This Week in The Journal

● Cellular/Molecular

Neuroprotective Growth Factors for Parkinson's Disease

Merja H. Voutilainen, Susanne Bäck, Eeva Pörsti, Liisa Toppinen, Lauri Lindgren, et al.

(see pages 9651–9659)

Parkinson's disease (PD) is caused by progressive degeneration of nigrostriatal dopaminergic neurons, and although therapies exist that alleviate motor symptoms of PD, none successfully prevent further degeneration. Neurotrophic factors have shown some potential as neuroprotective therapies *in vitro*, but those that showed the most promise in animal models—glial cell line-derived neurotrophic factor (GDNF) and neurturin—produced limited benefits in clinical trials. A plausible explanation for this failure is that GDNF and neurturin bind with high affinity to the extracellular matrix (ECM), which limits their diffusion *in vivo*. A relatively recently discovered molecule, mesencephalic astrocyte-derived neurotrophic factor (MANF), has lower affinity for ECM, and as reported by Voutilainen et al., it diffuses more broadly than GDNF when injected into the striatum of rats. MANF was at least as effective as GDNF in preventing behavioral symptoms and degeneration of dopaminergic neurons induced by injecting 6-hydroxydopamine into the striatum, a rat model of PD.

▲ Development/Plasticity/Repair

Enhancement of CNS Axon Regeneration by Spermidine

Kangwen Deng, Huifang He, Jin Qiu, Barbara Lorber, J. Barney Bryson, et al.

(see pages 9545–9552)

In experimental models of spinal cord injury, cutting the peripheral axonal branch of dorsal root ganglion neurons ("conditioning") several days before cutting central branches enables the latter to grow in the spinal cord. This effect appears to involve both increases in axons' propensity to grow and decreases in their susceptibility to inhibition of growth by myelin. Understanding the molecular pathways mediating this effect could guide development of regenerative therapies. One early step is elevation of cAMP, and *in vitro,* this increases expression of arginase I, an enzyme involved in polyamine synthesis. Deng et al. found that conditioning lesions *in vivo* likewise increased arginase expression and synthesis of polyamines, specifically the polyamine putrescine, which is subsequently converted to spermidine. Treatment with spermidine was as effective as cAMP or conditioning lesion in enabling axons to grow on myelin, and a single injection of spermidine increased regeneration of retinal ganglion neurons after nerve crush *in vivo*.

■ Behavioral/Systems/Cognitive

Temporal-Pattern Decoding in Electric Fish

Bruce A. Carlson

(see pages 9417–9428)

The temporal pattern of neuronal spikes can code both temporal and nontemporal information. A key question in neural computation is how responses of postsynaptic neurons are shaped by the temporal pattern of their inputs. Electric fish offer a useful system in which to address this question, because they communicate via electrical pulse sequences with varying interpulse intervals that are relatively easy to reproduce in the lab. Carlson discovered that neurons in the posterior exterolateral nucleus (ELp) of the midbrain are selective for specific interpulse intervals (IPIs). Most ELp neurons responded to a range of IPIs and could be classified as high-pass, low-pass, or band-pass depending on whether their responses diminished for IPIs higher and/or lower than their best IPI. In each group, responses of some neurons varied depending on whether IPIs were increasing or decreasing in a sequence of pulses. Collectively, these properties made different classes of neurons differentially suited for detecting different classes of communication signals.

Mormyrid electric fish, *Brienomyrus brachyistius*, communicate by producing electrical pulses with different patterns of interpulse intervals. Neurons in the midbrain are tuned to different intervals, and might be specialized to detect different categories of communication. See the article by Carlson et al. for details.

♦ Neurobiology of Disease

Thyroid Hormone Transporters in Mouse Neurons

Eva K. Wirth, Stephan Roth, Cristiane Blechschmidt, Sabine M. Hölter, Lore Becker, et al.

(see pages 9439 –9449)

The thyroid hormone 3′,3,5-triiodothyronine (T_3) regulates transcription of genes that control all stages of brain development, from neuronal and glial proliferation to synaptogenesis and myelination. To exert these effects, T_3 must be transported across plasma membranes and into cell nuclei where it binds to its receptors. The primary T_3 transporter in neurons is monocarboxylate transporter 8 (MCT8), and the importance of this transporter is revealed by the fact that its mutation causes Allan–Herndon–Dudley syndrome, characterized by profound mental retardation, severe motor defects, and abnormally high plasma levels of T_3. Surprisingly, mice lacking Mct8 show no overt behavioral abnormalities, although T_3 levels are elevated. Wirth et al. performed extensive analyses and found no anatomical or motor defects, but mutant mice exhibited decreased anxiety-like behaviors, thermal hypersensitivity, and grooming. They report that in developing mice, unlike in human fetuses, an additional T_3 transporter, L-type amino acid transporter 2, is expressed in neurons and may compensate for the loss of Mct8.