This Week in The Journal

Cellular/Molecular

Ca^{2+} and CaMKII Contribute to Hyperalgesic Priming

Luiz F. Ferrari, Oliver Bogen, and Jon D. Levine

(see pages 11002–11011)

Inflammation can prime nociceptive afferents, thereby intensifying and prolonging responses to subsequent inflammation even after the initial injury has healed. Such "hyperalgesic priming" might contribute to the development of chronic pain that occurs after repeated injury. In rats, induction of hyperalgesic priming requires activation of the ϵ isoform of protein kinase C (PKCϵ) and downstream activation of the translational regulator CPEB (cytoplasmic polyadenylation element binding protein). Delving deeper into this pathway, Ferrari et al. found that induction of hyperalgesic priming by a PKCϵ agonist was prevented by inhibiting either α calmodulin-dependent protein kinase II (αCaMKII, a target of CPEB) or ryanodine receptors (which release calcium from intracellular stores), or by buffering intracellular calcium. In contrast, injecting activated αCaMKII or ryanodine induced priming. Interestingly, unlike PKCϵ agonists, which induce hyperalgesic priming only in male rats, ryanodine and αCaMKII induced priming in both males and females, suggesting PKCϵ signaling pathways in males and females differ upstream of αCaMKII activation.

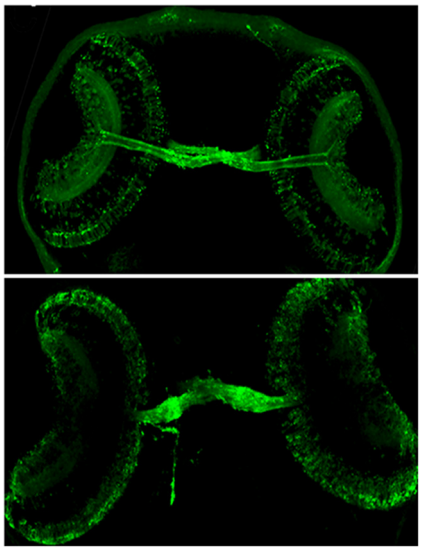
Development/Plasticity/Repair

G-Protein Receptors Regulate Semaphorin Receptor Expression

Alison L. Dell, Emma Fried-Cassorla, Hong Xu (徐洪), and Jonathan A. Raper

(see pages 11076–11088)

The midline is a major decision point for many types of projection neurons, including retinal ganglion cells (RGCs). In zebrafish, all RGC axons cross the midline and project to the contralateral tectum. Knocking down semaphorins (guidance molecules expressed at the midline) or the semaphorin receptor component neuropilin (expressed by RGCs) causes some RGCs to project ipsilaterally, suggesting that these molecules work together to promote midline crossing. Knocking down calcium-calmodulin adenylyl cyclases also causes ipsilateral misprojection, and Dell et al.



Whereas RGCs project contralaterally in normal zebrafish (top), some project ipsilaterally after $G\alpha_S$ is blocked (bottom). See the article by Dell et al. for details.

predicted that blocking signaling mediated by G-protein-coupled receptors (GPCRs), which regulate adenylyl cyclase activity, would produce a similar effect. Indeed, expressing dominant-negative constructs targeting the $G\alpha_S$ subunit, which stimulates adenylate cyclases, caused many RGCs to project ipsilaterally. Interestingly, this effect appeared to result from regulation of neuropilin1 expression by $G\alpha_S$-mediated signaling. These results indicate that activation of GPCRs by a cue at one choice point can potentially regulate a neuron's response to different cues as it approaches subsequent choice points.

Behavioral/Cognitive

Segmentation and Feature Discrimination Share Mechanisms

Dorita H. F. Chang, Zoe Kourtzi, and Andrew E. Welchman

(see pages 10962–10971)

Interacting with the visual world requires not only identifying relevant objects in complex ("noisy") scenes, but also discriminating among objects that have similar features. Chang et al. asked to what extent these processes interact, and in particular, how training on one task affects performance on another. Human participants were trained to discern stimuli based on binocular disparity (stereoscopic depth), motion, or orientation, which were presented either in a noisy background (segmentation task) or in a background that differed only slightly from the target stimulus (feature difference task). For each feature type (disparity, motion, or orientation), training on segmentation tasks improved performance only for that task, whereas training on feature-difference tasks improved performance on both tasks. On the other hand, training on segmentation tasks using one feature improved performance on segmentation using other features, whereas improved performance from feature-difference training did not generalize to tasks using other features. These results suggest that segmentation and feature discrimination use partially overlapping neural processes.

Neurobiology of Disease

Incentive Sensitization Requires Synaptic Changes in NAc

Xiaoting Wang, Michael E. Cahill, Craig T. Werner, Daniel J. Christoffel, Sam A. Golden, et al.

(see pages 11012–11022)

Rats given daily injections of cocaine develop behavioral sensitization, indicated by progressive increases in locomotion with successive cocaine treatment, as well as incentive sensitization, often described as "wanting," which is inferred from a faster rate of cocaine self-administration in instrumental conditioning tasks. Sensitization temporarily persists after cocaine delivery is halted, and during this period, both spine density and the surface expression of AMPA receptors (AMPARs) increase in the nucleus accumbens (NAc). How these changes are related to sensitization is unknown, however. Wang et al. found that Kalirin-7, a guanine-nucleotide exchange factor involved in excitatory synaptic plasticity in other systems, was upregulated in the NAc during cocaine withdrawal, and that knocking down Kalirin-7 before cocaine administration prevented increases in AMPAR expression and spine density. Interestingly, although knocking down kalirin-7 did not affect locomotor sensitization, it reduced pretreatment-induced increases in cocaine self-administration. These results suggest that increases in AMPAR expression and spine density that occur in the NAc after cocaine exposure and withdrawal contribute to incentive, but not locomotor sensitization.