

Listen to this: Study upends understanding of how humans perceive sound

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A key piece of the scientific model used for the past 30 years to help explain how humans perceive sound is wrong, according to a new study by researchers at the Stanford University School of Medicine.

The long-held theory helped to explain a part of the <u>hearing</u> process called "adaptation," or how humans can hear everything from the drop of a pin to a jet engine blast with high acuity, without pain or damage to the ear. Its overturning could have significant impact on future research for treating hearing loss, said Anthony Ricci, PhD, the Edward C. and Amy H. Sewall Professor of Otolaryngology and senior author of the study.

"I would argue that adaptation is probably the most important step in the hearing process, and this study shows we have no idea how it works," Ricci said. "Hearing damage caused by noise and by aging can target this particular molecular process. We need to know how it works if we are going to be able to fix it."

The study will be published Nov. 20 in *Neuron*. The lead author is postdoctoral scholar Anthony Peng, PhD.

Deep inside the ear, specialized cells called hair cells detect vibrations caused by air pressure differences and convert them into electrochemical signals that the brain interprets as sound. Adaptation is the part of this process that enables these <u>sensory hair cells</u> to regulate the decibel range over which they operate. The process helps protect the ear against sounds that are too loud by adjusting the ears' sensitivity to match the



noise level of the environment.

The traditional explanation for how adaptation works, based on earlier research on frogs and turtles, is that it is controlled by at least two complex cellular mechanisms both requiring calcium entry through a specific, mechanically sensitive ion channel in auditory hair cells. The new study, however, finds that calcium is not required for adaptation in mammalian auditory hair cells and posits that one of the two previously described mechanisms is absent in auditory cochlear hair cells.

Experimenting mostly on rats, the Stanford scientists used ultrafast mechanical stimulation to elicit responses from hair cells as well as high-speed, high-resolution imaging to track calcium signals quickly before they had time to diffuse. After manipulating intracellular calcium in various ways, the scientists were surprised to find that calcium was not necessary for adaptation to occur, thus challenging the 30-year-old hypothesis and opening the door to new models of mechanotransduction (the conversion of mechanical signals into electrical signals) and adaptation.

"This somewhat heretical finding suggests that at least some of the underlying molecular mechanisms for adaptation must be different in mammalian cochlear hair cells as compared to that of frog or turtle hair cells, where adaptation was first described," Ricci said.

The study was conducted to better understand how the adaptation process works by studying the machinery of the inner ear that converts sound waves into electrical signals.

"To me this is really a landmark study," said Ulrich Mueller, PhD, professor and chair of molecular and cellular neuroscience at the Scripps Research Institute in La Jolla, who was not involved with the study. "It really shifts our understanding. The hearing field has such precise



models—models that everyone uses. When one of the models tumbles, it's monumental."

Humans are born with 30,000 cochlear and vestibular hair cells per ear. When a significant number of these cells are lost or damaged, hearing or balance disorders occur. Hair cell loss occurs for multiple reasons, including aging and damage to the ear from loud sounds. Damage or impairment to the process of adaptation may lead to the further loss of hair cells and, therefore, hearing. Unlike many other species, including birds, humans and other mammals are unable to spontaneously regenerate these hearing cells.

As the U.S. population has aged and noise pollution has grown more severe, health experts now estimate that one in three adults over the age of 65 has developed at least some degree of hearing disability because of the destruction of these limited number of <u>hair cells</u>.

"It's by understanding just how the inner machinery of the ear works that scientists hope to eventually find ways to fix the parts that break," Ricci said. "So when a key piece of the puzzle is shown to be wrong, it's of extreme importance to scientists working to cure <u>hearing loss</u>."

Provided by Stanford University Medical Center

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