COMBINED EFFECTS: BIOLOGICAL REQUIREMENTS FOR NOISE INTERACTIONS

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Introduction The existence of this Noise Team reflects our understanding that the effects of given noise exposure can be influenced by a number of physical or chemical factors. The intent of this introduction is to examine the factors that lead to an interaction with noise.

The issue of noise and ototoxic drugs has been studied and we now have a reasonable understanding of the conditions leading to noise interactions. For example, drugs such as salicylates (aspirin) and loop diuretics, produce a temporary hearing loss and do not appear to interact with noise. Aspirin is commonly used and with large doses, it leads to a flat loss of up to 20 – 25 dB, but the hearing loss recovers within a day or two after the aspirin treatment has ended. The mechanism for aspirin induced hearing loss is not completely understood, but there is some evidence that outer hair cells *in vitro* show a loss of their contractile properties when bathed with artificial perilymph containing aspirin. Loop diuretics are used for kidney failure or congestive heart failure. They can produce a 40 – 50 dB temporary loss of sensitivity. The loop diuretic is active at stria vascularis where it disrupts the potassium (K) circuit to the endolymph and leads to a reduction in the 80 mV+ endolymphatic potential.

By contrast, ototoxic drugs such as cisplatin and the family of aminoglycoside antibiotics, cause permanent hearing loss and interact with noise. Gratton et al. (1988) reported that a noise exposure and cisplatin dose that were at the threshold of causing permanent threshold shifts (TTS), together caused significant hearing losses that were greater than the sum of either agent alone. In terms of mechanisms of hearing loss, both cisplatin and aminoglycosides initially target the outer hair cells (OHC), primarily at the basal cut of the cochlea. Furthermore, recent studies have revealed that both cisplatin and aminoglycosides alter the free radical/antioxidant balance in the cochlea. Thus, ototoxic drugs such as cisplatin or aminoglycosides that interact with noise, share with noise similar audiometric characteristics, as well as, similar cochlear pathology (loss of OHC at base of cochlea). In addition, both noise and these drugs lead to oxidative stress in the cochlea. The clinical implications of the drug/noise interactions is that the educational component of hearing conservation programs need to include information about drug interactions.

The drug/noise interactions are easily identified (i.e., one knows when the drug is given). There are other potential interactions that are more difficult to define. For example, there are experimental studies with animal models that show elevated core temperatures enhance the effects of noise and conversely, depressed core temperatures reduce the effects of noise. Given recent insights into free radical biology, the increased temperature will accelerate metabolism and thereby increase the rate of superoxide $0_2^{\bullet -}$ formation. Conversely, a decreased temperature will do the opposite. The contribution of increased ambient temperature is not known, but a reasonable question to pursue is whether temperature influences the effects of noise.

In the last ten years, there has been a growing awareness that industrial chemicals can interact with the effects of noise. Given the range of chemicals found in industry, there are many

potential pathways for influencing the cochlea, but two that are quite common are the interaction of noise and industrial solvents and noise and asphyxiants.

There is growing evidence that solvents, like toluene or styrene, are ototoxic as well as neurotoxic. One of the challenges to the industrial audiologist is to separate the central and peripheral changes in auditory function caused by the solvent. The peripheral effect of solvents appears to be primarily focused at the OHC in the base to middle region of the cochlea. The cause of OHC death is not known, but it is likely to involve damage to the lipid membranes of the OHC and the OHC die through the process of apoptosis. From a pathological perspective, styrene creates lesions in the cochlea that are similar to noise and there is growing evidence that styrene and noise can interact synergistically.

Asphyxiants, such as carbon monoxide or cyanide can be found in certain industrial settings. These are highly regulated chemicals and at low levels there is no consequence for hearing loss but there is evidence that at very low levels cyanide can interact with noise. Since one of the primary targets of cyanide is the mitochondria, cyanide intoxication inhibits mitochondrial respiration which leads to the increased generation of free radical formation. Since OHC are especially active, the cyanide poisoning is more toxic there. Damaging levels of noise exposure also create toxic free radicals in the cochlea. Thus, it is reasonable to expect the damaging effects of asphyxiants and noise, when added together, produce pathological changes greater than either agent alone.

In reviewing the critical features for an interaction, several trends emerge. First, all drugs/chemicals influence the balance of free radical/antioxidants. Second, all the drugs/chemicals that interact produce their major effects at the OHC in the basal half of the cochlea. The consistent vulnerability of the basal half of the cochlea is likely to be the result of antioxidant enzymes being less concentrated in the base than in the apical half of the cochlea.

Finally, the interaction of noise and drugs/chemicals has important implications for how the potential hazard for hearing loss is assessed. It is not enough to simply measure the noise when the environment contains other cochlear stressors. From an educational perspective, the training of industrial audiologists needs to be expanded to provide a perspective on other industrial pollutants.

References

Gratton, M., Salvi, R., Kamen, B., Henderson, D., and Poon, M. (1988) Combined effects of noise and cisplatin: effect on hearing. In: Recent advances in researches on the combined effects of environmental factors. O. Manninen, ed.