This Week in The Journal

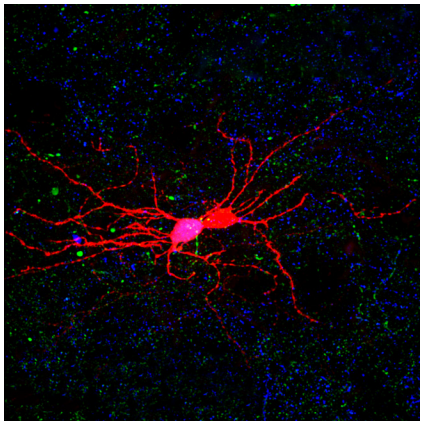
● Cellular/Molecular

Histamine Has Multiple Effects on Striatal Synapses

Tommas J. Ellender, Icnelia Huerta-Ocampo, Karl Deisseroth, Marco Capogna, and J. Paul Bolam

(see pages 15340–15351)

Histaminergic neurons, which reside in the hypothalamic tuberomamillary nucleus and project throughout the brain, are active during wakefulness, silent during sleep, and are involved in arousal and circadian regulation of various physiological functions. Although histamine afferents are relatively sparse in the striatum, this structure has one of the highest densities of histamine receptors in the brain. Nonetheless, the effects of histamine on striatal circuitry are poorly understood. Ellender et al. addressed this question with electrophysiological recordings of striatal medium spiny neurons (MSNs) expressing D1- or D2-type dopamine receptors. In both MSN subtypes, histamine caused depolarization, reduced EPSC amplitude at thalamic and cortical afferent synapses, and reduced IPSCs at MSN–MSN synapses. IPSCs elicited by fast-spiking interneurons were not affected. Histamine increased the paired-pulse ratio at corticostriatal and thalamostriatal synapses, suggesting it reduced the resting vesicle release probability. For thalamostriatal synapses, this resulted in a switch from short-term depression to facilitation.



Simultaneously recorded fast-spiking interneuron (pink) and MSN (red) in mouse striatal slice. Histamine has no apparent effect on synapses between these neuron types. See the article by Ellender et al. for details.

▲ Development/Plasticity/Repair

Snail Protein Reduces Retraction of Rodent Axons

Nasrin Nejatbakhsh, Cong-Hui Guo, Tom Z. Lu, Lin Pei, August B. Smit, et al.

(see pages 15231–15244)

Severed axons typically do not regenerate in the vertebrate CNS, not only because of physical barriers and inhibitory molecules in the environment, but also because the axons lose the ability to grow. Invertebrate CNS axons do regenerate, however, and identifying molecules that enable this regeneration may suggest ways to stimulate axonal growth in vertebrates. Nejatbakhsh et al. have identified one such molecule in snails: a putative calcium-binding protein, caltubin. Caltubin mRNA and protein were present in snail CNS neurites, and caltubin knockdown decreased neurite outgrowth in cultured neurons. After neurite transection, caltubin levels increased in both distal and proximal segments, suggesting it is locally synthesized in neurites. Furthermore, whereas distal neurites normally resumed extension after being severed, caltubin knockdown caused retraction, suggesting that local caltubin synthesis enables neurite extension. Interestingly, although no caltubin homolog has been identified in rodents, caltubin increased neurite outgrowth and reduced post-axotomy retraction when expressed in mouse cortical neurons.

■ Behavioral/Systems/Cognitive

Bats Use Sonar Aperture to Determine Object Size

Melina Heinrich, Alexander Warmbold, Susanne Hoffmann, Uwe Firzlaff, and Lutz Wiegrebe

(see pages 15618–15627)

Bats use biosonar to determine the distance, direction, and size of environmental objects. Determining distance is straightforward: it is proportional to the delay between sound emission and echo reception. Direction is determined by the difference in sound intensity between the two ears and/or by interference patterns produced by the shape of the ear. How bats discriminate object size, however, is not clear. One possible cue is echo loudness, which increases with object size. Another cue is sonar aperture—the spread of angles of incidence of echoes reaching the ear—which also increases with object size. Heinrich et al. found that bats can use either sonar aperture or echo intensity to determine object width, and that some neurons in the auditory cortex respond preferentially to given widths regardless of echo intensity. They propose that a combination of interaural intensity differences and the degree of interaural correlation in the echo envelope is used to encode sonar aperture.

♦ Neurobiology of Disease

Some HSPB1 Mutations Increase Microtubule Stability

Leonardo Almeida-Souza, Bob Asselbergh, Constantin d'Ydewalle, Kristof Moonens, Sofie Goethals, et al.

(see pages 15320–15328)

Charcot-Marie-Tooth (CMT) disease is a heterogeneous group of peripheral neuropathies involving demyelination (CMT1) or axonal loss (CMT2). Different CMT subtypes are caused by mutations in genes involved in various cellular processes, including mitochondrial dynamics, axonal transport, and protein trafficking. Mutations in the small heat-shock protein HSPB1 cause CMT2F, and a subset of these mutations increase HSPB1 affinity for its target proteins. Like other small HSPs, HSPB1 helps to prevent aggregation and facilitates refolding of partially unfolded proteins, and its targets include actin, neurofilaments, and microtubules. Almeida-Souza et al. report that some CMT-linked forms of HSPB1 have increased affinity for tubulin, and these mutants transiently increase microtubule stability. Unlike other microtubule stabilizers, mutant HSPB1 did not increase microtubule acetylation, and possibly as a result, microtubules depolymerized more rapidly after periods of stability. Given that other microtubule stabilizers are also associated with peripheral neuropathies, these data suggest that increased microtubule stability contributes to some forms of CMT.