This Week in The Journal

● Cellular/Molecular

Oxidative Stress in a Model of PD

Mechanism of Toxicity in Rotenone Models of Parkinson's Disease

Todd B. Sherer, Ranjita Betarbet, Claudia M. Testa, Byoung Boo Seo, Jason R. Richardson, Jin Ho Kim, Gary W. Miller, Takao Yagi, Akemi Matsuno-Yagi, and J. Timothy Greenamyre
(see pages 10756–10764)

The pathological hallmarks of Parkinson's disease (PD) include selective loss of nigrostriatal dopamine neurons and cytoplasmic inclusion bodies. Although the underlying mechanisms of cell death in PD are not fully resolved, several lines of evidence implicate mitochondrial dysfunction. Recently, rotenone, a pesticide that inhibits complex I of the mitochondrial electron transfer chain, has been shown to produce a PD-like syndrome in rats that includes death of dopamine neurons and motor deficits. Complex I inhibition could cause injury attributable to ATP depletion or to production of reactive oxygen species (ROS). Now, experiments by Sherer et al. indicate the latter as the probable cause of rotenone-induced toxicity. In neuroblastoma cells, rescue of complex I by transfection with the yeast protein NDI1 prevented toxicity. Depletion of ATP alone could not account for the action of rotenone in these cells. In contrast, rotenone-induced oxidative damage in brain slices was reduced by the antioxidants α-tocopherol (vitamin E) and coenzyme Q_{10}. Oxidative damage and cell-specific neurodegeneration were also present in brains of rotenone-treated rats. The report adds credence to the possible role of environmental factors and mitochondrial dysfunction in PD, and may renew interest in a therapeutic role for antioxidants.

▲ Development/Plasticity/Repair

De-Tuning and Re-Tuning Adult Auditory Cortex

Progressive Degradation and Subsequent Refinement of Acoustic Representations in the Adult Auditory Cortex

Shaowen Bao, Edward F. Chang, Jonathan D. Davis, Kevin T. Gobeske, and Michael M. Merzenich
(see pages 10765–10775)

During development and adulthood, the sensory cortex can be reorganized in response to correlated neuronal activity, but receptive field plasticity requires different circumstances in these two stages of life. During the early critical period, the sensory cortex is shaped by activity that lacks behavioral significance, whereas in adults, reinforcement or attention appears necessary for cortical reorganization. In this week's *Journal*, Bao et al. manipulated the organization of the adult primary auditory receptive field (AI) in rats. First, they paired pulsed noise stimulation to activate broadly correlated cortical activity with stimulation of the nucleus basalis (NB) to trigger cholinergic input. Noise pairing degraded the organization such that the AI resembled the nonprimary auditory cortex. In addition, spectral tuning broadened, and tonotopic maps were disrupted. However, by pairing NB stimulation with pulsed tone pips that triggered locally correlated activity, the AI regained its receptive field features over a 4 week trial period. It seems you can teach an old dog new tricks, provided they pay attention.

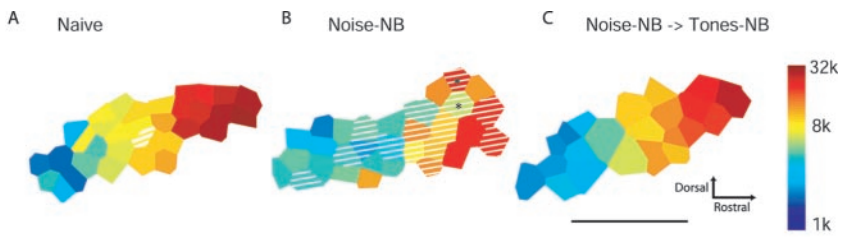
■ Behavioral/Systems/Cognitive

Swimming with Serotonin

Spike Timing-Dependent Serotonergic Neuromodulation of Synaptic Strength Intrinsic to a Central Pattern Generator Circuit

Akira Sakurai and Paul S. Katz
(see pages 10745–10755)

Usually spike timing is thought of as a means to alter homosynaptic plasticity. However, this week Sakurai and Katz describe spike-timing dependence of a heterosynaptic pathway in the mollusk *Tritonia diomedea*. In these pink-colored beasts, a central pattern generator circuit includes dorsal and ventral swim interneurons (DSIs and VSIs, respectively) and a cerebral interneuron C2. This circuit initiates the escape swimming response in efferent flexion neurons and keeps *Tritonia* out of the way of hungry echinoderms. The serotonergic DSI neurons modulate both C2 and VSI neurons. The authors analyzed the synapse between VSI and ventral flexion neurons. When VSI neurons fired within 10 sec of the neuromodulatory DSI neurons, the VSI-evoked synaptic response on motor neurons was greatly enhanced, but with an interval of $\geq$20 sec, the response was dampened. This biphasic response was also observed with simulated escape swim activity. Although the underlying cellular mechanisms remain to be explored, the timing seems matched to the practical needs of the escape response with enhancing activity when it is needed most.



A, B, Degradation of primary auditory cortical tonotopic maps by pairing noise with nucleus basalis stimulation. *C*, Subsequent pairing of pure tones with nucleus basalis stimulation refined the map. Hatched regions had receptive field irregularity index scores of $>$2. See the article by Bao et al. for details.