This Week in The Journal

Cellular/Molecular

TASK-2 Channels Help Respiratory Chemoreceptors Detect CO_2

Sheng Wang, Najate Benamer, Sébastien Zanella, Natasha N. Kumar, Yingtang Shi, et al.

(see pages 16033–16044)

Changes in brain CO_2 levels are detected by central respiratory chemoreceptors (CRCs) in the brainstem. CRCs stimulate circuits that drive breathing: they spike more and thus promote breathing when CO_2 levels rise, and they spike less when CO_2 levels drop, to prevent hyperventilation. Because pH is inversely related to CO_2 level, the CO_2 sensitivity of CRCs is assumed to be conferred by pH-sensitive channels; but the identity of such channels has remained unknown. Wang et al. now demonstrate that alkaline-activated TASK-2 channels—members of the two-pore domain family of background K^+ channels—underlie CRC sensitivity to low CO_2 levels. The response to alkalization (which occurs when CO_2 decreases) was diminished and sometimes absent in CRCs from mice lacking TASK-2 channels, whereas the response to acidification was largely preserved. Accordingly, the decrease in phrenic nerve activity caused by lowering CO_2 concentration was blunted in working heart–brainstem preparations from TASK-2-null mice, but the increase in activity induced by elevating CO_2 was maintained.

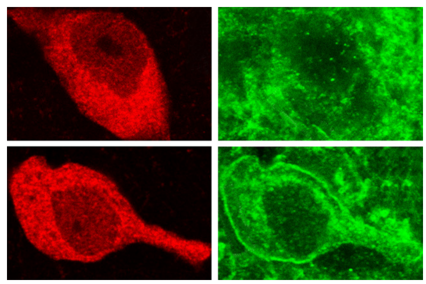
Systems/Circuits

Bipolar Cell Ion Channels Contribute to Parallel Processing

Theresa Puthussery, Sowmya Venkataramani, Jacqueline Gayet-Primo, Robert G. Smith, and W. Rowland Taylor

(see pages 16045–16059)

Different types of visual information are processed through different retinal circuits that project in parallel pathways to the brain. The best understood of these pathways in primates are the magnocellular and parvocellular pathways. Whereas the response properties of cells in the magnocellular pathway are ideal for detecting motion, cells in the parvocellular pathway are specialized for processing color and form. These specialized responses are thought to emerge in bipolar cells, partly through differential expression of voltage-gated ion channels. Indeed, Puthussery et al. found that in primate retina, voltage-gated sodium channels ($Na_V1.1$), T-type calcium channels ($Ca_V3.1$), and hyperpolarization-activated channels (HCN1) were expressed in diffuse bipolar cells that synapse onto ganglion cells of the magnocellular pathway, but not in midget bipolar cells of the parvocellular pathway. Interestingly, $Na_V1.1$ appeared to be expressed in axon initial segments and enable action potential generation, which has not previously been reported in bipolar cells. Together, the three channels likely contribute to producing transient responses necessary for motion detection.



Membrane expression of DORs (green) is higher in NAcs cholinergic interneurons (red) of highly conditioned mice (bottom) than in mice with weaker conditioned responses (top). See the article by Bertran-Gonzalez et al. for details.

Behavioral/Cognitive

δ-Opioid Receptor Expression Increases during Conditioning

Jesus Bertran-Gonzalez, Vincent Laurent, Billy C. Chieng, MacDonald J. Christie, and Bernard W. Balleine

(see pages 16060–16071)

Animals are more likely to perform a goal-directed behavior when cues indicate that the desired goal is obtainable. This is demonstrated in Pavlovian instrumental transfer (PIT) experiments, in which rodents press a lever more frequently when a conditioned stimulus indicates that the associated reward is present. The integration of Pavlovian and instrumental conditioning depends on corticolimbic projections to the nucleus accumbens shell (NAcs) and requires δ-opioid receptors (DORs). Bertran-Gonzalez et al. report that Pavlovian conditioning increased DOR expression on somatic membranes of NAcs cholinergic interneurons, making the neurons more responsive to DOR agonists. The increase was correlated both with the strength of conditioned responding and with increased irregularity in spike frequency of cholinergic interneurons—that is, an increased tendency to spike in bursts rather than tonically—which has previously been linked to associative learning. Although instrumental conditioning did not alter DOR expression after Pavlovian conditioning, PIT was stronger in mice with higher DOR expression, and a DOR antagonist blocked PIT.

Neurobiology of Disease

Soybean Phytosterol Reduces Aβ Production in Mice

Verena K. Burg, Heike S. Grimm, Tatjana L. Rothhaar, Sven Grösgen, Benjamin Hundsdörfer, et al.

(see pages 16072–16087)

Alzheimer's disease (AD) likely stems from accumulation and aggregation of β-amyloid (Aβ) peptides, which are derived from amyloid precursor protein (APP) by sequential cleavage by β- and γ-secretases. APP is a transmembrane protein that is transported to the plasma membrane, where it associates primarily with cholesterol-rich microdomains (lipid rafts). Association with these microdomains is thought to be essential for amyloidogenic processing of APP because cholesterol levels are correlated with Aβ load in AD patients and increasing cholesterol levels increases, whereas lowering cholesterol reduces Aβ production in mice. Disrupting lipid raft structure or function might therefore reduce Aβ accumulation and prevent AD. One way to disrupt rafts is to increase dietary intake of plant-derived cholesterol-like molecules (phytosterols). Indeed, Burg et al. discovered that stigmasterol, a phytosterol present at high levels in soybeans, displaced cholesterol in lipid rafts in neuroblastoma cells. Unlike cholesterol, which increased expression and activity of β- and γ-secretases, stigmasterol reduced activity of both secretases and thus reduced Aβ generation in mice.