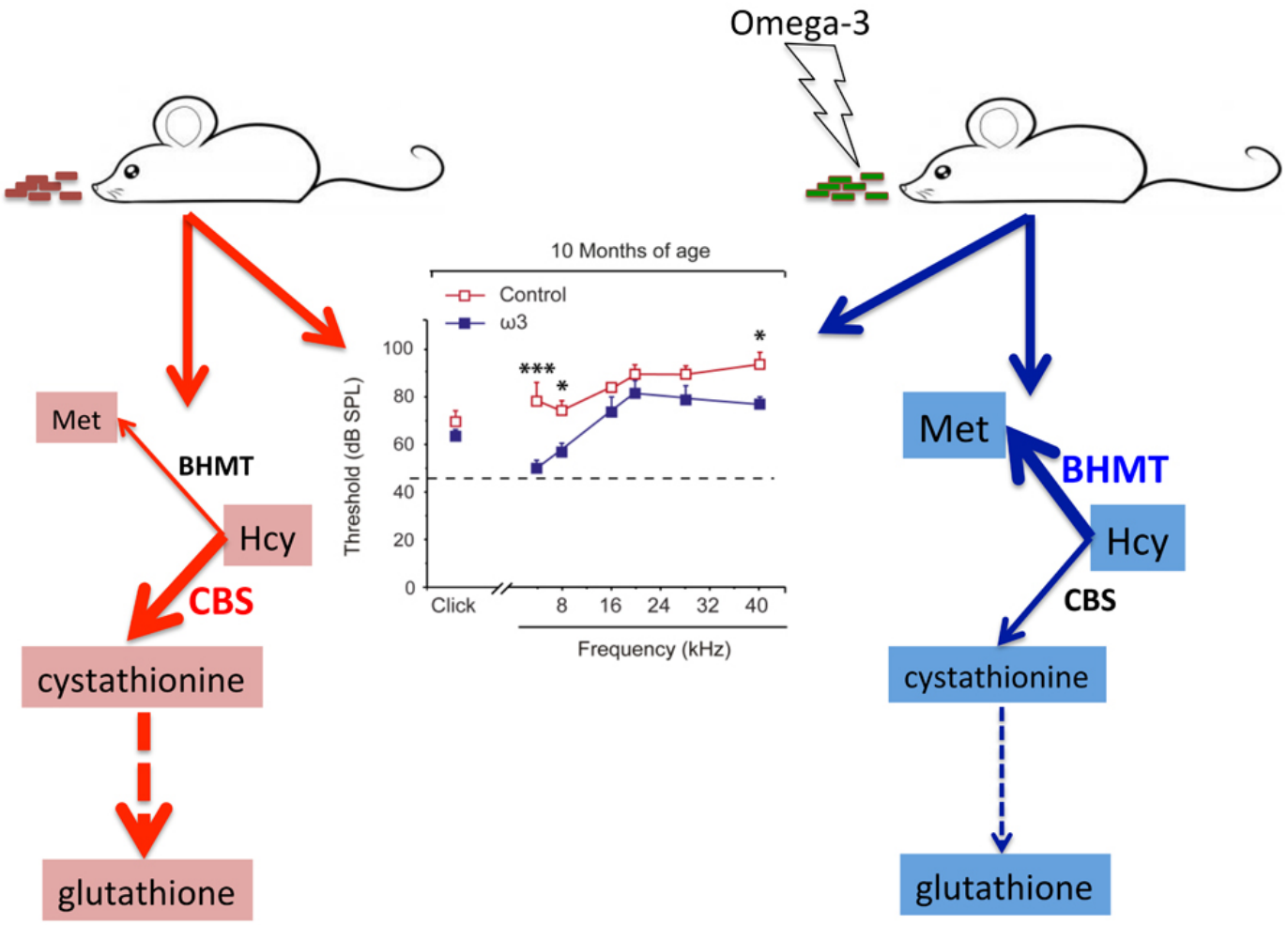
Omega-3 fatty acids ameliorate age-related hearing loss

We have evaluated the effects of a diet rich in omega-3 fatty acids on age-related hearing loss using a mouse model. These mice present early hearing loss, the symptoms appearing normally at 4 to 6 months of age. Therefore, the diet was given to the mice for 8 months, starting when they were 2 months of age and lasting until they became 10 months of age. Although the animals on the omega-3 rich diet did not like it much initially, after a short period they eat the same than those receiving a control diet and gained weight normally. During all this period the hearing capacity of the mice was evaluated every month using two types of audiometric tests, called auditory brainstem response (ABR) and distortion product otoacustic emissions (DPOAE). At 7 months of age the animals showed signs of hearing loss with both control and omega-3 rich diets. However, at 10 months of age significant differences were observed in mice on the omega-3 rich diet, which were able to detect lower intensities of the sound (threshold) emitted at several frequencies. Hence, mice eating the omega-3 supplement for a long period of time show the initial phases of hearing loss, probably due to their genetic background, but seem to delay the apparition of a second phase of auditory damage.



The second part of this study tried to identify how the omega-3 effects are produced, and for this purpose we had to sacrifice the animals in order to obtain the cochlea. This part of the inner ear contains the sensory organ, where the changes inducing hearing loss take place. Using this small tissue (6 mg in adult mice) we analyzed gene expression alterations of molecules involved in inflammatory processes, called cytokines, and certain marker genes involved in the control of oxidative stress. When we compared cochleae from young mice (4 month old) and mice 10 month old, all of them receiving a normal diet, it was possible to see that older animals show higher expression levels for cytokines promoting inflammation and a certain degree of oxidative stress. However, changes in the expression of these molecules in cochleae of mice 10 months old eating omega-3 rich diets were prevented, at least in part.

Next, we focused our attention in cochlear homocysteine metabolism, which is related to the production of antioxidant molecules and whose alteration in hearing loss was demonstrated previously. In this case, we analyzed both changes in gene expression and in protein levels. Differences in gene expression were measured in mice on a normal diet depending of their age;

specifically, key genes of this metabolic pathway reduce their expression in 10 months old mice. This expression changes did not correlate with alteration in the corresponding protein levels, and even in some cases followed opposite patterns. Altogether, the alterations in old mice eating a normal diet tend to favor elimination of homocysteine towards production of antioxidant molecules (cysteine and glutathione). What did the omega-3 rich diet did in the cochlea of mice 10 month old? Well, this diet helped in the maintenance of the expression levels exhibited by cochlea of young mice, and again, the proteins did not exactly follow this pattern. Overall, the omega-3 diet seems to induce the use of homocysteine for methionine synthesis, rather than for production of glutathione. These changes suggest an increase in homocysteine intracellular levels, which is known to participate in the inactivation and aggregation of proteins through its modification, but such an elevation was not detected. In summary, our results suggest that omega-3 diets have a protective effect against hearing loss.

Publication

Long-term omega-3 fatty acid supplementation prevents expression changes in cochlear homocysteine metabolism and ameliorates progressive hearing loss in C57BL/6J mice.
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