This Week in The Journal

● Cellular/Molecular

Chloride Uptake Affects E_{GABA} in the Axon Initial Segment

Stanislav Khirug, Junko Yamada, Ramil Afzalov, Juha Voipio, Leonard Khiroug, and Kai Kaila

(see pages 4635–4639)

It was recently discovered that GABAergic inputs from axo-axonic cells onto the axon initial segment (AIS) of cortical pyramidal cells is depolarizing, because the GABA receptor reversal potential (E_{GABA}) is more positive than the resting membrane potential at the AIS. Although this E_{GABA} is partly attributable to reduced expression of the K–Cl cotransporter (KCC2) and therefore reduced Cl extrusion in the AIS, Khirug et al. reasoned that this is insufficient to produce the observed E_{GABA}. To explore the role of Cl uptake in setting E_{GABA}, the authors recorded GABA responses in dentate granule cells from mice lacking the Na–K–2Cl cotransporter NKCCl. Local GABA uncaging in wild-type mice revealed that E_{GABA} was more negative in the AIS than in the soma. This difference was absent in NKCCl-null mice and was abolished in wild-type mice by a NKCCl blocker. These results suggest that Cl uptake by NKCCl contributes to the offset E_{GABA} at the AIS.

▲ Development/Plasticity/Repair

Perisomatic Glutamate Triggers Axon Retraction

Ryuji X. Yamada, Takuya Sasaki, Junya Ichikawa, Ryuta Koyama, Norio Matsuki, and Yuji Ikegaya

(see pages 4613–4618)

Growth cones are the principal sites where environmental cues are integrated to steer axon growth toward appropriate targets. But this week, Yamada et al. report that glutamate triggers axon retraction when applied locally to the soma of cultured dentate granule neurons, but not when applied to the axonal growth cone—even though glutamate receptors are present in axons. Perisomatic glutamate application initiated a calcium sweep that traveled down the axon. Retraction commenced shortly after the sweep reached the growth cone, regardless of the axon's length. The calcium sweep and retraction required calcium influx and release from internal stores, but intracellular calcium elevation by itself was unable to elicit the effect. When depolarizing current injection was paired with application of calcium ionophores, however, both the sweep and retraction occurred. The effects of glutamate were mimicked by AMPA, but not NMDA, and were inhibited by an antagonist of calcium-permeable non-NMDA glutamate receptors.

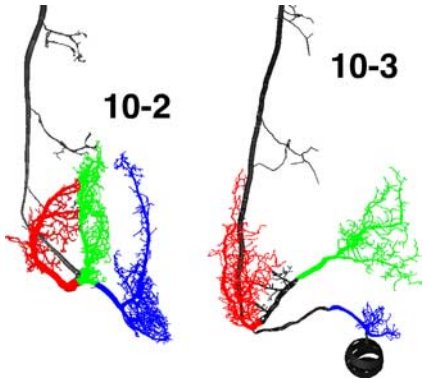
■ Behavioral/Systems/Cognitive

Calcium Imaging Reveals Different Computational Strategies in Crickets

Hiroto Ogawa, Graham I. Cummins, Gwen A. Jacobs, and Kotaro Oka

(see pages 4592–4603)

Crickets use air currents to detect and escape predators. All information about wind direction is processed by two pairs of interneurons (INs), IN 10-2 and 10-3. The dendrites of these four interneurons integrate inputs from many mechanosensory afferents, and their output is directionally tuned. Ogawa et al. used simultaneous presynaptic and postsynaptic calcium imaging to examine how afferent inputs to different dendritic branches of these interneurons are integrated to produce the directionally tuned response. They found that IN 10-2 and 10-3 integrated inputs differently, possibly due to differences in dendritic morphology. The directional tuning of each dendrite in IN 10-3 matched that of its presynaptic input, but not of the other dendrites, suggesting that each dendrite acted as a separate computational unit. In contrast, the directional tuning was similar across IN 10-2 dendrites (each was different from its inputs), suggesting that the dendrites acted as a single computational unit.



Drawings of IN 10-2 and 10-3, showing different dendritic compartments in different colors. See the article by Ogawa et al. for details.

♦ Neurobiology of Disease

Isoprostanes Increase Amyloid Plaques

Diana W. Shineman, Bin Zhang, Susan N. Leight, Domenico Pratico, and Virginia M.-Y. Lee

(see pages 4785–4794)

A promising new therapeutic target for Alzheimer's disease (AD)—the thromboxane receptor—is described this week. The thromboxane receptor is activated by isoprostanes, peroxidation products generated from arachidonic acid following oxidative stress. Two isoprostane isoforms are elevated in AD and AD-like diseases, but not in other neurodegenerative diseases. Shineman et al. report that injection of one of these isoprostanes increased the number of amyloid plaques in Tg2576 mice, a mouse model of AD. Activation of the thromboxane receptor increased levels of amyloid precursor protein (APP) and its cleavage products, including those that form plaques. The thromboxane receptor also increased the stability of APP mRNA by an unknown mechanism, and this likely provided more substrate for amyloid production. Significantly, thromboxane receptor antagonists reversed the effects of isoprostane injection and also reduced plaque formation in Tg2576 mice that were not treated with isoprostane, suggesting that these antagonists might reduce plaque formation in humans.