This Week in The Journal

● Cellular/Molecular

Don't Underestimate L-Type Channels

Thomas D. Helton, Weifeng Xu, and Diane Lipscombe

(see pages 10247–10251)

Neuronal L-type channels get a lot of credit for calcium entry into cell bodies and dendrites but little credit for calcium entry triggered by action potentials (APs). The somatodendritic L-type channels contribute to activity-dependent gene expression and plasticity but are thought to activate too slowly to open during an action potential. It seems this may not be the case. This week in the *Journal*, Helton et al. transiently expressed L-type channel subunits and evoked currents with voltage steps or AP waveforms. The activation rate of $Ca_v1.3$ channels was as fast as N-type $Ca_v2.2$ channels, whereas $Ca_v1.2$ channels opened more slowly. Both channels were as or nearly as efficient as $Ca_v2.2$ channels at allowing calcium entry in response to an AP waveform. Strikingly, the dihydropyridine antagonist nifedipine blocked $Ca_v1.2$ or $Ca_v1.3$ channel currents only after a train of 60 APs. Because block of these channels by nifedipine is state dependent, the role of L-channels in AP-triggered calcium influx may have been underestimated.

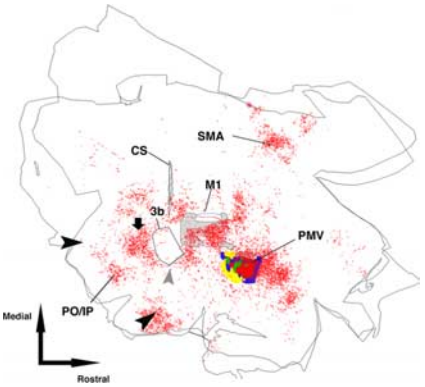
▲ Development/Plasticity/Repair

Rewiring Patterns after Cortical Injury

Numa Dancause, Scott Barbay, Shawn B. Frost, Erik J. Plautz, Daofen Chen, Elena V. Zoubina, Ann M. Stowe, and Randolph J. Nudo

(see pages 10167–10179)

Recovery after ischemic stroke is often far from complete. This week in the *Journal*, Dancause et al. examine the extent of cortical reorganization after a small cortical stroke in squirrel monkeys. The authors searched for connections between neurons that had projected to the area of ischemic damage and their new targets. Five months after a discrete ischemic lesion of the hand area of the primary motor cortex, motor performance had improved, but there were still deficits in fine motor control. At that point, the authors injected the hand area of the ventral premotor cortex (PMv) with biotinylated dextran amine to label axonal tracts. In contrast to control animals, PMv neurons of lesioned monkeys displayed greatly increased axonal sprouting and had forged new contacts with neurons in areas 1/2 of the primary somatosensory cortex and within the PMv. The authors propose that ischemic brain damage may trigger compensatory regrowth and rewiring of neuronal processes.



The pattern of labeled nerve terminals in a squirrel monkey 5 months after ischemic lesion in the primary motor cortex (M1). The tracer was injected in the ventral premotor cortex. The labeling in the area 1/2 hand representation (black downward arrow) was not present in control animals. See Dancause et al. for details.

■ Behavioral/Systems/Cognitive

Awareness and Declarative Memory

Christine Smith and Larry R. Squire

(see pages 10138–10146)

Memory can be subdivided into hippocampal-dependent declarative memory and the performance-based memory functions that underlie skill and habit learning. This week in the *Journal*, Smith and Squire revisit whether declarative memory is available to awareness. College students were trained with pairs of Japanese characters, one of which was always the "correct" choice over the other. Each set of five or six characters formed a hierarchical sequence (i.e., A > B > C > D > E). After training, novel pairs (e.g., BD) were presented to test learning through transitive inference. Subjects who reported awareness of the characters' hierarchy (on a posttest questionnaire) performed much better on the inference task, nearly always correctly choosing the higher-ordered character over the lower one. Unaware subjects and memory-impaired subjects with hippocampal damage performed poorly. The authors conclude that success on transitive interference tasks requires the hippocampus and depends on awareness of what is learned.

♦ Neurobiology of Disease

Nrf2 and Ischemic Neuroprotection

Andy Y. Shih, Ping Li, and Timothy H. Murphy

(see pages 10321–10335)

The transcription factor [nuclear factor erythroid 2-related factor 2 (Nrf2)] activates a set of genes that feature an antioxidant response element. The resulting gene products target reactive oxygen species and other ischemic byproducts. Normally tethered to a cytoplasmic regulatory protein, Nrf2 is freed by oxidative stress or electrophilic agents like the antioxidant *tert*-butylhydroquinone (tBHQ). This week in the *Journal*, Shih et al. report that tBHQ induced higher levels of Nrf2-activated enzyme activity in astrocytes from wild-type but not $Nrf2^{-/-}$ mice. The authors delivered tBHQ to rats and mice by intracerebral or intraperitoneal injection or by feeding for 3–7 d *in vivo*. The animals were then subjected to ischemia, either carotid occlusion or intracortical endothelin-1 injection. After 24 h, tBHQ-treated rats and wild-type mice displayed smaller infarcts and better neurological scores. $Nrf2^{-/-}$ mice fared worse. One month later, tBHQ-treated mice were functionally improved compared with control. The authors conclude that prophylactic Nrf2 activation may help protect against ischemia.