Unraveling the Pain of Sound: New Insights Into Hyperacusis

Hearing Health Foundation's partner Hyperacusis Research hosted a webinar in October 2025 that highlighted both the human impact of hyperacusis—pain triggered by everyday sounds—and the scientific progress being made to understand and treat it. The field was revolutionized in 2011 when Hyperacusis Research was founded by Bryan Pollard, who unfortunately passed away in 2022. Hyperacusis Research continues his legacy, and to date has awarded nearly $400,000 in research grants.

Several Types of Ear Pain

James Henry, Ph.D., a retired research audiologist, provided an overview of the potential mechanisms causing hyperacusis, including central auditory gain, middle ear muscle dysfunction, and specific nerve pathways. He also clarified distinctions between different types of sound sensitivity disorders, from otalgia to phonophobia.

Henry says loudness hyperacusis could be due to increased central auditory gain or to dysfunction in the middle ear muscles. Pain hyperacusis could be caused by dysfunction of the type II auditory neurons, which connect to outer hair cells in the cochlea. Another possible source is inflammation of the trigeminal nerve, which innervates the face, head, and ear.

Modeling Auditory Pain

Megan Beers Wood, Ph.D., of Vanderbilt University, a 2022–2023 Emerging Research Grants scientist generously funded by Hyperacusis Research, is modeling auditory pain in animals. She presented evidence that unmyelinated type II afferent neurons—which share characteristics with pain-sensing nerve fibers after tissue damage—may be a key component of pain hyperacusis.

Type II afferent neurons share characteristics with C-fibers, the primary pain-sensing neurons in the skin. These unmyelinated neurons express genes for pain-related neuropeptides like CGRP and Substance P, and respond to ATP, a chemical released by damaged cells. Noise exposure can cause physical and functional changes to these neurons, with an increase in the number of ribbon synapses connecting them to outer hair cells.

Wood's lab demonstrates that these nerves become activated after noise exposure and confirms that a functional cochlea is necessary to generate these auditory pain signals. In mice, auditory pain can be measured using changes in facial grimace and body position. Deaf mice cannot detect sound, demonstrating that the initial detection of sound by a functional cochlea is necessary for the generation of auditory pain.

HHF's Timothy Higdon (second from left) with (from left) Hyperacusis Research's Steven Barad, M.D., Michael Maholchic, and Ana Raab, at the ARO MidWinter Meeting in February 2025.

A Potential Pharmacological Treatment

Thanos Tzounopoulos, Ph.D., of the University of Pittsburgh, explained the "central gain" (neural hyperactivity) mechanism: After noise-induced damage reduces the signal from the ear, the brain turns up an internal gain to compensate, and neurons become hyperactive. This hyperactivity is caused by the dysfunction of potassium channels called KCNQ, which fail to open properly after noise injury.

An epilepsy drug, Retigabine, was previously shown to force these channels open but produced unacceptable side effects, and now Tzounopoulos and his team have developed a new, more specific molecule called RL81 that also opens KCNQ channels, quieting hyperactive neurons. RL81 is still in preclinical development. While drug delivery remains a challenge, this compound represents a promising new approach to correcting the neural hyperactivity underlying tinnitus. Once it enters testing, RL81 will likely be evaluated first for tinnitus.

For the full summary, see hhf.org/blogs/unraveling-the-pain-of-sound-new-insights-into-hyperacusis. Watch the full captioned video at youtube.com/watch?v=bKR4A0zY3uI. For more, see hhf.org/hyperacusis-research.

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