This Week in The Journal

● Cellular/Molecular

Prion Protein Modulates Calcium Buffering

Andrew D. Powell, Emil C. Toescu, John Collinge, and John G. R. Jefferys

(see pages 3877–3886)

Abnormal prion protein (PrP) is thought to cause spongiform encephalopathies such as Creutzfeldt-Jakob and mad cow disease, but the function of normal prion protein is unknown. Normal PrP is localized in synaptic membranes, and PrP-deficient mice show defects in neural transmission, including a reduced slow afterhyperpolarization (AHP) following trains of action potentials. Powell et al. explored mechanisms that might reduce the slow AHP, including dysfunction of calcium-dependent potassium channels, voltage-gated calcium channels, and calcium homeostasis. Using photorelease of calcium and calcium imaging, they found no defect in potassium or calcium channel function. Instead, they found an increase in calcium buffering and extrusion rate. These effects were mediated in part by an increase in calcium uptake into the endoplasmic reticulum via the sarco/endoplasmic reticulum pump calcium–ATPase (SERCA). How PrP interacts with SERCA and whether abnormal calcium buffering leads to prion disease still need to be explored.

▲ Development/Plasticity/Repair

GPI-Linked Ephrin Mediates Reverse Signaling in Manduca

Thomas M. Coate, Jacqueline A. Wirz, and Philip F. Copenhaver

(see pages 3846–3860)

Ephrins and Eph receptors engage in bidirectional signaling to direct cell migration and axon growth. Both transmembrane (type B) ephrins and those (type A) tethered to the plasma membrane via glycosyl-phosphatidylinositol (GPI) anchors can mediate reverse signaling triggered by Eph receptors. This week, Coate et al. report that interactions between a type A ephrin (MsEphrin), which is expressed in some *Manduca* neurons (DP cells), and the MsEph receptor, which is expressed in midline cells, are required to prevent improper midline crossing by DP cells and axons. By treating embryos with recombinant MsEphrin or MsEph receptor proteins that bound to their endogenous counterparts with or without activating endogenous signaling pathways, the authors showed that reverse signaling through MsEphrin, but not forward signaling through MsEph receptors, prevented midline crossing. Because *Manduca* express only single isoforms of ephrin and Eph receptor, they may prove useful for determining how guidance is mediated through GPI-linked ephrins.

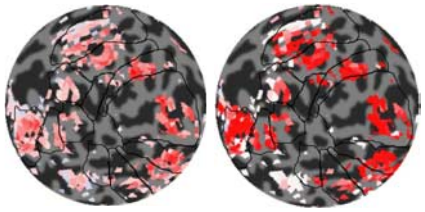
■ Behavioral/Systems/Cognitive

Retinotopy Prevails in Visual Cortex

Justin L. Gardner, Elisha P. Merriam, J. Anthony Movshon, and David J. Heeger

(see pages 3988-3999)

As we move our eyes, images of stationary objects fall on different portions of the retina. Because visual information is arranged in a retinotopic pattern in primary visual cortex, information about stationary objects is also represented in different regions of V1 as the eyes move. Nonetheless, our perception of the world is spatiotopic—we perceive stationary objects as remaining fixed in space despite eye movement. Hypothesizing that different cortical areas might use different frames of reference (retinotopic or spatiotopic), Gardner et al. used fMRI to map responses in 12 areas of human visual cortex as subjects gazed in different directions. In contrast to a previous study that reported spatiotopic mapping in the human middle temporal area, Gardner et al. found that every visual area had a retinotopic mapping. Multiple analyses supported this conclusion and indicated that the activity of every voxel that had a clear visual response fit better with retinotopic mapping.



Reference frame maps for the left occipital cortex of a human subject, based on two different indices. Red areas were retinotopic; white areas were ambiguous; spatiotopic regions would be blue. See the article by Gardner et al. for details.

♦ Neurobiology of Disease

Insoluble DISC1 Is Linked to Multiple Psychiatric Disorders

S. Rutger Leliveld, Verian Bader, Philipp Hendriks, Ingrid Prikulis, Gustavo Sajnani, Jesús R. Requena, and Carsten Korth

(see pages 3839–3845)

Mutations in the gene *Disrupted-in-schizophrenia* (DISC1) were recently found to segregate with schizophrenia, bipolar disorder, and depression in a large family. Leliveld et al. now report that abnormal DISC1 may be associated with sporadic cases of these diseases as well. Because deposition of insoluble proteins is a hallmark of several neurodegenerative diseases, the authors developed a procedure for isolating insoluble proteins from postmortem brain tissue. Immunostaining revealed the presence of insoluble DISC1 in ~20% of samples from an established, well diagnosed collection of patient brain tissue; it was not found in controls. Based on their subsequent transfection experiments, Leliveld et al. hypothesize that disruption of normal protein interactions of DISC1 leads to psychiatric disorders. The discovery that abnormal DISC1 is found in a subset of patients that presented with different diagnoses adds to accumulating evidence that current dichotomous classification schemes for psychoses and affective disorders may mask an underlying continuum of phenotypes.