This Week in The Journal

● Cellular/Molecular

Threshold Accommodation Increases Precision of Auditory Neurons

MacKenzie A. Howard and Edwin W Rubel

(see pages 12063–12074)

Sound localization is achieved by detecting differences in the time of arrival of sound at the two ears. Because the interaural time difference (ITD) can be tiny, spike timing of auditory inputs must be extremely precise. In birds, temporal precision increases when individual auditory nerve fibers converge on neurons in the nucleus magnocellularis (NM) that relay information to ITD detector neurons. This increased precision requires GABAergic inputs. Although the GABAergic input is depolarizing, it is subthreshold, and thus inhibits neuronal firing by activating voltage-sensitive potassium channels and inactivating voltage-sensitive sodium channels. Howard and Rubel show that this depolarizing inhibition shunts excitatory currents and raises spike threshold, and as a result, EPSPs elicited by auditory nerve inputs are likely to be subthreshold. Single subthreshold auditory inputs also transiently increase spike threshold, thus further narrowing the temporal window over which asynchronous EPSPs can sum to evoke a spike. Together, these mechanisms increase the temporal fidelity of NM neurons.

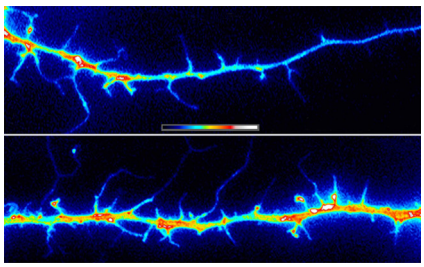
▲ Development/Plasticity/Repair

NGF Stimulates Branch Formation by Increasing F-Actin Patches

Andrea Ketschek and Gianluca Gallo

(see pages 12185–12197)

As axons grow, F-actin dynamics in the growth cone produce filopodia and lamellipodia. Extracellular cues stabilize a subset of these protrusions, allowing microtubules to extend into the growth cone. Actin-driven protrusion is then suppressed and the shaft consolidates around the microtubules, increasing axon length. But patches of dynamic F-actin continue to form along consolidated axon shafts. Filopodia that protrude from these patches can be stabilized to form axonal branches or synaptic boutons. If filopodia are not stabilized, however, the F-actin patches dissipate. Ketschek and Gallo show in cultured chick dorsal root ganglion neurons that NGF increases the number and rate of filopodia protrusions by increasing the number of F-actin patches along the axon. Activation of phosphoinositide 3-kinase, which colocalized with F-actin patches, was necessary for patch formation, as was activation of its downstream kinase, Akt. But other factors, such as the presence of mitochondria nearby, were required for filopodia to form from these patches.



Peptidergic activation of phosphoinositide 3-kinase (bottom panel) increased the number of filopodia emerging from axon shafts by increasing formation of actin patches. Axon in top panel treated with control peptide. See the article by Ketschek and Gallo for details.

■ Behavioral/Systems/Cognitive

Amblyopia Alters Properties of MT Neurons

Yasmine El-Shamayleh, Lynne Kiorpes, Adam Kohn, and J. Anthony Movshon

(see pages 12198–12209)

Abnormal early visual experience—resulting from misalignment, differential refraction, or occlusion of one eye—can cause amblyopia, characterized by loss of acuity, ocular dominance shifts, and other visual deficits that persist after the original abnormality is corrected. Numerous studies have indicated that these deficits result from abnormal development of connections in visual cortex. Most previous studies have focused on V1, but deficits in higher-order visual functions, such as motion perception, suggest that extrastriate visual areas are also affected. By recording single-unit activity, El-Shamayleh et al. found that neuronal properties in visual motion area MT are altered in amblyopic monkeys. Whereas MT neurons are strongly binocular in normal monkeys, most in amblyopic monkeys were more strongly driven by the normal eye. In addition, MT neurons failed to integrate motion over long temporal delays. Interestingly, changes in other properties of MT neurons, including direction selectivity, sensitivity to coherence, and preferred movement speed, depended on how amblyopia was produced.

♦ Neurobiology of Disease

ADAM-8 Protects Neurons by Cleaving TNF-α Receptors

Jörg W. Bartsch, Dirk Wildeboer, Garrit Koller, Silvia Naus, Andrea Rittger, et al.

(see pages 12210–12218)

ADAMs (a disintegrin and metalloproteases) are transmembrane proteinases that cleave the extracellular juxtamembrane region of other membrane proteins. This process of ectodomain shedding can rapidly downregulate the target protein, release soluble extracellular domains involved in extracellular signaling, or prime the target protein for secondary intracellular cleavage to produce an intracellular signaling molecule. In the CNS, ADAMs are involved in migration, axon guidance, and synaptic plasticity, but they also have roles in neuroinflammation and degeneration. Bartsch et al. show that ADAM-8 cleaves tumor necrosis factor α (TNF-α) receptor 1 and is neuroprotective in a mouse model of motor neuron disease. ADAM-8 is upregulated in CNS regions that undergo neurodegeneration in wobbler mice, and although ADAM-8 knockout did not affect survival or motor function in otherwise normal mice, it exacerbated muscle weakening, motor neuron degeneration, microglial activation, and premature death in wobbler mice. Furthermore, ADAM-8 knockout in otherwise wild-type mice greatly increased TNF-α-induced death in neuronal cultures.