This Week in The Journal

● Cellular/Molecular

Lipoamino Acids Inhibit T-Type Calcium Channels

Guillaume Barbara, Abdelkrim Alloui, Joël Nargeot, Philippe Lory, Alain Eschalier, et al.

(see pages 13106–13114)

Lipoamino acids, such as *N*-arachidonoyl glycine (NAGly), are endogenous fatty-acid–amino-acid conjugates that are structurally similar to endocannabinoids and exert similar effects. NAGly inhibits the enzyme that degrades the endocannabinoid anandamide, and this might explain some cannabinoid-like effects. But when cannabinoid receptors are inhibited, NAGly-induced analgesia persists, suggesting NAGly acts via a different mechanism. Because T-type calcium channels have been implicated in pain pathways and are inhibited by anandamide, Barbara et al. examined the effects of lipoamino acids on T-currents. Lipoamino acids strongly inhibited T-type channels and weakly inhibited high-voltage-activated calcium channels and sodium channels in mouse sensory neurons. The inhibition persisted in cell-free outside-out patches, indicating that lipoamino acids might act directly on the channels. Analysis of the current–voltage relationship suggested that lipoamino acids stabilize T-type channels in the inactivated state. Thermal analgesia produced by NAGly was absent in mice lacking T-type Cav3.2 subunits, suggesting inhibition of this channel is the main mechanism underlying NAGly-induced analgesia.

▲ Development/Plasticity/Repair

Nerve Transection Induces Circuit Reorganization in Tritonia

Akira Sakurai and Paul S. Katz

(see pages 13115–13125)

Many studies aim to stimulate recovery from CNS injury by promoting axonal regeneration to reestablish damaged connections. Unfortunately, regeneration is limited by numerous intrinsic and extrinsic factors, and despite much effort, stimulating regeneration has had limited success. Recovery of function can also result from reorganization of spared connections, however. Promoting such reorganization might therefore be an effective alternative strategy for treating injury. Sakurai and Katz show that functional reorganization of CNS circuits occurs in an invertebrate, *Tritonia*. Cutting the pedal commissure impaired escape swimming by eliminating a distal excitatory connection between neurons involved in the swim central pattern generator. The neurons remained connected proximally, however, by a weak excitatory synapse and a strong inhibitory synapse. Swimming recovered by 24 h posttransection because the inhibitory proximal connection weakened while the excitatory connection strengthened. Studying the cellular mechanisms underlying this reorganization in *Tritonia* might provide insights into how reorganization occurs in vertebrates.

■ Behavioral/Systems/Cognitive

Flies Integrate Visual and Vestibular Inputs to Stabilize Gaze

Stephen J. Huston and Holger G. Krapp

(see pages 13097–13105)

Many behaviors are controlled by inputs from multiple sensory modalities. Like most animals, flies combine visual and somatosensory information to guide head movements that stabilize the visual field. Huston and Krapp have studied how visual information from the eyes combines with gyroscopic information from specialized hind wings (halteres) to activate neck motor neurons that produce gaze-stabilizing head rotations. Although some motor neurons spiked in response to visual or haltere stimuli alone, others required inputs from both modalities. Oscillatory haltere movements evoked compound PSPs, and sometimes elicited action potentials that were phase-locked to the stimulus. In motor neurons that did not spike in response to visual stimuli alone, visual inputs generated small, sustained subthreshold depolarization. When combined with haltere stimulation, these visual stimuli increased neuronal spiking, which remained in phase with haltere movements. Haltere stimulation also altered spiking in neurons that responded to visual stimuli alone, entraining them to haltere oscillations.

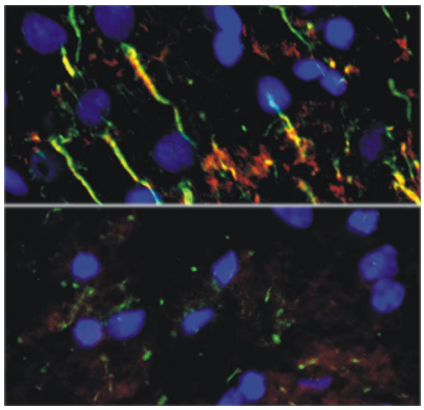
♦ Neurobiology of Disease

Ischemia Quickly Disrupts Axon Initial Segments

Dorothy P. Schafer, Smita Jha, Fudong Liu, Trupti Akella, Louise D. McCullough, et al.

(see pages 13242–13254)

The axon initial segment (AIS) and nodes of Ranvier are specialized cellular subdomains that contain unique cytoskeletal proteins—βIV spectrin and ankyrinG—that cluster voltage-sensitive sodium channels (Nav) at high density to enable spike initiation and propagation. Additionally, the AIS excludes somatodendritic proteins from the axon and thus helps to maintain neuronal polarity. Schafer et al. discovered that the AIS is particularly susceptible to damage by neuronal insult. In rats, transient ischemia caused loss of βIV spectrin and ankyrinG and subsequent loss of Nav at cortical AISs. Surprisingly, however, nodes were not disrupted. In cultures, oxygen–glucose deprivation disrupted both the AIS and neuronal polarity before causing significant cell death or degeneration. Inhibitors of the calcium-dependent protease calpain protected the AIS from disassembly *in vitro* and *in vivo*, but did not prevent cell death. NMDA receptor inhibitors reduced neuronal death however, suggesting treatment with both inhibitors could further limit damage from stroke.



Ischemia produced by unilateral middle cerebral artery occlusion disrupted the AIS in ipsilateral (bottom) but not contralateral (top) cortex. Blue, nuclei; green, βIV spectrin; red, Nav channels. See the article by Schafer et al. for details.