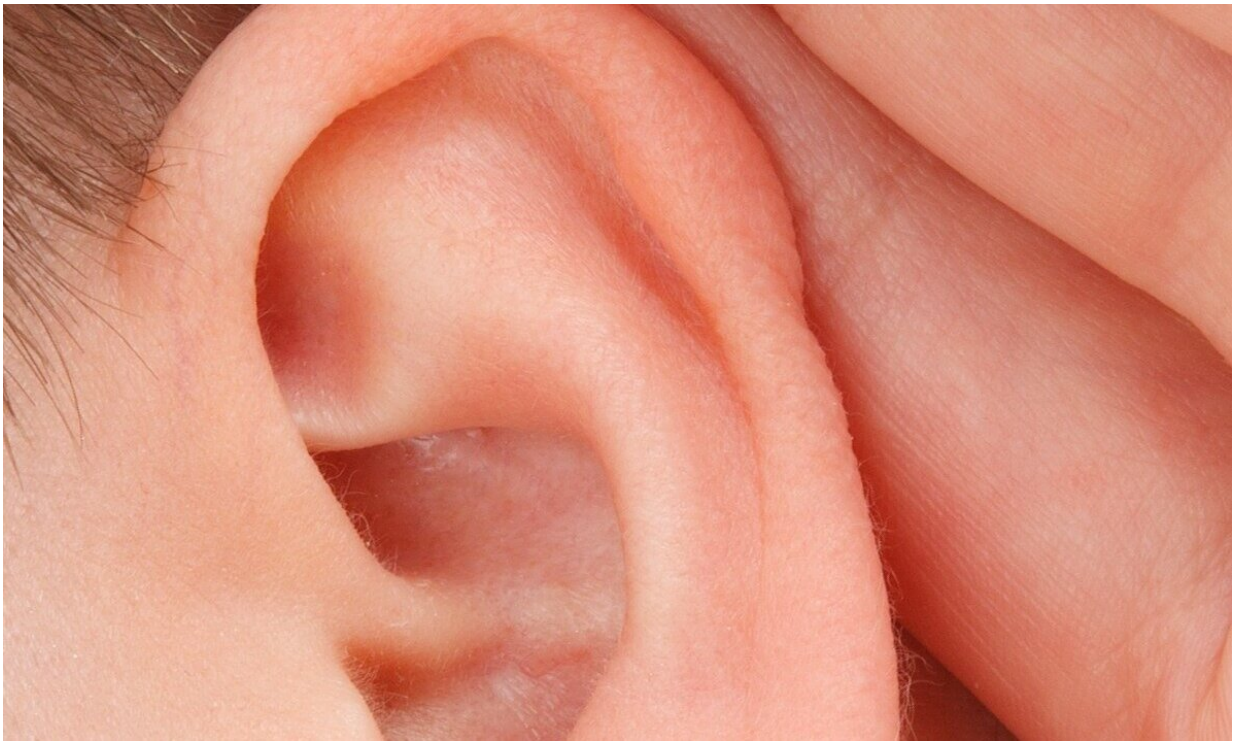
Bone disease medications may reverse hearing loss

July 20 2020, by Ryan Jaslow



Credit: CC0 Public Domain

Preliminary findings from Harvard Medical School researchers at Massachusetts Eye and Ear may pave the way for trials to test bone density medications for hearing loss.

Hearing loss caused by damaged nerves, whether from sound exposure

or aging, is irreversible. There are currently no medications approved by the Food and Drug Administration (FDA) to treat and reverse the most common type of hearing loss, called sensorineural hearing loss (SNHL). But a new animal study hopes to pave the way for future trials to see whether this type of treatment can be used in people.

New research led by Konstantina Stankovic, HMS associate professor of otolaryngology head and neck surgery at Mass. Eye and Ear, and Albert Edge, the Eaton-Peabody Professor of Otolaryngology Head and Neck Surgery at Mass. Eye and Ear, have found medications called bisphosphonates, which are commonly used to prevent bone density loss, were able to regrow damaged nerve connections in the inner ear in mice with SNHL. While the findings require further studying in animal models, the research team hopes it could be a promising target for conducting clinical trials in people with SNHL.

The discoveries were published July 14 in Frontiers in Molecular *Neuroscience*.

"This is a significant finding because it opens the possibility for repurposing bisphosphonates, which typically treat severe osteoporosis and metastatic bone disease, for the treatment of sensorineural hearing loss," said Stankovic, director of the Division of Otology and Neurotology at Mass. Eye and Ear. "We hope the promising results from this pilot study can lead to clinical trials within the next several years."

Damaged nerves

Disabling hearing loss affects 466 million people worldwide and 56 million in the United States—numbers that are expected to more than double over the next two decades. Hearing loss can take a toll on health and well-being, and untreated hearing loss costs more than $750 billion in health care spending each year worldwide, due to more hospital stays

and greater need for emergency rooms and clinical visits.

For typical hearing, sound waves travel through the ear canal before reaching the eardrum and the tiny bones of the middle ear. They are then converted into electrical signals in the inner ear and transmitted to the brain via the auditory nerve.

One type of hearing loss, called conductive hearing loss, occurs when sound transmission from the ear canal to the inner ear is impaired (such as by a middle ear infection, fluid, or impaired vibration of middle ear bones), leading to a reduction in sound levels reaching the inner ear and an inability to hear soft sounds.

Sensorineural hearing loss, on the other hand, occurs in the inner ear. The most common causes of hearing loss are noise exposure and aging, which results in loss of connections, called synapses, between nerve cells and sensory hair cells found in the inner ear. This type of SNHL is referred to as cochlear synaptopathy.

Research hopes

Previous research from Stankovic's lab looked to identify potential pathways to treat SNHL. Their analyses found that osteoprotegerin, a substance typically secreted by bone cells to inhibit bone remodeling, is highly produced by cochlear neurons and promotes their survival. In previous studies, doctors have observed that people with SNHL due to severe otosclerosis who take bisphosphonates have the ability to significantly improve their hearing loss and understand speech.

Word recognition is a sensitive measure of cochlear nerve function. That revelation, along with the previous results from the influence of the drug on the rapid increase and survival of cochlear stem cells, prompted the researchers' new study to determine the effects of bisphosphonates on

cochlear synaptopathy.

The scientists administered bisphosphonates to mice 24 hours after noise exposure. They found that the medication had a dramatic effect at regenerating the synapses between inner hair cells and spiral ganglion neurons found in the ear, and restoring cochlear function.

The team further suggested that their finding provides possible mechanisms that could explain why some patients in the clinic have improved their ability to recognize speech after bisphosphonate treatment. They also suggest that bisphosphonates are worth considering to reverse the loss of nerve connections for the treatment of human SNHL.

Stankovic cautioned that the research is still in its early phases. More research is needed, in animals and then in clinical safety and efficacy trials, before this could be a recommended treatment.

"It is our hope that, with further study, we can offer patients who have currently irreversible hearing damage a medication that might stall or reverse their hearing loss," she said.

More information: Richard Seist et al. Regeneration of Cochlear Synapses by Systemic Administration of a Bisphosphonate, *Frontiers in Molecular Neuroscience* (2020). DOI: 10.3389/fnmol.2020.00087

Provided by Harvard Medical School