This Week in The Journal

Contribution of T Channels to Visual Processing

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(see pages 5697–5710)

Thalamocortical neurons exhibit different spike patterns depending on whether T-type calcium channels are activated. Subthreshold depolarization after a period of hyperpolarization opens T channels, leading to further depolarization and a short, high-frequency burst of spikes. Depolarization inactivates the channels, however, and the cell must be hyperpolarized for >50 ms before the channels can be activated again. While T channels are inactivated, synaptic input can drive neurons to spike at low frequency, in an irregular pattern. This tonic mode predominates during alert states, whereas bursts alternating with hyperpolarization underlie the oscillations that characterize slow-wave sleep. Bursts also occur occasionally during alert states, however. For example, neurons in the lateral geniculate nucleus (LGN) sometimes produce spike bursts while animals watch movies of natural scenes. These bursts have been proposed to facilitate visual processing.

To elucidate the role of T channels and burst firing in visual processing, Alitto et al. recorded synaptically coupled pairs of retinal ganglion cells (RGCs) and LGN neurons during the presentation of visual stimuli. Because T channels can only be activated after a period of hyperpolarization, the authors used interspike interval in LGN neurons as a proxy for possible T channel involvement. The validity of this approach was supported by the finding that the probability of burst spiking in LGN neurons increased with interspike interval. Importantly, the efficiency of retinal spiking, that is, how often spiking in an RGC led to spiking in its postsynaptic LGN neuron, also depended on interspike interval in the LGN, and single RGC spikes were more likely to be followed by multiple LGN spikes as interspike interval increased. But the efficiency of RGC spikes increased with interspike intervals even in cases where the LGN neuron produced a single spike.

These results suggest that T channels in LGN neurons can facilitate the transmission of retinal information to the visual cortex even if the LGN neurons are not bursting. Because T channels are activated only after spike-free periods, they may contribute to visual processing primarily when visual stimuli appear suddenly or when animals have been inattentive. The channels may be especially important when visual stimuli are weak, and thus unable to elicit LGN neuron spikes without the contribution of T currents.

Eight-week-old adult-born granule cells from Tau^{VLW} mice (bottom) have shorter, less branched dendrites than those from wild-type mice (top). See Terreros-Roncal et al. for details.

Effects of Mutant Tau on Adult-Born Granule Cells

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(see pages 5794–5815)

Accumulation of abnormally phosphorylated forms of tau protein contributes to several neurodegenerative diseases, including Alzheimer's disease and frontotemporal dementia (FTD). In some forms of FTD, mutations in the tau gene promote hyperphosphorylation and aggregation of the protein, leading to atrophy of various frontal and temporal lobe structures, including the hippocampus. When human tau with FTD-linked mutations (Tau^{VLW}) is expressed in mice, it causes atrophy in the dentate gyrus, partly by reducing proliferation and survival of adult-born granule cells.

Terreros-Roncal et al. report that expression of Tau^{VLW} also alters the morphology and connectivity of adult-born granule cells in mouse dentate gyrus, particularly in cells born 4–8 weeks before morphology was examined. These cells had shorter dendrites with fewer distal branches than wild-type adult-born granule cells, and they were more likely to have more than one primary apical dendrite. In addition, the density of postsynaptic sites was lower in Tau^{VLW} adult-born granule cells than in controls, and the number of inputs to these cells from outside the dentate gyrus—as well as from excitatory neurons within the dentate gyrus—was reduced. The size of granule cell axonal arbors in hippocampal areas was also smaller in mutant mice than in controls. In contrast, Tau^{VLW} granule cells received more input from local inhibitory neurons than wild-type cells, and the dentate gyrus of mutant animals had more GABAergic neurons that expressed Neuropeptide Y and higher levels of presynaptic and postsynaptic markers of inhibitory synapses than controls. Furthermore, expression of Egr-1, a marker of neuronal activation and plasticity, was reduced in mutant granule cells. Notably, similar changes in morphology and inhibitory synaptic markers were found in the dentate gyrus of people who had FTD. Environmental enrichment or activating mutant granule cells using designer receptors exclusively activated by designer drugs reversed many of the abnormalities found in adult-born granule-cells of Tau^{VLW} mice.

These results suggest that mutations that promote tau hyperphosphorylation slow the development of adult-born granule cells and disrupt the cells' integration into hippocampal circuits in rodents. Similar abnormalities occur in people with FTD, although adult neurogenesis is far less prominent in humans than in rodents. Therefore, increasing neuronal activity may ameliorate deficits in FTD.

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