Sergeyenko.
of moderate noise exposure (tions from the ear to the brain were lost forever. terminals. The ear was healthy, but the connec-
to normal there was an acute loss of afferent nerve
were left intact, but even after thresholds returned
the noise-exposed cochleae showed the hair cells
remained affected. Careful histological analyses of
reaction potentials (CAPs).

tory brainstem responses (ABRs), and compound

documented this shift through distortion
enough to cause a temporary threshold shift. In-
level noise for two hours—
(2015;68[1]:6
Hear J
)
clinical implications—including in
searchers have argued that hidden hearing loss is a wide-
neural degeneration tar-
and normal hair cell function despite a profound loss of the
neural infrastructure thought to be critical for auditory pro-
cessing in noise (although this remains to be shown empiri-
cally).

This so-called or “hidden hearing loss” (or “cochlear neu-
opathy”) has captivated auditory scientists, and provides an
elegant hypothesis for the cause of age-related hearing dif-
Plack. Trends Hear 2014;18], auditory processing disorder
(Bharadwaj. J Neurosci 2015;35[5]:2161-2172), tinnitus
(Schaette. J Neurosci 2011;31[38]:13452-13457), and hy-
Additionally, understanding this pathophysiology can point to
a clinical strategy for pharmacological interventions if ever
a drug be discovered to regenerate synapses. Several re-
searchers have argued that hidden hearing loss is a wide-
spread phenomenon in humans and are working to discover
a diagnosis, and have argued that this work has important
clinical implications—including in The Hearing Journal (Zeng.
Hear J 2015;68[1]:6):
- It has been posited hidden hearing loss explains age-related
hearing difficulty, auditory processing disorder, tinnitus, and
hyperacusis. How does a single injury manifest (at a mini-
imum) as four distinct pathologies? What are the factors
that lead two people to suffer the same acute injury, but
develop different phenotypes? How does this peripheral
injury interact with predispositions, lifestyle factors, and
cognitive factors such as attention or working memory in
contributing to patient outcomes?
- An analogy has been drawn between hidden hearing loss
and auditory neuropathy, the latter of which is character-
ized by normal hair cell function with an absent ABR. Many
authors have suggested that hidden hearing loss is akin to
a mild form or auditory neuropathy, especially given the
presumed behavioral consequences of the peripheral deaf-
fertation. This analogy fails to consider a competing hy-
thesis for neuropathy, however, which suggests these
listeners have plenty of afferent synapses that simply fire
dys synchronously ([Starr. Brain 2003;126[Pt 7]:1604-1619]).
The dys synchro hypothesis is supported by computa-
tional modeling of neuropathy. Additionally, the protein
otof erlin has been implicated in neuropathy because it
regulates synaptic vesicle release at the afferent connec-
tions to inner hair cells ([Roux. Cell 2006;127[2]:277-289],
but is not necessary for ribbon synapse formation. Finally,
we note an extremely rare but fascinating syndrome, tem-
perature-dependent auditory neuropathy. These listeners
exhibit transient auditory neuropathy when they have a fe-
ver, but their auditory function is otherwise essentially nor-
mal ([Starr. Ear Hear 1998;19[3]:169-179]. We highly
doubt they undergo an immediate deafferentation when
febrile and reaafferentation when their temperature returns
to normal. Together, this evidence questions the extent to
which hidden hearing loss is similar to auditory neuropathy.

Not-So-Hidden Hearing Loss
By Nina Kraus, PhD, & Travis White-Schwoch

G Kujawa and MC Liberman published a paper that instantly became a modern clas-
sic (Kujawa. J Neurosci 2009;29[45]:
14077-14085). They exposed mice to a
single, moderate-level noise for two hours—

Subsequent work has shown a similar effect following a life
33[34]:13686-13694], and that this neural degeneration tar-
gets the high threshold, low spontaneous rate nerve fibers
that fire in noise ([Furman. J Neurophysiol 2013;110[3]:
577-586]). Thus, an animal can have a normal audiogram
and normal hair cell function despite a profound loss of the
neural infrastructure thought to be critical for auditory pro-
cessing in noise (although this remains to be shown empiri-
cally).

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Dr. Kraus, left, is a professor of auditory neuroscience at Northwestern University, investigating the neuro-biology underlying speech and music perception and learning-associated brain plasticity. Mr. White-Schwoch, right, is a data analyst in the Auditory Neuroscience Laboratory (brainvolts.northwestern.edu), where he focuses on translational questions in speech, language, and hearing.
Dyssynchronous synaptic activity at the inner hair cell afferents would be qualitatively distinct from a loss of those afferents.

- What are the consequences of a peripheral deafferentation for central auditory function? Caspary and colleagues have documented a profound loss of inhibitory neurotransmission in older animals that they have long since hypothesized may be a maladaptive compensatory gain for the loss of afferent input (Caspary, J Exp Biol 2008;211[Pt 11]:1781-1791). This hypothesis is supported by recent work by Polley and colleagues, who attribute many of the communicative difficulties experienced by listeners with auditory neuropathy to maladaptive central plasticity as opposed to peripheral deafferentation per se (Chambers. Neuron 2016;89[4]:867-879). These observations are also consistent with work in humans that shows, for example, that older adults with normal hearing thresholds exhibit poor neurophysiological processing of sound (Anderson. J Neurosci 2012;32[41]:14156-14164).

- How would a diagnosis of hidden hearing loss guide treatment in the clinic? There are no ways to regenerate neurons, and although there are efforts to develop a drug much more research is required. If somebody has normal thresholds, they are likely not a candidate for amplification and certainly not for implantation. Listeners already know that they have problems hearing in everyday settings—what they are looking for is a strategy to improve their listening success.

- This leads us to our last question. Just how hidden is hidden hearing loss? We define it as a hearing problem that cannot be explained by a threshold shift on the audiogram, but we all know the audiogram is not a good measure of everyday listening skills. There’s nothing hidden about a patient who struggles to understand speech in everyday environments—in fact, that’s pretty blatant. Perhaps we would be better off thinking of this as “not-so-hidden hearing loss.”

What are the factors that lead two people to suffer the same acute injury, but develop different phenotypes?

This work provides game-changing understanding into potential mechanisms underlying listening difficulties, and has posited elegant hypotheses that make strong predictions about factors contributing to these difficulties. But while this work may one day offer strategies for diagnosis and management, many questions stand between not-so-hidden hearing loss and the clinic.