Trends in Neurosciences

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Review

Cellular Computations Underlying Detection of Gaps in Sounds and Lateralizing Sound Sources

Donata Oertel,[1,*] Xiao-Jie Cao,[1] James R. Ison,[2,3] and Paul D. Allen[4]

In mammals, acoustic information arises in the cochlea and is transmitted to the ventral cochlear nuclei (VCN). Three groups of VCN neurons extract different features from the firing of auditory nerve fibers and convey that information along separate pathways through the brainstem. Two of these pathways process temporal information: octopus cells detect coincident firing among auditory nerve fibers and transmit signals along monaural pathways, and bushy cells sharpen the encoding of fine structure and feed binaural pathways. The ability of these cells to signal with temporal precision depends on a low-voltage-activated K^+ conductance (g_{KL}) and a hyperpolarization-activated conductance (g_h). This 'tale of two conductances' traces gap detection and sound lateralization to their cellular and biophysical origins.

Timing Information in the Processing of Sound

In mammals, acoustic information arises in the cochlea and is transmitted to the ventral cochlear nuclei (VCN). Three groups of VCN neurons extract different features from the firing of auditory nerve fibers: octopus, stellate, and bushy cells, which in turn convey that information along separate pathways through the brainstem. Two of these pathways process temporal information: octopus cells detect coincident firing among auditory nerve fibers and transmit signals along monaural pathways, while bushy cells sharpen the encoding of fine structure and feed binaural pathways. The ability of these cells to signal with temporal precision depends on both g_{KL} and g_h conductances. Mice with genetically altered g_h and g_{KL} have deficits in detecting temporal gaps and in lateralizing sounds, and these sensory deficits parallel the slowing of electrical events in octopus and bushy cells, respectively.

Processing temporally precise auditory information underlies both monaural and binaural functions. For instance, the ability of mammals to detect temporal gaps in sounds is a monaural function. The detection of gaps is crucial for mammals to determine the biological significance or meaning of sounds. In humans it is required for understanding speech [1–5]. People with auditory neuropathy whose gap-detection thresholds are elevated have difficulty understanding speech even when their hearing thresholds are near-normal. The ability to detect a gap of 3 ms [3] requires that neurons encode offsets and onsets of sounds with a temporal precision of at least 1 ms.

Localizing the azimuthal direction of sound origin, by contrast, is a binaural function. This function relies on comparisons of timing and intensity between the two ears [6]. The

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Two conductances enable auditory brainstem neurons to carry acoustic information in the timing of firing: the g_h conductance mediated through HCN channels and the g_{KL} conductance mediated through Kv1 channels.

Deletion of crucial subunits of those ion channels differentially alters the biophysical properties of auditory neurons and also alters the ability of mice to detect gaps in sounds or lateralize sound sources.

Biophysical changes in the binaural pathways through bushy cells of the ventral cochlear nucleus parallel deficits in sound lateralization.

Biophysical changes in octopus cells of the ventral cochlear nucleus, which form a disynaptic monaural pathway through the brainstem to the inferior colliculus, parallel and can account for deficits in gap detection.

[1]Department of Neuroscience, School of Medicine and Public Health, University of Wisconsin, Madison, WI 53705 USA
[2]Department of Brain and Cognitive Sciences, Meliora Hall, University of Rochester, Rochester, NY 14627, USA
[3]Department of Neuroscience, University of Rochester Medical Center, Rochester, NY 14642, USA
[4]Department of Otolaryngology, University of Rochester Medical Center, Rochester, NY 14642, USA

*Correspondence: doertel@wisc.edu (D. Oertel).

computation of interaural time and intensity requires that the delays in the neuronal pathways from the two sides are matched in the superior olivary complex [7,8]. The temporal precision in the computation of interaural time requires, in addition, the ability to measure the magnitude of tiny temporal disparities. Differences in the relative time of arrival of sounds at the two ears are small even in animals with large heads, <0.5 ms in humans. Under optimal conditions human subjects can resolve differences in location of 1° that correspond to interaural time differences of ~10 μs [9,10].

In this review we discuss progress in understanding the processing of temporally precise auditory information, with emphasis on how two cellular conductances in VCN neurons make temporal processing possible. Genetic tools have made it possible to pinpoint specific links between these cellular conductances and the perceptual functions of gap detection and sound localization. We conclude with a discussion of some of the open questions in field, including how the detection of synchronous firing in response to broadband transient sounds by octopus cells could help to bind together the spectral components of individual sound sources into a single percept.

Ascending Pathways from the Ventral Cochlear Nucleus Convey Timing Cues

Type I spiral ganglion cells in the cochlea receive input from inner hair cells through their peripheral process and transmit signals through their central processes, the auditory nerve fibers, to the VCN. These myelinated auditory nerve fibers convey acoustic information to three groups of principal cells in the VCN – octopus, stellate, and bushy, cells – each of which form separate parallel pathways through the brainstem (Figure 1).

Octopus cells extract information from many (>60 in mice) fibers tuned to a broad range of frequencies [11,12], each of which activates only a small conductance (<2 nS in mice) and produces a very small (<3 mV in mice) excitatory postsynaptic potential (EPSP). They signal the presence of the onset of broadband sounds with extraordinary temporal precision [13–15] and project to the contralateral superior paraolivary nucleus (SPON) [16,17] and to the columnar area of the ventral nucleus of the lateral lemniscus (VNLL) [16,18,19] (Figure 1A).

Bushy cells extract information gleaned from the timing of firing of few auditory nerve fiber inputs. They receive few (in mice 2–6) large, somatic, end bulb terminals of auditory nerve fibers [20]. These terminals activate large conductances (in mice 22 ± 15 nS) that can deliver large synaptic currents that produce large EPSPs. All three subtypes of bushy cells are involved in binaural pathways. Large spherical bushy cells feed timing information to the medial superior olivary (MSO) nuclei on both sides, while globular bushy cells project to the medial nucleus of the trapezoid body (MNTB) which in turn signals the timing of contralateral sounds to the lateral superior olivary nuclei (LSO). Small spherical bushy cells excite neurons in the ipsilateral LSO [21]. All subtypes of bushy cells also innervate parts of the VNLL [22–25] (Figure 1A,B).

Lastly, stellate cells (also called T stellate [26], type I multipolar [27], chopper [28], or planar multipolar [29] cells), largely jettison timing information. These sharply tuned neurons receive input from only few auditory nerve fibers (5–6 in mice) that activate conductances of modest amplitude (4.6 ± 3 nS) [20]. Stellate cells project broadly, including to the ipsilateral LSO [30], possibly to the SPON [22,31], and to the VNLL [19,32–34] (Figure 1B).

Monaural and binaural pathways through the brainstem are largely separate. Within target areas of the VCN – the superior olivary complex and the lemniscal nuclei – the SPON and the VNLL process acoustic information that comes from only one ear (Figure 1, top), whereas the MSO and LSO nuclei compare acoustic features from the two ears (Figure 1, bottom).