This Week in The Journal

● Cellular/Molecular

Moving Calcium from Store to Store

Yu Mi Choi, Shin Hye Kim, Sungkwon Chung, Dae Yong Uhm, and Myoung Kyu Park

(see pages 12127–12136)

Most cells, including neurons, have developed multiple safeguards to keep internal calcium low; thus, calcium signals are usually restricted to areas near the source of calcium influx or of release from intracellular stores. In this issue, Choi et al. take a look at the topology of endoplasmic reticulum (ER) calcium stores in isolated dopamine neurons from postnatal day 9–14 rats. The ER essentially consists of a convoluted set of tunnels that winds throughout the cell. The authors used imaging to detect calcium transients, local application of caffeine to release calcium, and fluorescence recovery after photobleaching to measure calcium diffusion. Because cell bodies contained more ER, and thus a larger calcium pool, than each dendrite, the ER in cell bodies served as a calcium reservoir. As a result, the ER in dendrites repeatedly released calcium in response to local stimulation without running dry, as the dendrite stores were rapidly refreshed from reservoirs in the cell body.

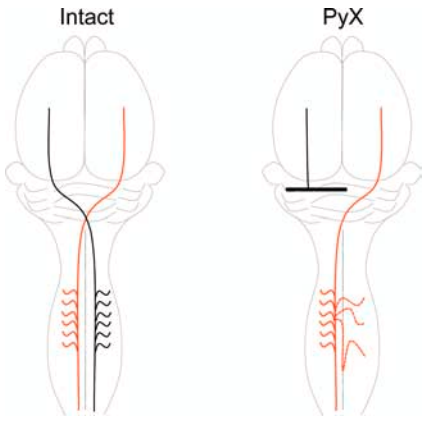
▲ Development/Plasticity/Repair

Nogo and Axonal Growth Revisited

William B. J. Cafferty and Stephen M. Strittmatter

(see pages 12242–12250)

Several molecules associated with myelin sheaths can keep damaged axons from regenerating. But studies examining one of these myelin-associated inhibitors, Nogo-A protein and its main receptor NgR1, have had surprisingly mixed results when assessed in knock-out mice. To clear up some of the confusion, Cafferty and Strittmatter examined the roles of Nogo-A and NgR1 in mice whose left or right medullary pyramid had been cut. This corticospinal tract lesion does not produce an astrocytic scar and thus is well suited for analyzing myelin-mediated inhibition of axonal growth. Four weeks after injury, transgenic mice lacking either Nogo-A or NgR1 showed a dramatic increase in collateral sprouting of labeled corticospinal axon collaterals crossing from the intact side of the spinal cord to the denervated side. These same animals do not show long-distance regeneration after dorsal hemisection, indicating that the injury-induced axonal growth varies with fiber tract and lesion paradigm.



The left panel shows the mature termination pattern of the corticospinal tract. The right panel shows the location of a pyramidotomy (black, right panel) and the predicted sprouting response in the right side of the spinal cord. See the article by Cafferty and Strittmatter for details.

■ Behavioral/Systems/Cognitive

Timing in the Substantia Nigra

Marjan Jahanshahi, Catherine R. G. Jones, Georg Dirnberger, and Christopher D. Frith

(see pages 12266–12273)

Timing is everything. Take away motor timing, and you cannot tap your finger to a tune on the radio; take away perceptual timing, and you cannot guess at how long you have been waiting for the elevator. This week, Jahanshahi et al. examined the roles of the cerebellum and basal ganglia in several timing tasks. Using positron emission tomography scanning, the authors measured brain activity while subjects performed three tasks: "short" (500 ms) and "long" (2 s) time reproduction tasks in which the subjects pressed a button after the perceived interval and a control task in which they responded immediately after a tone. Both time reproduction tasks produced activation in the cerebellum and basal ganglia structures. When the time reproduction tasks were compared with the control tasks, there was timing-specific activation in the left substantia nigra and left lateral premotor cortex, suggesting a role for basal ganglia and associated cortical projections in temporal processing.

♦ Neurobiology of Disease

Dynactin 1 Dysregulation in a Mouse Model of SBMA

Masahisa Katsuno, Hiroaki Adachi, Makoto Minamiyama, Masahiro Waza, Keisuke Tokui, Haruhiko Banno, Keisuke Suzuki, Yu Onoda, Fumiaki Tanaka, Manabu Doyu, and Gen Sobue

(see pages 12106–12117)

Expansion of a trinucleotide CAG repeat within the first exon of the androgen receptor gene causes spinal and bulbar muscular atrophy (SBMA). This inherited neurodegenerative disease targets motor neurons in adult males, whereas female carriers are usually unaffected. Katsuno et al. report that the mechanism may involve impaired retrograde axonal transport. In a transgenic mouse model of SBMA, the authors found that neurofilaments and synaptic vesicles accumulated in the terminals of motor neurons, consistent with a defect in retrograde axonal transport. Expression of dynactin 1, an axonal-motor-associated protein, was reduced in SBMA neurons and in the ventral horns of SBMA patients, possibly as a result of a disruption in transcription by mutant protein. Consistent with this idea, overexpression of dynactin 1 in cells expressing mutant SBMA reduced toxicity, and oral treatment of SBMA mice with a histone deacetylase inhibitor to promote gene transcription restored dynactin 1 levels in spinal motor neurons.