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# PROTECTING AGAINST NOISE TRAUMA BY SOUND CONDITIONING

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The World Health Organization estimates that more than 12% of the world population is at risk for developing noise-induced hearing loss. At present, sound conditioning presents one means of reducing the deleterious effects of noise trauma. This phenomenon is now known to occur in a variety of mammals, including gerbils, chinchillas, guinea pigs, rabbits, rats, mice, and, of most importance, human subjects. A variety of sound conditioning paradigms have been proven successful in preventing morphological and physiological damage. Proposed mechanisms include the upregulation of endogenous antioxidants, the number of NMDA receptors, heat shock proteins, calcium buffering systems, and neurotrophic factors. Further studies are needed to understand the protective mechanisms afforded by sound conditioning. It is convincible that sound conditioning will benefit human subjects and provide a treatment for noise-induced hearing loss. The data presented in this review describe the current status and understanding of the phenomenon of sound conditioning.


## 1. INTRODUCTION

A number of recent studies have shown that the susceptibility of the inner ear to noise trauma can be reduced by prior exposure to an acoustic stimulus. The existence of the resistance to noise trauma was first suggested by Miller *et al.* [1] in 1963 on the basis of experiments in cats. These authors demonstrated that when cats were exposed to interrupted noise for 16 continuous days, the threshold shifts declined during the latter part of the exposure compared to the thresholds obtained on the first day. Two distinct paradigms are employed to reduce the susceptibility of the inner ear to noise trauma. The first uses a low-level, non-damaging continuous acoustic stimulus before the traumatic exposure. This phenomenon has been termed sound "conditioning" and has been demonstrated on a number of species including guinea pigs, gerbils, rabbits, and rats [2–9].

The second paradigm uses an interrupted schedule at sound levels that produce a temporary threshold shift during the first few days of exposure. However, as the daily exposure continues, the degree of threshold shift is reduced, in some cases to no threshold shift despite an ongoing exposure. This reduction has been termed "toughening" or resistance to noise-induced hearing loss.

Toughening has been demonstrated in chinchillas, guinea pigs, and gerbils [9–20]. In low-level, continuous conditioning studies, several investigators have reported that the conditioning stimulus should not cause significant temporary or permanent threshold shifts or hair cell damage, in order to be maximally effective in preventing subsequent hearing loss and hair cell damage. In some cases, this has been accomplished by using a relatively low level of intensity for the conditioning stimulus [2]. In other cases, a period of "rest" has been

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interposed between the conditioning and damaging stimuli, in order for thresholds to recover to pre-conditioning levels [3].

It is important that the sound conditioning parameters are correctly chosen. A good example of choosing the wrong stimulus parameters for sound conditioning is exemplified in a study by Fowler *et al.* [21]. In this study, the mouse was chosen as the experimental animal to determine the effect of sound conditioning on a subsequent high-intensity noise exposure. The mice were conditioned either to a continuous sound conditioner or to an interrupted paradigm. No protective effect was demonstrated with either paradigm. The mouse appeared particularly resistant to the high traumatic noise exposure (12 or 24 h) whereas they were particularly sensitive to the continuous sound conditioning stimulus, which induced a threshold shift.

These results are intriguing when one considers the relatively low intensities used in the continuous training (threshold shifts induced) compared to either the interval training (threshold shifts not induced) or the traumatic exposure. These results cannot be explained on the basis of energy. For example, the interval training (96 dB *SPL*, 6 h/d for 10 d) resulted in nearly 4 times the total energy of the animals trained continuously at 80 dB *SPL* for 24 d. Obviously, hearing loss was not related to total acoustic energy in any simple manner. Employing equal energy may also not be an appropriate method for comparing the effects of interrupted and continuous conditioning paradigms. The lack of conditioning in the mouse might be a peculiarity of this species. However, it seems more parsimonious to conclude that the stimuli used in this particular study were inappropriate.

Recently, Yoshida and Liberman [22] demonstrated the protective effect of sound conditioning against subsequent noise trauma in mice. These investigators used two different conditioning paradigms, i.e., one of 1 week duration and the other of 15 min duration. After both sound conditioning protocols, increased amplitudes of distortion product otoacoustic emissions were found. Both sound conditioning paradigms resulted in reduction of noise-induced PTS from a subsequent high-level exposure. These findings are not in contradiction to Fowler's study [21] since different sound conditioning parameters were used. These two studies emphasize the importance of selecting suitable parameters. If protection is not found in a given condition, it is important that the results be interpreted with caution. One obvious explanation would be that optimal sound conditioning parameters were not tested.

It has been reported that low-level acoustic stimulation could slow, but not prevent, genetically determined hearing loss in mice [23]. In order to delay the hearing loss, it was important to initiate the low-level stimulation before the onset of hearing loss. These findings expand the possibilities of protecting against hearing loss by sound conditioning such that pre-treatment can also protect against hereditary-based hearing loss. Another interesting finding regarding sound conditioning in the mouse was recently demonstrated [22]. The conditioner used in this case was whole body heat stress. When the mice were primed with heat stress and then subjected to noise trauma a protection against hearing loss was evident compared to the group not heat stressed [24]. Both these findings in mice suggest that sound conditioning may have a wider range of applications in preserving hearing than previously thought. Table 1 illustrates some of the different paradigms that have been used to protect against trauma by preconditioning.

## 2. CONCLUSIONS

Many hypotheses have been advanced to explain the protective effects of sound conditioning, but the vast majority of studies are inconclusive. There is increasing evidence

TABLE 1

| Species | Conditioner | Pause | Trauma | Reference |
|---|---|---|---|---|
| Chinchilla | OBN 0·5 kHz, 95 dB, 6 h/d 10 d | 5 d | Impulse noise, 150 dB | Henselman *et al.* [18] |
| Chinchilla | OBN 0·5 kHz, 95 dB, 6 h/d 10 d | max 60 d | OBN 0·5 kHz, 106 dB, 48 h | McFadden *et al.* [20] |
| Gerbil | OBN(1·4–5·6 Hz) | max 3 week | OBN (1·4–5·6 Hz) 110 dB, 1 h | Ryan *et al.* [3] |
| Gerbil | OBN at 2 kHz, 74 dB, 10 d | 2 d | OBN at 2 kHz, 107 dB, 48 h | White *et al.* [9] |
| Gerbil | OBN at 2 kHz, 80 dB, 6 h/d 10 d | 2 h | OBN at 2 kHz, 107 dB, 48 h | White *et al.* [9] |
| Guinea pig | 1 kHz, 81 dB, 24 d | None | 1kHz, 105 dB, 72 h | Canlon *et al.* [7] |
| Guinea pig | 6·3 kHz, 78 dB, 13 d | None | 6·3 kHz, 100 dB, 24 h | Canlon *et al.* [26] |
| Guinea pig | BBN, 85 dB, 5 h/d 10 d | 5 d | 2–20 kHz, 110 dB, 5 h | Yamasoba *et al.* [25] |
| Rat | OBN at 4 kHz, 55–95 dB, 10 h | 10 h | OBN at 4 kHz, 105 dB, 13 h | Pukkila *et al.* [8] |
| Rabbit | OBN at 1kHz, 95 dB, 3 weeks | | 4·215 kHz, 95 dB, 5 min | Franklin *et al.* [13] |
| Mouse | OBN (8–16 kHz), 89 dB, 15 m | 24 h | OBN (8–16 kHz) 100 dB, 2 h | Yoshida *et al.* [22] |
| Mouse | Heat stress (41·5°C) | 6 h | OBN (8–16 kHz) 100 dB, 2 h | Yoshida *et al.* [24] |
| Mouse | BBN (4–25 kHz), 70 dB, 12 h | | Hereditary hearing loss | Willott *et al.* [23] |
| Human | Music, 70 dBA, 6 h/d 5 d | None | OBN 2 kHz, 105 dB, 10 min | Miyakita *et al.* [17] |

for endogenous protective systems in the cochlea, which, if enhanced, can provide protection against subsequent trauma. Endogenous cochlear protective systems characterized to date include endogenous antioxidants or free radical scavengers, calcium buffering systems, heat shock proteins (HSPs), glutamate receptors, and neurotrophic factors.

All these events can result in damage to tissues, proteins, lipids, and DNA, partly via membrane lipid peroxidation. Depending upon the severity of the damage, the hair cells may die (necrosis or apoptosis) or survive with varied functional activity. The upregulation of cochlear antioxidant enzymes would be one means of causing a localized protection for all cochlear structures, including the outer hair cells and the efferent nerve endings by sound conditioning. However, a recent study showed that unilateral protection from acoustic trauma was afforded after unilateral sound conditioning [25]. These findings suggest that an overall stress-related mechanism underlying sound conditioning is not the complete cause for protection.

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