Individual Susceptibility to Noise-Induced Hearing Loss: An Old Topic Revisited

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Abstract

The wide range in susceptibility to noise-induced hearing loss has intrigued researchers and hearing conservationists alike. Some of these differences in variability have been attributed to various intrinsic factors such as eye color, gender, age, etc. However, a review of controlled research shows that the influence of these intrinsic variables is relatively small and cannot explain the wide range of hearing loss observed in demographic studies. Furthermore, uncontrolled variables or unrecognized drug and noise interaction may obscure the relation between noise exposure and hearing loss. With the growing understanding of the physiology of the auditory system, new possibilities are emerging that may explain the range of susceptibility. A review of the role of acoustic reflex effectiveness, cochlear efferent function, and history of noise exposure provide a perspective for future strategies in predicting susceptibility to noise-induced hearing loss.

Audiologists and otologists have for a long time recognized the threat to the auditory system from exposure to high levels of noise. Over 9 million Americans are exposed to noise levels of 85 dB or higher on their job (EPA, 1981) and are, therefore, at risk of developing noise-induced hearing loss (NIHL). There are a large number of people who are exposed to dangerous levels of noise in recreational activities, although it is difficult to assess their number. Well-controlled large scale demographic studies show that not all individuals exposed to a given noise develop the same degree of hearing loss. A particularly dramatic example for the wide range in susceptibility to NIHL comes from the Taylor, Pearson, Mair, and Burns (1965) study of a group of weavers. This is a very informative study because each of the weavers had a relatively well-documented history of exposure to noise, the noise conditions were stable throughout their work history, and they were all screened for otological or medical conditions. In spite of the homogeneity of the group and the careful approach, the data as seen in Figure 1 are characterized by extreme variability. For instance, at 3 kHz, there is a relatively even distribution of hearing loss from 10 to 70 dB HL.

Other demographic studies report equal or greater degrees of variability (Burns & Robinson, 1970; Passchier-Vermeer, 1973). Surprisingly, controlled laboratory studies of temporary threshold shift (TTS) (Davis, Morgan, Hawkins, Galambos, & Smith 195) and permanent threshold shift (PTS) in experimental animals (Henderson & Hamemik, 1988) often report similar ranges of variability. Thus, it is reasonable to assume that there is a wide range of biological factors contributing to susceptibility to NIHL. Furthermore, an interaction of other environmental agents with the noise exposure may also influence the effect of a given noise exposure. The interaction effects of such biological and environmental factors has been the focus of several papers (Boettcher, Henderson, Gratton, Danielson, & Byrne, 1987; Humes, 1984; Humes & Jesteadt, 1991). Further, the National Institutes of Health consensus report (1990) outlines some of these factors and discusses other issues relevant to the study of NIHL. Some of these factors are briefly reviewed here. However, the primary focus of this article is to review some of the recent developments in our understanding of basic auditory processes and possible mechanisms involved in determining an individual's susceptibility to NIHL and to suggest some strategies in developing future tests in predicting the susceptibility to NIHL.

Approaches to Predicting NIHL

After World War II, the U.S. government became concerned about the exceptionally high incidence of permanent sensorineural hearing loss among the returning soldiers. One of the first steps was to commission extensive laboratory studies of experimentally induced TTS in human subjects. The paper, "*Temporary Deafness Following Exposures* to Tone and Noise," by Davis et al (1950) is the report of a series of experiments on the relation between frequency, level and duration of the exposure and the resultant hearing loss, changes in loudness, diplacusis, and tinnitus. Because the experimentally induced temporary changes in hearing parallelled the reports

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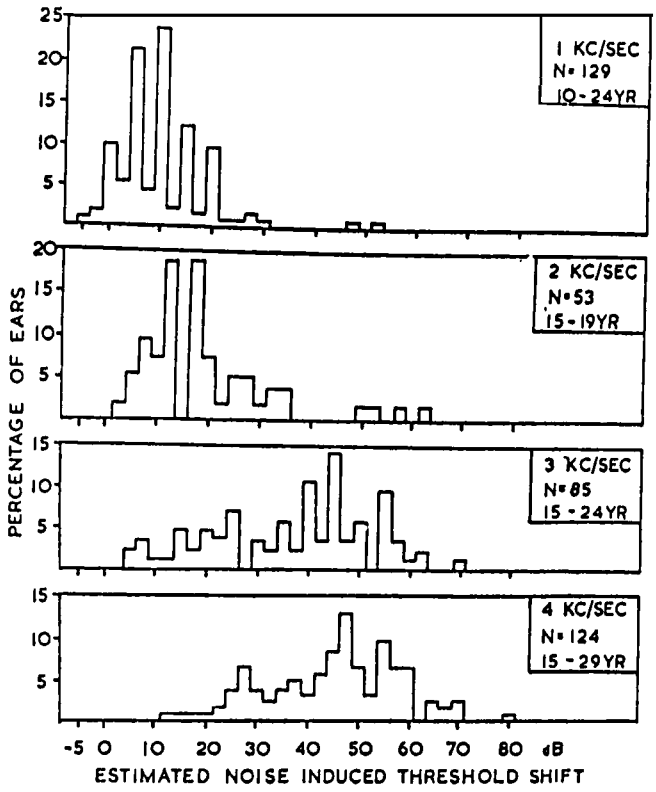

FIGURE 1. Distribution of hearing loss in a group of workers from a weaving industry (Taylor et al, 1965).

from field studies of NIHL, the assumption was made that there was a high correlation between TTS and PTS.

Given the assumed relation between TTS and PTS, it was hypothesized that an individual's TTS after a controlled exposure could be used to predict his vulnerability to PTS from longer or more intense exposures. Specifically, individuals who show extreme reactions to noise exposures that produce TTS would also suffer proportionately greater amounts of PTS from more severe exposures. This was an attractive idea that was expanded and formalized in to the National Academy of Sciences and National Research Council's position in evaluating noise exposures (Kryter, 1973). However, as Ward and Turner (1982) and Ward (1983) point out, the suitability of TTS measures in predicting PTS is questionable, especially in the case of interrupted and impulse noise exposures. In the few experimental studies that provide a direct perspective on the correlation between TTS and PTS within the same subjects, Henderson, Hamerink, and Sitler (1974) reported that the degree of TTS immediately after an exposure was not a good predictor of the eventual PTS. A compromise solution was offered by Kraak (1981), who proposed to predict PTS from the integrated value of TTS at several times after a noise exposure. Although Kraak's approach has theoretical advantages, it is not practical to make multiple threshold determination for several days after a noise exposure.

Today, use of TTS tests to assess susceptibility to PTS is not seriously advocated, primarily because of the ambiguous correlation between TTS and PTS and the possible threat of litigation from producing even small amounts of temporary hearing loss.

Nonauditory Predictors of Susceptibility

Certain nonauditory intrinsic factors may influence an individual's susceptibility to NIHL. Intrinsic factors that have been implicated in affecting the susceptibility include eye color, gender, age, and smoking, among others.

Eye Color

Eye color as a factor affecting susceptibility to NIHL was studied by Carter (1980) and Carlin and McCrosky (1980). There were some trends in the data suggesting that blue-eyed individuals may be more susceptible to NIHL than subjects with greater melanin content in their eyes. However, the differences were small and limited to specific frequencies.

Gender

At least two studies have reported substantial differences in susceptibility to NIHL between men and women. After 9 yr of exposure to a noise at 97 dB (A), Gallo and Glorig (1964) observed a 20 dB difference in the noise-induced permanent threshold shift (NIPTS) between men and women. Likewise, Berger, Royster, and Thomas (1964) observed a 20 dB difference (after correcting for aging) between male and female workers exposed to a noise with a L_{eq} of 89 dB for 9 yr, with men incurring greater hearing loss than women. However, it is unclear if these were inherent biological differences in their response to noise or were merely a reflection of differences in the lifestyles. Given the current awareness of gender differences in several health problems, well-controlled studies are warranted to address this question.

Age

In demographic studies, age is a potentially important variable for long duration exposures (20-40 yr) where the interaction of presbycusis and NIHL is possible. There are indications that subjects in either end of the age continuum appear to have increased susceptibility to NIHL.

Sensitivity Period. Bock and Seifter (1978) reported

that during development, hamsters exhibit increased susceptibility to NIHL. This increase in susceptibility is seen in TTS as well as PTS. Likewise, Lenoir, Bock, and Pujol (1979) reported change in susceptibility with age, with the greatest susceptibility being on postnatal ages of 16 through 40 days. Similar observations were made by Henry (1984a,b) using mice. He reported that the sensitivity period in these animals was the second month of life, whereas their cochleas may reach maturity at 1 mo (Shnerson & Pujol, 1983).

Price (1976) compared the susceptibility of young kittens and adult cats to NIHL. All the animals were subjected to a 5 kHz pure tone for 50 min. Changes in CM were measured to assess the hearing loss. Price observed that the young and the adult animals were equally susceptible up to a critical range of intensities beyond which the younger animals were more vulnerable.

The "sensitive period" data come from animal models where the development of the auditory system is incomplete at birth and proceeds after birth. On the other hand, the development of the human auditory system is complete by 18th week of pregnancy and the maturation is complete in the last trimester. Pujol (1992) has suggested that the latter would therefore correspond to the "sensitive period." Exposure to noise in utero may result in hearing loss in the child. Daniel and Laciak (1982) reported that 35 of the 75 infants born to mothers exposed to noise in a weaving industry (noise level of 100 dB) showed high-frequency hearing loss. Similarly, Lalande, Hetu, and Lambert (1986) reported a threefold increase in the risk of hearing loss in children born to mothers exposed to 85 to 95 dB of industrial noise. Furthermore, they observed a correlation between low-frequency noise exposure and hearing loss at 4 kHz. Although these results are very important and highly relevant for early identification, they must be interpreted cautiously until more controlled, laboratory studies confirm their findings.

Aging. The effect of aging on hearing loss has been a subject of debate. McCrae (1971) reported that older subjects exposed to noise had greater hearing loss than younger subjects. On the other hand, Henry (1982) reported that aged mice were less susceptible than young adult mice. In a recent study, Shone, Altschuler, Miller, and Nuttall (1991) observed that mice with presbycusis were more susceptible to NIHL than age-matched controls with no hearing loss. Aged animals without presbycusis had the same susceptibility as the younger subjects. Likewise, Mills (1992) reported an additive effect of presbycusis on NIHL. Given that the aging/noise literature is not definitive, there is no compelling reason to expect that older subjects are at an increased risk to incur NIHL.

Smoking

Individuals who smoke may be more susceptible to noise than those who do not. Chung, Wilson, Gannon, and Mason (1982) hypothesized that the increased susceptibility may be due to carbon monoxide in the smoke, and they estimated that smoking increased the level of PTS in a population of workers by about 3 to 6 dB. Recently, Prince and Matanoski (1991) reported that a history of smoking increased the predicted rate of hearing loss over time for workers exposed to high occupational noise levels. The relation between smoking and hearing loss is difficult to establish because of the numerous health problems associated with smoking.

Thus, several nonauditory characteristics of the individual may contribute to his/her hearing loss from exposure to noise. However, results of research in these areas are equivocal, and the effects, if any, can only account for a small part of the large variability in NIHL.

Confounding Factors in Population Studies

Recent research has strongly hinted that some of the variability seen in large scale demographic studies may be related to unrecognized interactions with certain drugs or uncontrolled interactions with other physical factors in the work place.

Ototoxic Drugs

The effects of ototoxic drugs have been discussed in depth elsewhere (Boettcher, Gratton, Bancroft, & Spongr, 1992). At least five categories of ototoxic drugs have been identified: aminoglycoside antibiotics, anti-neoplastic agents, loop-inhibiting diuretics, salicylates, and quinine compounds. Loop-inhibiting diuretics do not appear to increase NIHL (Vernon, Brummet, & Brown, 1978; Kisiel & Bobbin, 1982) and the effects of quinine toxicity on NIHL is yet unclear. However, there is clear evidence that noise-induced damage is exacerbated by certain aminoglycoside antibiotics and antineoplastic agents.

Aminoglycoside antibiotics are potent antibacterial agents used against gram negative infections. Some of these drugs are known to be ototoxic and/or vestibulotoxic. Physiological and histological data show that the noise-induced hearing and hair cell losses are increased by concurrent administration of gentamicin, kanamycin, and neomycin

(Brown, Brummett, Meikle, & Vernon, 1980; Dayal, Koksanian, & Mitchell, 1971; Dodson, Bannister, & Douek, 1982; Gannon, Tso, & Chung, 1979; Jauhianien, Kohoren, & Jauhianien, 1972; Ryan & Bone, 1982). For a given level of noise exposure, Brown et al (1980) reported a "threshold dose" of interaction such that kanamycin doses below the threshold did not exacerbate the noise-induced damage. Interestingly, there is some evidence that noise exposure followed by kanamycin administration caused more histological damage than concurrent exposure to the two agents (Ryan & Bone, 1982).

Cisplatin, a common antineoplastic agent, causes hearing and hair cell loss similar to the aminoglycoside antibiotics. Gratton, Salvi, Kamen, and Saunders (1990) studied the interaction effects of noise and cisplatin using seven groups of chinchillas. One group was exposed to cisplatin alone. Three groups were exposed to a 0.5 kHz octave band noise (OBN) alone (at 70, 85, or 100 dB SPL). The remaining three groups were exposed to noise and were also administered cisplatin. Although cisplatin alone resulted in little or no hearing loss, it did interact with noise to increase the amount of hearing loss significantly (Fig. 2). Animals being treated with cisplatin were, thus, more vulnerable than animals exposed to noise alone. This is an important finding because it is possible for workers to receive cisplatin on an outpatient basis and be exposed to noise at the workplace.

The exacerbating potential of salicylates on NIHL is controversial. Eddy, Morgan, and Carney (1976) observed that chinchillas receiving salicylates and noise exposure incurred greater hearing loss than those exposed to noise alone. Likewise, McFadden and Plattsmier (1983) reported an increase in temporary hearing loss from a pure-tone exposure when salicylates were administered. Other studies show no increase in susceptibility to NIHL in animals treated with salicylates. Woodford, Henderson, and Hamerink (1978) observed no significant interaction between salicylates and continuous or impulse noise. Similarly, Bancroft, Boettcher, Salvi, and Wu (1991) observed no increase in TTS or PTS from a 0.5 kHz OBN (85 or 105 dB SPL) when salicylates were concurrently administered. Likewise, hair cell loss resulting from concurrent administration of noise and salicylates was not significantly different from the loss resulting from noise alone. Furthermore, administration of salicylates alone resulted in little or no hair cell loss (Spongr, Boettcher, Saunders, & Salvi, 1992)

In summary, aminogyloside antibiotics and antineoplastic agents like cisplatin can interact significantly with noise, resulting in greater hearing loss than could be caused by either agent alone. On the other hand, salicylates, the more commonly taken drugs, do not appear to markedly increase the risk associated with exposure to noise.

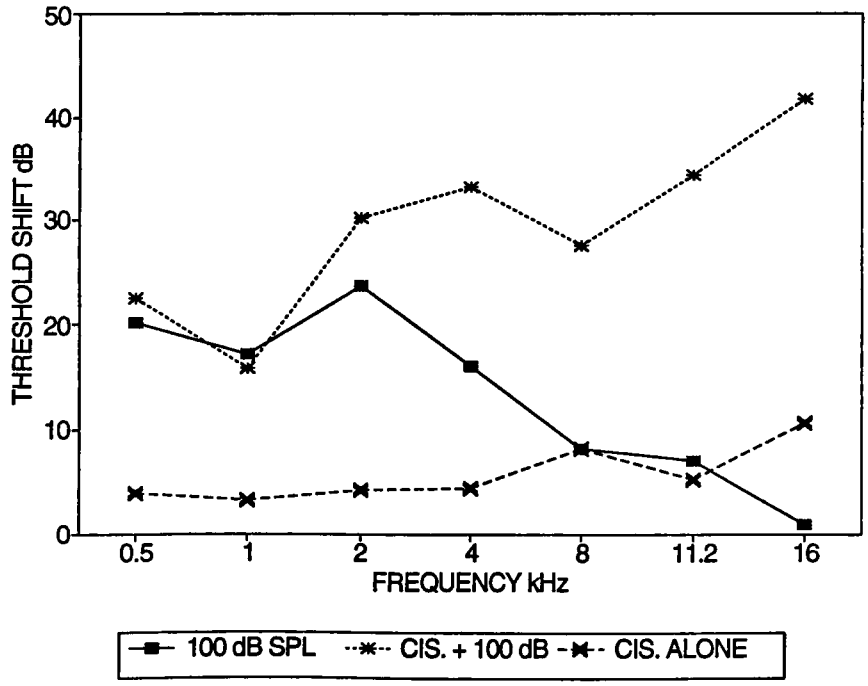

FIGURE 2. Permanent hearing loss from cisplatin or from exposure to 0.5 kHz OBN 100 dB SPL or their combination (redrawn with permission from Gratton, 1989).

Environmental Agents

Many occupational environments are contaminated by both noise and airborne toxins. Recent data suggest that some gaseous toxins may exacerbate the effects of noise. Toluene, a very common solvent (used in paints), is known to cause high-frequency hearing loss (Johnson, Juntunen, Nylen, Borg, & Hogland, 1988; Pryor, Dickinson, Feeney, & Rebert, 1984). Barregard and Axelsson (1984) observed that ship painters exposed to both toluene and high-frequency noise (from air-pressure painting machines) incurred greater hearing loss than would be expected from exposure to the noise alone. Johnson, Nylen, Borg, and Hoglund (1990) reported that rats exposed to toluene (1000 ppm, 16 hr/day, 5 days/week, 2 weeks) and then to noise (100 dB L_{eq}, 10 hr/day, 7 days/week, 4 weeks) incurred greater hearing loss than those exposed to noise alone. Reversal in the order of exposure resulted in no interaction between the two agents.

Similarly, exposure to carbon monoxide (1200 ppm, 210 min) along with noise exposure (broadband, 110 dB for 2 hr) also results in greater hearing loss (15-20 dB at high frequencies) than from noise exposure alone (Fechter, Young, & Carlisle, 1988). Likewise, workers exposed to carbon disulphide (lipid solvent used in manufacturing rayon) showed greater hearing loss from the noise in the factory (86-89 dBA) than workers exposed to same levels of noise alone (Morata, 1989).

Several other substances encountered in the workplace may affect the auditory system. These include lead and trimethyltin (Clerici, Ross, & Fechter, 1991; Fechter, Young, & Nuttall, 1986). However, their potential to interact with noise, and, thereby, alter the susceptibility to NIHL is yet unexplored.

The importance of uncontrolled agents in the population of individuals with NIHL is difficult to assess because of the difficulty in determining the amount of exposure to the chemical pollutant. However, now that we are aware of these interactions of noise and other ototoxic agents, it would be important to account for their influence in future demographic studies.

Auditory Variables Associated with Susceptibility to NIHL

The most common measure of an individual's auditory function is the threshold of hearing. However, as previously discussed, individuals with similar hearing thresholds may not be equally susceptible to NIHL. Noise begins to stress the auditory system only when sound levels exceed the 75 to 85 dB (A) range. When the auditory system is stimulated at these levels and above, both the acoustic reflex and the efferent auditory nervous system are likely to be fully operative. Neither of these mechanisms is a significant factor at threshold levels of response. Thus, it is reasonable to ask if the differences in susceptibility to NIHL may in fact stem from inherent physiological differences in the suprathreshold functioning of the auditory system of the individual. The remainder of the article focuses on the possible relation between individual susceptibility and the effectiveness of acoustic reflex, functioning of the efferent auditory nervous system, and the differences attributable to noise exposure history.

Acoustic Reflex

In addition to their role in attenuating sound during speech production (Borg & Counter, 1989), the middle ear muscles may play a protective role against loud sounds (Kato, 1913) by attenuating the sound transmitted through the middle ear. Moller (1965) recorded the changes in the acoustic transmission when the tensor tympani and the stapedius were activated by electrical stimulation individually and in combination. His results indicated that the tensor tympani caused relatively small changes in transmission and that its effects were restricted to low frequencies. On the other hand, contraction of the stapedius muscle affected transmission of low as well as high frequencies, with the smallest effect being at 2 kHz. Simultaneous contraction of the two muscles were observed to bring about only a slightly greater decrease in transmission than the contraction of the stapedius alone (Moller, 1965).

Using human subjects who could voluntarily contract their middle ear muscles, Reger (1960)

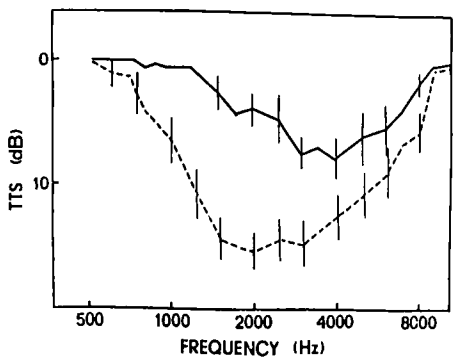

FIGURE 3. The average TS after exposure to noise on the unaffected side (solid line) and affected side (dashed line) in patients with Bell's palsy. Notice that the primary increase in TTS is at mid-frequencies, but there is also a small increase in TTS at higher frequencies (reprinted with permission from Zakrisson et al, 1980)

demonstrated that their contraction could elevate the hearing thresholds by 20 to 30 dB at frequencies below 2 kHz, with the maximum effect at low frequencies (125 and 250 Hz). In other words, the contraction of middle ear muscles acted like a high-pass filter tuned to 2 kHz.

Zakrisson, Borg, Liden, and Nilsson (1980) used subjects with Bell's palsy to examine the role of acoustic reflex in the development of NIHL. Bell's palsy is the result of facial nerve dysfunction and is associated with paralysis of the stapedius muscle. Zakrisson et al exposed their subjects to recorded shipyard noise at 102 dB(A) for 15 min via earphones. Soon after the noise exposure, substantially greater threshold shifts (TS) were recorded on the affected side than on the unaffected side (Fig. 3).

The protective role of the stapedius muscle is not confined to TTS, but also extends to PTS. In an experiment using rabbits, Borg, Nilsson, and Engstrom (1983) deactivated the stapedius on one side of their experimental animals. Each animal was exposed only on one side at a time to high levels of shipyard noise (120, 125, and 130 dB(A), L_{eq} 15 min). Hearing thresholds were monitored using brain stem evoked potentials. Borg et al observed that PTS was 30 to 40 dB greater in the ears with deactivated stapedius muscles than in control ears. On the side with intact stapedius, hearing loss was primarily confined to 0.5 and 1 kHz with a small depression at high frequencies. Ears with denervated stapedius incurred large TS at all the frequencies below 8 kHz. Similar differences were also observed morphologically with extensive hair cell loss in ears with deactivated stapedius.

Colletti and Sittoni (1986) used a more comprehensive evaluation of the acoustic reflex and examined its role in determining the susceptibility to NIHL. In addition to the acoustic reflex threshold, they measured the onset latency, rise time, amplitude, offset latency, and decay time. Their subjects were industrial workers with history of exposure to metallurgic and mechanical noise. Colletti and Sittoni selected three groups of subjects. The first two groups had similar exposure histories (15 yr), but differed in the magnitude of hearing loss. Group A had mild hearing loss that fell between 1 and 2 SD above the average group audiogram for all the workers in the factory (Fig. 4a). The second group (group B) had considerably greater hearing loss than group A, which fell between 1 and 2 SD below the mean. The third group (group C), like group A, had mild hearing loss, but was exposed to the noise for only 5 yr.

Acoustic reflex parameters, including onset time, latency, strength of contraction, adaptation, and decay time (Fig. 4b) were measured for each of these groups. Figure 4, c and d, shows the reflex onset and strength of contraction. All the reflex parameters tested were with in normal limits in the case of group A (Fig. 4, a—d). On the other hand, group B showed abnormalities in reflex threshold as well as in suprathreshold parameters. It may be questioned whether the differences between groups A and B are true differences in the acoustic reflex or are simply a reflection of greater hearing loss in group B. The answer to this question comes from group C, whose hearing loss matched that of group A. Subjects in this group had normal reflex thresholds, but showed abnormalities such as decreased amplitude and faster decay at suprathreshold levels. Thus, the groups with greater hearing loss in relation to the duration of exposure (groups B and C) also showed abnormalities in acoustic reflex. Based on their findings, Colletti and Sittoni (1986) suggested that the stapedius reflex plays an important role in protecting the inner ear against noise.

Colletti and Sittoni (1986) also presented normative data (Fig. 4e) on the distribution of reflex amplitude as a function of stimulus level. Given the large variability, it is an interesting possibility that at least some of the differences in susceptibility might be attributable to differences in the functioning of the acoustic reflex. A study with pre- and postexposure measurements of these parameters using an animal model would help clarify the role of acoustic reflex in determining the susceptibility to NIHL. If the effect is as strong as in Colletti and Sittoni's report, then it may be possible to use some measures of acoustic reflex functioning as predictors of susceptibility to NIHL.

Efferent Auditory Nervous System

Since the pioneering work of Rasmussen (1946, 1953) and Spoendlin (1969), we have been aware of the extensive efferent system in the cochlea. Several studies (Galambos, 1956; Sohmer, 1965; Weiderhold & Peake, 1966) have shown that activation of the efferent system causes an inhibition or reduction in both VIIIth nerve single unit responses and the VIIIth nerve action potential. There has been a renewed interest in the cochlear efferent system and the possible role it may play in NIHL. To appreciate recent research on the efferent system, it is useful to review its anatomy.

The efferent auditory nervous system (EANS) is primarily comprised of the crossed- and uncrossed-

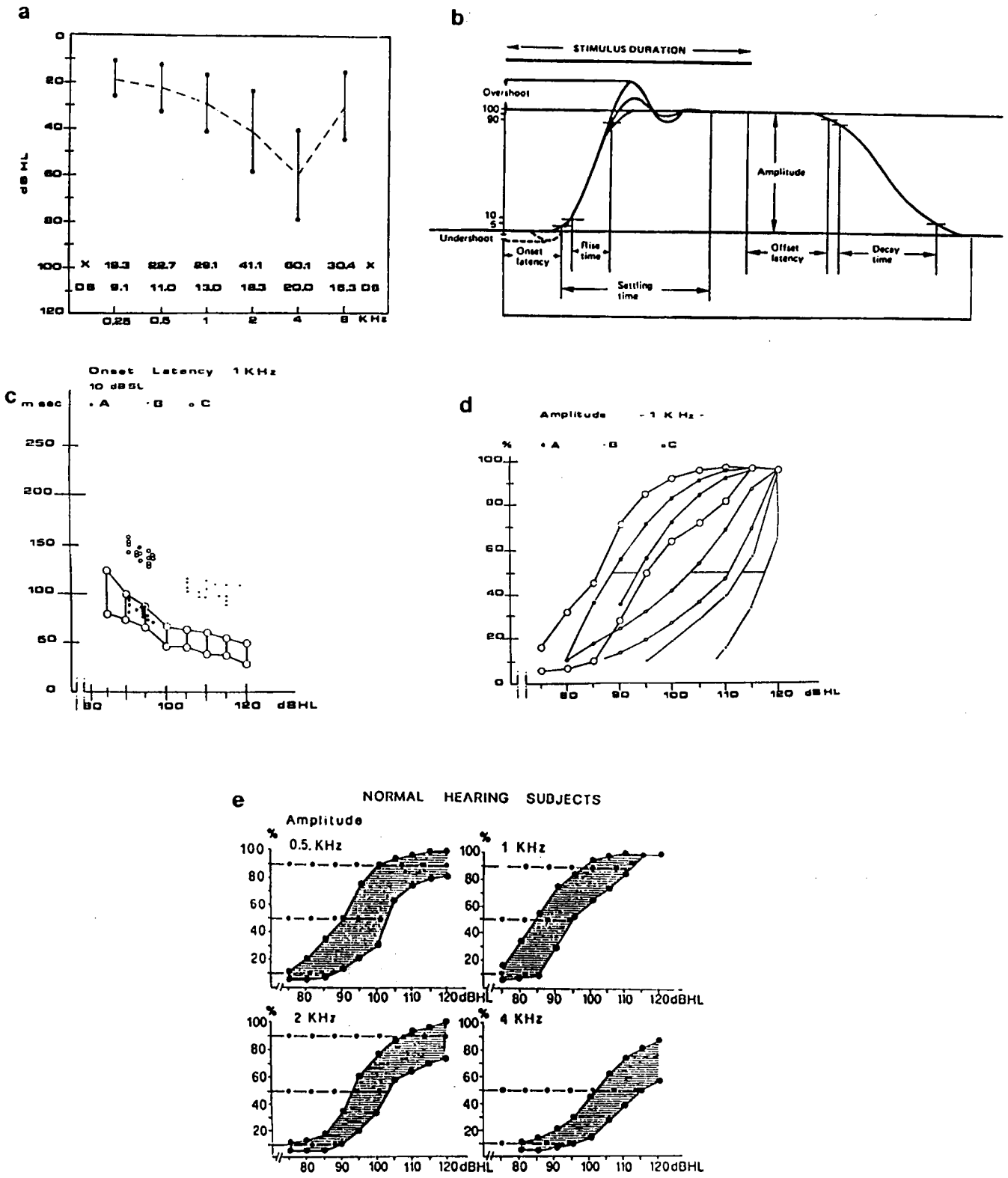

FIGURE 4. (a) Audiogram depicting the mean and SD of thresholds of the workers in Colletti and Sittoni's study.(b) Parameters of acoustic reflex measured in their study. (c) Differences in the onset time of reflex in the three groups. (d) Differences in strength of contraction in the three groups. (e) Range of acoustic reflex thresholds in a group of normal-hearing subjects (reprinted with permission form Colletti & Sittoni, 1986).

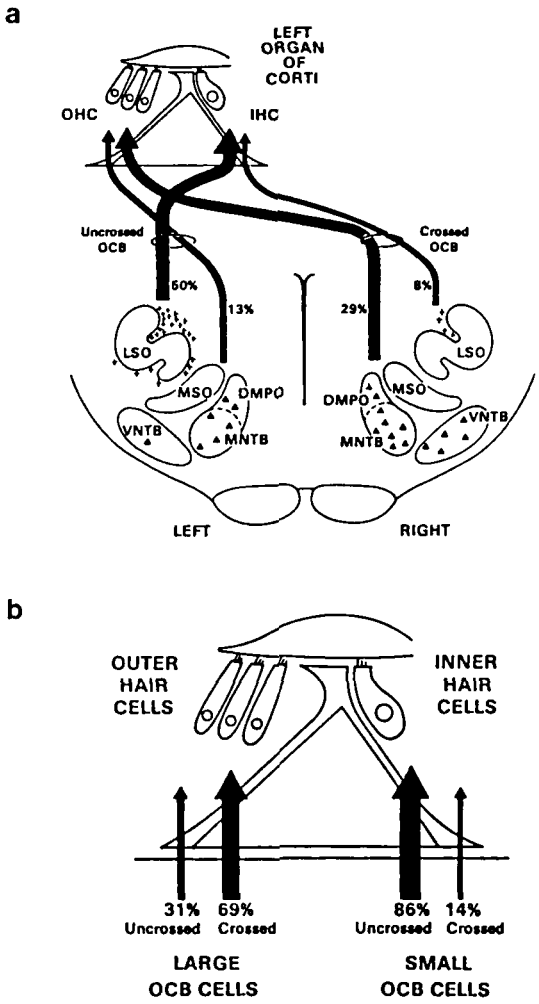

FIGURE 5. (a) Schematic representation of the origins and terminations of the OCB in the cat. Crosses represent small OCB neurons and triangles represent large OCB neurons. Symbols of each kind and the widths of the lines originating from each region are proportional to neuronal contribution. Abbreviations: DMPO, dorsomedial periolivary nucleus; IHC, inner hair cell; LSO, lateral superior olivary nucleus; MNTB, medial nucleus of the trapezoid body; MSO, medial superior olivary nucleus; OCB, olivocochlear bundle; OHC, outer hair cell; VNTB, ventral nucleus of the trapezoid body. (b) The relative proportions of crossed and uncrossed olivocochlear neurons contributing to each of the two efferent synaptic fields within the organ of Corti (reprinted with permission from Warr, 1978).

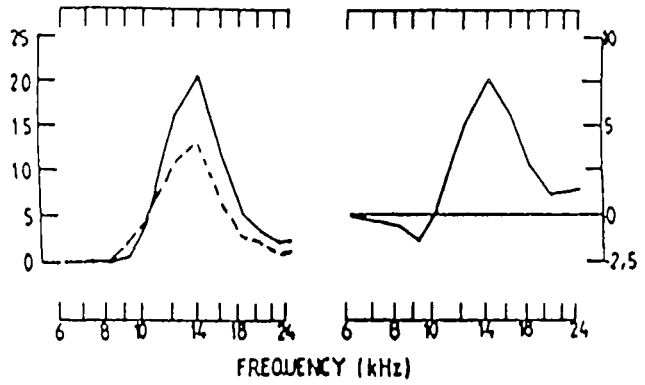

FIGURE 6. TS 5 min after exposure to a 10 kHz pure tone. Control group (solid line) shows substantially more TTS than the experimental group (dotted line) during contralateral stimulation. Y-axis represents the N_1 threshold shift (left) and the differences in TS (right). (reprinted with permission from Rajan & Johnstone, 1983)

olivocochlear bundle (OCB). The origins and the terminations of the OCB in cat as described by Warr (1978) are presented in Figure 5 (a and b). A part of the EANS originates from small fusiform neurons near the lateral superior olivary nucleus (LSO). Another set originates at the large cells near the medial superior olivary nucleus (MSO). Most of the neurons originating at the MSO project to the outer hair cells (OHCs) on the contralateral side, although a small number have ipsilateral projections to OHCs. Neurons from small cells in the LSO project primarily to the ipsilateral inner hair cells (IHCs). Some project to the contralateral IHCs. The dominant efferent innervation on the OHC is part of a reflex arc that begins with the VIIIth nerve, cochlear nucleus, contralateral MSO, and returns to the ipsilateral OHC.

The role of the efferent system in NIHL is still an open question. Trahiotis and Elliot (1970) compared TS from broadband noise exposures at 107 dB in control and experimental animals (cats) with sectioned crossed efferent systems. Results in the two groups were similar except at 4 kHz, where the control animals showed a reduction with repeated exposures, but the experimental animals did not. The difference between the groups being small and the number of subjects being only three in each group renders it difficult to draw any conclusions.

Using a similar approach, Handrock and Zeisburg (1982) studied the role of the EANS on the development of TTS and PTS in guinea pigs. Their experimental group consisted of animals with severed OCB, whereas in the control group, the OCB was intact. Hearing thresholds were determined using compound action potential (CAP) measurements for 1 min, and 8 days after exposure to a 4 kHz OBN, at 120 dB for 5 min. No differences were observed in the TS of the two groups. However, when the level was raised to 125 dB and the duration increased to 30 min, the experimental group manifested greater PTS (40 dB) than the control group (16.6 dB). Handrock and Zeisburg

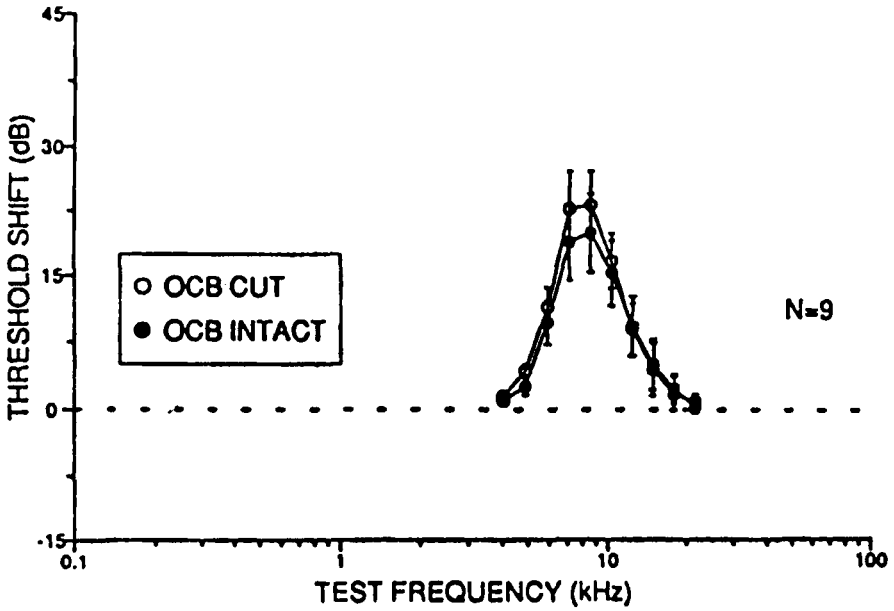

FIGURE 7. Comparison of average TS seen in experimental versus control ears of nine animals unilaterally de-efferented and then binaurally exposed to a 6 kHz tone at 100 dB for 10 min (reprinted with permission from Liberman, 1992).

(1982) concluded that the inhibitory action of the efferent system is in full effect only after extreme strain on the cochlea.

Rajan and Johnstone (1983) reported that TTS from a high-frequency tone (10 kHz at 103 dB SPL for 1 min) can be decreased by contralateral stimulation or contralateral cochlear destruction in guinea pigs (Fig. 6). They suggested that this reduction in TS is attributable to the inhibitory influence of the efferent feedback pathway.

This hypothesis was confirmed by administering strychnine (a nonspecific agent also known to block the EANS). An injection of strychnine abolished the contralateral protective effect, rendering the ipsilateral ear as vulnerable as the control ears. Similar results were obtained when the efferent system was stimulated electrically (Rajan, 1988a,b).

In an experiment using cats, Liberman (1992) could not replicate Rajan and Johnstone's results. To rule out the effect of the acoustic reflex, Liberman cut both the middle ear muscles. The animals were unilaterally de-efferented and were exposed to a 6 kHz tone at 100 dB for 10 min. Liberman observed no significant difference between the TS in the control and experimental ears (Fig. 7). Additional stimulation of the EANS to the control ear using electrical stimulation (to achieve maximum activation) did not result in any difference between the two sides.

More recent evidence (Reiter & Liberman, 1991) suggests that the differences in the results of Rajan and Johnstone's (1983, 1988a,b) and Liberman's (1992) studies may be attributed to the differences in the methodology. Reiter and Liberman could replicate Rajan and Johnstone's results only under monaural stimulation and only when the animals were carbogen ventilated. The effect was absent during binaural exposures. They concluded that the protection is attributable to either the middle ear muscle reflex or is a shock-evoked effect (Reiter & Liberman, 1991). However, it must be remembered that these experiments used single acute exposures, an experimental design that is often plagued with high levels of variability.

The cochlear efferent system continues to be an enigma. Basic research has elucidated its anatomical structure; electrophysiological experiments show that it has a tonic influence on the organ of Corti, and stimulation of the efferent system increases CM and decreases AP. However, there still is no clear perspective on the efferent system's potential role in NIHL.

Noise Exposure History

The effect of noise on the auditory system is determined by a combination of the acoustics of the exposure and the physiological and mechanical properties of the ear. In the last few years, it has become apparent that an individual's susceptibility to both temporary and permanent hearing loss can be influenced by prior exposure to moderate levels of noise. Although it is a relatively new idea, data supporting this idea can be traced back to the work of Miller, Watson, and Covell (1963). In one of their experiments, they exposed monaural cats to broadband noise at 115 dB for 7.5 min/day for 17 days. The first exposure produced a TTS of 35 dB at 4 kHz. By the end of the fifth day, the same exposure produced only 15 dB of TTS. The authors discussed

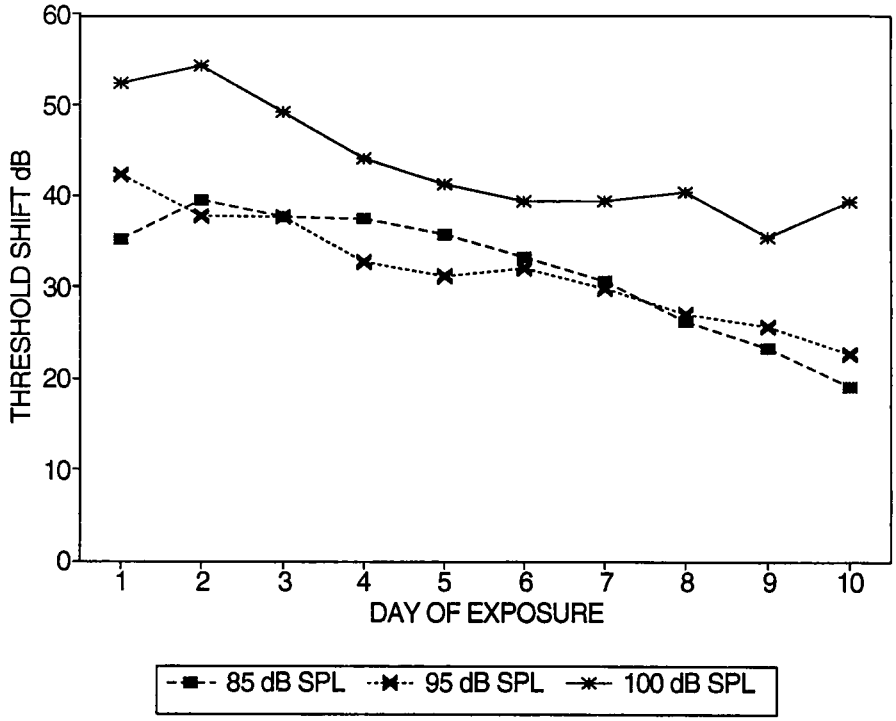

FIGURE 8. Average TS ($N = 9$) after exposure to a 0.5 kHz OBN at 95 dB SPL for 6 hr a day. Notice the trend toward decrease in TS over the days of exposure (modified from Subramaniam et al, 1991a).

a number possibilities for the unexpected decrease in the TS, including the idea that the auditory system's response to noise could be moderated by prior exposure. However, this hypothesis remained untested for the next 25 yr.

Several recent experiments also showed the progressive decrease in hearing loss with intermittent exposures. Clark, Bohne, and Boettcher (1987) exposed a group of chinchillas to an OBN centered at 0.5 kHz at 95 dB for 6 hr/day for 36 days. Another group was exposed to the same noise for 15 min/hr for 144 days. The animals were tested using behavioral

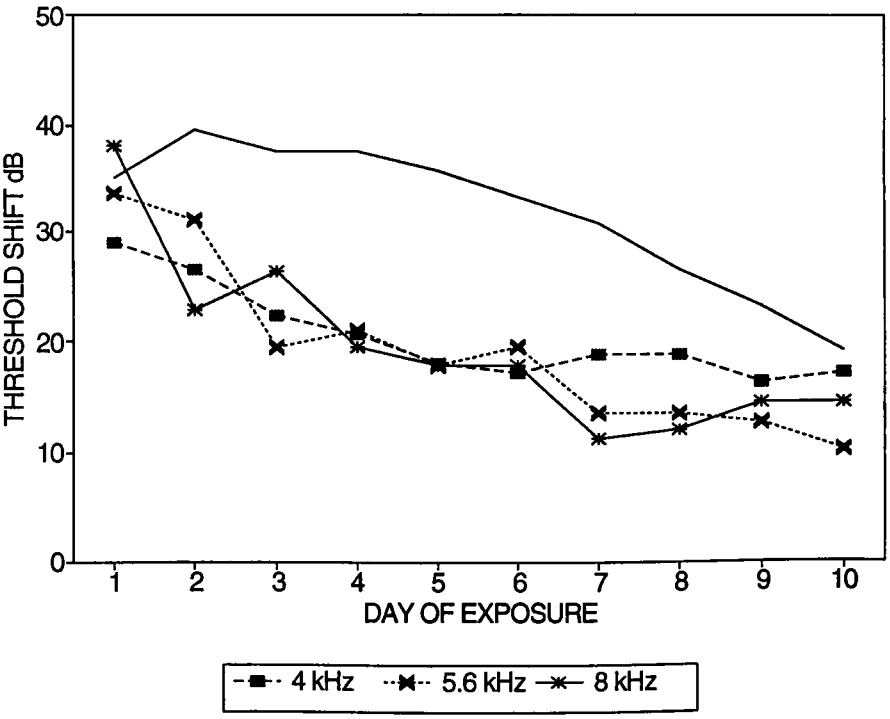

FIGURE 9. TS over the 10 days of exposure to 4 kHz OBN at 85 dB SPL for 6 hr a day, measured at three frequencies. Changes in TS from similar exposures at 0.5 kHz measured at 1 kHz is presented (solid line) for comparison.

audiometry. The TS peaked during the first few days of exposure and then decreased (up to 30 dB) with repeated exposures. Byrne, Henderson, Saunders, Powers, and Farzi (1988) reported essentially the same results, but in their experiment, thresholds were tested using evoked potential recording. Replication of the results with electrophysiological measures suggests that the reduced TS or "toughening" with repeated exposures reflects some fundamental changes in the auditory system rather than a change in the subjects' listening strategy.

The studies of repeated noise exposures are quite clear and dramatic. Using different techniques and experimental animals, one reliably finds 10 to 30 dB less TS with repeated exposures. A logical next question would be to explore the generality of the toughening phenomena (i.e., how does it depend on the level, duration, and frequency of the conditioning exposure?).

Effect of Exposure Level

The effect of exposure level on toughening was examined using monaural chinchillas (Subramaniam, Campo, & Henderson, 1991a). The animals were exposed to an OBN centered at 0.5 kHz for 6 hr/day for 10 days at one of the three levels: 85, 95, or 100 dB SPL. Thresholds were determined at octave frequencies from 0.5 to 16 kHz using evoked potential recording. As expected, the magnitude TS depended on the level of exposure, the greatest shift resulting from the 100 dB exposures (Fig. 8). However, all three groups of animals demonstrated toughening or reduction in TS with repeated exposures. Furthermore, toughening was not limited to the exposure frequency, but was seen at frequencies up to 8 kHz.

Effect of Exposure Frequency

The toughening effect is also seen with high-frequency exposures. When chinchillas were exposed to an OBN centered at 4 kHz at 85 dB SPL for 6 hr/day for 10 days, considerable reductions were seen in TS at and above the exposure frequency (Fig. 9) (Subramaniam, Campo, & Henderson, 1991b). A 12 dB reduction was seen at the exposure frequency (4 kHz) and a 24 dB reduction was recorded at one-half (5.6 kHz) and one octave (8 kHz) above the exposure frequency. Little or no hearing loss was seen below the exposure frequency. Interestingly, the development of toughening for the high-frequency exposure appeared to be faster than those seen for the low-frequency exposure (Fig. 9).

Although the effects of interrupted exposures are interesting, it would be even more important if these "conditioning" exposures protect the subject against PTS from future exposures.

Protection from Subsequent Exposures

Low- and Mid-Frequency Exposures. Canlon, Borg, and Flock (1988) were the first to study the effect

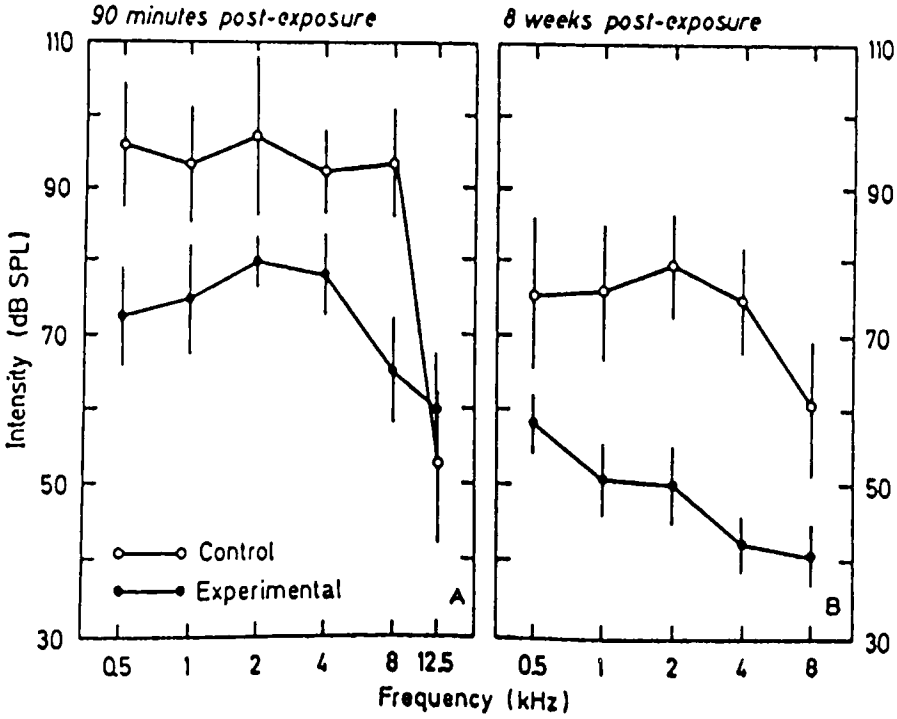

FIGURE 10. PTS in the experimental group (which received 24 days of "conditioning") and the control group after exposure to a 1 kHz tone at 105 db SPL (reprinted with permission from Canlon

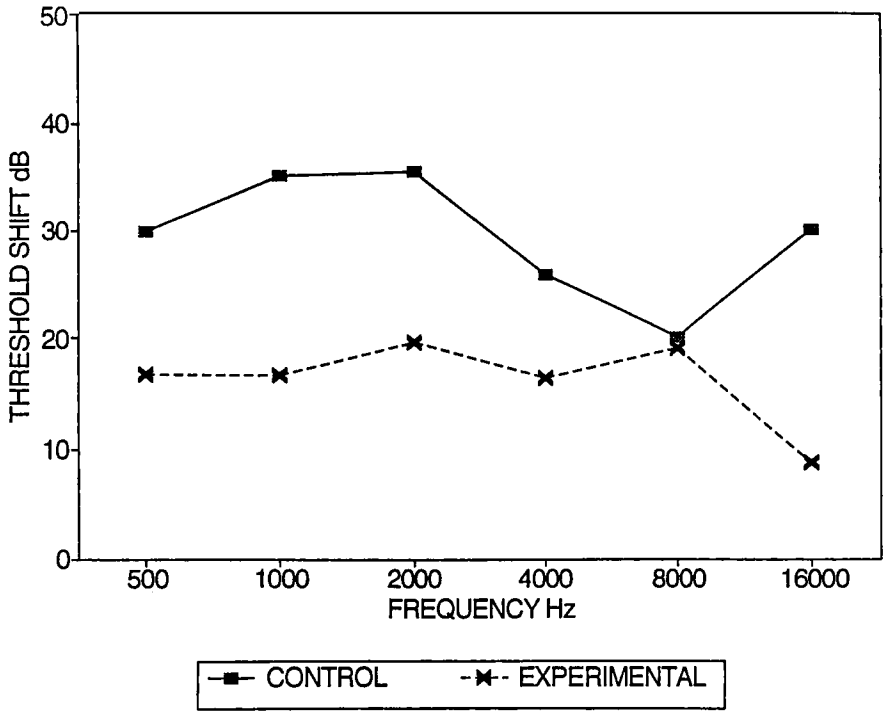

FIGURE 11. The difference in PTS between the experimental group, which received a 10 days of "conditioning" exposures, and control groups after 0.5 kHz 106 dB SPL exposure for 48 hr (Campo et al, 1991).

of low-level exposures on hearing loss from subsequent high-level exposures. They exposed a group of guinea pigs to a 1 kHz tone at 81 dB for 24 days. This group of experimental subjects was then exposed to the same tone at 105 dB SPL for 72 hr. A control group of animals were exposed only to the higher level noise. Hearing thresholds were recorded before and after the noise exposures. The animals that were initially exposed to the lower level developed less TS than the control group (Fig. 10).

Canlon et al's (1988) results were replicated in another study by Campo, Subramaniam, and Henderson (1991). Here the experimental animals (chinchillas) were exposed to an OBN centered at 0.5 kHz at 95 dB for 6 hr/day for 10 days. The animals

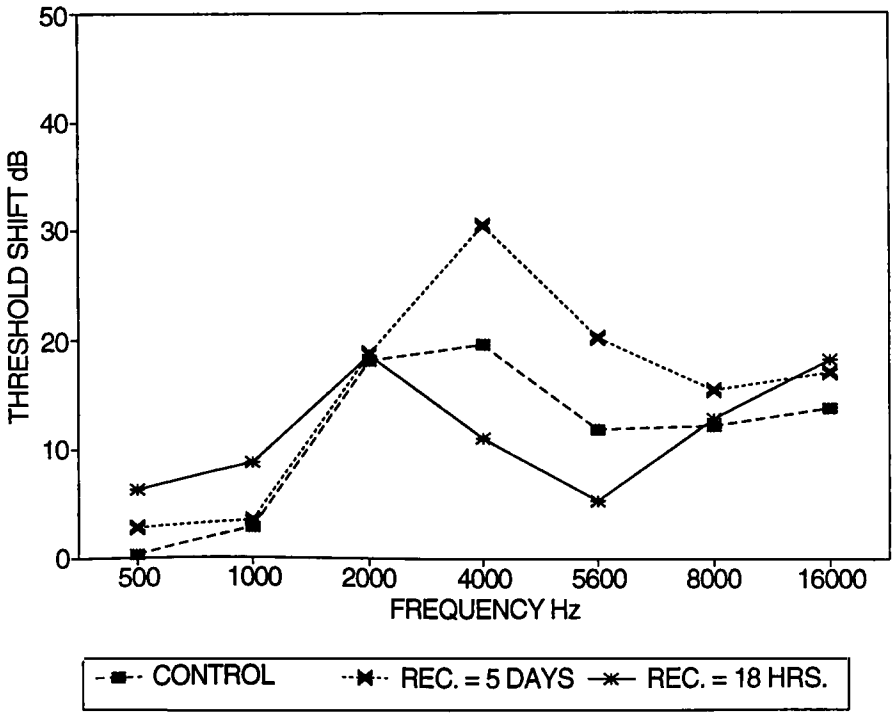

FIGURE 12. PTS after a 4 kHz OBN exposure at 100 dB SPL for 48 hr. The experimental groups were "conditioned" with the same noise at 85 dB for 6 hr a day for 10 days. One group was allowed to recover for 5 days and the second group was allowed to recover for 18 hr. The control group received only the higher level exposure (Subramaniam et al, 1992).

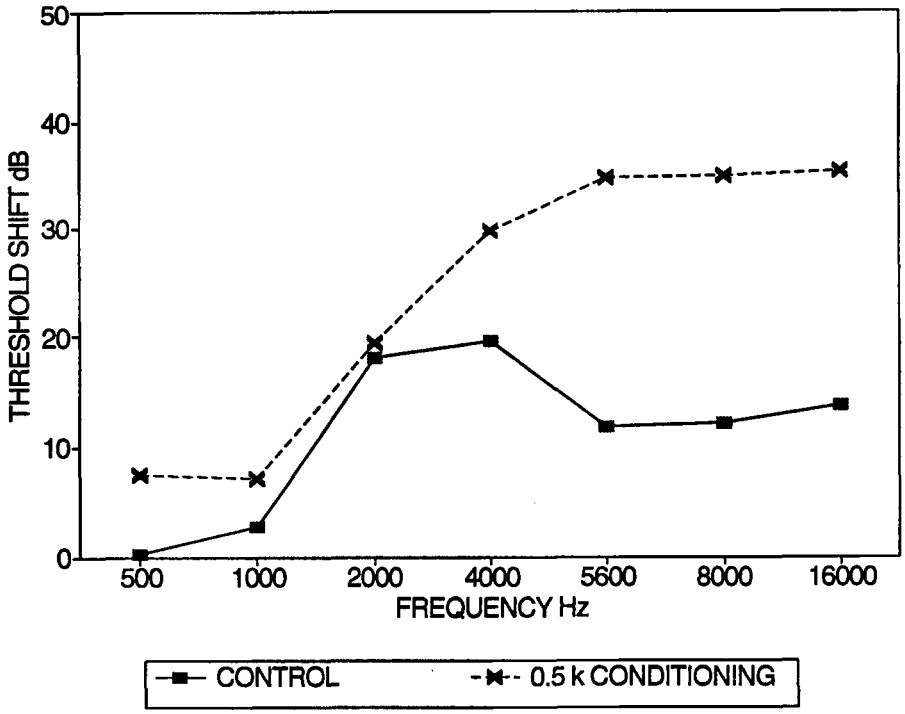

FIGURE 13. PTS after 4 kHz OBN exposure at 100 dB SPL for 48 hr. The experimental group was "conditioned" using a 0.5 kHz OBN at 95 dB SPL for 6 hr a day for 10 days. The control group was exposed only to the higher level (Subramaniam et al, 1991c).

were then allowed to recover for 5 days before subjecting them to a higher level exposure (106 dB) for 48 hr. Thresholds measured just before the 106 dB exposures indicated complete recovery in hearing. TS compared with those of a control group exposed only to 106 dB indicated substantially lower TS in the case of the experimental group (Fig. 11).

High-Frequency Exposures. Subramaniam, Henderson, Campo, and Spongr (1992) repeated the Campo et al (1991) study with a 4 kHz OBN exposure rather than a 0.5 kHz OBN exposure. The experimental animals were first exposed to the 4 kHz OBN at 85 dB SPL for 6 hr/day for 10 days, allowed to recover for 5 days, and then exposed to the same noise at 100 dB for 48 hr. TS were compared with those of a control group exposed to 100 dB only. All the experimental animals showed a consistent reduction in TS during the 10 days of "conditioning" exposures. However, contrary to expectations, after the 100 dB exposure, the experimental animals actually incurred greater hearing loss than did the controls, the difference being statistically significant at 4 and 5.6 kHz ($p < 0.05$). The experiment was repeated with a second experimental group. This group of animals was allowed to recover for only 18 hr after the last conditioning exposure and before the 100 dB exposure for 48 hr. PTS (at 4 and 5.6 kHz) in the 18-hr recovery group were significantly lower ($p < 0.01$) than those in the 5-day recovery group. The 18-hr recovery group also had lower PTS than the controls, but the difference was statistically significant only at 4 kHz ($p < 0.01$) (Fig. 12). The results of this experiment raise the possibility that the 10-day set of exposures may render the ear resistant to future higher level exposure, but the effect may dissipate quickly in the case of high-frequency exposures.

Low-Frequency Conditioning and High-Frequency Traumatic Exposure. In the experiments discussed above, the conditioning and the traumatic exposures were at the same frequency. Recall that the low-frequency conditioning exposures (Subramaniam et al, 1991a) also produced a "toughening" effect at high test frequencies when the exposure levels were 95 and 100 dB SPL. To determine if this would in turn provide protection against a high-frequency exposure, chinchillas conditioned with 0.5 kHz OBN at 95 dB SPL for 6 hr/day for 10 days were exposed to a 4 kHz OBN at 100 dB for 48 hr after 5 days of recovery (Subramaniam, Henderson, & Spongr, 1991c). Thresholds recorded at the end of 4 weeks of recovery indicated substantially greater hearing loss (15-30 dB from 4 to 16 kHz) than the control animals ($p < 0.01$), indicating that the experimental animals were actually more vulnerable (Fig. 13).

In summary, a comparison with the low and the high frequency data emphasizes the base versus apex difference. It may be recalled that the animals previously conditioned with a low frequency and allowed to recover for 5 days were actually protected from the higher level exposure at the same frequency (Campo et al, 1991). On the other hand, identical exposure schedules with the high-frequency noise

rendered the animals slightly more vulnerable than the controls (Subramaniam et al, 1992). Animals conditioned with a low-frequency noise and later exposed to the high-frequency noise were even more vulnerable (Subramaniam et al, 1991c). These results suggest a possible difference in the mechanism involved in the development of toughening and protection from subsequent exposures at low and high frequencies.

Mechanisms Involved in "Toughening"

Little is known about the mechanisms underlying the toughening phenomenon. Various hypotheses have been postulated, including strengthening of the acoustic reflex and/or the efferent auditory nervous system and structural/functional changes in the cochlea (Canlon et al, 1988; Canlon, Borg, & Lofstrand, 1992; Fiorino, Gratton, Subbanna, Bianchi, & Henderson, 1989).

Current theories of hearing suggest that most if not all afferent information is processed by IHCs, and that the role of OHCs is to increase the sensitivity and facilitate the mechanical tuning properties of the basilar membrane through contraction and elongation of the OHCs upon stimulation (see Brownell, 1990). The contribution of the OHCs appear to be most important to the hearing range of 0 to 50 dB (Ryan & Dallos, 1975). Thus, it would be interesting to know if the OHCs play a role in the development of toughening.

After low-level, long-term (81 dB, 24 days) stimulation, Canlon et al (1992) observed increased membrane recycling (vesicles, coated vesicles, and tubulo-vesicular cisternae) at the presynaptic region of the OHCs. This was also accompanied by increased resynthesis of transmitter substance. Canlon et al (1992) suggested that such a membrane recycling could be one of the underlying mechanisms for the protection against noise trauma.

Thus, although various mechanisms have been suggested to play a role, it is yet unclear as to the extent to which these contribute to the development of toughening from repeated noise exposures. Some of the unexplored areas include changes in histochemistry, such as the development and changes in heat shock proteins (Wenthold, Schneider, Kim, & Deschsne, 1992) with interrupted exposures.

The realization that a subject's history of exposure to noise may be a relevant factor in their future susceptibility to more traumatic noise is an interesting idea that raises a number of questions: (1) Over what intensity range is the toughening exposure effective? (2) What is the time course of the toughening effect (i.e., is the toughening process initiated by the first low-level exposure or does it actually need exposures that last 10 to 20 days and is the amount of protection dependent upon the duration of toughening exposures) (e.g., 10 days versus 20 days)? (3) How long does the toughening effect last (i.e., if the time interval between toughening exposures and the traumatic or higher level exposure is increased, does the protective effect remain the same)? (4) Do toughening exposures using continuous noise exposures offer protection against impulse or impact noise? (5) What is the biological basis for the toughening effect: Can it be attributed to changes in the efferent system or are these changes more peripheral? Is it associated with stress or heat shock proteins or changes in the transmitters? (6) From a clinical perspective, what are the suprathreshold changes associated with toughening (i.e., is toughening associated with changes in tuning curves, spread of masking, etc.)?

Conclusions

1. The large variability in demographic studies of NIHL is not simply a reflection of the sampling problem, because similar variability is seen in laboratory studies of TTS with human subjects and in studies of PTS and hair cell loss with animal subjects. It is likely that the variability stems from multiple causes. Thus, an effective screening procedure for susceptibility to NIHL is likely to require assessment of several factors.

2. In the large scale demographic studies, it is likely that some of the variability can be attributed to interactions between the noise exposure and other agents such as ototoxic drugs, carbon monoxide, and solvents.

3. Early attempts to predict susceptibility to NIHL using nonauditory characteristics of the subject (i.e., gender, eye color, smoking, age, etc.) can only account for minor amounts of variability across the subjects in their susceptibility to NIHL.

4. Attempts to predict a subject's potential for PTS from TTS or response to a short, relatively high-level noise exposure have not been very successful. Direct measurements of the relation between TTS and PTS in experimental animals have shown little or no correlation, especially with interrupted and impulse noise exposures.

5. Recently, there has been a re-evaluation of the possible factors related to the auditory system contributing to susceptibility. These include differences in acoustic reflex functioning, the role of the efferent system, and the subject's history of noise exposure. Retrospective studies suggest that the

acoustic reflex plays a significant role in determining the susceptibility to NIHL. There is also a growing body of literature that indicates that an individual can be protected from the effects of noise by prior exposure to a lower level noise. Results of the auditory variables affecting susceptibility are of potential interest and warrant further research.

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