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Antioxidant-enriched diet does not delay the progression of age-related hearing loss

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Abstract

Oxidative stress has been linked to noise- and drug-induced as well as age-related hearing loss. Antioxidants can attenuate the decline of cochlear structure and function after exposure to noise or drugs, but it is debated as to whether they can protect from age-related hearing loss. In a long-term longitudinal study, 10-month old female CBA/J mice were placed on either a control or antioxidant-enriched diet and monitored through 24 months of age. Supplementation with vitamins A, C, and E, L-carnitine and α-lipoic acid significantly increased the antioxidant capacity of inner ear tissues. However, by 24 months of age, the magnitude of hearing loss was equal in both groups. Likewise, there were no significant differences in hair cell loss or degeneration of spiral ganglion cells. We conclude that dietary manipulations can alter cochlear antioxidant capacity but do not ameliorate age-related sensorineural hearing loss in the CBA/J mouse.

Keywords

Antioxidant diet; reactive oxygen species; age-related hearing loss; CBA/J mice

1. Introduction

Recent research (see Willott and Schacht, 2010 for a review) has placed age-related hearing loss in animals –at least in the case of sensorineural presbycusis – into the category of oxidant-stress related events. Other auditory pathologies linked to oxidative stress, such as those induced by drugs or noise, can be ameliorated by antioxidants. Whether or not the progression of presbycusis is amenable to dietary manipulations, however, is controversial. Some studies suggest success but others have failed (Bielefeld et al., 2008). Caloric restriction, known to extend longevity and slow age-related deterioration, has inconsistent effects in different mouse strains ranging from slowing hearing loss to accelerating it.

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Supplementary data
Supplementary data associated with this article can be found in the online version.

2. Experimental Procedures

One hundred female CBA/J mice were placed either on a diet supplemented with multiple antioxidants or a control diet, and monitored from 10 to 24 months of age. Inner ear pathology was characterized by the accepted standards of auditory threshold shifts, loss of hair cells, and deterioration of spiral ganglion cells. Antioxidant levels in cochlear tissues were quantified using the Total Antioxidant Power Assay Kit (Oxford Biomedical Research, Oxford, MI, USA).

3. Results

The efficacy of antioxidant supplementation was first tested in a subgroup of animals. After two months, total antioxidant capacity of the inner ear had increased two-fold from 0.23 ± 0.07 to 0.42 ± 0.21 mM uric acid equivalents (n = 8 each; $p < 0.05$). Auditory performance at 10 months (ABR thresholds) at frequencies of 4, 12, 24, and 48 kHz was comparable between the control and antioxidant groups (50 animals each). ABR were measured again at 12, 18, and 24 months of age at all four frequencies. Thresholds increased with age but there were no significant differences between the two groups at any time or frequency. The percentage of mice meeting the criteria for hearing loss (≥40 dB) was also not different (Suppl. Fig. 1A). Consistent with the ABR results, hair cell loss and degeneration of spiral ganglion cells were the same in the two groups at 24 months of age (Suppl. Fig. 1B and C).

4. Discussion

The key finding is that an antioxidant-enriched diet does not delay age-related auditory pathology across all measured parameters (auditory thresholds, loss of hair cells, and degeneration of spiral ganglion cells). The conclusion is particularly strong as this long-term intervention begins at an age of normal auditory function and ends close to the expected life span of the animals. Importantly, the antioxidant cocktail enhanced the redox status of the inner ear and included compounds effective in attenuating the influence of ototoxic drugs and noise.

Our result seems to contrast with some earlier reports (see Willott and Schacht, 2010) which, however, need to be critically assessed. Rats on vitamin supplements throughout their lifespan maintained a minimally better auditory sensitivity than their cohorts on placebo, but most animals had died during the study and the result was based on only three to four survivors per group. Dogs fed an antioxidant diet for the last three years of their lives showed less neuronal degeneration in the cochlea than animals on a normal diet. However, the dogs had a lifetime of exposure to excessive noise in their kennels. Hence, damage and protection may have been related to acoustic trauma. Antioxidants delay “age-related” hearing loss in C57BL/6J mice (Someya et al., 2009), but this mutant strain harbors the $Cdh23^{ahl}$ allele that predisposes to a non-physiological accelerated hearing loss. Another recent study shares our conclusions: rats at the ages of 15, 18, and 24 months receiving acetyl L-carnitine to enhance mitochondrial bioenergetics for 30 to 90 days had no better hearing than controls (Bielefeld et al., 2008).

The results do not support the benefit of antioxidant intervention in age-related hearing loss. This does not imply that the nutritional status of the animal or the antioxidant balance of the inner ear is not important to the preservation of hearing. Deficiencies might indeed affect auditory performance but for normally maintained animals, supplementation is not effective.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

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