A stress-response system in the ear protects against hearing loss

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An in vivo study shows for the first time that there is a stress-response system within the cochlea that mirrors the signaling pathways of the body's fight or flight response. Researchers have identified a hormone-like signaling system of the inner ear that sets baseline hearing sensitivity and helps protect against noise-induced hearing loss.

"Our research shows, for the first time, that the cochlea's protective mechanism is likely to be largely a locally-produced phenomenon. The current theory of protection is that signals from the cochlea travel to the brain and back. While this theory does work under certain circumstances, we have known that it requires moderately-high intensity sounds to function. Our study demonstrates that a previously unrecognized signaling system involved in noise-induced hearing loss exists entirely within the ear. This signaling system works at lower intensity sounds - typical of our everyday environment - than the pathway involving the brain," explained Doug Vetter, PhD, senior author and lecturer in the department of neuroscience at Tufts University School of Medicine.

"The local signaling system that we identified in the cochlea mirrors the molecular signaling pathways of the body's physiological fight-or-flight response, which is triggered by the release of molecules from the adrenal glands during times of physical stress. It may be that activation of the cochlea's protective mechanism from physical stress changes the way the cells of the inner ear respond to the next exposure. In this way, protection may be established based on previous exposures, and prior to

the next exposure to potentially damaging sounds," continued Vetter.

As many as 26 million Americans, or 15 percent of the adult population, suffer from hearing loss, some of which may have been caused by exposure to loud noise, according to an estimate by the National Institute on Deafness and Other Communication Disorders (NIDCD) at the National Institutes of Health. Noise-induced hearing loss is one of the most common occupational injuries in the United States, and is most prevalent in the general manufacturing, mining, and construction industries. Daily exposure to noise, including listening to music too loudly, can also result in permanent hearing damage. In order to prevent noise-induced hearing loss, NIDCD suggests that "a good rule of thumb is to avoid noises that are 'too loud,' and 'too close' or that last 'too long.'"

Vetter and colleagues focused on a specific receptor for corticotropin-releasing factor (CRF), a peptide that acts as a hormone and neurotransmitter. In the typical hormone signaling system served by CRF, the hypothalamus secretes CRF in response to stress and triggers the release of glucocorticoids, which are involved in the body's immune and inflammatory responses.

Mice that were missing a gene responsible for making CRFR2, a specific CRF receptor, had increased sensitivity to sound. While this may seem to be an advantage, when exposed to an environment of broad frequency sounds similar in intensity to normal conversation, Vetter and colleagues found that the mice with a genetic deficit of CRFR2 receptors experienced significant hearing damage, while normal mice experienced no hearing loss at all. In another experiment, mice were exposed to high intensity sound levels, comparable to that of a passing subway train at about ten feet, or most MP3 players at maximum volume. As expected, under these conditions, the mice with the normal CRFR2 genes experienced some hearing loss, but the mice lacking the CRFR2 genes experienced twice as much hearing loss compared to the

normal mice.

"Our research shows that the CRFR2 receptors have a role in the cellular reaction to environmental stressors acting on the inner ear, such as moderate and loud noise exposure. Identifying the role of CRF receptors in the inner ear may ultimately help us understand why some individuals are more susceptible than others to noise-induced hearing loss. It is possible that there is some variability in the activity or expression of the receptors," said first author Christine Graham, a graduate student in neuroscience at the Sackler School of Graduate Biomedical Sciences at Tufts.

The study was published in the May issue of *Neurobiology of Disease*.

More information: Graham CE, Basappa J, Vetter DE. Neurobiology of Disease. 2010. (May); "A corticotropin-releasing factor system expressed in the cochlea modulates hearing sensitivity and protects against noise-induced hearing loss." 38(2): 246-258, doi:10.1016/j.nbd.2010.01.014

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