This Week in The Journal

Cellular/Molecular

Growth Cone Crosstalk

Semaphorin 3F Antagonizes Neurotrophin-Induced Phosphatidylinositol 3-Kinase and Mitogen-Activated Protein Kinase Kinase Signaling: A Mechanism for Growth Cone Collapse

Jasvinder K. Atwal, Karun K. Singh, Marc Tessier-Lavigne, Freda D. Miller, and David R. Kaplan (see pages 7602–7609)

A semaphore, a visual signaling mechanism with moving arms or flags commonly seen on railroads, is an apt descriptor for the semaphorin family of axon guidance molecules. Growth cones are directed by positive and negative cues, including nerve growth factor (NGF) and the semaphorins. In this week’s Journal, Atwal et al. examine the interaction of NGF and Semaphorin 3F (Sema 3F) in cultured rat sympathetic neurons that express the NGF receptor [tyrosine receptor kinase A (TrkA)] and the Sema 3F coreceptor (neuropilin-2). Their results show that Sema 3F causes growth cone collapse by antagonizing the downstream actions of NGF. Although Sema 3F did not prevent phosphorylation of TrkA, it did reduce phosphorylation of other downstream proteins in the PI3 (phosphatidylinositol 3)-kinase–Akt and MEK (mitogen-activated protein kinase kinase–ERK) extracellular signal-regulated kinase pathways. The Sema 3F-driven collapse was partially rescued by overexpression of the adaptor protein Gab-1 (growth-associated binder 1), a hyperactivator of these signaling pathways. Although these two pathways are unlikely to be the sole mediators of semaphorin signaling, the results reveal another layer in the signaling crosstalk involved in regulating axonal growth dynamics.

Development/Plasticity/Repair

GABA and Retinal Wave Dynamics

Developmental Modulation of Retinal Wave Dynamics: Shedding Light on the GABA Saga

Evelynne Sernagor, Carol Young, and Stephen J. Eglen (see pages 7621–7629)

Synaptic connections in the embryonic visual system are refined by spontaneous, propagating waves of retinal activity that are generated and controlled largely by glutamate and acetylcholine. In turtles, the waves become narrower and slower ~1 week before hatching. After hatching, the waves become restricted to small patches and eventually disappear in a process that is thought to be experience dependent. In this issue, Sernagor et al., using calcium imaging of turtle retina, reveal a mechanism for the disappearance of spontaneous bursting activity, a developmental switch in GABA responses from excitatory to inhibitory. The change in wave behavior correlated with upregulation of KCC2, the chloride-extruding neuronal cotransporter, consistent with a shift in the chloride equilibrium potential from depolarizing to hyperpolarizing. If animals were dark-reared, spontaneous propagating waves persisted, as did excitatory GABA responses. This work identifies inhibitory GABAergic activity as a visual experience-dependent stop signal for retinal waves.

Behavioral/Systems/Cognitive

Cross Training in Nociceptive Reflexes

Developmental Learning in a Pain-Related System: Evidence for a Cross-Modality Mechanism

Alexandra Waldenström, Jonas Thelin, Erik Thimansson, Anders Levinsson, and Jens Schouenborg (see pages 7719–7725)

To correctly respond to painful stimuli, animals must react with specific muscle movements that power the appropriate escape response. The development of nociceptive withdrawal reflexes is experience dependent. Waldenström et al. pondered how this might occur given that noxious stimuli are thankfully uncommon during early life. Might animals use non-noxious stimuli to learn to respond correctly to pain? The authors examined the development of a nociceptive withdrawal reflex in rats after a brief heat stimulus to the tail. Tail movement away from the stimuli began at postnatal day 10 (P10) (“correct response”) and was ~90% correct by P21. Interestingly, this adaptation occurred even when the tail was deprived of any noxious stimuli by either encasement in a tube or application of topical analgesics. However, removal of tail hairs to prevent tactile sensation blocked nociceptive responses and adaptation, indicating that low-threshold mechanoreceptors are necessary for adaptation to the noxious stimulus. Removal of hairs in adult rats did not alter the reflex. The authors suggest that this cross-modality adaptive response during early development is driven by normally activated mechanosensors that influence the strength of synapses involved in the withdrawal reflex. It seems in this case, “no pain, no gain” is not the operating principle.

Micrographs of rhodamine–phalloidin-stained growth cones treated with NGF (top panels) or NGF plus Sema 3F (bottom panels). See Figure 2 B of Atwal et al. for details.