This Week in The Journal

● Cellular/Molecular

Zinc Inhibition of Kainate Receptors

David D. Mott, Morris Benveniste, and Raymond J. Dingledine

(see pages 1659–1671)

This week, Mott et al. present evidence that zinc inhibits glutamatergic kainate receptors in a pH-dependent manner. Zinc is packaged with glutamate in mossy fiber terminals, which synapse onto CA3 pyramidal cells. Mott et al. found that zinc chelators increased kainate receptor-dependent facilitation of field EPSPs produced by 100 Hz stimulation of mossy fibers in rat hippocampal slices. Furthermore, exogenous zinc abolished kainate-mediated miniature EPSCs (mEPSCs) without affecting AMPA-mediated mEPSCs. When mossy fibers were stimulated antidromically, kainate increased firing synchrony and the size of the population spike; this potentiation was also blocked by zinc. Examination of kainate receptors expressed in oocytes revealed that those with KA1 and KA2 subunits were most sensitive to zinc. Lower pH reduced zinc inhibition of kainate receptors, with greatest effects on KA2-containing receptors. Because neurotransmission alters synaptic pH, these data suggest that activity can modulate kainate receptor function by modulating inhibition by zinc.

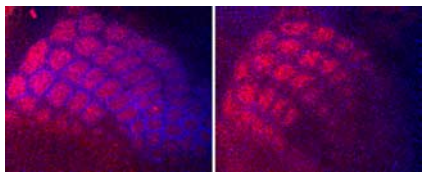
▲ Development/Plasticity/Repair

Effects of Neurofibromin on Cortical Organization

Mark E. Lush, Yun Li, Chang-Hyuk Kwon, Jian Chen, and Luis F. Parada

(see pages 1580–1587)

Neurofibromin, the tumor suppressor protein mutated in neurofibromatosis type 1 (NF1), is important for cortical development, report Lush et al. this week. Using the Cre/Lox method, the authors produced mice in which neurofibromin was knocked out only in cortical progenitors and thus was absent from most cortical neurons and astrocytes. Although these mice had normal numbers of cortical neurons and no obvious defects in cortical layering or thalamic inputs, the organization of the neurons was disrupted. Aggregation of neurons was disrupted throughout the somatosensory cortex, but this was particularly obvious in the barrel cortex, where the barrel structure was completely absent. Nonetheless, expression levels of other proteins known to disrupt barrel formation, including NMDA receptors, phospholipase C-β1, protein kinase A-RIIβ, and SynGAP, were unchanged in these mice. It is conceivable that similar defects in cortical organization might underlie intellectual deficits and autism spectrum disorders seen in some NF1 patients.



Nuclear staining (blue) shows that neurons do not segregate into barrels in the somatosensory cortex of neurofibromin conditional knock-out mice (right), although thalamic axon (red) innervation and segregation is similar to controls (left). For details, see the article by Lush et al.

■ Behavioral/Systems/Cognitive

Filtering Self-Generated Sensory Information

Nathaniel B. Sawtell and Alan Williams

(see pages 1598–1612)

As an animal explores its surroundings, its own movements create sensory feedback that it must distinguish from sensory signals from the environment. Sawtell and Williams have studied this problem in mormyrid electric fish. Mormyrids sense their environment by producing an electric field and sensing perturbations to this field via electrosensory receptors that cover their bodies. Sawtell and Williams show that the activity of these electroreceptors is strongly affected by tail movements—more strongly, in fact, than by nearby objects. In contrast, secondary sensory neurons in the electrosensory lobe (ELL), a cerebellar-like structure, are much more sensitive to object locations than to tail movements. As a result, the output of ELL neurons carries much more information about environmental objects than the sensory afferents. This transformation partly depends on proprioceptive inputs about tail position, which provide input to neurons of the ELL via parallel fibers.

♦ Neurobiology of Disease

New and Improved Mouse Model for Alzheimer's Disease

Donna M. Wilcock, Matthew R. Lewis, William E. Van Nostrand, Judianne Davis, Mary Lou Previti, Nastaran Gharkholonarehe, Michael P. Vitek, and Carol A. Colton

(see pages 1537–1545)

Most attempts to create transgenic mice that exhibit all the pathological features of Alzheimer's disease (AD)—amyloid-β (Aβ) plaques, neurofibrillary tangles of hyperphosphorylated tau, and neuronal loss—have been only partially successful. This week's report by Wilcock et al. is therefore a welcome advance. The authors produced mice that have a mutant form of amyloid precursor protein (APP) and that also lack inducible nitric oxide synthase (iNOS). These mice showed levels of Aβ staining similar to that in mice with mutant APP alone, but they had greater defects in spatial learning. Furthermore, unlike APP single-mutant mice, the double mutants had significant neuronal degeneration and increased phosphorylation and aggregation of tau, particularly in the hippocampus and subiculum—brain regions that expressed high levels of APP. Moreover, neurons expressing neuropeptide Y were especially susceptible to death in these mice, as in human AD patients, further strengthening the usefulness of this mouse as a model for AD.