This Week in The Journal

**Cellular/Molecular**

**Na^+**-Activated K^+ Channels Contribute to Nociceptor Sensitization

Megan O. Nuwer, Kelly E. Picchione, and Arin Bhattacharjee

(see pages 14165–14172)

Inflammatory molecules sensitize peripheral nociceptors, making them responsive to innocuous stimuli. Sensitization is mediated by protein kinase A (PKA), but the ion channels involved are not known. PKA increases expression of voltage-gated sodium channels, but knock-out of these channels does not eliminate inflammation-induced sensitization. PKA also decreases potassium currents, but the percentage change in current was reportedly small. Nuwer et al. noted, however, that the latter studies were conducted in sodium-free medium, and therefore could not identify effects on sodium-activated potassium (KNa) channels, which are highly expressed in nociceptors. With physiological sodium concentrations, a PKA activator caused a 50% decrease in potassium current injection, as does activation of PKA.

**Development/Plasticity/Repair**

Post-Ischemic Spine Recovery Depends on Perfusion Level


(see pages 14116–14126)

When a cerebral blood vessel is blocked, loss of perfusion causes neuronal death. But because vessels are interconnected, some tissue normally supplied by the blocked vessel receives blood from collateral branches of unaffected arteries. Although neurons in this peri-infarct region are damaged, they can recover, and remapping of lost functions to these neurons might underlie functional recovery. Mostany et al. elaborated changes in neurons and capillaries in the peri-infarct region in vivo in mice. Artery occlusion caused an immediate decrease in blood flow and dendritic spine density on cortical pyramidal neurons. Within 2 months, spine density recovered as more spines were generated and maintained. In fact, in distal peri-infarct areas, spine density was higher 3 months after occlusion than before. In contrast, perfusion never fully recovered. Interestingly, although initial spine loss was independent of blood flow, areas with the highest perfusion immediately after occlusion showed the greatest recovery of spine density in subsequent weeks.

**Behavioral/Systems/Cognitive**

Tonic and Phasic Firing Differentially Affect D1 and D2 Receptors

Jakob K. Dreyer, Kjartan F. Herrik, Rune W. Berg, and Jørn D. Hounsgaard

(see pages 14273–14283)

Midbrain dopaminergic neurons are spontaneously active, and their tonic firing maintains low levels of dopamine in target regions. In response to certain external events, however, dopaminergic neurons spike in bursts followed by pauses. Whereas tonic release is thought to enable behavioral selection and switching, phasic spiking likely encodes value, e.g., the desirability of a stimulus or the difference in value between received and expected rewards. Differential activation of low-affinity D1 receptors and high-affinity D2 receptors might underlie these functions. To predict how different firing patterns might affect dopamine concentration and receptor activation, Dreyer et al. created a computer model based on experimental data. Tonic firing caused widespread activation of D2 receptors with minimal activation of D1 receptors. Bursts had a proportionately larger effect on D1 receptors, whereas subsequent pauses caused greater reduction in D2 receptor activation. Therefore, a shift from tonic to phasic firing patterns resulted in a shift from primarily D2 receptor activation to greater D1 receptor activation.

**Neurobiology of Disease**

Reactive Fibrous Astrocytes Retract, Then Extend Processes

Daniel Sun, Ming Lye-Barthel, Richard H. Masland, and Tatjana C. Jakobs

(see pages 14008–14019)

Upon CNS injury, astrocytes undergo molecular and morphological changes. Reactive astrocytes likely limit damage by regulating inflammation, repairing the blood–brain barrier, taking up excess glutamate, and releasing neuroprotective molecules. Protoplasmic astrocytes residing in gray matter are well studied because they occupy distinct domains and their processes minimally overlap. In contrast, fibrous astrocytes, which primarily occupy white matter, are less well studied, because they are difficult to distinguish from each other. Sun et al. used mice expressing green fluorescent protein in a subset of astrocytes to investigate morphological changes in fibrous astrocytes during reactive astrocytosis. At the optic nerve head, fibrous astrocytes had long processes oriented perpendicular to the nerve, and they formed tubes through which axons projected. After nerve crush, astrocytic processes initially retracted, thickened, and became disorganized. Subsequently, the processes returned to normal length and thickness, but they remained disorganized, filling the tubes, and thus forming a glial scar.

Transverse sections through the glia lamina at the optic nerve head show orientation and morphology of normal (left) and reactive (right) astrocytes. See the article by Sun et al. for details.