This Week in The Journal

Recurrent Loops between Thalamus and Somatosensory Cortex

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(see pages 2849–2858)

Much of the information the cortex receives from peripheral and subcortical structures passes through the thalamus; and the thalamus also conveys information between cortical areas. Thalamic nuclei that receive sensory information from the periphery were originally thought to relay this information to primary sensory cortical areas without modification. But work over the past few decades has demonstrated that primary cortical areas project back to the thalamus to regulate incoming sensory information. Primary cortex also projects to higher-order thalamic areas, which then convey the information to secondary sensory and motor cortical areas. Recent work has also detailed recurrent loops between cortex and thalamus. For example, neurons in the anterolateral motor (ALM) cortex innervate neurons in the ventromedial (VM) thalamus that project back to ALM. Similar recurrent loops have been found between VM and the medial prefrontal cortex, and between the posterior (PO) nucleus and primary motor cortex (M1). Guo et al. now show that recurrent cortico-thalamo-cortical loops also occur between primary somatosensory cortex (S1) and both PO and the ventral posterolateral (VPL) nucleus, a primary somatosensory nucleus of the thalamus.

Anterograde and retrograde tracers injected into the forelimb region of S1 revealed that S1 axon terminals overlapped extensively with VPL and PO regions containing S1-projecting neurons. Consistent with this, activation of channelrhodopsin-expressing terminals of S1 corticothalamic axons evoked large EPSCs in S1-projecting VPL and PO neurons. Similarly, activation of S1 pyramidal tract axons evoked large EPSCs in S1-projecting PO neurons. In contrast, S1 axons overlapped minimally with M1-projecting neurons in PO, and activation of either corticothalamic or pyramidal

tract S1 axons evoked weak EPSCs in M1-projecting PO neurons. Conversely, pyramidal tract axons from M1 overlapped extensively with M1-projecting neurons in PO, and activation of M1 axons evoked much stronger EPSCs in M1-projecting neurons than in S1-projecting neurons.

These results suggest that corticothalamic and pyramidal tract axons in S1 and pyramidal tract axons in M1 provide substantial input to thalamic neurons that project back to the same area, with minimal input to neurons that project to the other area. This type of recurrent loop has been proposed to help maintain sensory and motor representations during ongoing task performance. Future work should test this hypothesis.

Acetylcholine alters the pattern of activity across the population of granule cells (B) in the cerebellum, possibly altering the output of Purkinje cells (A). Drawing by Santiago Ramón y Cajal, 1899; Instituto Cajal, Madrid, Spain.

Effects of Acetylcholine on Cerebellar Activity

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(see pages 2882–2894)

The cerebellum has roles in motor coordination, motor learning, and cognition. How it contributes to these functions remains poorly understood, but the circuitry it uses to do so has been known for decades. The sole cerebellar output neurons are Purkinje cells, each of which receives strong excitatory input from a

single inferior olive neuron via a climbing fiber and weaker excitatory input from numerous granule cells via parallel fibers. Granule cells receive sensorimotor information from the spinal cord, brainstem, and other areas via excitatory mossy fibers. Cerebellar Golgi cells also receive excitatory input from mossy fibers, and they in turn provide feedforward and tonic inhibition to granule cells. This basic circuit is repeated many times across the cerebellar cortex (Jörntell, 2016, *J Physiol* 595:11).

Neuromodulators are thought to shape the function of cerebellar circuits, but how they do so has rarely been addressed. Therefore, Fore et al. examined how acetylcholine affects cerebellar circuit function. Focal application of acetylcholine to Golgi cells in cerebellar slices caused a prolonged outward current and suppression of spiking, which were mediated by M2 muscarinic receptors. Consistent with this, muscarine produced a long-lasting decrease in spontaneous and evoked IPSCs, as well as tonic inhibitory current, in granule cells. At the same time, muscarine reduced the amplitude of EPSCs evoked in granule cells by mossy fiber activation, likely via a presynaptic mechanism. Similarly, muscarine reduced the amplitude of mossy-fiber-evoked EPSCs in Golgi cells.

The reduction in inhibitory and excitatory input to granule cells in the presence of muscarine had heterogeneous effects on spiking across the granule-cell population. Spiking increased in some cells and decreased in others. A computational model suggested that the effect on spiking depended on the relative amount of baseline excitation and inhibition a cell received: cells that received predominantly inhibitory input at baseline showed an increase in spiking, whereas those that received less synaptic inhibition showed a decrease in spiking in the presence of muscarine.

These results suggest that by decreasing both inhibition and excitation of cerebellar granule cells, acetylcholine can influence which granule cells are activated by mossy fiber inputs. How this affects behavioral output in different contexts must be investigated in future studies.

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