This Week in The Journal

Cellular/Molecular

High-Frequency Firing, MSO-Style
Luisa L. Scott, Paul J. Mathews, and Nace L. Golding
(see pages 7887–7895)

Sound localization requires precise comparisons of binaural input in brainstem centers including the medial superior olivary (MSO). MSO output is encoded as trains of action potentials, placing a premium on high temporal fidelity. This week, Scott et al. examined the membrane properties of MSO neurons that underlie this special role. The authors reported that MSO neurons between postnatal day 14 (P14) and P38. From P14 to P21, incoming somatic EPSPs became shorter along with a reduction in input resistance and membrane time constant, suggesting an increased somatic membrane conductance. Furthermore, somatic action potential amplitude declined, and dual dendrite/soma recording indicated that action potentials arose from the soma in the axon. These changes were mediated by a threefold increase in low voltage-activated potassium current containing the Kv1.1 subunit. The increase in Kv1.1 narrows the window for temporal summation and thus enhances processing of binaural input.

Development/Plasticity/Repair

A Combinatorial Approach to Sensory Axon Regeneration
Michael P. Steinmetz, Kevin P. Horn, Veronica J. Tom, Jared H. Miller, Sarah A. Busch, Dileep Nair, Daniel J. Silver, and Jerry Silver
(see pages 8066 – 8076)

Injured dorsal root ganglion (DRG) neurons retain some regenerative capacity. However, regrowth of their central processes is limited by lack of trophic support and inhibitory factors such as chondroitin sulfate proteoglycans and growth cone-collapsing factors. This week, Steinmetz et al. countered this problem with a combinatorial approach. Using an in vitro assay, the authors challenged cultured DRG neurons to cross a proteoglycan gradient that mimicked the dorsal root entry zone (DREZ). Neurons were “preconditioned” with agents that recruit macrophages and stimulate axon outgrowth, such as zymosan. Acute treatments had little effect, but 7 d of zymosan preconditioning in vivo produced only a modest increase in neurite crossings in vitro. However, zymosan pretreatment, when combined with chondroitinase ABC in vitro digestion of proteoglycans, markedly enhanced axonal regeneration. Even more striking were the results of combined treatment in vivo: after a root crush, there was regrowth through the DREZ and re-establishment of functional synapses.

Behavioral/Systems/Cognitive

Memory Consolidation and the VOR
Charles D. Kassardjian, Yao-Fang Tan, Ji-Yeon J. Chung, Raquel Heskin, Michael J. Peterson, and Dianne M. Broussard
(see pages 7797 – 7895)

The consolidation of memories may involve sites remote from where they form. This week, Kassardjian et al. explored motor memory consolidation using the cat vestibulo-ocular reflex (VOR), which holds the visual world steady during rapid head movements. Sensory input from the vestibular labyrinth influences eye movements, shifting gaze in the opposite direction of the head movements. Cats were fitted with goggles that miniaturize the visual world, and then they were rotated for 60 min. This maneuver induces a decrease in VOR gain, a short-term motor memory. Immediately after rotation, injection of the AMPA–kainate receptor antagonist 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX) into the cerebellar flocculus disrupted the change in VOR gain. Similarly, learning was disrupted by rotation in darkness, indicating that consolidation had not occurred. After 3 d of learning, however, CNQX injections were much less effective. The authors suggest that after initial memory formation, the consolidation phase involves a site outside of the cerebellum.

Neurobiology of Disease

Parkin and One of Its Substrates, p38
Han Seok Ko, Rainer von Coelln, Sathya R. Sriram, Seong Who Kim, Kenny K. K. Chung, Olga Plentikova, Juan Troncoso, Brett Johnson, Roya Safary, Eyleen L. Goh, Hongjiong Song, Bum-Joon Park, Min Jung Kim, Sunghoon Kim, Valina L. Dawson, and Ted M. Dawson
(see pages 7968 – 7978)

One of the familial forms of Parkinson’s disease (PD), autosomal recessive juvenile parkinsonism (AR-JP), arises from a mutation in parkin, a ubiquitin ligase that normally targets proteins for degradation. This week, Ko et al. make a case that accumulation of a parkin substrate could be important in the pathogenesis of PD. In the ventral midbrain/hindbrain of parkin-deficient mice, the authors report an upregulation of the aminoacyl-tRNA synthetase cofactor p38, but not of other substrates, including CDCrel-1, α-synuclein, parkin-associated endothelin-like receptor, cyclin E, synaptotagmin XI, or β-tubulin. The brains of AR-JP patients also accumulated p38, but not other putative parkin substrates. In idiopathic PD, S-nitrosylation of parkin inhibits its function, potentially leading to accumulation of p38. Indeed, p38 was elevated in dopaminergic neurons of PD brains. Adding to the evidence, the authors report that p38 directly interacted with parkin and that p38 overexpression in mice led to dopaminergic cell death.