Antioxidant Therapy Prevents Presbycusis in C57BL6 Mice
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ABSTRACT
Problem Addressed: Presbycusis, or age-related hearing loss, is characterized by gradual, progressive sensorineural hearing loss which accompanies aging with associated decreased speech recognition in noisy environments, slowed central processing of acoustic stimuli and impaired sound localization. In addition to impairing one’s ability to communicate effectively, presbycusis jeopardizes one’s autonomy, presents a safety concern and has been correlated with an increased incidence of clinical depression and social withdrawal. By 2025, it is estimated that approximately 25 million Americans will be affected, thus this presents a major public health concern. The purpose of this study is to evaluate the potential of antioxidant therapy, including two novel antioxidants, in the prevention of presbycusis.

Methods and Measures: C57BL6 mice were assigned to treatment or control groups. Treatment groups of mice were fed with a combination of two novel antioxidants, L-cysteine-glutathione mixed disulfide and ribose cysteine, as well as vitamin B12, folic acid, and ascorbic acid. Antioxidant therapy effectively decreased threshold shifts in association with aging.

Clinical Significance of Study: Combination antioxidant therapy may prove a safe and cost-effective method of preventing presbycusis in our growing elderly population.


METHODS AND MATERIALS
•Animal model: C57BL6 mice
•Initiation of hearing loss at 6 month
•Profound hearing loss by 18 month
•Antioxidant Therapy Composition - NW-nitro-L-arginine-methyl ester (250mg/kg) - L-cysteine-glutathione mixed disulfide (200mg/kg) - Ribose-cysteine (200mg/kg) - Vitamin B12 (80mcg/kg) - Folic Acid (100mcg/kg) - Ascorbic Acid (200mg/kg)

RESULTS
Figure 1: Timeline of Auditory Brainstem Response (ABR) Assessment
Figure 2: Baseline ABR Data by Experimental Group
Figure 3: ABR Threshold Shifts at 7 Months of Age

Figure 4: ABR Threshold Shifts at 9 Months of Age
Figure 5: ABR Threshold Shifts at 12 Months of Age

The etiology of age-related hearing loss is theorized to be multifactorial. Oxidative damage is thought to be a major etiologic factor. Changes in inducible nitric oxide synthase expression (an enzyme responsible for the production of reactive nitrogen species), superoxide dismutase expression (an enzyme essential in the breakdown of reactive oxygen species), heat shock protein 70 (a protein involved in cellular defense against oxidative damage), and mitochondrial genome deletions associated with oxidative damage have been demonstrated in association with ARHL. Within the literature, a number of antioxidants have been studied for the prevention of ARHL including cyanocobalamin, ascorbic acid, Vitamin E, melatonin, folic acid, lipoic acid, L-carnitine, and resveratrol.

The administration of a high dose combination antioxidant therapy in this study within C57BL6 mice, an accepted animal model of presbycusis, appeared to attenuate the progression of ARHL. Although this study was limited by sample size, the findings were statistically significant. The combination nature of the antioxidant therapy confounds the findings. These results are promising in the possibility of attenuation of age related hearing loss with high dose combination antioxidant therapy. Further study is necessary to ascertain optimal dosing and combination of agents.

REFERENCES

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