

This Week in The Journal

● Cellular/Molecular

Modeling Electrophysiological Diversity

Cengiz Günay, Jeremy R. Edgerton, and Dieter Jaeger

(see pages 7476–7491)

Variations in morphology and ion-channel expression largely determine the electrophysiological properties of neurons. To investigate whether such variations are sufficient to explain the electrophysiological variability of globus pallidus neurons recorded in brain slices, Günay et al. created >100,000 computer models using three realistic morphologies and variable levels of nine ionic conductances. The models' properties (e.g., spike threshold, waveform, afterhyperpolarization, firing rate) largely replicated the variability recorded in real neurons. Most properties were influenced by multiple conductances, and most conductances influenced multiple properties. Furthermore, complex interactions between conductances produced great variability in the magnitude of the effect produced by changing a single conductance; even the sign of the effect could change, depending on the density of the other conductances in a model. Impressively, the authors validated the model approach by using low doses of channel blockers to decrease conductance density in real neurons and produce the variability predicted by the model.

▲ Development/Plasticity/Repair

Neuronal Death Pathways

Li-ying Yu, Mart Saarma, and Urmas Arumäe

(see pages 7467–7475)

Programmed cell death pathways are generally divided into two broad categories: the intrinsic pathway, in which cellular stress (e.g., oxidative stress) leads to release of cytochrome *c* from mitochondria, which leads to activation of caspase-9, which activates effector

caspases that degrade cellular proteins; and the extrinsic pathway, in which extracellular ligands bind to death receptors, which activate Fas-activated death domain (FADD) protein, which leads to activation of caspase-8, which activates effector caspases. This week, Yu et al. describe the apoptosis pathway activated by withdrawal of GDNF and BDNF from cultured midbrain dopaminergic neurons. The normal intrinsic pathway was not involved, because cytochrome *c* was not released from mitochondria. Nonetheless, caspase-9 was involved. Death-receptor pathways were also involved, because blocking FADD or caspase-8 prevented apoptosis. Interestingly, this apoptosis pathway is different than that induced by withdrawal of GDNF from sympathetic neurons.

■ Behavioral/Systems/Cognitive

Receptive Field Properties in Mouse Visual Cortex

Cristopher M. Niell and Michael P. Stryker

(see pages 7520–7536)

Niell and Stryker have performed a broad quantitative study of the receptive field properties of neurons in mouse visual cortex and classified the neurons based on laminar position and waveform (narrow spiking vs broad spiking, which are thought to correspond to inhibitory and excitatory neurons, respectively). Despite the poor visual acuity and lack of cortical columnar organization in mice, mouse visual cortical neurons have many of the properties seen in other species, including orientation and spatial-frequency tuning, simple and complex responses, and contrast-invariant tuning. The results provide information about the optimal stimulus parameters to use in future studies of mouse visual processing, and most importantly, they open the door to using mouse genetic strategies such as targeted gene disruption and exogenous gene expression to investigate how the cortex generates well-established sensory response properties.

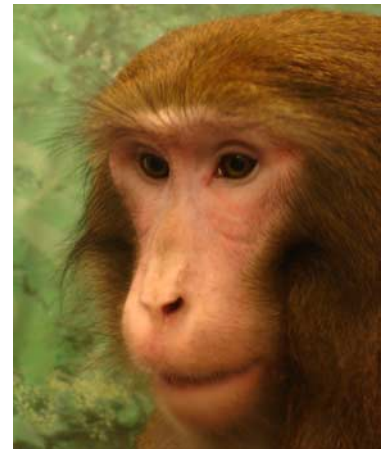
◆ Neurobiology of Disease

Unexpected Effects of Dopamine Withdrawal and Replacement

Li Liang, Maholn R. Delong, and Stella Papa

(see pages 7537–7547)

A prominent model of Parkinson's disease (PD) posits that chronic dopamine depletion causes opposite effects on striatal medium spiny neurons of the direct (striatonigral) and indirect (striatopallidal) pathways. Specifically, striatonigral neurons (~50% of the population) are thought to express primarily D₁ receptors and be less excitable in PD, whereas striatopallidal neurons are thought to express primarily D₂ receptors and be more excitable in PD. Moreover, L-DOPA is thought to reverse PD symptoms by reversing these changes in excitability. Experiments reported by Liang et al. contradict this model. The authors recorded individual striatal neurons in parkinsonian monkeys before and after administering L-DOPA. Contrary to expectations, all parkinsonian neurons had a higher firing rate than previously reported for striatal neurons in normal monkeys. Furthermore, L-DOPA further increased firing rate in 64% of neurons. Thus, excitability appears to be increased in neurons of both pathways, and L-DOPA actions do not simply reverse this effect.



After exposure to the toxin MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), macaques develop parkinsonian symptoms. A long-lasting hypothesis about the neuronal bases of these symptoms needs refinement. See the article by Liang et al. for details.