This Week in The Journal

Central Effects of Neurod1 Knock-Out in Inner Ear

Iva Macova, Kateryna Pysanenko, Tetyana Chumak, Martina Dvorakova, Romana Bohuslavova, et al.

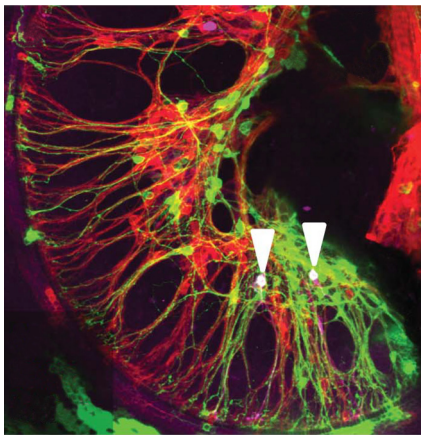
(see pages 984–1004)

Primary sensory afferents project to the CNS in an organized fashion, creating sensory maps in target areas. In the auditory system, spiral ganglion neurons innervate different portions of the organ of Corti from base to apex, and their central projections maintain this order as they innervate cochlear nuclei, where they create a cochleotopic—and thus tonotopic—map. Although molecular cues guide the initial formation of this map, subsequent sensory input refines it. Consequently, partial sensory deprivation can distort the map, with areas deprived of input being taken over by adjacent areas.

How much sensory disruption can central plasticity overcome? Can activity-dependent plasticity rearrange scrambled input to form a functional map, for example? To answer this question, Macova, Pysanenko, et al. knocked out Neurod1—a transcription factor essential for auditory system development—selectively in the inner ear. This greatly disrupted the organization of fibers innervating the cochlea. Afferents innervating the base and apex were intermingled, and some afferents sent collaterals to both regions. Furthermore, some spiral ganglion neurons innervated vestibular organs. Central projections in the auditory-vestibular nerve were similarly intermingled, and no cochleotopic map was evident in cochlear nuclei. Pure-tone stimulation increased levels of the activity-regulated gene c-fos in cells distributed throughout the cochlear nuclei, demonstrating the lack of a tonotopic map.

The effects of peripheral Neurod1 deletion extended to the inferior colliculus, which receives input from cochlear nuclei. Frequency-tuning curves in this area were wider than normal in mutant mice, and they had multiple peaks. The threshold for excitation of inferior colliculus neurons was also elevated in mutant mice, likely as a consequence of increased thresholds in the auditory nerve. Alterations in the auditory pathway also affected behavior. Whereas normal mice show greater startle responses to white noise than to pure tones, mutant mice had large startle responses for both, suggesting they perceived pure tones as broad-spectrum noise. In addition, white-noise pre-pulses produced stronger attenuation of startle responses in mutant mice than in controls.

These results indicate that the ability of central plasticity to overcome peripheral sensory disruption is limited. Future work should investigate the effects of this disruption on more complex functions, such as auditory associative conditioning, and determine whether auditory training can reduce deficits.



In mice lacking Neurod1 in the inner ear, axons innervating the apex (green) and base (red) of the organ of Corti are intermingled, and a few send collaterals (purple) to vestibular nuclei. See Macova, Pysanenko, et al. for details.

How Lampreys Stop Swimming

Swantje Grätsch, François Auclair, Olivier Demers, Emmanuella Auguste, Amer Hanna, et al.

(see pages 1044–1057)

Locomotion in vertebrates is driven by central pattern generating circuits in the spinal cord. The activity of these circuits depends on input from the brainstem. Specifically, neurons in the mesencephalic locomotor region (MLR) initiate, maintain, and terminate locomotion via projections to the reticular formation, which contains neurons that control spinal locomotor circuits. Previous work in lampreys found that reticulospinal neurons involved in MLR-induced swimming could be divided into three groups: neurons that produced a transient spike burst at the onset of swimming, neurons that spiked robustly throughout swim episodes, and neurons that spiked in bursts at both the beginning and end of swim bouts. The latter cells also exhibited spike bursts when sensory-evoked or spontaneous swimming stopped, and activating the neurons stopped ongoing swimming, whereas inhibiting them prolonged swimming. Therefore, the cells were named stop cells.

Delving deeper into the neural control of locomotor termination, Grätsch et al. investigated the source of inputs driving the swim-termination burst in stop cells. They found that low-intensity stimulation of MLR evoked short-latency EPSPs in stop cells, and these EPSPs were unaffected by divalent cations, suggesting they were monosynaptic. When MLR stimulation was strong enough to induce swimming, stop cells exhibited the characteristic termination burst, and the number of spikes in this burst increased with stimulus strength. When stimulation was sufficiently strong, swimming outlasted the stimulation. In such cases, delivery of a second, equally strong stimulus prolonged the swim episode. Remarkably, however, when the intensity of the second stimulation was 40–50% of the first, swimming stopped within 7 s, thus shortening the swim bout. This effect was blocked by glutamate receptor antagonists injected into the stop-cell region of the brainstem. Importantly, low-intensity stimulation of MLR also stopped swimming evoked by sensory stimuli. Finally, retrograde labeling suggested that MLR neurons that innervate stop cells are distributed throughout the MLR and are intermingled with cells that innervate other swim-related reticulospinal neurons.

These results suggest that neurons in the MLR activate stop neurons in lamprey via direct glutamatergic projections. Many intriguing questions remain to be answered, including why only low-intensity MLR stimulation stops swimming. Intracellular recordings from MLR neurons might help to answer such questions.

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