This Week in The Journal

Cellular/Molecular

Stereocilia Staircase Is Not Required for Mechanotransduction
Ruben Stepanyan and Gregory I. Frolenkov
(see pages 4023–4034)

The apical surface of hair cells has numerous stereocilia that are arranged by height, forming a staircase pattern. Rigid, oblique tip links connect the top of each stereocilium to the side of a taller, adjacent stereocilium. Deflection of the hair cell bundle toward the tallest stereocilium is thought to increase tension on tip links, thereby opening mechanotransduction channels. Subsequently, calcium influx through the channels rapidly deactivates them. Some studies have suggested that the staircase arrangement of stereocilia, along with the oblique orientation of tip links, is essential for mechanotransduction. But Stepanyan and Frolenkov report that mechanotransduction is essentially normal in inner hair cells (IHCs) from mice lacking myosin-XVa, even though the stereocilia have uniform height and are connected by horizontal top-to-top links. On the other hand, the IHCs lacked fast adaptation, and mechanotransduction channels were activated by deflection of the bundle in multiple directions, indicating that the staircase pattern is important for these characteristics.

Development/Plasticity/Repair

Resting Microglia Monitor Synaptic Activity
Hiroaki Wake, Andrew J. Moorhouse, Shozo Jinno, Shinichii Kohsaka, and Junichi Nabekura
(see pages 3974–3980)

Microglia are the brain’s primary immune cells. Upon activation by pathological insults, microglia become highly motile, migrating to sites of injury and phagocytosing cellular debris. Even in unactivated states, however, microglia extend and retract processes, apparently surveying the local environment. Wake et al. used two-photon microscopy and thin-skull transcranial imaging to observe fluoroescently labeled microglia and neurons in undisturbed mouse cortex. Microglia continually extended and retracted processes. When a process contacted a dendritic spine or axonal bouton, it paused for 4–5 min, and presumed individual synaptic sites were contacted by microglial processes about once per hour. Reducing synaptic activity, e.g., by silencing the retinas to limit input to visual cortex, caused retraction of microglial processes and reduced the frequency of contacts with synapses. In contrast, ischemic insult prolonged contact between microglia and synapses, often to >1 h. Some synapses disappeared after prolonged microglial contact, suggesting microglia contribute to synapse elimination.

Behavioral/Systems/Cognitive

Visual Training Restores Perception in Cortically Blind Patients
Krystel R. Huxlin, Tim Martin, Kristin Kelly, Meghan Riley, Deborah I. Friedman, W. Scott Burgin, and Mary Hayhoe
(see pages 3981–3991)

Damage to primary visual cortex (V1) causes loss of conscious vision in the affected fields, but persistent connections to other visual areas can produce “blindsight,” in which patients detect some features of visual stimuli without consciously seeing them. Although visual training has been reported to improve visual perception in such patients, past studies were marred by uncontrolled confounds, such as patients learning to monitor blind field stimuli with preserved regions of V1. A study by Huxlin et al. controlled for these variables and demonstrated full recovery of motion discrimination and contrast sensitivity after daily training for many weeks. Recovery was limited to the trained visual field location, but it generalized to untrained tasks, and subsequent training of other visual field locations ultimately restored sensitivity in each of these regions. Conscious perception of stimuli increased in parallel with improved performance, so that a vague sense of “something there” eventually yielded to recognition of the stimulus as a pattern of moving dots.

Neurobiology of Disease

Activity Regulates Synaptic Accumulation of Aβ
Atul Deshpande, Hideki Kawai, Raju Metherate, Charles G. Glabe, and Jorge Buciglio
(see pages 4004–4015)

Amyloid β (Aβ) oligomers are major contributors to cognitive decline in Alzheimer’s disease. Aβ accumulates at synapses in hippocampus and cortex, inhibits LTP, and impairs learning. Deshpande et al. have found that stimulating synaptic activity, either electrically or with glutamate or KCl, increases the accumulation of exogenously applied Aβ oligomers at synapses in hippocampal slices, whereas blocking synaptic activity prevented this effect. The authors hypothesized that zinc—which is concentrated in synaptic vesicles, is released during synaptic activity, and binds and promotes oligomerization of Aβ—may contribute to synaptic accumulation of Aβ. Indeed, a zinc (and copper) chelator reduced Aβ accumulation at synapses in both stimulated and unstimulated hippocampal slices. Furthermore, Aβ did not accumulate at synapses in mice lacking a zinc transporter. Synaptic accumulation of Aβ also required NMDA receptor activation. Interestingly, copper is released when NMDA receptors are active, suggesting that metal ions from both presynaptic and postsynaptic sources may contribute to Aβ accumulation.