This Week in The Journal

Movement-Related Activity in Human Cerebellar Dentate Nucleus

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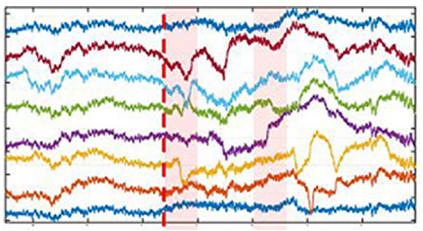
(see pages 5186–5197)

Bidirectional communication between the cerebral cortex and the cerebellum is required for many brain functions. For example, motor planning and coordination are thought to be mediated by indirect communication between the dentate nucleus—one of three deep cerebellar nuclei—and premotor and motor cortical areas. The importance of this communication is apparent when ischemic stroke damages the corticopontocerebellar tract. This results in hypoactivation of the cerebellum and reduced cerebellar output. When this occurs, the prospect for motor recovery is reduced. Notably, however, 30 Hz electrical stimulation of the dentate nucleus increases recovery of motor function after experimental stroke in rodents. Clinical trials are now underway to determine whether such stimulation can improve functional recovery in stroke patients with persistent motor deficits.

Examination of corticocerebellar communication during movement in humans has not heretofore been possible because noninvasive methods for recording brain activity do not yield clear signals from the cerebellum. Fortunately, 10 people participating in phase 1 of the clinical trial of dentate nucleus stimulation agreed to provide such data. As these volunteers performed a visually guided, fluctuating grip task, Gopalakrishnan et al., recorded oscillatory activity in the participants' motor cortex and dentate nucleus using EEG and implanted electrodes, respectively. Recordings from motor cortex in people with moderate motor impairment showed the normal reduction in synchronous activity (i.e., reduced power) in the low-beta (~20 Hz) range at movement onset, reflecting increased cortical activity and excitability. Notably, power in the low- and high-beta ranges was inversely correlated with task performance. Neural synchrony in thedentate nucleus also decreased with movement onset in moderately impaired participants. In contrast, severely impaired people showed increased synchronization in both areas at movement onset. During an ongoing grip, power at alpha (~10 Hz) and low-beta frequencies in the dentate nucleus and motor cortex was correlated. In addition, coherence between the two areas was higher, indicating increased communication, during the hold phase than between trials. Finally, coherence in the low-beta range was correlated with task performance.

These results confirm that communication between motor cortex and dentate nucleus is essential for normal motor function in humans. Future work should determine whether and how this communication changes as motor function improves in stroke patients



Local field potential recorded from cerebellar dentate nucleus in a person performing a grip task. Dashed vertical line indicates time of movement onset. See Gopalakrishnan et al, for details.

Regulation of Gut Motility by NPY Neurons

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(see pages 5212–5228)

As food is consumed, muscles in the stomach relax, allowing expansion of the stomach cavity. The muscles then contract to mix and grind food and push it into the small intestine. The strength of stomach contractions and the rate of gastric emptying are controlled by excitatory and inhibitory efferents from the dorsal motor nucleus of the vagus (DMV). The activity of efferent neurons, in turn, is regulated by local interneurons and input from the nucleus of the solitary tract (NTS). The NTS and DMV contain heterogeneous populations of excitatory and inhibitory neurons, however, and the functions of many of these remain unclear. Bellusci et al. now elucidate the function of two populations: those that express neuropeptide Y (NPY) and those that express somatostatin.

NPY-expressing neurons were found in both the NTS and DMV. NPY-expressing fibers were found throughout both structures, and their terminals surrounded the somata of both somatostatin-expressing neurons and DMV neurons that projected to the stomach. NPY neurons also formed synapses with each other. Approximately half of NPY-expressing neurons were likely glutamatergic, whereas ~22% were likely GABAergic. Photoactivation of channelrhodopsin-expressing NPY neurons in brainstem slices evoked both excitatory and inhibitory currents in DMV efferent neurons and somatostatin-expressing neurons. Consistent with previous work showing that somatostatin-expressing NTS neurons release GABA or glycine, photoactivation of these neurons inhibited NPY neurons and stomach-projecting DMV neurons.

Photoactivation of NPY or somatostatin-expressing NTS neurons *in vivo* increased the amplitude of gastric contractions and increased gastric motility, whereas photoactivation of either neuronal subtype in the DMV reduced contractions and motility. Conversely, photoinhibition of archT-expressing NPY neurons in the NTS reduced gastric motility whereas photoinhibition of DMV NPY neurons increased motility. But photoinhibition of somatostatin-expressing NTS or DMV neurons had the same effects as photoactivating these neurons, possibly because the inhibition of some neurons led to the disinhibition of others.

These results suggest that both NPY and somatostatin-expressing neurons in the NTS and DMV regulate the output of DMV neurons that project to the stomach. Thus, these neurons regulate the speed at which food moves through the stomach, thereby influencing digestion. Whether NPY neurons make direct or indirect synapses with excitatory or inhibitory DMV efferent neurons remains to be determined.

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