Now hear this: Mouse study sheds light on hearing loss in older adults

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(PhysOrg.com) -- Becoming "hard of hearing" is a standard but unfortunate part of aging: A syndrome called age-related hearing loss affects about 40 percent of people over 65 in the United States, and will afflict an estimated 28 million Americans by 2030.

"Age-related hearing loss is a very common symptom of aging in humans, and also is universal among mammal species, and it's one of the earliest detectable sensory changes in aging," says Tomas Prolla, a professor of genetics and medical genetics at the University of Wisconsin-Madison.

Prolla is senior author of a paper in today's (Nov. 9) *PNAS* that looks at the genetic roots of this type of hearing loss, which is not due to noise exposure.

The study has identified a gene that is essential to age-related hearing loss, a condition marked by deaths of sensory hair cells and spiral ganglion neurons in the inner ear. These cells are at the heart of the conversion of vibrations into nerve impulses that the brain can decipher, and yet these cells cannot be regenerated.

In mice, the new study shows that the damage starts with free radicals, which are key suspects in many harmful changes of aging. Free radicals trigger a process called apoptosis, or programmed cell death, by which damaged cells "commit suicide." Apoptosis is often beneficial, as it eliminates cells that may be destined for cancer.

Before the study, it was already clear that "aging was associated with a major loss of hair cells and ganglion cells, so it was plausible that programmed cell death was playing a role in hearing loss," says Prolla. "We also thought that oxidative stress — the presence of free radicals — contributes to age-related hearing loss, so we put two and two together and showed that oxidative stress does indeed induce age-related hearing loss."

In mice, Prolla and the study's first author, Shinichi Someya, a postdoctoral researcher at UW-Madison, found that the suicide program was operating in hair cells and spiral ganglion neurons, and that the suicide program relied on activity in a suicide gene called bak.

Activity of the bak gene "is required for the development of age-related hearing loss," says Someya. "The strongest evidence for this was the fact that a strain of mice that did not have the bak gene did not show the expected hearing loss at 15 months of age."

In one way, the new results are a bit unusual, Prolla admits. "In most genetic diseases, it's a mutation that causes the disease. In our study, a mutation in the gene prevents the disease."

Someya says he measured mouse hearing with an instrument like that used to test hearing in newborns. "It's a standard test for infants. We place electrodes on the skin above the brain, and when they respond to a sound an electric current is generated from the brainstem, and we detect that current."

The new results, obtained with collaboration from the universities of Florida, Washington and Tokyo, hint that the oxidative stress and hearing loss may be preventable. Although antioxidants have been widely used, with generally disappointing results, to prevent free-radical damage in aging, Someya and Prolla found that two oral antioxidants

were effective. "One of the most surprising findings was that these two — alpha lipoic acid and coenzyme Q10 — were very specific in their protection against apoptosis and hearing loss," says Prolla.

Programmed cell death is triggered by mitochondria, small units inside cells that process energy for the cell. But when the mitochondria receive signals indicating that the cell is damaged, they break up and begin the process of apoptosis.

Confirming the importance of mitochondria in hearing loss, both of the helpful antioxidants are known to make mitochondria less responsive to oxidative stress.

The study provides strong evidence linking free radicals, the bak gene and hearing loss, Prolla says. "We wanted to know how oxidative stress leads to deaths of these critical cells, and when we looked at mice without bak, they were entirely protected from age-related hearing loss. One of our major findings is that free-radical damage does not kill the cell directly, but rather induces the pathway to programmed cell death. Mice without bak still accumulated oxidative damage, but did not undergo programmed cell death, did not lose hair cells or these neurons, and their hearing was fine."

Bak may play a role in other age-related conditions, Prolla adds. "This study focused on hearing loss, but there is evidence that other diseases associated with the loss of neurons, like Parkinson's or Alzheimer's, are associated with oxidative stress, and it's possible that the bak protein plays a role in apoptosis in those diseases as well. We are very intrigued by the possibility that blocking bak may have broader utility against neurodegeneration."

Source: University of Wisconsin-Madison (news : web)