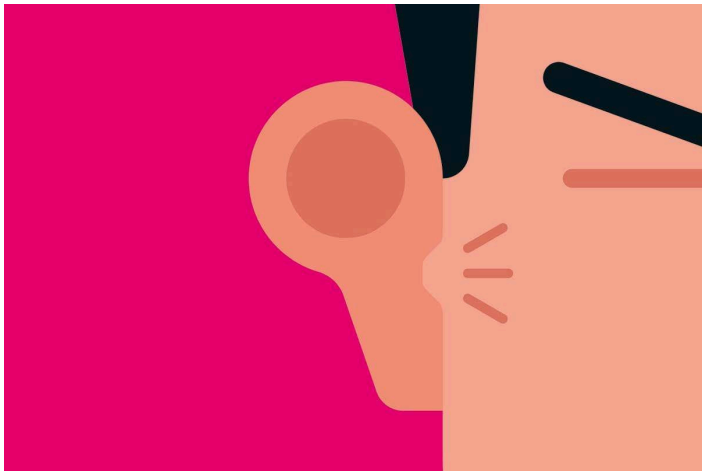
A new understanding of tinnitus and deafness could help reverse both

Investigations of the paradoxical link between tinnitus and hearing loss have revealed a hidden form of deafness, paving the way to possible new treatments

By Clare Wilson on April 17, 2024



Pâté

Working as a DJ in Liverpool, UK, a decade ago, James Rand would often leave work hearing strange sounds that he knew weren't real — a high-pitched whine or a low rumble. These symptoms of tinnitus always disappeared by the time he awoke… until, one day in 2017, they didn't.

A doctor confirmed that the sounds had probably been caused by Rand's exposure to loud music for hours at a time. There were no treatments, bar ways to help him get used to it. "I knew I was never going to hear silence again," he says. "It was incredibly depressing."

Today, though, the prospects for treating tinnitus aren't so bleak. New research has led to neurostimulation devices that reduce the sounds' volume. Moreover, several treatments are in development that could even silence tinnitus completely. "For the first time, we're talking about a possible cure," says Stéphane Maison at Harvard Medical School.

These insights have also shed light on a common cause of hearing loss. In fact, they suggest that some of the same treatments for tinnitus could also restore hearing in people who have

become partially deaf with age. “It has completely changed the way we think about hearing loss,” says Maison.

What is tinnitus?

Tinnitus is one of the most common long-term medical conditions, affecting up to a quarter of older adults. While the whining and rumbling experienced by Rand are common forms, others may hear whistling, humming, clicking or even musical hallucinations. The sounds can be intrusive and distracting, sometimes leading to depression, anxiety and difficulties sleeping. They can also interfere with hearing. Rand was worried it would affect his job as a music producer, his main career. “I work in music and I’d killed my ears,” he says. “I spent a long time being angry at myself.”

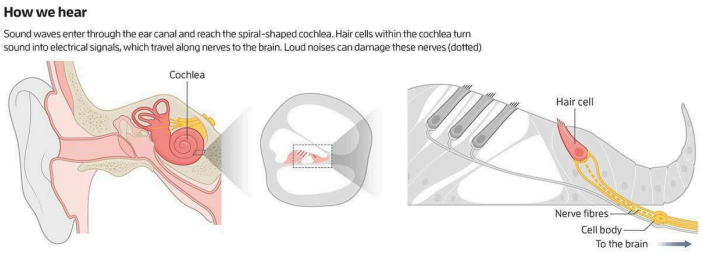
When someone first seeks help for tinnitus, doctors usually try to rule out potentially treatable causes, such as a build-up of earwax or a reaction to medication. But most people end up being advised to find some way to live with it, using strategies such as talking therapies, hearing aids to stop tinnitus interfering with real sounds, or white noise to mask tinnitus sounds while going to sleep.

That is set to change. In the past 15 years, major advances have come from investigating the links between tinnitus and hearing loss. Doctors have long known of the connection between the two conditions. For instance, if people have hearing loss at certain sound frequencies, they often hear a whine at the same pitch. It is even possible to trigger temporary tinnitus by wearing heavy-duty earplugs for several days to mimic hearing loss.

Yet the link between tinnitus and hearing loss is paradoxical: the former is hearing things that aren’t there, while the latter is being unable to fully hear. The leading explanation for this link is that the loss of input from the ears causes the brain to compensate by becoming more sensitive — sometimes called the central gain theory. As a result, the brain creates the illusory sounds of tinnitus in a similar way to how someone with an amputated limb may feel phantom sensations from the missing body part.

But there is a problem with this hypothesis. There are some people, like Rand, who have tinnitus but have normal results on hearing tests — up to a quarter of those with the condition, by some estimates.

An explanation for this has come from our growing understanding of how hearing can be damaged. Ordinarily, sound waves pass through the eardrum and reach fluid inside a spiral chamber within the inner ear called the cochlea (see graphic, below). Cells with tiny hairs that are buffeted by this fluid turn sound waves into electrical impulses that travel along nerves to the brain. These hair cells gradually die off as we get older, especially the ones that register high-frequency sounds. For a long time, the assumption was that loud noise also damages hearing by killing hair cells. But in 2009, work in mice discovered another culprit.



Sharon Kujawa and Charles Liberman at Harvard Medical School showed that, under moderate noise overexposure, the nerve fibres that carry signals from hair cells to the brain are more vulnerable to noise damage than hair cells are. What's more, the damage doesn't affect all the fibres equally. While they look similar, in reality, there are at least three different types, letting us process sounds at different volumes: quiet, intermediate and loud. The ones that process loud sounds are most susceptible to damage. "This got people's attention," says Liberman.

The findings — which were replicated in a variety of different animals — have several important implications. The first is that, if hearing loss that happens with ageing follows the same pattern, it explains why it is so common for older people to have difficulties understanding speech in noisy surroundings, like in a restaurant. Presumably, in some people, the nerve fibres that respond to quiet sounds are fine, but the nerves that respond to loud sounds have been damaged, says Liberman.

Tinnitus and hidden hearing loss

A second implication relates to the cause of tinnitus. People who have the condition but have good hearing, according to the standard hearing test known as an audiogram, have long been a stumbling block for the central gain theory. However, if they had damage solely to their loud nerve fibres, this wouldn't show up as hearing loss in an audiogram, which only measures the quietest sounds that people can hear. This strengthens the case for the central gain theory. "It presented a new way to think about people whose audiograms are normal, but who have tinnitus," says Liberman.

Two years later, Roland Schaette and David McAlpine at University College London showed this could indeed be happening in people, as well as animals. They found that people with tinnitus but normal results in hearing tests had lower activity in the nerves leading from the ear to the brain, compared with those without tinnitus and normal hearing — supporting the idea that the brain is getting less input from the damaged "noisy nerves" and so responds by generating the phantom sounds of tinnitus. The researchers also proposed that the condition of having hearing problems only in noisy environments be called hidden hearing loss, a term that has stuck. These findings have since been confirmed in larger groups of people, including in work by Liberman, Maison and others published in November 2023.

The evidence that noise exposure can affect cochlear nerves to cause hidden hearing loss, even before it kills hair cells, is starting to be taken more seriously, says Liberman. But it is still unknown how common this form of hearing loss is, as it is such a recent discovery.

Rand says that his experience fits the description of hidden hearing loss. Standard tests indicate his hearing is fine, but he has difficulties understanding speech in noisy environments. “My hearing is quite bad if I’m walking with my son with the background sound of cars,” he says. “I’m constantly having to stick my ear closer to him.”

The crucial 2009 findings in mice have a further implication, and it is one that offers hope about new treatments. The old idea, that the main effect of noise exposure is to kill hair cells, meant that to reverse the damage, new hair cells would have to be created — a formidable challenge. But repairing cochlear nerve fibres may be more achievable. The animal work showed that the initial damage is to the nerves’ synapses — the connections they make with the hair cells — progressing along to the first part of the fibre. What remains is a crucial part of the nerve cell called the cell body, along with the second half of the nerve fibre, which continues on to the brain. “The exciting thing is that the cell body and the rest of the fibre can remain alive [after the initial damage] for decades,” says Maison.

Regrowing nerves

That is good news because previous work has shown that fibres and synapses can be coaxed to regrow by natural signalling molecules called neurotrophins. In the ear, focus has turned to one called neurotrophin-3, which normally promotes synapse formation in the ear in developing embryos, says Gabriel Corfas at the University of Michigan.

One hurdle is that neurotrophins are large protein molecules, which makes them hard to deliver to the inner ear, but there are possible workarounds. Corfas and his colleagues have used gene therapies to boost levels of neurotrophin-3 in the inner ears of mice, which leads to synapse growth. In one experiment, they were even able to give the animals more synapses than normal, which gave them superior hearing.

Niliksha Gunewardene at the Bionics Institute in Melbourne, Australia, and her colleagues have recently shown that in animals, an injection of neurotrophin-3-loaded nanoparticles into the ear releases the compound for several weeks. Further along is a French firm called Cilcare, which has several drugs in the works that trigger production of multiple neurotrophins. Its lead compound — which Cilcare isn’t yet identifying publicly — has already been shown to be safe in people when given orally for a different medical condition. The firm is due to start a trial next year in people with hidden hearing loss, with or without tinnitus.

Treating tinnitus

Strategies such as these, which could potentially reverse both hearing loss and tinnitus, may still be some years away from reaching the clinic. But a different approach, designed to turn down the volume of tinnitus, is already starting to bear fruit. It is based on further insights about exactly how the brain produces these phantom sounds. Work by several groups has shown that this happens primarily within a site at the base of the brain called the cochlear nucleus, where the cochlear nerve fibres enter and make connections with brain cells. According to studies in animals, this is where activity is raised to compensate for the lack of input from the ears. “The circuits become self-stimulating,” says Susan Shore at the University of Michigan. “And the rest of the brain thinks there’s a sound in the absence of external sound.”

Loud noise can damage the nerves that send signals from the ears to the brain. Charlie Raven/Alamy

Despite its name, the cochlear nucleus also has inputs from other parts of the body, including touch neurons from the face, jaw and neck, which may be to suppress sounds caused by movements of the body, such as chewing. This could explain why many people with tinnitus can change the pitch or loudness of their phantom sounds by moving their jaw or neck, and also why tinnitus occasionally begins after a head injury, says Shore.

Homing in on the site where tinnitus sounds are generated has enabled attempts to hack this process. There are now two companies producing devices aimed at reducing tinnitus symptoms by providing sounds alongside electrical stimulation of touch neurons. The idea is that, over time, this reduces the overactivity of the auditory circuits within the cochlear nucleus.

A firm co-founded by Shore, called Auricle, uses electrodes placed on the jaw or neck to deliver stimulation, followed 5 milliseconds later by pulses of sound at the same frequency as the person’s tinnitus. In a trial in 99 people, using this equipment for 30 minutes a day for six weeks reduced the loudness of their tinnitus compared with a control treatment that delivered the sound alone. Auricle is in the early stages of an approval application.

Neuromod Devices, a company based in Dublin, Ireland, has already received approval for a similar device called Lenire, which was launched in Europe in 2019 and in the US last year.

Lenire delivers electrical stimulation to the tongue at the same time as the person listens to sounds through headphones. The firm has carried out three trials showing that the severity of people's tinnitus reduced with the treatment, although it didn't compare the stimulation with a placebo version, which would have been a more rigorous test, says Will Sedley at Newcastle University, UK.

It is possible that both strategies — to regrow the damaged parts of cochlear nerves and to turn down activity in the cochlear nucleus via electrical stimulation — could help people with tinnitus, says Sedley. But he warns that there are potential downsides if people pin their hopes on eradicating their symptoms. At the moment, the approach with the most supporting evidence is using talking therapies that help people learn to live with the sounds, he says. "I've heard a number of people talk about declaring war on their tinnitus," he says. "What's really evidence-based and currently available are ways to make peace with it."

That philosophy chimes with Rand's experience. Contrary to his initial fears, his symptoms didn't interfere with his music career and he has now come to terms with his tinnitus. "It doesn't feel that intrusive in the day and I have grown used to it at night," he says.

At work in mixing studios, however, Rand is fastidious about making sure sound levels don't get too high, so as to avoid further hearing damage. And he advises everyone to wear hearing protection at clubs and concerts. "You get one pair of ears, so look after them," he says. "I miss silence and guarantee you would too if you lost it."

Prevention is better than a cure

Most people are aware that excessive noise exposure can lead to hearing loss and tinnitus (see main story). But it is hard for people to know exactly how loud is too loud, says Will Sedley at Newcastle University, UK.

Damage to the ears can be caused by both short bursts of very loud noise and prolonged exposure to moderately loud noise. Common sources of dangerously loud noise include work environments, such as factories, the military and the music and e-sports industries.

Outside work, we may damage our ears at concerts, in nightclubs or by listening to music via headphones at too loud a setting. "There are very clear noise exposure guidelines. My impression is they are ignored by everybody, whether it's the listener or people who run concerts, clubs and bars," says Sedley.

He recommends that people follow the "60-60" rule when using headphones, which means you should listen at no more than 60 per cent of the maximum volume for no longer than 60 minutes.

"For any venue, if it's uncomfortably loud, wear earplugs," says Sedley. "If you come out with temporary tinnitus, that means you [also] have temporary hearing loss and you've also accrued a little bit of permanent hearing damage."

Clare Wilson is a health reporter at New Scientist