Which neurons survive the glutamate storm?

Eric D. Young
Center for Hearing and Balance, Department of Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland

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TRAUMATIC SOUND EXPOSURE CAUSES SENSORINEURAL HEARING LOSS (SNHL) by destroying or damaging the neural elements of the cochlea (Young 2011). Until recently, the focus of SNHL research was on the hair cells (HCs), the transducer cells in the cochlea (Fig. 1). Severe acoustic trauma destroys HCs, leading to loss of function in damaged regions (Engström et al. 1966). Less severe trauma can cause subacute damage to HCs, such as disrupting the transducer elements on their stereocilia (Liberman and Dodds 1984). HCs survive but transduce with reduced sensitivity and selectivity.

Recently it has been found that spiral ganglion neurons are an additional locus of the primary lesion in SNHL, perhaps as important as the HCs (Kujawa and Liberman 2009). In cases of moderate acoustic trauma that is insufficient to permanently damage HCs, there can be loss of a significant fraction of spiral ganglion neurons. The loss occurs even if almost all HCs remain and recover their sensitivity to sound following the trauma. The mechanism of the loss of spiral ganglion neurons seems to be excitotoxicity due to glutamate release during the acoustic exposure (Puel et al. 1994). Loss of nerve fibers reduces the number of fibers connected to each inner HC, normally 10–30 fibers per cell, but seems to leave an otherwise normal cochlea.

Loss of a fraction of the auditory nerve fibers with preservation of HCs, called cochlear neuropathy, produces a hearing loss in which threshold is normal because it depends on intact HCs. Nevertheless, the representation of sound at suprathreshold levels may be abnormal because of loss of auditory nerve fibers or consequent changes in the central nervous system. It is the nature of the neural representation of sound that is the focus of a recent paper by Furman et al. (in press). Interest in this question is intensified by the existence of auditory neuropathy, a form of clinical hearing impairment with many similarities to cochlear neuropathy. In particular, audiometric thresholds can be near normal, and outer HC function can be present, as judged by otoacoustic emissions testing, but suprathreshold processing can be compromised in a variety of ways (Starr et al. 1996; Zeng et al. 2005).

Furman and colleagues (in press) ask which subgroups of auditory nerve fibers survive cochlear neuropathy. In the normal ear, fibers can be divided into two to three groups with somewhat different properties. Fibers in the majority group (~60%) have substantial spontaneous activity (>20 spikes/s, HSR) in the absence of sound. These neurons have low thresholds, essentially equal to the audiometric threshold, and limited dynamic ranges (20–40 dB); at higher sound levels, these fibers are at or near rate saturation, meaning that their rates change little or not at all as the stimulus changes. The remaining fibers have low (<1) or medium (1–18) rates of spontaneous activity (LMSR), higher thresholds, and wider dynamic ranges.

Research has long been directed toward showing how the wide auditory dynamic range of hearing (over 100 dB) is created from the overlapping (much smaller) dynamic ranges of these subpopulations of auditory nerve fibers (e.g., Vienneister 1988; Colburn et al. 2003; Delgutte 1990). Generally, LMSR fibers provide a better representation of sound at high sound levels and in background noise, including in the difficult listening conditions important in human communication (Costalupes et al. 1984; May et al. 1996). Consistent with this, LMSR fibers innervate the cochlear nucleus more profusely than HSR fibers, with some projections into regions poorly innervated by HSR fibers and with heavier terminal patterns everywhere (Liberman 1991, 1993). Together, these findings suggest that LMSR fibers may play a critical role in sound perception, especially in difficult listening conditions.

Furman and colleagues (in press) characterize the properties of auditory-nerve fibers in guinea pigs following an acoustic trauma that produces cochlear neuropathy. Consistent with auditory neuropathy, otoacoustic emissions are normal in these animals, indicating normal outer HC function, and the auditory brainstem responses have normal thresholds, but reduced amplitude, consistent with neuropathy. Furman and colleagues report that auditory nerve fibers in these animals have normal tuning, thresholds, dynamic ranges, and adaptation. The major difference is a reduced number of LMSR fibers.

In normal animals, LMSR fibers innervate the modiolar side of the inner HC, whereas HSR fiber synapses are scattered (Fig. 1). LMSR fibers also have larger presynaptic ribbons (Merchan-Perez and Liberman 1996). To look for an anatom-
ical correlate of the apparent selective loss of LMSR fibers, Furman and colleagues measured the size and location of synaptic ribbons in their animals. Surprisingly, there were more large ribbons in the neuropathy animals, and they were scattered over the whole of the base of the inner HC, opposite the expectation from the measured spontaneous activity.

This paper poses several interesting questions. First, the anatomical characteristics of the HC/nerve-fiber synapse are apparently plastic and perhaps also is the spontaneous rate. To resolve what is going on, it will be necessary to clear up uncertainties about the determinants of auditory spontaneous activity (Yi et al. 2010). Second, it will be interesting to see if the remaining fibers in the cochlear neuropathy animals have the characteristics of fibers of the same spontaneous rate classes in normal animals. That is, do the properties of the LMSR fibers in normal animals derive from some correlate of the anatomical ribbon size or from some encoding feature related to spontaneous rate? Third, it will be interesting to know what is the central distribution of synaptic terminals in neuropathy animals. This paper makes obtaining answers to these questions urgent.

DISCLOSURES

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REFERENCES


