This Week in The Journal

● Cellular/Molecular

A Supersensitive Phosphorylation Site on Kv2.1

Hiroaki Misonou, Milena Menegola, Durga P. Mohapatra, Lauren K. Guy, Kang-Sik Park, and James S. Trimmer

(see pages 13505–13514)

Voltage-dependent K^+ (Kv) channels are activated by changes in the cell membrane potential, but phosphorylation of residues in the subunits can significantly alter the extent of activation. A recent mapping of the Kv2.1 channel, a member of the Kv family present on most hippocampal and cortical pyramidal neurons, identified not one, not two, but 16 such sites. This week, Misonou et al. looked at two of these sites, S563 and S603, in more detail. The authors tested the effects of stimuli that cause increased neuronal activity such as kainate-induced seizures, or decreased neuronal activity such as deep anesthesia in rat brains *in vivo*. The authors also tested glutamate excitation of cultured neurons. In each case, S603 was much more sensitive. Increased neuronal activity led to calcineurin-mediated dephosphorylation, whereas reduced activity increased phosphorylation, providing a bidirectional and graded means to regulate channel function and in turn neuronal activity.

▲ Development/Plasticity/Repair

Development without Death

Robert R. Buss, Thomas W. Gould, Jianjun Ma, Sharon Vinsant, David Prevette, Adam Winseck, Kimberly A. Toops, James A. Hammarback, Thomas L. Smith, and Ronald W. Oppenheim

(see pages 13413–13427)

The developing nervous system of vertebrates initially generates an excess of neurons. About one-half of these neurons are then eliminated through programmed cell death, or apoptosis. Although many studies have focused on the mechanism of apoptosis and how to prevent it, few have looked at the fate of the "excess" neurons when their death was prevented. This week, Buss et al. did just that. They examined neuromuscular development in three animal models in which apoptosis was blocked: knock-out mice lacking the proapoptotic gene *Bax*, transgenic mice overexpressing the survival factor MyoGDNF (myogenin glial cell line-derived neurotrophic factor), and chick embryos paralyzed by treatment with curare. All animals had an excess of axons projecting to target muscles, but motoneurons were smaller, and many axons failed to myelinate or form functional synapses. The phenotypes of the three animal models also differed in some features, consistent with distinct compensatory changes.

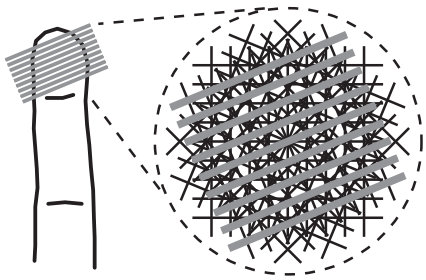
■ Behavioral/Systems/Cognitive

Orientation Tuning in Macaque Somatosensory Cortex

Pramodsingh H. Thakur, Paul J. Fitzgerald, John W. Lane, and Steven S. Hsiao

(see pages 13567–13575)

Previous work has shown that many neurons in the second somatosensory (S2) cortical region show orientation tuning, somewhat akin to that observed in the visual cortex. This week Pramodsingh et al. honed in on a single finger pad of two rhesus monkeys and show that this orientation tuning involves multiple mechanisms. They indented the skin of a finger pad with a motorized bar at eight different orientations and nine different locations and recorded from single neurons in the macaque S2 region. Some cells had simple cell-like receptive fields, but many neurons showed position invariant responses. That is, their firing was selective for a narrow band of orientations, and the preferred orientation was the same in any location across the finger pad. The range of response properties indicated that tuning results from a region of pure position invariance, bands of excitation and inhibition that are not centered on the finger pad, or a combination of these mechanisms.



A single distal finger pad with an indented oriented bar that was rotated to one of eight orientations (22.5 degree increments) and indented into the skin at one of nine positions per orientation. See the article by Thakur et al. for details.

♦ Neurobiology of Disease

Adenosine A_{2A} Receptors and L-DOPA-Induced Dyskinesias

Danqing Xiao, Elena Bastia, Yue-Hang Xu, Caroline L. Benn, Jang-Ho J. Cha, Tracy S. Peterson, Jiang-Fan Chen, and Michael A. Schwarzschild

(see pages 13548–13555)

Treatment of Parkinson's disease with L-3,4-dihydroxyphenylalanine (L-DOPA) has its limits. Continued treatment often leads to adaptive behavioral responses and, in particular, involuntary movements referred to as L-DOPA-induced-dyskinesia (LID). Because adenosine A_{2A} receptors are highly expressed in striatum, there has been interest in their use in nondopaminergic treatments. Xiao et al. wanted to know whether blocking A_{2A} receptor signaling would relieve symptoms of LID in hemiparkinsonian mice. Using the *Cre/lox* system, the authors knocked out A_{2A} receptors in the forebrains of transgenic mice. These mice developed fewer abnormal involuntary movements and rotational responses during chronic L-DOPA treatment, similar to mice that received low doses of A_{2A} receptor antagonists along with L-DOPA. Thus A_{2A} receptors in forebrain neurons may contribute to the behavioral sensitization to L-DOPA, perhaps indicating that A_{2A} antagonists could reduce the risk of LID.