This Week in The Journal

● Cellular/Molecular

Sodium Channel Redistribution and Neuropathic Pain

Redistribution of $Na_V1.8$ in Uninjured Axons Enables Neuropathic Pain

Michael S. Gold, Danny Weinreich, Chang-Sook Kim, Ruizhong Wang, James Treanor, Frank Porreca, and Josephine Lai

(see pages 158–166)

Pain resulting from chronic nerve injury or damage (so-called neuropathic pain) is a common and debilitating condition. Many studies indicate that tetrodotoxin-resistant (TTX-R) sodium channels are highly expressed in nociceptors, the sensory neurons that mediate pain. It has also been suggested that a reduction in TTX-R expression or function reduces pain. Similarly, because axonal injury causes hyperexcitability, it has been proposed that increases in sodium channel expression in injured neurons account for neuropathic pain. However, Gold et al. present evidence that sodium channel redistribution contributes to neuropathic pain. They ligated lumbar nerves 5 and 6, a standard rat model of neuropathic pain. Tactile sensitivity increased, and withdrawal latencies to thermal stimuli decreased 7 d after injury. The authors compared the characteristics of neurons in the L4 dorsal root ganglion (DRG) (uninjured) with the L5 DRG (injured). They found that the $Na_V1.8$, a TTX-resistant sodium channel that is exclusively expressed in primary sensory neurons, was downregulated in injured DRG cell bodies, but $Na_V1.8$ immunoreactivity and TTX-R sodium channels were increased along the sciatic nerve, primarily because of redistribution of TTX-R sodium channels to axons of uninjured nerves. Thus both changes in expression and redistribution of sodium channels may underlie neuropathic pain.

▲ Development/Plasticity/Repair

Inducible Nitric Oxide Synthase and Neurogenesis

Expression of Inducible Nitric Oxide Synthase after Focal CerebralIschemia Stimulates Neurogenesis in the Adult Rodent Dentate Gyrus

Dong Ya Zhu, Shu Hong Liu, Hong Suo Sun, and You Ming Lu

(see pages 223–229)

The neurogenesis of neurons in the adult brain has been studied intensively over the past few years, particularly in the dentate gyrus of the hippocampus. Neurogenesis of granule cells occurs at a basal rate and can be increased by stimuli including stress, exercise, and seizures. In this issue, Zhu et al. examine neurogenesis after cerebral ischemia in a rat model of focal cerebral ischemia (90 min occlusion of the middle cerebral artery). One week after ischemia, they found increased neurogenesis as well as a threefold increase in expression of inducible nitric oxide synthase (iNOS). Of note, iNOS is not generally expressed in the brain except after inflammation. The increased neurogenesis was blocked by iNOS inhibitors administered in the 5 d after ischemia, There was a concomitant reduction in the area of ischemic damage. Ischemia in iNOS-deficient mice also produced a smaller area of damage, and these animals did not show enhanced neurogenesis. The authors argue that reduced neurogenesis by iNOS inhibition is not simply an indirect result of reduced ischemic injury, and that nitric oxide may be directly involved in repair after ischemic brain injury.

■ Behavioral/Systems/Cognitive

Imaging Financial Rewards

Differential Response Patterns in the Striatum and Orbitofrontal Cortex to Financial Reward in Humans: A Parametric Functional Magnetic Resonance Imaging Study

Rebecca Elliott, Jana L. Newman, Olivia A. Longe, and J. F. William Deakin

(see pages 303–307)

Functional neuroimaging provides neuroscientists with the opportunity to examine the neural substrates of behaviors that would seem to be uniquely human. Money would certainly seem to be such a uniquely human reward. However, imaging studies over the past several years have revealed that brain regions involved in financial reward are also involved in other rewards in animals, such as food. In this issue, Elliott et al. make use of a parametric functional magnetic resonance imaging design to detect patterns of activation in brain regions involved in financial reward. Healthy student volunteers at the University of Manchester (Manchester, UK) were asked to pick green or blue squares from a series of targets presented on a screen. A correct response resulted in the appearance of a coin on the screen. The value of the coin reward was also continuously displayed at the bottom of the screen. Four test series ranged from "minimum wage" (10 pence) to "lucrative" (1 pound). They found that the striatum and amygdala responded in an all-or-none manner to the reward, whereas premotor cortex responses increased with increasing reward. Orbitofrontal areas showed a complex pattern of response, responding at the extremes of the reward spectrum. The authors speculate that striatal neurons respond during the expectation and detection of a reward, whereas orbitofrontal areas may be involved in coding relative rather than absolute values of reward.