This Week in The Journal

● Cellular/Molecular

Abnormal Myelin in Mice Lacking ClC-2

Judith Blanz, Michaela Schweizer, Muriel Auberson, Hannes Maier, Adrian Muenscher, Christian A. Hübner, and Thomas J. Jentsch

(see pages 6581–6589)

The hunt for genes that increase susceptibility to disease is fraught with twists and turns. Heterozygous mutations in the plasma membrane chloride channel ClC-2 have been linked to human epilepsy in three families. However, Blanz et al. found a quite different phenotype in mice that were either heterozygous or deficient in *Clcn2*. This widely expressed chloride channel is activated by cell swelling, lowered pH, and voltage. Mice lacking *Clcn2* showed spongiform vacuolation of the central white matter, basically a picture of fluid-filled holes between myelin sheets. This pattern was apparent at 2 months of age and increased further with age. The peripheral nerves were unaffected. Blindness was the most obvious consequence of ClC-2 loss, presumably from the retinal damage described previously in these mice. However, neurons appeared normal, and there was no effect on seizure threshold. The pattern of white matter injury suggests that ClC-2 is involved in extracellular ion homeostasis in oligodendrocytes.

▲ Development/Plasticity/Repair

EGFR Inhibitors and Spinal Cord Injury

Matthias Erschbamer, Karin Pernold, and Lars Olson

(see pages 6428–6435)

After spinal cord injury (SCI), physical and molecular barriers inhibit axon regeneration. These impediments arise in part from a glial scar consisting of reactive astrocytes as well as astrocytic release of growth inhibitors such as chondroitin sulfate proteoglycans. These astrocytic events can be triggered by activation of the epidermal growth factor receptor (EGFR). Thus, Erschbamer et al. tested the potential benefit of permanently blocking the receptor after SCI. Rats received a contusion injury, and for 14 d received intrathecal injection of either vehicle or the irreversible EGFR inhibitor PD168393 (4-[3(bromophenyl)-amino]-6-acrylamidoquinazoline) at the injury site. Treated rats showed greater and faster recovery in locomotion, sensory function, bladder control, and weight gain compared with control-treated rats. Drug-treated animals also had more spared myelin and more axons reactive for serotonin or tyrosine hydroxylase. Injury caused a marked upregulation of EGFR in the spinal cord, particularly in astrocytes.

■ Behavioral/Systems/Cognitive

Medial Prefrontal Cortex Activity and Facilitation of Learning

Rony Paz, Elizabeth P. Bauer, and Denis Paré

(see pages 6542–6551)

Consolidation of hippocampal-dependent memories presumably involves long-term storage of information that gradually moves to the neocortex through multisynaptic pathways. This week, Paz et al. investigated how the medial prefrontal cortex (mPFC) might facilitate this transfer. In a trace-conditioning task, cats learned to expect a liquid food reward (Gerber's pureed "sweet potatoes and turkey") after a visual conditioned stimulus (CS). The authors made simultaneous recordings from neurons in mPFC, perirhinal (PR) cortex, and entorhinal (ER) cortex. They then measured correlated activity in ER and PR that followed firing of mPFC neurons. Early in the training, mPFC firing evoked an increased correlation betweeen ER and PR firing, but in no particular direction. As learning solidified, the mPFC-induced correlation increased and included the conditioned stimulus. The correlation also was directional, specifically from ER to PR neurons, the direction expected for signal transfer from hippocampus to neocortex.

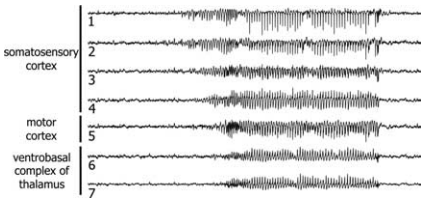
♦ Neurobiology of Disease

A Focal Onset in a Rat Model of Absence Seizures

Pierre-Olivier Polack, Isabelle Guillemain, Emilie Hu, Colin Deransart, Antoine Depaulis, and Stéphane Charpier

(see pages 6590–6599)

In this week's *Journal*, Polack et al. pinpoint the origin of seizure activity in Genetic Absence Epilepsy Rats from Strasbourg (GAERS). Absence seizures such as childhood absence or petit mal are typically considered as arising without a seizure "focus," i.e., a highly circumscribed area from which seizure activity originates. However, the authors show that GAERS does not follow the rule. After implanting recording electrodes, the authors measured local field potentials in somatosensory and motor cortex as well as the thalamus of freely moving GAERS rats. The vast majority of spike-and-wave discharge activity arose from the face area of the somatosensory cortex. The authors next made intracellular recordings from neurons in each layer of the S1 somatosensory cortex. Compared with neurons in the upper layers, layer 5/6 neurons were consistently more depolarized and fired spontaneously between seizures. Their activity during seizures preceded firing in other cortical and thalamic areas, thus constituting a bona fide seizure focus.



In freely moving GAERS rats, local field potentials revealed that slow wave discharges, indicative of absence seizures, began in the somatosensory area before propagating to motor cortex and thalamus. See the article by Polack et al. for details.