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NEUROSCIENCE

HIDDEN HEARING LOSS

Jackhammers, concerts and other common noisemakers may cause irreparable damage to our ears in unexpected ways *By M. Charles Liberman*

FOOTBALL FANS OF THE SEATTLE SEAHAWKS AND THE KANSAS CITY CHIEFS ROUTINELY compete at home games to set the Guinness World Record for the noisiest stadium. On October 1, 2014, the Chiefs hit the latest peak: 142.2 decibels (dB). That level is like the painful, blistering roar of a jet engine at 100 feet—a typical example that hearing experts give for a noise that is more than loud enough to cause hearing damage. After the game, the fans were ecstatic. They reveled in the experience, noting the ringing in their ears or the feeling that their eardrums were about to explode. What was happening inside their ears was far from wonderful, however.

A hearing test, if administered before and immediately after the game, might have shown a marked deterioration. The softest sound that a fan could have heard before kickoff—say, whispered words—might no longer be detectable by halftime. The thresholds for hearing might have risen by as much as 20 to 30 dB by the final whistle. As the ringing in fans' ears subsided over the course of a few days, the output of the hearing test, an audiogram, might well return to baseline, as the ability to hear faint sounds returned.

Scientists long thought that once thresholds returned to normal, the ear must have done so as well. Recently my colleagues and I have shown that this presumption is not true. Exposures that lead to only a temporary rise in thresholds can, nonetheless, cause immediate and irreversible damage to fibers in the auditory nerve, which conveys sound information to the brain. Such damage may not affect the detection of tones, as shown on the audiogram, but it can hamper the ability to process more complex signals. This newly recognized condition is called hidden hearing loss because a normal audiogram can hide the nerve damage and the hearing impairment associated with it.

As a person continues to abuse their ears, the toll on the nerve fibers can mount. In fact, such damage may contribute to the gradual deterioration in the ability of the middle-aged and elderly to discriminate the subtleties of speech. Hid-

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den hearing loss, however, is by no means confined to older adults. The latest research suggests that it is occurring at ever younger ages in industrial society because of greater exposure to loud sounds, some avoidable, some not.

A SENSORY MARVEL

THE VULNERABILITY of the ear stems from its awe-inspiring sensitivity, which allows it to function across a vast range of sound levels. Our ability to just make out a quiet sound at frequencies near 1,000 oscillations per second, or 1,000 hertz (Hz)—in other words, the threshold at which we can perceive that sound—is defined as zero decibels. Using this logarithmic measure, each 20-dB increase in sound level corresponds to a 10-fold increase in the amplitude of the sound waves. At 0 dB, the bones of the middle ear, whose vibrations drive the hearing process, move less than the diameter of a hydrogen atom. At the other extreme, such as the pain-inducing levels of more than 140 dB at the record-setting Chiefs game, the ear is forced to deal with sound waves that are 10 million times greater in amplitude.

Hearing begins as the outer ear funnels sound waves through the ear canal to the eardrum, which vibrates and sets the bones of the middle ear in motion. The resulting vibrations then make their way to the inner ear's fluid-filled tube, the cochlea—the location of hair cells that occupy a spiraling strip of tissue called the organ of Corti. These cells get their name from hairlike protrusions known as stereocilia that extend in bundles from one end of the cells. Hair cells most sensitive to low frequencies lie at one end of the cochlear spiral, and those most sensitive to high frequencies lie at the other end. As sound waves bend the "hairs," these cells convert vibrations to chemical signals, emitting a neurotransmitter molecule—glutamate—at the other end, where the hair cells form synapses with the fibers of the auditory nerve.

At the synapse, the glutamate released from a hair cell crosses a narrow cleft to bind to receptors on the end, or terminal, of an auditory nerve fiber. Each terminal is at one end of a nerve cell that extends a long fiber, an axon, to its other end in the brain stem. Glutamate bound to nerve fibers triggers an electrical signal that travels the entire length of the auditory nerve to the brain stem. From there the signals move through a series of parallel neural circuits that traverse various regions—from the brain stem to the midbrain and thalamus—and finish their journey at the auditory cortex. Together this complex circuitry analyzes and organizes our acoustic environment into a set of recognizable sounds, whether it be a familiar melody or the wail of a siren.

Hair cells come in two types, termed outer and inner. Outer hair cells amplify the sound-induced motions in the inner ear, whereas inner hair cells translate these motions into the chemical signals that excite the auditory nerve. The inner cells are most directly responsible for what we think of as "hearing" because 95 percent of auditory nerve fibers form synapses only with inner hair cells. Why so few fibers connect the outer hair cells to the brain remains a mystery, but it has been theorized that the fibers connected to outer hair cells may be responsible for the pain that we all suffer when the loudness of a sound wave approaches 140 dB.

Historically hearing loss has been assessed mainly by audiograms. Ear doctors have long known that workers pounding sheet metal into boilers often had permanent hearing loss for tones in the middle-frequency region. Audiograms record our ability to detect tones at octave-frequency intervals: for example 250, 500, 1,000, 2,000, 4,000 and 8,000 Hz. In the early stages of noise-induced hearing loss, the audiogram exhibits what is called the boilermaker's notch, an inability to detect sounds in the middle frequencies of the human hearing range.

In the 1950s and 1960s epidemiological studies of workers in noisy factories showed a clear relation between length of employment and a decline in hearing acuity. The initial deficit near 4,000 Hz tended to spread to other frequencies over time. Many older workers lost hearing entirely above 1,000 or 2,000 Hz. Such high-tone loss causes a severe hearing impairment because much of the information in speech is in the frequency range that has become unresponsive.

Human studies such as these inspired the federal government in the 1970s to establish noise guidelines to limit workplace exposures. Today several federal agencies regulate noise levels on the job, including the National Institute for Occupational Safety and Health and the Occupational Safety and Health Administration, and different agencies suggest different limits. The lack of precise agreement reflects the challenges in assessing noise-damage risk. The problems are twofold. First, there are enormous individual differences in noise susceptibility: there are what might be described as "tough" ears and "tender" ears. That means regulators must choose what percentage of the population they want to protect and what level of hearing loss is acceptable. The other problem is that the effects of noise on hearing result from a complex combination of duration, intensity and frequency of sounds to which a person is exposed.

Currently OSHA mandates that sound levels not exceed 90 dB for an eight-hour day. The risk of noise damage above 90 dB is roughly proportional to the total energy that is delivered to the ear (duration multiplied by intensity). For each additional 5 dB above the eight-hour standard, OSHA guidelines recommend a halving of exposure time—in other words, a worker should not be exposed to 95 dB for more than four hours daily or to 100 dB for more than two hours a day. By these measures, the 142-dB-plus exposure of football fans vying for the Guinness noise record would exceed OSHA guidelines in around 15 seconds. Of course, OSHA does not regulate noise levels for fans at football games or even for U.S. farms, where teenagers driving tractors and combines all day are at serious risk of hearing loss.

For the past 60 years hearing special-

IN BRIEF

Conventional wisdom holds that loud noises cause muffled sound or ringing in the ears, but the ears soon recover.

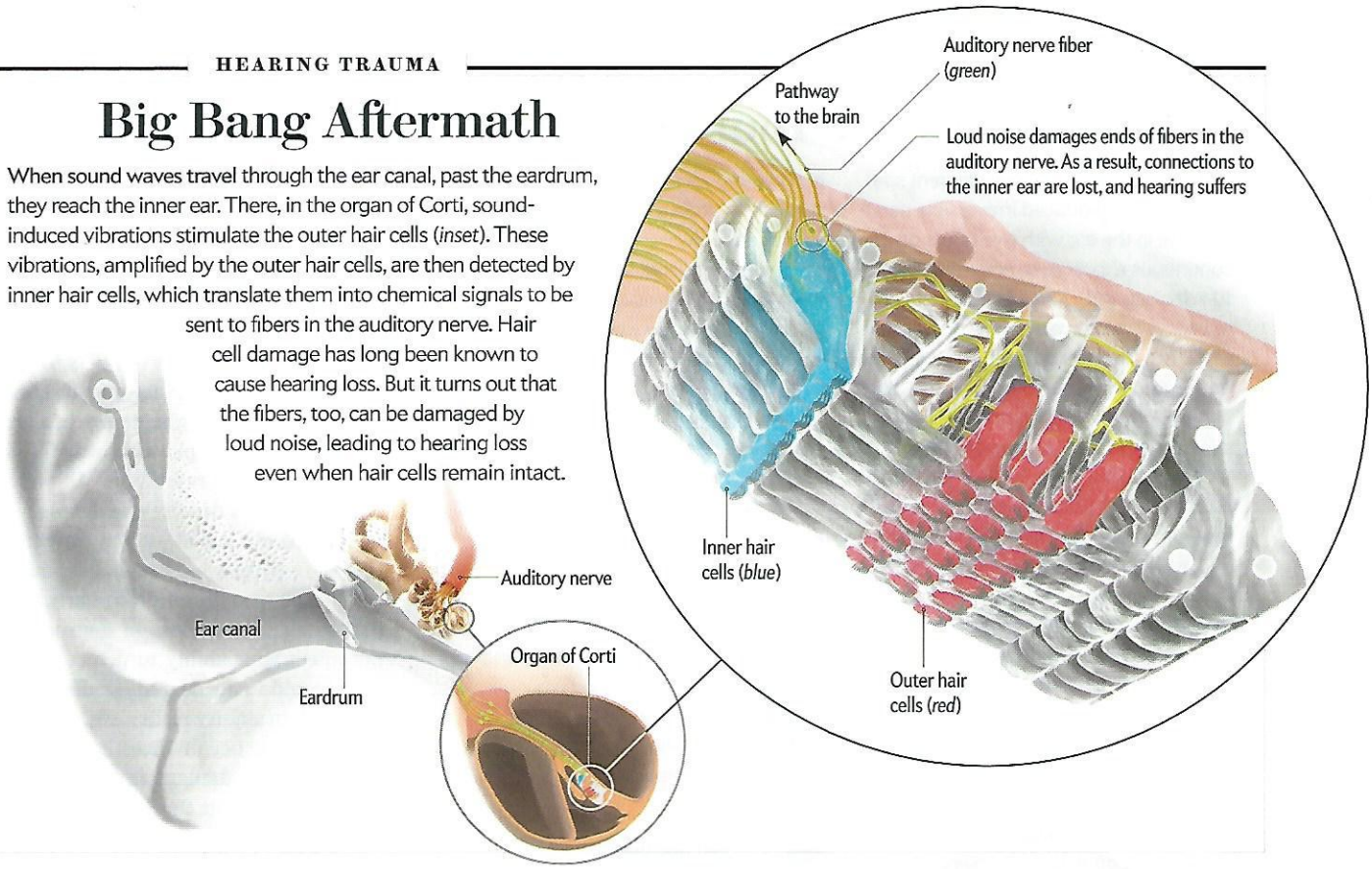
Elevated noise levels can produce permanent damage to auditory nerve fibers that carry sound into the brain.

Hidden hearing loss that results may allow someone to hear sounds without making out what a speaker is saying.

A drug that lets the damaged nerve fibers recover may be one solution to this ubiquitous problem.

Big Bang Aftermath

When sound waves travel through the ear canal, past the eardrum, they reach the inner ear. There, in the organ of Corti, sound-induced vibrations stimulate the outer hair cells (*inset*). These vibrations, amplified by the outer hair cells, are then detected by inner hair cells, which translate them into chemical signals to be sent to fibers in the auditory nerve. Hair cell damage has long been known to cause hearing loss. But it turns out that the fibers, too, can be damaged by loud noise, leading to hearing loss even when hair cells remain intact.



ists have assumed that routine readings of an audiogram reveal everything we need to know about noise-induced damage to hearing. Indeed, the audiogram will show if there has been damage to the inner ear's hair cells, and investigations from the 1940s and 1950s revealed that hair cells were among the most vulnerable cells in the inner ear to acoustic overexposures.

Experiments in animals, some performed in our laboratory, have shown that outer hair cells are more vulnerable than inner ones, that hair cells in the section of the cochlea that detects high-frequency tones are more vulnerable than those in the low-frequency region, and that, once lost, hair cells never regenerate. Even before the cells degenerate, loud noise can damage the bundles of stereocilia atop the cells, and this damage is also irreversible. When damage to or death of hair cells occurs, hearing thresholds are elevated—the radio must be turned up, or a colleague across the table must raise his or her voice.

More incisive study of cochlear damage in humans has been hampered by the fact that the tiny hair cells cannot be biopsied safely or imaged in a living individual with any existing technique. Damage associated with noise-induced hearing loss in humans has been studied only in people who have donated their ears for scientific study after death.

In part because of these limitations, the question of whether hearing loss is unavoidable in the aging process—or whether it is a consequence of repeated exposure to the clamor of modern life—continues to puzzle hearing scientists. A tantalizing hint came from a study in the 1960s, in which researchers sought out groups living in uniquely quiet environments, such as the Mabaan tribe in the Sudanese desert. Hearing testing was significantly better in Mabaan men, from 70 to 79 years old, compared with a group of American men of the same age. Of course, these studies cannot tease out other differences between an average American and the typical Mabaan, such as those related to genetic background or diet.

DEEP DAMAGE

RECENT INVESTIGATIONS by my colleagues and me into the effects of noise on hearing have added a sobering new dimension to our understanding of the dangers of acoustic overexposure. Scientists and clinicians have long known that some of the hearing impairment from noise exposure is reversible and that some is not. In other words, at times hearing thresholds return to normal a few hours or days after an exposure—other times recovery will be incomplete, and the higher threshold will persist forever. Hearing scientists used to think that if the threshold sensitivity recovered, the ear had completely recovered. We now know that this is not true.

The loud pop of Fourth of July firecrackers or the roar of the crowd at a football game not only affects the hair cells, it also damages the auditory nerve fibers. We and others showed in the 1980s that overly loud noise causes damage to the terminals of the nerve fibers where they form synapses with hair cells. The swelling and eventual rupture of the terminals probably occur in response to excess release of the signaling molecule glutamate from the overstimulated hair cells. Indeed, too much glutamate release anywhere in the nervous system is toxic. The conventional wisdom had been that these noise-damaged fibers must recover or regenerate after intense noise exposure because auditory thresholds can return to normal in ears that showed massive nerve swelling immediately after exposure.

In my lab, we were skeptical that such

Illustration by Bryan Christie

How to Protect Your Hearing

In animal studies in several different species, we have produced irreversible nerve damage in the ear with two hours of continuous exposure to noise at 100 to 104 decibels (dB). There is every reason to believe that human ears are just as sensitive. Most daily exposures in our lives do not continue for that long. Nevertheless, it is prudent to avoid unprotected exposure to any sounds in excess of 100 dB.

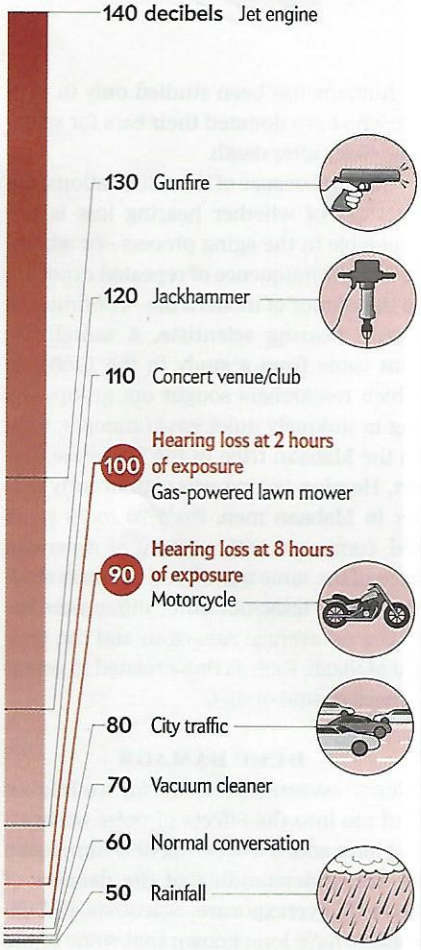
Many sounds in daily life take us into a danger zone. Concert venues and clubs routinely produce peak levels of 115 dB and average levels in excess of 105 dB. Gas-powered leaf blowers and lawn mowers reach levels at the users' ears between 95 and 105 dB, as do power tools such as circular saws. Frequency of the sounds matters. The more high-pitched whine of a belt sander is more dangerous at the same decibel level than the lower-pitched roar of an undermuffled motorcycle. Jackhammers produce levels of 120 dB even for passersby, and the rapid-fire impulses of the metal rod on concrete produce lots of the dangerous high-pitched sounds.

What can we do? These days almost all of us have access to surprisingly accurate sound-level meters in our pockets or purses. There are numerous free or inexpensive apps for iOS and Android phones that provide reliable readings of sound pressure produced by a musical instrument or a car backfiring to within 1 to 2 dB of the most expensive professional sound-monitoring equipment. The app for iOS that worked best for me, Sound Level Meter Pro, is still under $20 and gave me readings in my laboratory that were accurate to less than 0.1 dB.

Once you are aware of which sounds in your environment are potentially dangerous, the good news is that effective ear protection is cheap, easy to use and extremely portable. If properly inserted, the foam-type insert plugs can attenuate the sound level by 30 dB in the most dangerous frequency regions. Roll one between your fingers to squeeze it into the thinnest cylinder you can and then quickly insert it as deeply in your ear canal as you can. It is no more difficult or dangerous to do so than putting in earbud headphones. Let them slowly expand, and within a minute you are ready to rock and roll.

If you are attending a concert, these foam earplugs provide too much sound muffling. When you want to hear the sound but just at a lower (safe) level, use "musicians' ear plugs." Several brands are available online for $10 to $15 a pair. They are designed to provide 10 to 20 dB of sound attenuation, with equal muffling of low- and high-pitched sounds, so that the timbre of music is unaffected.

Most important, pay attention to what your ears are telling you. If you have left an event or an activity sensing that sounds seem muffled, like you have cotton in your ears, or if you have ringing in your ears, odds are that you have destroyed some auditory nerve synapses. Don't despair but try not to let it happen again. —*M.C.L.*



badly damaged synapses could regenerate in the adult ear. We also knew that noise-induced nerve damage would not necessarily be reflected in the standard testing because animal studies dating back to the 1950s showed that loss of auditory nerve fibers, without loss of hair cells, does not affect the audiogram until the loss becomes catastrophic, greater than 80 percent. It appears that you do not need a dense population of nerve fibers to detect the presence of a tone in a quiet test booth. By analogy, take a digital image of a group of people and sample it repeatedly, each time at a lower resolution. As you decrease the pixel density, the details of the image become less clear. You can still tell there are people in the picture, but you cannot tell who they are. Similarly, we hypothesized, diffuse loss of neurons need not affect your ability to detect a sound, but it could easily degrade understanding of speech in a noisy restaurant.

When we began investigating noise-induced nerve damage in the 1980s, the only way to count the synapses between auditory nerve fibers and inner hair cells was with a technique called serial-section electron microscopy, a highly laborious process requiring roughly a year of work to analyze the nerve synapses on only a few hair cells from one cochlea.

Twenty-five years later my colleague Sharon G. Kujawa of Massachusetts Eye and Ear and I were trying to determine whether one episode of acoustic overstimulation in the ears of young mice could accelerate the onset of age-related hearing loss. The noise to which we exposed the animals was designed to produce only a temporary elevation of auditory thresholds and thus no permanent hair cell damage. As expected, the rodent cochleas looked normal a few days after exposure. But as we examined the animals from six months to two years later, we saw an accumulating loss of auditory nerve fibers, despite the presence of intact hair cells.

Fortunately, much had been learned since the 1980s about how to explore the molecular structure of these synapses. Antibodies had become available that could bind to, and tag with, different fluorescent markers, structures on each side of the synapse between the inner hair cell and auditory nerve fiber. The tags allowed us to count synapses easily under a light microscope. We quickly accumulated data showing that a few days after noise expo-

SCIENTIFIC AMERICAN ONLINE Watch a video of how the auditory system works at ScientificAmerican.com/aug2015/how-hearing-works

Graphic by Amanda Montañez

sure, when the auditory threshold had returned to normal, as many as half of the auditory nerve synapses were gone and never regenerated. The loss of the rest of the neurons—the cell bodies and the axons that project to the brain stem—became evident within a few months. By two years, half of the auditory neurons had completely disappeared. As soon as the synapses were destroyed, the affected fibers were of no use and did not respond to sounds of any intensity.

In the past few years we have documented noise-induced degeneration of synapses in mice, guinea pigs and chinchillas—and in postmortem human tissue. We have shown in the animal studies and in human ears that the loss of connections between auditory nerve fibers and hair cells occurs before the threshold elevations associated with hair cell loss. The idea that auditory nerve damage causes a kind of hidden hearing loss—an important component of noise-induced and age-related hearing impairment—has now become widely accepted, and many auditory scientists and clinicians are working to develop tests to determine if the problem is widespread and if our noisy lifestyles are leading to an epidemic of ear damage in people of all ages.

REPAIRING NERVES

PUT IN ITS SIMPLEST TERMS, the audiogram, the gold standard test of hearing, measures auditory thresholds and is a sensitive gauge of cochlear hair cell damage. Yet it is a very poor indicator of damage to auditory nerve fibers. Our research has shown that the nerve damage of hidden hearing loss does not affect the ability to detect the presence of sound, but it most likely degrades our ability to understand speech and other complex sounds. In fact, it may be a significant contributor to the classic complaint of the elderly: "I can hear people speaking but can't make out what they are saying."

Audiologists have long known that two people with similar audiograms can perform very differently on so-called speech-in-noise tests, which measure the number of words correctly identified as the level of a background noise increases. Previously they have ascribed these differences to brain processing. Our research suggests that much of it arises because of differences in the surviving population of auditory nerve fibers.

Hidden hearing loss may also help explain other common hearing-related complaints, including tinnitus (ringing in the ears) and hyperacusis (inability to tolerate even sounds of moderate loudness). These conditions often persist even when an audiogram flags no problem. In the past, scientists and clinicians have pointed to the normal audiogram of a tinnitus or hyperacusis sufferer and concluded, again, that the problem must arise in the brain. We suggest instead that the damage may have taken place in the auditory nerve.

Our research raises questions about the risks of routine exposure to loud music at concerts and clubs and via personal listening devices. Although noise-induced hearing loss is clearly a problem among professional musicians, even those playing classical music, epidemiological studies of casual listeners have consistently failed to find substantial impact on their audiograms. The federal guidelines developed to minimize noise damage in the U.S. workforce are all based on the presumption that if postexposure thresholds return to normal, the ear has fully recovered. As we have learned, this assumption is wrong; thus, it naturally follows that present noise regulations may be inadequate to prevent widespread noise-induced nerve damage and the hearing impairment that it causes.

To tackle this question, we need better diagnostic tests for auditory nerve damage, short of counting synapses in postmortem tissue. One promising approach is based on an existing measure of the electrical activity in auditory neurons, called the auditory brain stem response (ABR). The ABR can be measured in an awake or sleeping subject, fitted with scalp electrodes to measure electrical activity (electroencephalography) in response to the presentation of tone bursts of different frequencies and sound-pressure levels. Historically the ABR test has been interpreted largely on a pass-fail basis: the presence of a clear sound-evoked electrical response is interpreted as normal hearing, and the absence of a response is evidence of impairment.

In animal work, we have shown that the amplitude of the ABR at high sound levels is very informative: it grows in proportion to the number of auditory nerve fibers that retain a viable connection with inner hair cells. Correspondingly, a recent epidemiological study inspired by our research has used a variant of the ABR test on a group of British college students with normal audiograms and found smaller response amplitudes among those who report having been repeatedly exposed to the din of clubs and concerts.

In search of potential treatments for hidden hearing loss, we are now asking whether we can reverse the noise-induced degeneration by treating the surviving neurons with chemicals designed to regrow nerve fibers, reestablishing connections to inner hair cells. Although the synapses themselves are destroyed immediately after the noise exposure, the slowness of the degeneration of the rest of the nerve (its cell body and axons) makes us optimistic that normal function can be restored in many human subjects. We have had encouraging results in animal studies by delivering neurotrophins (nerve growth promoters) directly to the inner ear.

Hidden hearing loss may soon be treatable by injection through the eardrum of gels that slowly release neurotrophins to restore synapses months or years after a noise insult. They would be administered immediately after exposure to loud noise, such as the explosion at the finish line of the Boston Marathon in 2013 that damaged the hearing of more than 100 spectators. An otologist may one day be able to deliver drugs to the cochlea using a minimally invasive treatment for noise-induced ear damage as easily as an ophthalmologist corrects a myopic eye by laser surgery of the lens. SA

MORE TO EXPLORE

Adding Insult to Injury: Cochlear Nerve Degeneration after "Temporary" Noise-Induced Hearing Loss. Sharon G. Kujawa and M. Charles Liberman in *Journal of Neuroscience*, Vol. 29, No. 45, pages 14,077–14,085; November 11, 2009.

Synaptopathy in the Noise-Exposed and Aging Cochlea: Primary Neural Degeneration in Acquired Sensorineural Hearing Loss. Sharon G. Kujawa and M. Charles Liberman in *Hearing Research*. Published online March 11, 2015.

FROM OUR ARCHIVES

Regaining Balance with Bionic Ears. Charles C. Della Santina; April 2010.

scientificamerican.com/magazine/sa