This Week in The Journal

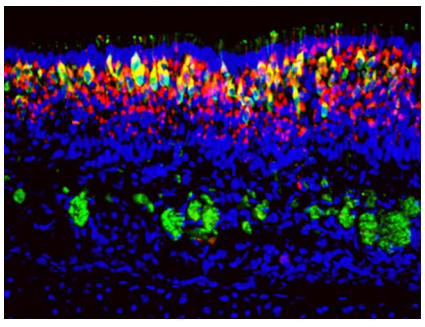
Cellular/Molecular

"Goofy-Nosed" Mice Lack Novel Protein and Keen Olfaction

Tomomi Kaneko-Goto, Yuki Sato, Sayako Katada, Emi Kinameri, Sei-ichi Yoshihara, et al.

(see pages 12987–12996)

Through the olfactory system, we perceive a rich diversity of odorants transmitted from the olfactory epithelium to the brain by olfactory receptors, G-proteins, and other intracellular signaling molecules. Unclear, however, is how the nose perceives its stimuli so keenly. Kaneko-Goto et al. describe a novel olfactory-specific, Golgi-associated protein they call Goofy that emerged as essential to olfactory sensitivity in rodents. A signal sequence trap screen of olfactory epithelial cDNA turned up Goofy, a membrane-associated protein confined to mature and immature sensory neurons of the olfactory epithelium and vomeronasal organ. After odorants bind at receptors on dendritic cilia of olfactory sensory neurons, action potential firing requires adenylyl cyclase III (ACIII) signaling. With disruption of Goofy expression, olfactory neurons appeared normal, but ACIII was no longer localized to the sensory cilia, and the cilia themselves were shortened. The mice, described as "Goofy-nosed," displayed dampened electrophysiological and behavioral olfactory responses to odorants, defects that the authors propose stemmed from Goofy-dependent mislocalization of ACIII.



Olfactory epithelium of a young mouse labeled with antibodies against Goofy (red), an olfactory marker protein (green), and a marker of DNA (blue). See Kaneko-Goto et al. for more information.

Systems/Circuits

Electrical Synapse Rectification Complicates Simple Circuits

Gabrielle J. Gutierrez and Eve Marder

(see pages 13238–13248)

Gap junctions allow neurons in circuits to communicate more seamlessly, but they can also have desynchronizing effects. While microscopy provides visual evidence of these electrical synapses, an understanding of their electrophysiological nature requires intracellular recordings. Rectification, the propensity of an ion channel to pass current more easily in one direction than the other, has been well described in ion channels at chemical synapses, but the hemichannels that form gap junctions can also feature this property when formed of different subunits. Using computational modeling of a simple five-neuron circuit including electrical and chemical synapses, Gutierrez and Marder show this week that the effects of electrical synapse rectification depends on the direction of current flow restriction and the intrinsic properties of each neuron. The findings illustrate how even simple networks can have vastly different output patterns depending on the composition of their gap junctions, which can vary widely. This little-studied synaptic property emerges as a mighty factor in modulating circuit robustness.

Behavioral/Cognitive

Emotional Context, Not Content, Determines Learning Pathway

Nathan M. Holmes, Shauna L. Parkes, A. Simon Killcross, and R. Frederick Westbrook

(see pages 13112–13125)

The emotional context of sensory stimuli, it now appears, determines the brain circuitry that handles them. Holmes et al. implanted rats with a cannula to infuse pharmacological agents into the perirhinal cortex (PRh) or the basolateral amygdala (BLA), temporarily suspending neuronal activity there. Their experiments showed that learning (and un-learning) an association between novel, neutral stimuli—a tone and a light—depend on the PRh. In contrast, when one stimulus was previously paired with a shock to make it signal danger, the BLA but not the PRh was required for processing. More surprising was the authors' finding that BLA activity also mediated learning of neutral stimuli when the stimuli were presented in a threatening environment, suggesting that context alone can shift sensory processing to a distinct subcortical pathway through the amygdala rather than the PRh pathway. The findings may have far-reaching implications for anxiety disorders such as posttraumatic stress disorder, in which people perceive harmless stimuli as potentially dangerous.

Neurobiology of Disease

Autonomic Dysreflexia Triggers Immune Suppression after SCI

Yi Zhang, Zhen Guan, Brenda Reader, Todd Shawler, Shweta Mandrekar-Colucci, et al.

(see pages 12970–12981)

One of the many devastating consequences of spinal cord injury (SCI)—particularly when it occurs in the upper thoracic or cervical spine—is autonomic dysreflexia, in which visceral or somatic stimuli trigger sympathetic reflexes that go unchecked because supraspinal control over sympathetic preganglionic neurons is lost. Zhang et al. show that autonomic dysreflexia leads to immune suppression, a previously mysterious after-effect of SCI that leaves patients susceptible to risky infections. In T3 SCI mice, circulating glucocorticoids and norepinephrine rose precipitously after spontaneous autonomic dysreflexia peaked, which occurred several weeks after injury. Additionally, leukocytes were depleted, spleen atrophied, and immunization failed to raise antibodies; these outcomes were prevented by blocking glucocorticoid and norepinephrine receptors. When the authors elicited autonomic dysreflexia in SCI mice at earlier times after injury with colorectal distension, similar immunosuppressive effects arose. Notably, the findings were supported in a single volunteer patient who experienced a spike in circulating norepinephrine and a drop in leukocytes after the micturition reflex.