This Week in The Journal

Transient LTP in Hippocampus and Prefrontal Cortex

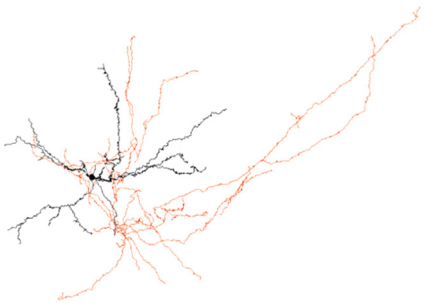
Bruno Pradier, Katherine Lanning, Katherine T. Taljan, Colin J. Feuille, M. Aurel Nagy, et al.

(see pages 5750–5758)

A modern Heraclitus might say you could not activate the same synapse twice. Indeed, synapses are continually changing as a result of synaptic activity or the lack thereof. In rodent hippocampus, for example, the amplitude of EPSCs evoked in CA1 pyramidal neurons by single CA3 spikes is much greater after high-frequency stimulation of CA3 afferents than before. With repeated testing, the synaptic potentiation decays, but within minutes it reaches a plateau level that persists for many hours and is thus called long-term potentiation (LTP)—one of the best-studied forms of synaptic plasticity. Relatively little is known about the initial, rapidly decaying potentiation, but intriguingly, the decay appears to be driven by synaptic activity: the initial level of potentiation persists for longer periods if test pulses are delivered infrequently. Furthermore, the mechanisms underlying the initial and long-term plateau phases of potentiation are thought to be distinct (Park et al., 2014 Philos Trans R Soc Lond B Biol Sci 369:20130131).

Pradier et al. found that unlike the plateau phase of LTP, the initial phase, which they call labile-LTP, could be evoked in hippocampal slices in the presence of an NMDA receptor antagonist. Notably, labile-LTP could also be evoked in the prefrontal cortex. Consistent with previous work, labile-LTP was accompanied by a decrease in the paired-pulse ratio; moreover, as labile LTP decayed, paired-pulse ratio increased. This suggests that labile-LTP results from an increase in presynaptic release probability. In support of this hypothesis, chelating calcium throughout the slice prevented induction of labile-LTP, whereas chelating calcium selectively in the postsynaptic cell did not. Unlike other forms of potentiation involving increases in presynaptic release probability, however, labile-LTP did not require synaptotagmin 7 (a presynaptic calcium-binding protein) or RIM1α (a component of the vesicle release machinery). An inhibitor of multiple protein kinases prevented induction of labile-LTP, however.

These data confirm that once evoked, labile-LTP persists for long periods if the synapse remains inactive. The results support the hypothesis that the mechanisms underlying labile-LTP are distinct from those that produce the more-commonly-studied plateau phase of LTP. Beyond requiring calcium and protein kinases, however, the mechanisms of labile-LTP remain unknown. Future work should address this issue, as well as determining the function of this form of plasticity.



3D reconstruction of a SABI, showing dendrites (black) and axon (red). See Assous, Faust, et al. for details.

A New Type of GABAergic Interneuron in the Striatum

Maxime Assous, Thomas W. Faust, Robert Assini, Fulva Shah, Yacouba Sidibe, et al.

(see pages 5688–5699)

The striatum integrates input from across the cerebral cortex to regulate motivated behaviors. Approximately 95% of striatal neurons are medium spiny neurons (MSNs), which provide the output of striatal processing. The remaining 5% of neurons are cholinergic and GABAergic interneurons, which shape the activity of MSNs. Research over the past decade has revealed a surprising diversity in striatal GABAergic interneurons, with different populations identified by their expression of tyrosine hydroxylase, calretinin, neuropeptideY, somatostatin, parvalbumin, and/or 5HT3a serotonin receptors (5HT3aRs). Some of these groups can be subdivided further based on electrophysiological properties and/or morphology.

Assous, Faust, et al. have discovered yet another unique population of GABAergic interneurons in mouse striatum. These neurons express 5HT3aR, but unlike previously described 5HT3aR-expressing interneurons, they are spontaneously active in brain slices. The neurons do not express proteins that characterize other spontaneously active striatal interneuron populations, however. Moreover, unlike other spontaneously active neurons, the 5HT3aR-expressing population fired in bursts rather than tonically. Therefore the authors named these cells spontaneously active bursty interneurons (SABIs). The most notable characteristic of SABIs was that—unlike any previously described striatal GABAergic interneuron—they rarely made direct synaptic connections with MSNs, either as the presynaptic or the postsynaptic cell. Instead, optogenetic inhibition of 5HT3aR-expressing interneurons typically led to delayed inhibition of MSNs, suggesting that SABIs tonically inhibit other GABAergic interneurons that inhibit MSNs when SABIs are inactivated.

Thus, SABIs are a previously unrecognized population of striatal GABAergic interneurons that preferentially inhibit other interneurons rather than MSNs. As such, SABIs might influence which MSNs can be activated by afferent input to produce state-dependent responses. To elucidate possible functions of these neurons, future work should identify their synaptic targets and record their activity patterns *in vivo*.

This Week in The Journal was written by Teresa Esch, Ph.D.