White et al., 1998). Since different species and noise parameters have been used, such dif-

* Corresponding author. Tel.: +1 (518) 564 7700; Fax: +1 (518) 564 7827; E-mail: roger.hamernik@plattsburgh.edu

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ferences in results might be expected. The purpose of the experiment reported here was to determine if an auditory system with a small but stable noise-induced hearing loss (NIHL), could be toughened by an interrupted exposure paradigm known to produce large and consistent toughening across a broad range of frequencies. The experiment is also germane to the issue of the damaged ear theory of Davis et al. (1950) and the more recent experiments reported by Mills (1992).

2. Methods

Chinchillas (1–2 years old) were used as the experimental subjects. Each animal was made monaural by the surgical destruction of the left cochlea. Brainstem (inferior colliculus) auditory evoked potentials (AEPs) were used to estimate pure-tone thresholds and surface preparation histology was used to quantify sensory cell populations. Additional methodological details can be found in Ahroon et al. (1996).

2.1. Noise exposures

All the exposures consisted of narrow band impacts (NBI) 400 Hz wide, having a 1 kHz center frequency, presented at the rate of 1 impact/s. All noise stimuli were generated digitally using a virtual instrument developed using the LabView™ software package. A fixed-length pulse was fed through a fourth order, band-pass Butterworth filter. The resulting waveform was played though the computer's (Macintosh Quadra 840 AV) sound output and fed to an AB International Precedent Series 900A amplifier. The output of the amplifier was fed to a JBL Model 2445J speaker with model 2360H horn and Model 2360T transition piece. Fig. 1 shows the relative spectrum and temporal waveform of the 115 dB peak SPL NBI. Waveforms and spectra at the 121 dB peak SPL level were qualitatively similar.

During exposure, individual chinchillas were confined to cages (10×11×16 inches) with free access to food and water. A maximum of six animals was exposed at a time. Peak SPLs in the exposure field were uniform to within 2 dB. The four groups of animals were exposed to one of the following impact presentation protocols:

- Group 1 ($n=12$): the 121 dB traumatic exposure followed after 30 days by the 115 dB toughening exposure (trauma/toughening group).
- Group 2 ($n=12$): the 115 dB toughening exposure followed after 30 days by the 121 dB traumatic exposure (toughening/trauma group).
- Group 3 ($n=10$): the traumatic exposure; 121 dB peak SPL, 24 h/day for 5 days.

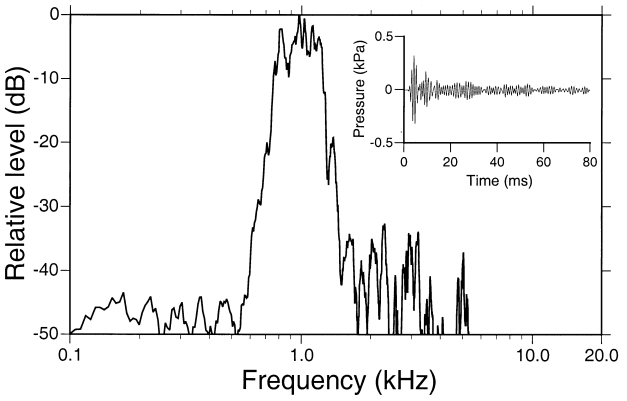

Fig. 1. The spectrum and temporal waveform of the 115 dB peak SPL impact that was used as the toughening stimulus. The 121 dB peak SPL narrow-band impact that was used as the traumatizing noise had a spectrum and waveform that was qualitatively similar to the 115 dB peak SPL impact.

- Group 4 ($n=6$): the toughening exposure; 115 dB peak SPL, 6 h/day for 10 days.

It should be noted that the number of animals in control Groups 3 and 4 was reduced relative to the experimental groups. The same two exposure paradigms used for Groups 3 and 4 were used in previously reported work (Hamernik and Ahroon, 1998) with nine animals per group and produced essentially the same results that were found in Groups 3 and 4. Thus, an effort was made to minimize the number of animals used without sacrificing the value of the controls.

2.2. Threshold testing

Thresholds for all AEP audiograms were measured at octave intervals from 0.5 to 16.0 kHz. The mean (in dB SPL) of three threshold determinations measured on different days defined each animal's pre-exposure audiogram. For the 10-day interrupted exposure paradigm, a complete audiogram was measured immediately prior to the first exposure and following the first and last two daily 6 h exposures in order to quantify the magnitude of the toughening phenomenon. The amount of TS_R, at each audiometric test frequency, was defined as the difference between the threshold measured at a given frequency following the first day exposure and the mean of the thresholds measured following exposure on days 9 and 10.

A complete audiogram was measured once daily during each of the five exposure days of the uninterrupted (traumatic) exposures and the average (in dB SPL) taken over the five days established the mean asymptotic threshold levels and shifts (ATS). Thirty days following each exposure protocol for each experimental group, three AEP audiograms were measured again on differ-

ent days and averaged for each animal to establish the stable or permanent postexposure threshold levels and shifts (PTS).

2.3. Histology

Thirty days following the final noise exposure and after the last AEP test protocol, each animal was killed, under anesthesia, and the right auditory bulla removed and opened to gain access to the cochlea for perfusion. Fixation solution consisting of 2.5% glutaraldehyde in veronal acetate buffer (final pH = 7.3) was perfused through the cochlea. After 12–24 h of fixation the cochlea was postfixed in 1% OsO_4 in veronal acetate buffer. Surface preparation mounts of the entire organ of Corti were prepared and inner and outer hair cell (IHC, OHC) populations were plotted as a function of frequency and location using the frequency–place map of Eldredge et al. (1981). Missing cells were identified by the characteristic phalangeal scars which form in the 30-day period prior to death. For the purpose of this presentation, sensory cell population data is presented as group averages (in percent missing) taken over octave band lengths of the cochlea centered on the primary AEP test frequencies.

2.4. Statistical analysis

The dependent variables reported in this paper are (1) AEP thresholds and threshold shifts, before, during and following noise exposure(s) and (2) sensory cell losses in octave-band lengths of the cochlea. Comparisons of groups of animals receiving different treatments were accomplished by mixed model analyses of variance with repeated measures on at least one factor (frequency). The probability of a type I error was set at 0.05 for all analyses. Statistically significant main effects of frequency are expected in most of the following analyses because of the frequency-specific nature of not only the chinchilla audiogram (Fay, 1988) but also of the noise stimuli. For this reason any main effects of frequency will not be repeatedly discussed in the following presentation of results. Analysis of variance summary tables may be obtained from the authors.

2.5. Animal care

The care and use of the animals used in this study were approved by the Plattsburgh State University of New York Institutional Animal Care and Use Committee. In conducting the research described in this report, the investigators adhered to the Guide for Care and Use of Laboratory Animals, as promulgated by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Resources Commission on Life Sciences, National Academy of Sciences-National Research Council, revised 1985.

3. Results

In some of the following figures the shaded region on the AEP audiograms represents the mean normative AEP audiogram (±1 S.D.) based on a population of 924 chinchillas. The bars on the data points in each figure represent one standard error of the mean; where no bar is shown the standard error was less than the size of the datum symbol.

The initial group mean thresholds for each of the groups is shown in Fig. 2. In general, the group mean thresholds fall within ±1 S.D. of laboratory norms. Statistical analyses indicated that there were significant differences among the groups as a result of the approximately 10 dB spread in thresholds at 1, 4 and 16 kHz.

Fig. 3 shows the group mean ATS, PTS and sensory cell loss for the trauma-only control, Group 3. Also shown in the upper panel, for the Group 1 (trauma/toughening) animals, is the mean ATS measured over the course of the 5-day traumatic exposure and the mean PTS measured 30 days following the same traumatic exposure (i.e. immediately prior to the toughening exposure of the Group 1 animals). Fig. 3 demonstrates the similarity in the response of Groups 1 and 3 to only the traumatizing noise. (Since the Group 1 animals will be receiving a toughening exposure 30 days following the traumatic exposure their sensory cell population is not shown in Fig. 3.) The traumatic exposure produced on the order of 40 to 60 dB ATS in the two groups. A two-way ANOVA with repeated measures on one factor (frequency) indicated no statistically significant differences between the two groups. There was,

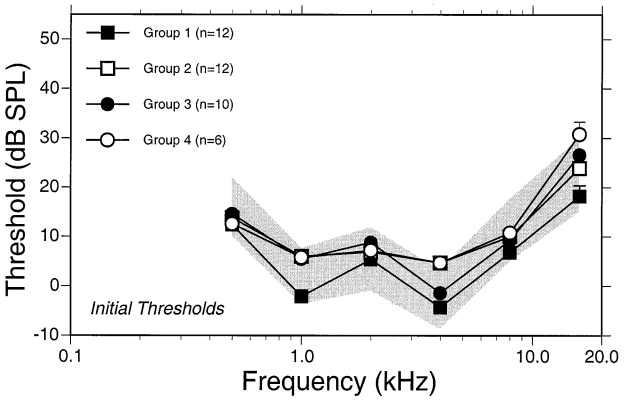

Fig. 2. Initial mean thresholds for the two experimental Groups 1 and 2 and the two control Groups 3 and 4 measured prior to any noise exposures. The shaded area represents the mean preexposure thresholds ±1 S.D. from the laboratory norm based on 924 chinchillas.

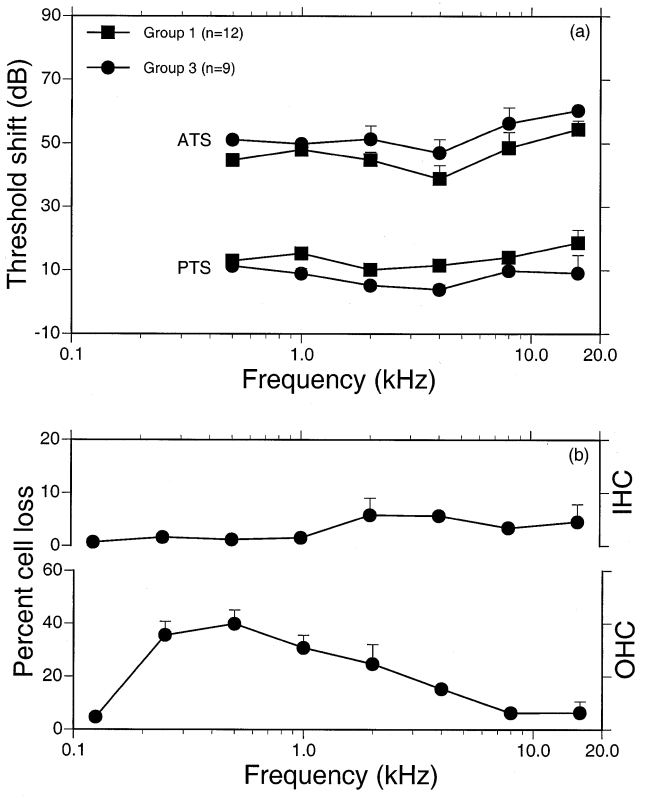

Fig. 3. (a) Group mean asymptotic threshold shift (ATS) and permanent threshold shift (PTS) in the Group 1 (trauma/toughening) and Group 3 (trauma-only) animals that were exposed to the traumatic noise. (b) Group mean outer and inner hair cell (OHC, IHC) losses in the trauma-only control Group 3 animals.

however, a statistically significant main effect of group in the PTS analysis indicating that the Group 1 animals had a significantly greater PTS (<10 dB). This is clearly seen in Fig. 3a. Thus, the Group 1 animals that will receive, in 30 days, the toughening exposure had a slightly greater PTS than the trauma-only control group. The mean PTS in the control Group 3 did not exceed 10 dB. This loss was accompanied by the moderate (up to 40%) OHC loss between 0.25 and 2.0 kHz shown in Fig. 3b. Group 3 also showed a small but larger than normal loss of IHCs from 2.0 kHz to the basal end of the cochlea.

Fig. 4 shows the effects of the toughening noise exposure on the toughening-only control Group 4 and on the experimental Group 2 that will receive the traumatic exposure 30 days following the completion of the toughening exposure. The upper panel shows the $TS_R = TS_1 - TS_{9/10}$ for the toughening-only control Group 4 animals and for the experimental Group 2 (toughening/trauma) animals. Both groups show a considerable amount of toughening which varies from about 10 dB at 0.5 kHz to a maximum of over 20 dB at 4 kHz. The primary difference between these two groups is the large amount of toughening seen in the Group 2 animals at 8 kHz although the analysis of variance indicated no statistically significant differences between the two groups. The middle panel shows the PTS for the two groups. There were no statistically significant differences between the groups and both groups returned to normal pretoughening thresholds. Sensory cell losses for the toughening-only control Group 4 are shown in the bottom panel of Fig. 4. There were small ($<10\%$) OHC losses at several frequencies and about a mean loss of 10% IHCs at 8 kHz. These sensory cell losses, while small, are larger than would be expected in non-exposed animals. As indicated in the introduction, sensory cell losses have been reported following some toughening noise exposure paradigms. (Note: problems developed with the AEP plug in one animal in Group 2 just prior to the final 30-day testing. Thus, the sample size in Fig. 4b is $n = 11$.)

Fig. 5 shows the group mean thresholds measured

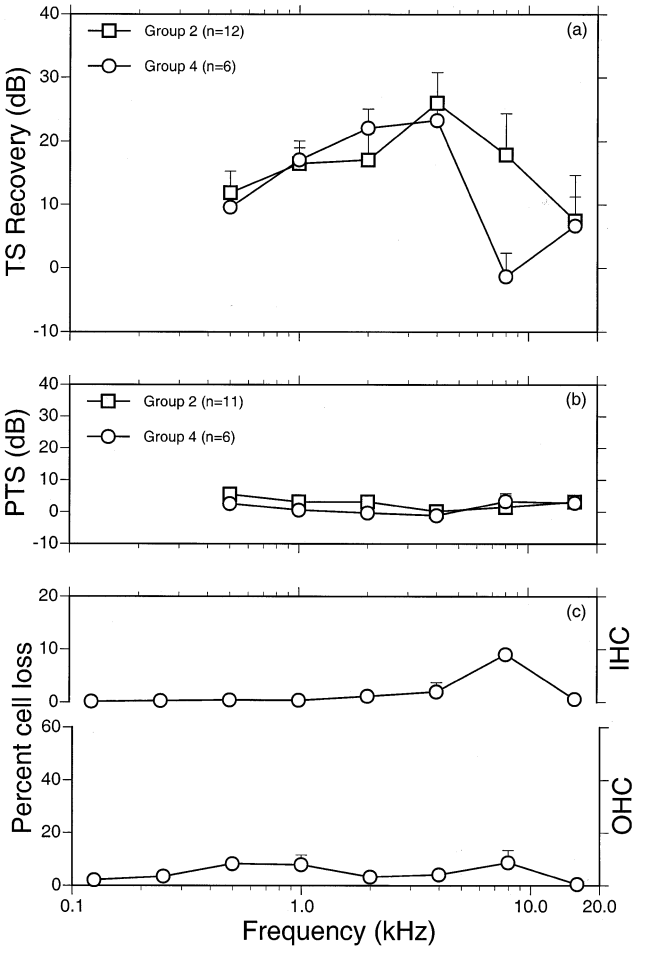

Fig. 4. (a) Group mean threshold shift (TS) recovery and (b) group mean permanent threshold shift in the Group 2 (toughening/trauma) and Group 4 (toughening-only) animals that were exposed to the toughening noise paradigm. (c) Group mean outer and inner sensory cell losses measured 30 days following noise exposure in the Group 4 animals that were only toughened.

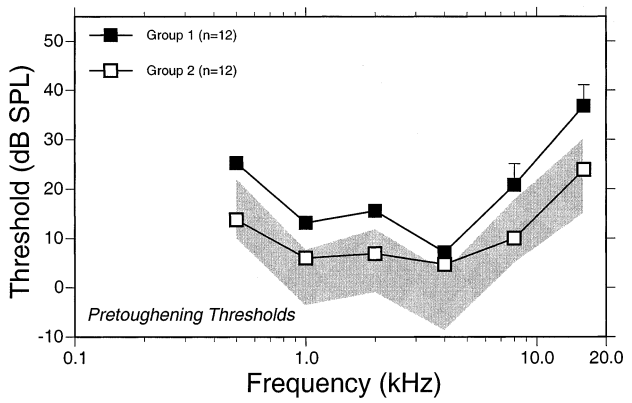

Fig. 5. Mean thresholds of the two experimental groups (Group 1 (trauma/toughening) and Group 2 (toughening/trauma)) measured just prior to the toughening exposure. The shaded area represents the mean preexposure thresholds ±1 S.D. from the laboratory norm based on 924 chinchillas.

just prior to introducing Groups 1 (trauma/toughening) and 2 (toughening/trauma) into the toughening noise. For Group 1 these are the thresholds that reflect the PTS produced by the 5 day traumatic noise that was completed 30 days earlier and shown in Fig. 3a. Thus, the two groups enter the toughening noise exposure with different thresholds, which in the case of the Group 1 animals were elevated by the traumatic noise exposure which yielded a mild PTS. The thresholds for the Group 2 animals are the normal pre-exposure thresholds. Based on the sensory cell loss shown in Fig. 3b for the Group 3, trauma-only animals, we can assume that the Group 1 (trauma/toughening) animals are entering into the toughening exposure with a similar moderate sensory cell loss.

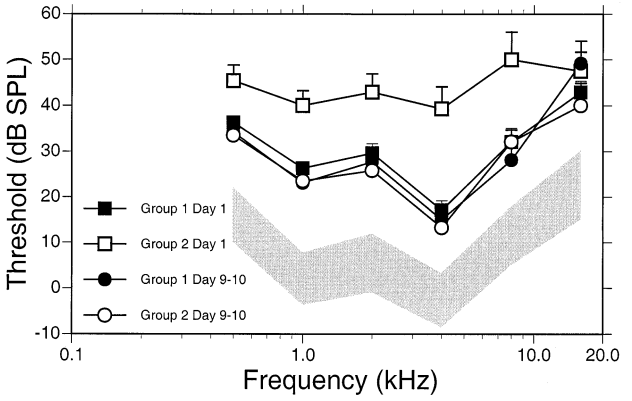

Fig. 6. Group mean AEP thresholds for the two experimental groups (Group 1 (trauma/toughening) and Group 2 (toughening/trauma)) measured immediately following the first 6 h exposure of the toughening noise and the average thresholds measured after the ninth and tenth days of the toughening exposure. The shaded area represents the mean preexposure thresholds ±1 S.D. from the laboratory norm based on 924 chinchillas.

The mean response of the Group 1 animals to the toughening noise is compared in Fig. 6 with the response of the Group 2 (toughening/trauma) animals that have at this point received only the toughening exposure. Fig. 6 shows the absolute thresholds for the two groups measured following the first 6 h daily exposure and the mean thresholds measured after the ninth and tenth day exposure. In Fig. 6, for any frequency, the vertical distance between each pair of open symbols is the amount of toughening measured in the Group 2 animals, while the vertical distance between each pair of filled symbols is a measure of the amount of toughening in the Group 1 animals. It is clear in Fig. 6 that the Group 1 animals (filled symbols) showed no toughening at any frequency. Also, their thresholds following the first 6 h exposure are substantially lower than those of Group 2. The Group 1 animals showed the same thresholds following the first day's exposure as they did after the last two days' exposures and these were the same as the mean Group 2 thresholds measured following the exposures on days 9 and 10.

The results of this set of experiments are summarized in Fig. 7 where the AEP TSs and sensory cell populations for Groups 1, 2 and 3 are shown. There is no

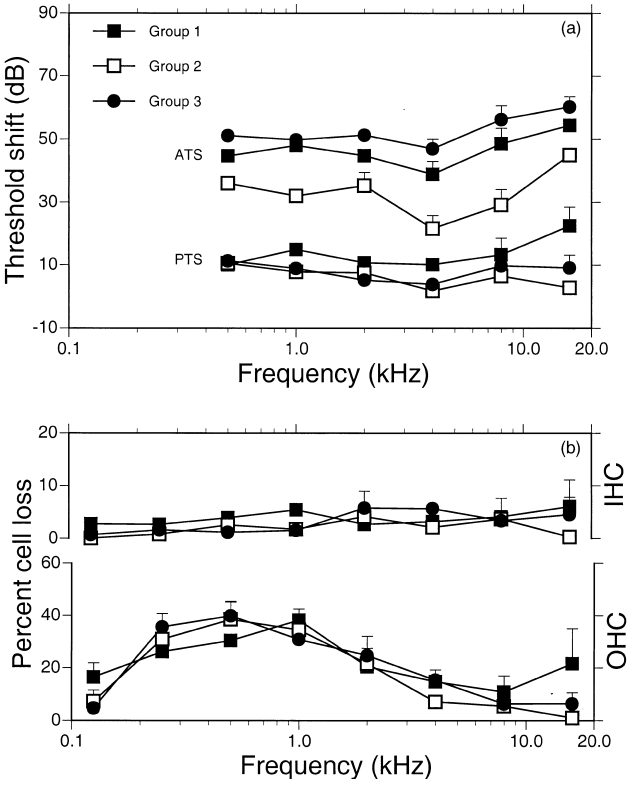

Fig. 7. (a) Group mean asymptotic and permanent AEP threshold shifts and (b) group mean outer and inner sensory cell losses (OHC, IHC) for the groups that received the traumatic exposure; Group 1 (trauma/toughening), Group 2 (toughening/trauma) and Group 3 (trauma-only).

statistically significant difference in the ATS in Groups 1 and 3. That is, the animals that were first traumatized and then given the toughening noise (Group 1) responded to the ATS producing traumatic noise the same way as the trauma-only control Group 3. However, the Group 2 animals that were toughened prior to receiving the traumatizing noise showed a statistically significant reduction in ATS. When the PTS (measured 30 days after all exposures were completed) across these three groups is compared there is a main effect of group and an interaction (i.e. differences in PTS are dependent on frequency). Removal of the 16 kHz data points yields no statistically significant differences among the groups. Comparison of IHC losses across the three groups produces statistical results similar to those reported for PTS (i.e. no significant differences if the 16 kHz data are eliminated from the analysis, otherwise there is a significant group effect and an interaction). There were no statistically significant differences among the OHC losses for the three groups. Thus, the permanent changes in the evoked response audiograms and sensory cell populations were the same in Groups 1, 2 and 3 that were exposed to the traumatic noise, regardless of whether or not the animals were ever subjected to the toughening noise or whether the toughening noise preceded or followed the traumatic noise.

4. Discussion

As indicated in Section 1, a variety of noise stimuli presented in an interrupted exposure paradigm will produce a TS_R. There are, however, a couple of interesting studies in the literature where no TS_R was observed. Saunders et al. (1977) using a 4 kHz octave band of noise (OBN) exposed the same group chinchillas, 6 h/day for 9 days at levels that varied from 57 to 92 dB SPL. The daily cyclic pattern of TS and recovery at a given level was the same each day. There was no evidence of any TS_R. However, Subramaniam et al. (1992) also exposed chinchillas to a 4 kHz OBN at 85 dB SPL, 6 h/day for 10 days and reported a large TS_R.

Using 113 dB peak SPL noise impacts presented 1/s as the stimulus for an interrupted noise exposure paradigm (8 h/day for 5 days) Henderson et al. (1979) showed a cyclic daily pattern of TS and recovery similar to that reported by Saunders et al. In both of these studies the upper bound for the TS that was measured was the ATS that was produced by the same stimulus but presented on an uninterrupted schedule. Hamernik et al. (1994), using impacts similar to those of Henderson et al., but with a 2 h shorter duty cycle, reported a large TS_R. There is arguably no compelling reason why the above two pairs of studies should be in conflict.

Hamernik and Ahroon (1999) exposed chinchillas to a 0.5 kHz OBN at 95 dB SPL, 6 h/day for 10 days in order to produce a TS_R. Their experimental group consisted of 12 animals. They reported that seven of the animals developed large TS_R at a number of test frequencies consistent with other studies in the literature. What was unusual was that five of the animals did not develop a TS_R but rather their daily TSs increased to levels that would be expected from an ATS producing exposure paradigm as reported in Henderson et al. (1979). There was no obvious explanation for this dichotomy in the response to the interrupted noise exposure.

In this present report the Group 1 animals prior to their toughening exposure have a moderate noise-induced PTS (Fig. 5) as a result of their traumatic 5-day exposure and an inferred moderate OHC loss (Fig. 3) that is greatest in the apical half of the cochlea and slowly falls off toward the base. This group shows no TS_R, rather the thresholds measured after the first 6 h exposure and those measured after the ninth/tenth day of the exposure show no statistically significant differences. Further, there are no statistically significant differences between these thresholds and those measured after the ninth/tenth day exposures in the Group 2 animals that received the same toughening exposure but had not yet received the traumatic exposure. Thus, the noise-damaged auditory system has shifted its threshold in response to the toughening noise exposure to the toughened threshold of the undamaged system. While based on a limited data set, it appears that the damaged cochlea will not develop a TS_R. It is interesting that there are interrupted noise exposures that produce a systematic TS_R as a result of a toughening exposure and also generate a PTS and sensory cell loss (Boettcher et al., 1992; Hamernik and Ahroon, 1998), while an auditory system with a moderate preexisting loss (Group 1) could not be toughened. Also note that the toughening-only Group 4 animals shown in Fig. 4a show no TS_R at 8 kHz. This group also showed a moderate OHC and IHC loss ($\sim$10%) at 8 kHz. Since our exposures should not have produced much sensory cell loss in the high frequencies, the 8 kHz losses may have been preexisting. Based on the results of the Group 1 (trauma/toughening) animals, this loss may have contributed to the lack of a TS_R seen at 8 kHz.

In the Group 2 animals that were first toughened and then exposed 30 days later to the traumatic noise the ATS was significantly lower than in the control Group 3 and the Group 1 animals (Fig. 7). However, despite the lower ATS in Group 2 there was no statistically significant difference in the PTS in Groups 1, 2 and 3 for frequencies between 0.5 and 8.0 kHz. The sensory cell loss data shown in Fig. 7b is in general agreement with the AEP audiometric data in that there is no sub-

stantial difference in the sensory cell losses among these three groups.

A compound threshold shift (CTS), which is measured after a traumatic noise exposure including those producing an ATS, is considered to consist of TTS and PTS. The data presented in Figs. 6 and 7 would suggest that there is a physiological process, responsible for a component of TTS, that is subject to manipulation by some noise exposures. The extent to which this manipulation of the absolute magnitude of a CTS results in a protective effect (i.e. less PTS and sensory cell loss from a subsequent traumatic exposure) is not clear. A number of studies using a toughening paradigm have shown consistent protective effects (e.g. McFadden et al., 1997; Subramaniam et al., 1993; Campo et al., 1991). Our results using impact noise, while showing clear toughening effects, that is a TS_R, have not shown protective effects (Hamernik and Ahroon, 1998, 1999; Ahroon and Hamernik, 1999). An obvious difference between our work and others referenced is our use of high-level impact noise which may have different or more subtle damaging effects on the sensory structures of the cochlea. Such damage which would not be reflected in the cochleogram, may be sufficient to cause the cochlea to no longer be susceptible to the protective effects of a 10 to 30 dB TS_R. However, Henselman et al., 1994, using 150 dB peak SPL impulses to produce a trauma showed that the toughened cochlea develops a large protective effect. Thus, level and stimulus type would not appear to offer a convincing explanation of the above differences in results. Additional discussion of this issue can be found in Hamernik and Ahroon (1999).

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References

Ahroon, W.A., Hamernik, R.P., 1999. Noise-induced hearing loss in the noise-toughened auditory system. Hear. Res. 129, 101–110.

Ahroon, W.A., Hamernik, R.P., Lei, S.-F., 1996. The effects of reverberant blast waves on the auditory system. J. Acoust. Soc. Am. 100, 2247–2257.

Boettcher, F.A., Spongr, V.P., Salvi, R.J., 1992. Physiological and histological changes associated with the reduction in threshold shift during interrupted noise exposure. Hear. Res. 62, 217–236.

Campo, P., Subramaniam, M., Henderson, D., 1991. The effect of 'conditioning' exposures on hearing loss from traumatic exposure. Hear. Res. 55, 195–200.

Clark, W.W., Bohne, B.A., Boettcher, F.A., 1987. Effects of periodic rest on hearing loss and cochlear damage following exposure to noise. J. Acoust. Soc. Am. 82, 1253–1264.

Davis, H., Morgan, C.T., Hawkins, J.E. et al., 1950. Temporary deafness following exposure to loud tones and noise. Acta Otolaryngol. 88 (Suppl.), 1–57.

Eldredge, D.H., Miller, J.D., Bohne, B.A., 1981. A frequency–position map for the chinchilla cochlea. J. Acoust. Soc. Am. 69, 1091–1095.

Fay, R.A., 1988. Hearing in Vertebrates. Hill-Fay Associates, Winnetka, IL.

Hamernik, R.P., Ahroon, W.A., 1998. Interrupted noise exposures: threshold shift dynamics and permanent effects. J. Acoust. Soc. Am. 103, 3478–3488.

Hamernik, R.P., Ahroon, W.A., 1999. Susceptibility of the noise toughened auditory system to noise-induced trauma. Hear. Res. 132, 140–148.

Hamernik, R.P., Ahroon, W.A., Davis, R.I., Lei, S.-F., 1994. Hearing threshold shifts from repeated 6-h daily exposure to impact noise. J. Acoust. Soc. Am. 95, 444–453.

Henderson, D., Hamernik, R.P., Hynson, K., 1979. Hearing loss from simulated work-week exposure to impulse noise. J. Acoust. Soc. Am. 65, 1231–1237.

Henselman, L.W., Henderson, D., Subramaniam, M., Sallustio, V., 1994. The effect of 'conditioning' exposures on hearing loss from impulse noise. Hear. Res. 78, 1–10.

McFadden, S.L., Henderson, D., Shen, Y.H., 1997. Low-frequency 'conditioning' provides long-term protection from noise-induced threshold shifts in chinchillas. Hear. Res. 103, 142–150.

Miller, J.D., Watson, C.S., Covell, W.P., 1963. Deafening effects of noise on the cat. Acta Otolaryngol. 176 (Suppl.), 1–91.

Mills, J.H., 1992. Noise-induced hearing loss: Effects of age and existing hearing loss. In: Dancer, A.L., Henderson, D., Salvi, R.J., Hamernik, R.P. (Eds.), Noise-Induced Hearing Loss. Mosby Yearbook, St. Louis, MO, pp. 237–245.

Saunders, J.C., Mills, J.H., Miller, J.D., 1977. Threshold shift in the chinchilla from daily exposure to noise for six hours. J. Acoust. Soc. Am. 61, 558–570.

Subramaniam, M., Campo, P., Henderson, D., 1991. The effect of exposure level on the development of progressive resistance to noise. Hear. Res. 52, 181–188.

Subramaniam, M., Henderson, D., Campo, P., Sponger, V.P., 1992. The effect of 'conditioning' on hearing loss from a high frequency traumatic exposure. Hear. Res. 58, 57–62.

Subramaniam, M., Henderson, D., Sponger, V.P., 1993. Protection from noise induced hearing loss: is prolonged 'conditioning' necessary? Hear. Res. 65, 234–239.

White, D.R., Boettcher, F.A., Miles, L.R., Gratton, M.A., 1998. Effectiveness of intermittent and continuous acoustic stimulation in preventing noise-induced hearing and hair cell loss. J. Acoust. Soc. Am. 103, 1566–1572.