This Week in The Journal

Ear Occlusion Alters Transmission at Endbulbs of Held

Xiaowen Zhuang, Wei Sun, and Matthew A. Xu-Friedman

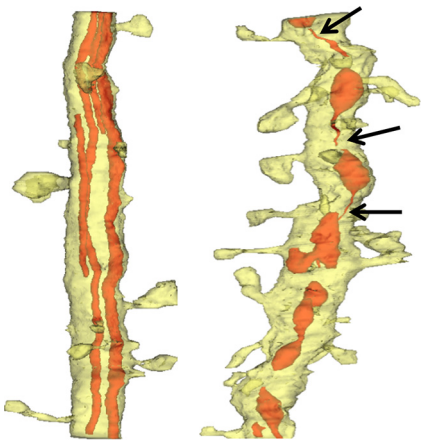
(see pages 323–332)

When sensory input is disrupted during early postnatal life, developing sensory circuits are altered, sometimes resulting in long-term perceptual deficits. In human infants, auditory stimulation can be distorted by otitis media, a common inflammatory disease in which viscous fluid fills the middle ear. If otitis media occurs during the auditory critical period and is severe enough to produce conductive hearing loss, it can cause long-lasting deficits in auditory processing that may affect language development. Although studies on the effects of otitis media are often confounded by a failure to assess hearing, animal studies consistently indicate that auditory distortion during critical periods causes long-lasting changes in auditory circuits (Whitton & Polley 2011 J Assoc Res Otolaryngol 12:535). Most such studies have focused on the auditory cortex; considerably less is known about the effects of auditory deprivation at earlier stages in the auditory pathway.

Zhuang et al. addressed this question by measuring the effects of temporary conductive hearing loss on synaptic transmission at endbulbs of Held, the synapses between auditory nerve fibers and bushy cells of the anteroventral cochlear nucleus. They examined how ear occlusion affected the number of release sites, probability of vesicle release, quantal size, and postsynaptic physiology in mouse brainstem slices.

Endbulb of Held synapses normally show paired-pulse depression, indicating a high probability of vesicle release. Paired-pulse depression was significantly enhanced after one week of ear occlusion, suggesting the probability of vesicle release increased further. Although EPSC amplitudes often increase when release probability increases, this was not observed after ear occlusion, probably because the number of release sites decreased at the same time. The input resistance, excitability, and spike probability of postsynaptic cells also decreased after ear occlusion. In contrast, quantal size, indicated by the amplitude of miniature EPSCs, was unchanged.

Both the release probability and the number of release sites returned to control levels within one week after ear occlusion was removed. Although this suggests auditory deprivation does not produce permanent changes at endbulb of Held synapses, occlusion took place relatively late in postnatal development in these experiments, and occlusion was reversed after only three days. Because previous experiments indicate that the persistence of deprivation-induced changes strongly depends on the timing and duration of deprivation, future studies should investigate whether manipulating these variables produces longer lasting changes at endbulbs of Held.



Mitochondria are long and tubular in dendritic segments from sham-operated mice (left), but they are fragmented in ischemic mice (right). Thin segments interconnecting some mitochondria in dendrites of ischemic mice (arrows) suggest fission is ongoing. See Kislin et al. et al. for details.

Ischemia Causes Mitochondrial Fragmentation

Mikhail Kislin, Jeremy Sword, Ioulia V. Fomitcheva, Deborah Croom, Evgeny Pryazhnikov, et al.

(see pages 333–348)

Mitochondria are best known for their role in ATP production, but they have several additional functions, including sequestering calcium, eliciting viral immune responses, and driving apoptosis of damaged cells. Although usually portrayed as small, capsule-shaped organelles, mitochondria assume a variety of shapes *in vivo*. The reason for this structural diversity is poorly understood, but different shapes are thought to be optimal for different functions. For example, mitochondrial fusion can create long organelles that efficiently generate ATP, whereas fission creates smaller mitochondria that are more mobile and thus able to reach sites requiring ATP more quickly. Fission also precedes mitochondrial degradation by autophagy, and it facilitates release of pro-apototic factors (Pernas and Scorrano 2016 Ann Rev Physiol 78:505).

To better understand how mitochondrial dynamics affect their function, we must learn what shapes mitochondria take under different conditions. Such studies have generally been done *in vitro*, where imaging is easiest, but results from these studies must be confirmed *in vivo*. Therefore, Kislin et al. used two-photon imaging to examine fluorescently labeled mitochondria in mouse layer 1 cortical dendrites *in vivo*, and to determine whether ischemia and other insults cause mitochondrial fragmentation, as suggested by *in vitro* work.

In healthy brains, mitochondrial length varied: while most were $<5\ \mu$m long, some stretched more than 20 μm. All insults—transient global ischemia, permanent focal ischemia, focal laser lesions, and mild photodamage—caused mitochondrial fragmentation, but the extent and duration of fragmentation depended on the severity of the injury. Most notably, when global dendritic structure was maintained, mitochondria eventually regained their normal tubular structure. This occurred within 2 h if perfusion was quickly restored after global ischemia, but in other cases it took a week, if it occurred at all.

These results confirm that mitochondria fragmentation occurs after even mild brain injury *in vivo*. The finding that mitochondrial recovery takes a week even after mild damage indicates that it is a slow process, likely involving biogenesis of new organelles. This suggests that mitochondrial fragmentation leads to mitophagy after brain injury. How fragmentation affects neuronal survival remains to be determined.

This Week in The Journal was written by Teresa Esch, Ph.D.