This Week in The Journal

Cellular/Molecular

Opening Mechanotransducer Channels
Anthony J. Ricci, Helen J. Kennedy, Andrew C. Crawford, and Robert Fettiplace
(see pages 7831–7839)

Rapid sensory transduction in hair cells is made possible by the direct coupling of stereocilia displacement to ion channels. This week, Ricci et al. examined the extraordinarily fast (and thus difficult to measure) kinetics of these mechanotransducer (MET) channels, and how kinetics shapes transduction. MET channels open rapidly in response to deflections of the hair bundle and then adapt (close) in a calcium-dependent manner. The authors took advantage of slower adaptation in turtle hair cells tuned to low frequencies to measure activation kinetics. The channels opened in two phases: a fast invariant process and a slower process determined by the stimulus amplitude. The dependence on stimulus amplitude supports the view that channel gating is triggered by mechanical displacement. High-frequency cells, measured in low calcium to reduce adaptation, activated approximately twofold faster. The authors conclude that channel activation and adaptation kinetics impose a bandpass filter on transduction.

Development/Plasticity/Repair

Cortical Folding Patterns in Williams Syndrome
(see pages 7840–7846)

Williams syndrome (WS) results from a microdeletion on chromosome 7q11.23. WS patients show cognitive deficits in visuospatial construction and behavioral abnormalities that include hypersocial behavior, anticipatory anxiety, and phobias. The macroscopic appearance of the cortex is also abnormal, presenting an opportunity to examine the relationship between genetics, gyral patterning, and cognition. To this end, Kippenhan et al. compared the cortical geometry of high-functioning WS patients with controls, matched for age, sex, and IQ (intelligence quotient), using high-resolution magnetic resonance imaging. The authors calculated gray matter volume with voxel-based morphometry. In WS patients, the depth of the left intraparietal sulcus (PS) was reduced, as was the PS gray matter volume. WS subjects also had significant reductions in the left collateral sulcus and the orbitofrontal cortex. These areas correspond to an area previously shown to have functional abnormalities in WS, suggesting a critical role of the PS in this disorder.

Behavioral/Systems/Cognitive

Endogenous Opiates and the Placebo Effect
 Jon-Kar Zubieta, Joshua A. Bueller, Lisa R. Jackson, David J. Scott, Yanjun Xu, Robert A. Koepppe, Thomas E. Nichols, and Christian S. Stohler
(see pages 7754–7762)

Much to the chagrin of drug designers and sometimes to the benefit of patients, placebos can have powerful effects on medical management. This week, Zubieta et al. add to the evidence that the placebo effect on the subjective assessment of pain involves the endogenous opioid system. During a pain challenge, volunteer subjects were given an intravenous injection that they were led to believe might have analgesic properties. The painful stimulus, the infusion of a few milliliters of hypertonic saline into a jaw muscle, was adjusted to maintain constant pain intensity and to prevent tissue swelling. The authors used positron emission tomography in combination with a μ-opioid receptor-selective radiotracer to examine the brain regions activated and the contribution of μ-opioid receptors. The placebo induced activation in the rostral anterior cingulate, dorsolateral frontal cortex, insular cortex, and nucleus accumbens in parallel with lower ratings of pain intensity.

Neurobiology of Disease

Imaging in Early Alzheimer’s Disease
 Randy L. Buckner, Abraham Z. Snyder, Benjamin J. Shannon, Gina LaRossa, Rimmon Sachs, Anthony F. Fotenos, Yvette I. Sheline, William E. Klunk, Chester A. Mathis, John C. Morris, and Mark A. Mintun
(see pages 7709–7717)

This week, Buckner et al. analyzed the distribution of affected regions in the brains of Alzheimer’s disease (AD) patients compared with healthy controls. Their purpose was to explore an apparent mismatch between hypometabolism and areas of atrophy in AD patients. The authors used a longitudinal analysis of amyloid deposition and brain atrophy patterns in early-stage AD patients and mined previous functional and metabolic imaging studies of healthy adults. Regions that were metabolically active in “default” states in young adults were the same as those that showed metabolic abnormalities early in AD. Default states refers to regions that show relatively increased metabolic activity at rest or in the absence of a task. There was a correlation between amyloid deposition, atrophy, and hypometabolism in posterior cortical regions and the medial temporal lobe, areas that are active during memory retrieval. The authors suggest that there may be a relationship between activity patterns and later amyloid deposition.