This Week in The Journal

Spike-Independent LTP in Hippocampus

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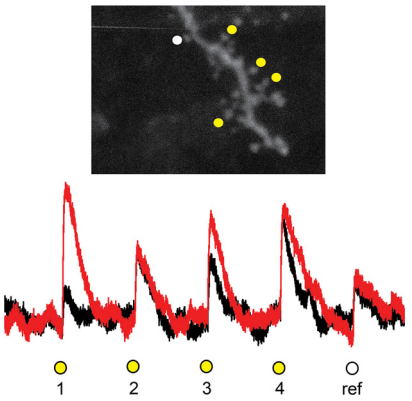
(see pages 2593–2605)

Synaptic plasticity is essential for circuit formation and learning, but the rules governing plasticity can differ among cell types and even across the dendritic arbor. The best studied forms of synaptic plasticity are spike-timing dependent, but potentiation can also occur in the absence of action potentials. In hippocampal pyramidal cells, for example, synapses can be potentiated if their activation coincides with dendritic spikes (Bono et al., 2017 Curr Op Neurobiol 46:136), and simultaneous activation of multiple spines on distal portions of basal or oblique dendrites can strengthen those synapses even in the absence of dendritic spikes. Magó et al. now detail the rules governing action-potential-independent plasticity in these dendrites.

Near-synchronous activation of 3 spines spaced ~3 μm apart on distal dendrites was usually sufficient to induce long-term potentiation (LTP) in at least one of the stimulated spines, even though the stimulation did not evoke dendritic spikes. In contrast, LTP rarely occurred when the interspine distance was increased to 5 μm, unless the number of coactivated spines was increased to elicit dendritic spikes. The occurrence of dendritic spikes also allowed LTP to spread to nearby unstimulated spines, and it decreased the number of synchronous activation events required to evoke LTP.

In contrast to spines on distal dendrites, stimulation of as many as 16 closely spaced spines on proximal dendrites was insufficient to induce LTP in the absence of dendritic spikes. But when dendritic spikes were elicited by stimulating somewhat more distal spines along with proximal spines, LTP was induced at the proximal spines regardless of whether somatic action potentials were evoked.

These data confirm that LTP can be produced by coactivation of closely spaced distal dendritic spines in the absence of regenerative dendritic spikes, but they also show that dendritic spikes increase the distance over which LTP can occur. In contrast, dendritic spikes or back-propagating action potentials are necessary for inducing LTP in proximal spines. The difference in LTP requirements is likely related to the higher impedance of thin, distal dendrites, which allows greater voltage changes in response to a given input. Spike-independent potentiation of distal synapses might be necessary because the large electrotonic distance between the spike initiation zone and distal dendrites limits spike-dependent plasticity.



Near-synchronous activation of four spines (indicated by filled yellow circles) on a distal dendritic branch increased the amplitude of EPSPs in two of those spines (red trace) compared with baseline (black trace). This protocol did not alter EPSP amplitude in unstimulated spines (open circle). See Magó et al. for details.

How Spinal Cord Stimulation Might Promote Recovery after SCI

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(see pages 2633–2643)

Restoring motor function after spinal cord injury (SCI) is a longstanding goal of neuroscience research, but progress toward this goal has been disappointingly slow. Nevertheless, there is hope for people with SCI. Nearly all spinal injuries are incomplete, and spared axons can sprout to restore some lost function. Indeed, many patients exhibit spontaneous recovery within the first year of injury. Moreover, several recent studies have shown that electrical stimulation of the spinal cord, when paired with physical therapy, can enhance such recovery, even restoring the ability to walk in some cases. The stimulation is assumed to enhance synaptic plasticity that strengthens spared connections and stabilizes newly sprouted fibers (Hofer and Schwab, 2019 Curr Op Neurol 32:828). The precise mechanisms remain poorly understood, however.

To learn how transcutaneous spinal cord stimulation (TESS) might promote functional recovery after SCI, Benavides et al. measured electrophysiological responses [motor-evoked potentials (MEPs)] in arm muscles elicited by stimulation of motor cortex or the junction between the medulla and spinal cord. TESS consisted of either single 200 μs pulses delivered at 30 Hz or blocks of five 5 kHz pulses delivered at 30 Hz, and it was delivered over the cervical spinal cord in healthy adults and people with cervical SCI. Both TESS patterns increased the amplitude of muscle responses elicited by cervicomedullary stimulation, but only single-pulse TESS increased the amplitude of muscle responses elicited by stimulation of motor cortex. TESS using 5 kHz pulses did not alter cortical MEPs, likely because it enhanced intracortical inhibition. Notably, hand motor function in SCI patients improved more with 5 kHz TESS than with single-pulse TESS.

These results suggest that TESS facilitates recovery of motor function by enhancing communication between corticospinal neurons and motor neurons and/or by increasing motor neuron excitability. The authors hypothesized that increased intracortical inhibition during TESS with 5 kHz pulses might have resulted from activation of spinal afferent fibers, leading to feedforward inhibition from somatosensory to motor cortex. This might improve motor performance by reducing activation of antagonist muscles. Future work should test this hypothesis and aim to refine TESS procedures to promote greater motor recovery in more patients.

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