This Week in The Journal

● Cellular/Molecular

Pyramidal Cells Might Not Excite GABAergic Terminals

Court Hull, Hillel Adesnik, and Massimo Scanziani

(see pages 8991–8995)

In 2007, researchers found that triggering single spikes in mouse cortical pyramidal cells occasionally evoked IPSCs in nearby pyramidal cells. This led to a controversial hypothesis: pyramidal neurons directly excite presynaptic terminals of GABAergic interneurons, evoking localized transmitter release. Neither electrophysiological nor electron-microscopical evidence for such synapses had previously been reported in neocortex, although similar mechanisms exist in spinal cord and thalamus. Hull et al. tried to replicate the results, but could only do so if cesium was included in the whole-cell recording electrode, as had been done previously. Recording the same cell sequentially with potassium- then cesium-based internal solution doubled the size of EPSCs evoked in fast-spiking interneurons. When action potentials were blocked, photostimulation of glutamate release from pyramidal cells never evoked IPSCs in nearby pyramidal cells. These results suggest that pyramidal cell IPSCs require spiking by inhibitory interneurons, and that cesium might increase the probability of such spiking.

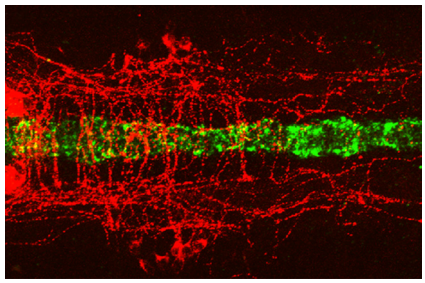
▲ Development/Plasticity/Repair

Slit, Netrin, and HSPGs Act Together to Position Descending Axons

Edda Kastenhuber, Ursula Kern, Joshua L. Bonkowsky, Chi-Bin Chien, Wolfgang Driever, et al.

(see pages 8914–8926)

Descending corticospinal axons project in distinct pathways. The position of these tracts is determined during development by guidance cues, including substrate-bound molecules, such as heparan sulfate proteoglycans (HSPGs), and gradient-forming diffusible cues secreted by the midline, including attractive cues, e.g., Netrin, and repulsive cues, e.g., Slit. Kastenhuber et al. studied the role of these molecules in positioning diencephalic dopaminergic projections in zebrafish. In mutants lacking the Slit receptor Robo2, the dopaminergic axonal tract did not maintain its normal lateral position, but rather shifted toward the midline as it extended; some axons crossed the midline. Knockdown of Netrin or its receptor, DCC, in mutant embryos largely rescued the phenotype, but had no detectable effect in wild type. When Slit was expressed ubiquitously, many axons crossed the midline and lateral fascicles did not form. Reducing levels of HSPGs, which normally surround growing dopaminergic axons, also caused axons to shift medially and occasionally cross the midline.



Misexpression of Slit in a non-graded distribution disrupts formation of lateral fascicles by descending dopaminergic axons (red) and causes many axons to cross the midline (green). See the article by Kastenhuber et al. for details.

■ Behavioral/Systems/Cognitive

Vestibular Responses in MST Are Independent of Gravity

Sheng Liu and Dora E. Angelaki

(see pages 8936–8945)

To determine the direction they are heading, animals use information from multiple sensory sources, including "optic flow" of images across the retina and head movement encoded by the vestibular system. Interpretation of this information is complicated because the same sensory responses are produced by multiple stimuli: optic flow is produced by gaze shifts as well as by whole-body translation, and otolith organs respond to gravitational acceleration as well as head movements. Neurons in the medial superior temporal area (MST) in visual cortex respond to information from multiple modalities and appear to encode heading direction. To better understand how the brain disambiguates heading-related from other sensory signals, Liu and Angelaki have characterized the responses of macaque MST neurons to combinations of tilts, rotations, and translation. Their results indicate that MST neurons encode acceleration and velocity independently of head position relative to gravity, suggesting that gravity-related signals are filtered out before vestibular information reaches MST.

♦ Neurobiology of Disease

Activation of TGF-β Pathway Contributes to Epileptiform Activity

Luisa P. Cacheaux, Sebastian Ivens, Yaron David, Alexander J. Lakhter, Guy Bar-Klein, et al.

(see pages 8927–8935)

Head injury can produce epilepsy, and disruption of the blood–brain barrier (BBB) can be an intermediate step. The serum protein albumin is required for BBB disruption to produce epileptic activity. Albumin is taken up by astrocytes after it binds to TGF-β receptors, and blocking these receptors has been shown to prevent albumin-induced epileptiform activity. Cacheaux et al. extend these findings, showing that activation of the TGF-β signaling pathway with TGF-ß1 replicates the ability of albumin to evoke epileptiform activity in rat neocortical slices. The delay in epileptogenesis after injury suggests transcriptional activation is required. The authors report that gene expression changes evoked by TGF-β1, albumin, and BBB breakdown are similar, further supporting the hypothesis that the TGF-β pathway is a prime contributor to the development of seizure activity. Changes included upregulation of inflammatory mediators and ionotropic glutamate receptor subunits, and downregulation of voltage-gated potassium channels and $GABA_A$, NMDA, and metabotropic glutamate receptor subunits.