This Week in The Journal

Golgi Cells Have Active Dendrites

Stephanie Rudolph, Court Hull, and Wade G. Regehr

(see pages 15492–15504)

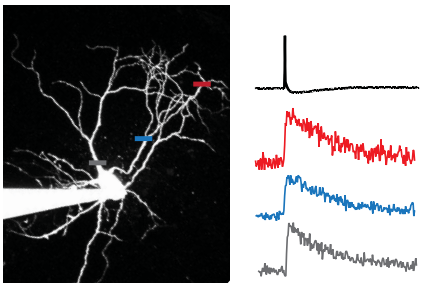
The cerebellum coordinates multijoint movements and contributes to motor learning. These functions require precise spike timing in Purkinje cells, the cerebellar output neurons. Purkinje cell spiking is driven partly by granule cells, which receive information about ongoing movements from mossy fibers, and the timing and spatial extent of granule cell output is determined largely by inhibitory input from spontaneously active interneurons called Golgi cells.

Golgi cell spiking is modulated by excitatory input from both mossy fibers and granule cells. How these inputs are integrated in Golgi cell dendrites remains poorly understood. Finding no evidence for active conductances in Golgi cell dendrites, Vervaeke et al. (2012, Science 30: 1624) hypothesized that dendritic gap junctions enable granule cell inputs to influence Golgi cell activity. Although gap junctions likely do contribute to dendritic processing in Golgi cells, Rudolph et al. now show that Golgi cell dendrites also express voltage-gated channels.

If dendrites lacked active conductances, one would expect signals to decay with distance from the soma. But calcium imaging in rat cerebellar slices revealed that action potentials caused uniform calcium elevation throughout Golgi cell dendrites. Moreover, applying a voltage-gated sodium channel (VGSC) blocker selectively to dendrites reduced spike-associated calcium elevation in distal dendrites. In addition, blocking T- and R-type voltage-gated calcium channels (VGCCs) attenuated calcium elevation selectively in distal dendrites, while blocking N-type channels reduced calcium elevation only in proximal dendrites.

Blocking voltage-gated channels also had functional consequences. Blocking N-type channels decreased the amplitude of the spike afterhyperpolarization and increased the spike rate of Golgi cells. In contrast, T-type channel blockers had little effect on baseline firing frequency. Nonetheless, blocking T-type channels attenuated rebound spiking after hyperpolarization and reduced the amplitude of EPSPs evoked by stimulation of granule cell axons.

These experiments suggest that VGSCs help depolarize distal dendrites to enhance activation of T-type VGCCs, which in turn amplify responses to granule cells and promote rebound bursting. Meanwhile, N-type VGCCs located near the soma appear to be tightly coupled to calcium-activated potassium channels, which regulate the spontaneous spike rate of Golgi cells. Thus, Golgi cell dendrites have multiple types of voltage-sensitive channels that are differently distributed and serve distinct roles in ensuring the precise timing of cerebellar output.



Injecting current into a Golgi cell soma (left) evoked an action potential (right, top trace) that caused similar increases in calcium in distal (red), middle (blue), and proximal (gray) dendrites. See Rudolph et al. for details.

Low-Threshold Spikes Are Generated Globally

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(see pages 15505–15522)

T-type voltage-gated Ca^{2+} channels (T channels) underlie bursting in many neuronal types besides Golgi cells (discussed in "Golgi Cells Have Active Dendrites," above). T channels have a lower activation threshold than other voltage-gated channels, and their opening leads to further membrane depolarization and channel activation. This regenerative process can depolarize a cell sufficiently to generate action potentials, called low-threshold spikes (LTS). Because T channels rapidly inactivate and cannot be reactivated until the membrane is hyperpolarized, they often contribute to rhythmic bursting activity.

Although the importance of T channels in generating LTS is well-documented, how LTS are generated is less clear. LTS could be initiated at T-channel hot-spots near the soma (like action potentials) or in dendrites (like NMDA-receptor-dependent Ca^{2+} spikes), and propagate from there. Alternatively, T channels could be activated simultaneously throughout the dendritic arbor, resulting in a global increase in Ca^{2+}. Connelly et al. investigated these possibilities in rat thalamocortical and thalamic reticular nucleus (TRN) neurons, whose T-channel-dependent rhythmic bursting drives slow-wave sleep.

If LTS are generated locally, then LTS should be generated whenever the local membrane potential surpasses a given threshold. This was not the case in dendrites: greater dendritic depolarization was required to elicit LTS when current was injected into the dendrite than when current was injected into the soma. This suggests that the soma must be depolarized above some threshold to elicit LTS. If LTS propagate from the soma to dendrites, however, blocking somatic T channels should block LTS. It did not. Moreover, reducing dendritic T channel conductance inhibited LTS generation in a computational model. Together, these data suggest that LTS involve global activation of T channels and does not require propagation of the signal.

Thalamocortical and TRN neurons shared dendritic electrical properties that explain the global nature of LTS. Specifically, the input impedance increased with distance from the soma, while the transfer impedance remained constant. Consequently, somatic current injection produced nearly uniform voltage changes throughout the dendrites, whereas dendritic current injection produced smaller voltage changes in the soma than in the dendrite. By preventing LTS from occurring unless the entire cell is depolarized, these properties might help stabilize and synchronize rhythmic bursting during slow-wave sleep and other LTS-dependent neuronal activity.

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