Putting the 'Neural' Back in Sensorineural Hearing Loss

By Sharon G. Kujawa, PhD

In many forms of sensorineural hearing loss, permanent threshold elevations are associated with hair cell damage or loss. These losses have received much experimental attention and are a primary focus of prevention and treatment efforts (*Hear Res* 2013;297:42-51).

Recent work in noise and aging, however, has revealed a much more insidious process that progressively interrupts communication between sensory hair cells and auditory neurons, ultimately leading to death of the neurons themselves. These neurodegenerative changes are likely very common, occurring even in ears with normal threshold sensitivity and a full complement of hair cells. As a result, they challenge our traditional approaches to diagnosis and management.

IMPLICATIONS FOR PUBLIC HEALTH

The inner hair cell–cochlear nerve fiber synapse is the primary conduit through which information about the acoustic environment is transmitted to the auditory nervous system. In ears that age normally–without noise exposure, for example–synapses are lost gradually throughout life. Such losses are seen in the cochlea long before the age-related decline of threshold sensitivity or hair cells (*J Neurosci* 2013;33[34]:13686-13694).

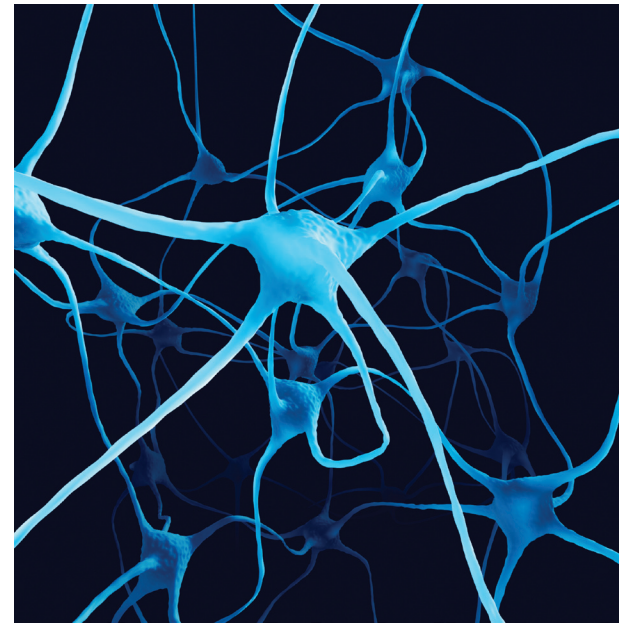
Noise produces similar, but immediate, synaptic losses and then accelerates aging, even for exposures that produce reversible threshold shifts and no hair cell loss (*J Neurosci* 2006;26[7]:2115-2123; *J Neurosci* 2009;29[45]:14077-14085).

Synaptic losses at short postexposure times are restricted to cochlear frequency regions with maximum acute threshold shifts and are followed by proportional spiral ganglion cell declines in the same cochlear regions. As animals age, losses spread to cochlear regions that initially appeared uninvolved in the noise insult.

Noise-induced cochlear neurodegeneration has now been observed in several mammalian species, and there is no reason to suspect that humans will be an exception. However, this widespread primary neurodegeneration has remained hidden for many years.

While thresholds are sensitive metrics of hair cell damage, they are relatively insensitive to diffuse loss of cochlear synapses and cochlear neurons. For example, distortion product otoacoustic emissions (DPOAEs) are unaffected because their generation requires only presynaptic processes.

Neural response thresholds like the auditory brainstem response (ABR) are not affected because the noise targets cochlear neurons with high thresholds (*J Neurophysiol* 2013;110[3]:577-586). Behavioral audiometric thresholds are unaffected for the same reason and because stimulus detection requires less neural information than stimulus discrimination.



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Although thresholds fail to capture the communication failure, my colleagues and I have identified key indicators evident in the suprathreshold neural response.

Primary cochlear neurodegeneration is a likely contributor to a variety of auditory perceptual abnormalities common with aging and after noise, including speech-in-noise difficulties (*Front Syst Neurosci* 2014;8:26), tinnitus (*J Neurosci* 2011;31[38]:13452-13457), and hyperacusis (*J Neurophysiol* 2010;104[6]:3361-3370).

These sobering findings have important implications for public health. One question is, once an ear has been exposed to noise, can the noise insult influence future changes in the ear and hearing, such as those that accrue with age?

Traditionally, the focus has been on thresholds, and an absence of delayed threshold shifts after exposure has been taken as evidence that noise effects will not occur later. Recent work using powerful new tools provides clear evidence that delayed effects can happen, though.

The current goal of federal noise exposure guidelines aims to protect against permanent threshold shifts, assuming that reversible threshold shifts are associated with cochlear recovery and a safe exposure. Accumulating evidence suggests that this assumption is unwarranted.

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