

St. Jude finds 'dancing' hair cells are key to humans' acute hearing

St. Jude Children's Research Hospital investigators have found that an electrically powered amplification mechanism in the cochlea of the ear is critical to the acute hearing of humans and other mammals. The findings will enable better understanding of how hearing loss can result from malfunction of this amplification machinery due to genetic mutation or overdose of drugs such as aspirin.

Sound entering the cochlea is detected by the vibration of tiny, hair-like cilia that extend from cochlear hair cells. While the cochlea's "inner hair cells" are only passive detectors, the so-called "outer hair cells" amplify the sound signal as it transforms into an electrical signal that travels to the brain's auditory center. Without such amplification, hearing would be far less sensitive, since sound waves entering the cochlea are severely diminished as they pass through the inner ear fluid.

In their studies, Zuo and his colleagues have sought to establish the mechanism by which outer hair cells produce such amplification. Specifically, they wanted to distinguish between two amplification theories—called "stereociliary motility" and "somatic motility"—that have resulted from previous studies of the auditory machinery.

The stereociliary theory holds that amplification is produced by intricate vibrations of the bundles of cilia extending from the outer hair cells. The somatic motility theory proposes that the sound signal is amplified by an amplifier protein, called prestin, embedded in the hair cell membrane. Prestin is powered by voltages within the membrane that are produced by mechanical sound vibrations.

"This motility is also called 'dancing' because when you electrically stimulate an outer hair cell with a sound, the cell body spontaneously elongates and contracts along with the sound," said Jian Zuo, Ph.D., associate member of the St. Jude Department of Development Neurobiology. "It is very dramatic to see these hair cells 'dance' with the sound." Zuo is the senior author of a report on this work that appears in the May 8 issue of the journal "Neuron."

Since the prestin protein is the key component of somatic motility, in previous experiments Zuo and his colleagues genetically knocked out prestin in mice and tested the effects on hearing. Those mice showed a hearing defect that indicated a malfunction of somatic motility. While the knockout experiments were strong evidence for the role of somatic motility, the affected mice also showed structural abnormalities in their outer hair cells, Zuo said, thus complicating the interpretation.

In the new experiments to more unequivocally establish the role of somatic motility, the researchers genetically altered mice to have only subtle alterations in the prestin protein. These alterations only compromised prestin's function as an amplifier but did not otherwise affect the outer hair cell structure or function, the researchers' analysis showed.

"We found that these mice showed exactly the same kinds of hearing deficiency as the previous knockout mice," Zuo said. "Therefore, we believe that these experiments eliminate criticism of our earlier experiments with the knockout mice." The new experiments, Zuo said, thus firmly establish that the "dancing" somatic motility of the outer hair cells is critical to cochlear amplification.

However, he noted, "With this study we still cannot really exclude stereociliary motility from contributing to cochlear amplification, because eliminating somatic motility also reduces ciliary motility. So, it is not

possible to totally isolate either form of motility. In fact, we hypothesize that the two mechanisms might work together in different aspects of amplification.”

By finding prestin’s role in hearing Zuo and his colleagues may help scientists better understand the mechanisms of hearing loss. “For example, an overdose of aspirin causes a high-frequency hearing loss by inhibiting prestin’s function,” Zuo said. “Also, there is evidence that many cases of high-frequency hearing loss are caused by defects in the cell’s molecular machinery that involves prestin. And two mutations that have been detected in the prestin gene in humans are reported to be associated with deafness.”

Source: St. Jude Children's Research Hospital

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