This Week in The Journal

● Cellular/Molecular

Few Prefrontal Pyramidal Cells Express Dopamine D1 Receptors

Hannah J. Seong and Adam G. Carter

(see pages 10516–10521)

Dopaminergic projections to the prefrontal cortex (PFC) modulate its role in several functions, including attention, working memory, and self-control. The projections terminate predominantly in deep layers, where D1 dopamine receptors (D1DRs) are sparsely distributed. To better understand the distribution and function of D1DRs, Seong and Carter performed whole-cell recordings in PFC slices taken from BAC transgenic mice in which a fluorescent dye was expressed under control of D1DR promoter elements. A small subset of neurons expressed D1DRs, and these were concentrated in deep layers. D1DR-expressing pyramidal neurons in layer 5 differed from nearby pyramidal neurons both morphologically and electrophysiologically: their apical dendrites were shorter and less branched, their resting membrane potentials were more hyperpolarized, they showed minimal activation of hyperpolarization-activated channels, and they were more likely to exhibit burst spiking upon depolarization. A D1 receptor agonist increased the depolarization-induced spiking of D1DR-expressing neurons, and this effect required activation of protein kinase A.

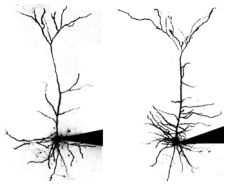
▲ Development/Plasticity/Repair

Adolescent Nicotine Exposure Affects Plasticity in Adult PFC

Natalia A. Goriounova and Huibert D. Mansvelder

(see pages 10484–10493)

Although nicotine has some positive effects, such as enhancing attention in people with cognitive disorders, chronic nicotine use—particularly during adolescence, when prefrontal cortical (PFC) circuits are developing—can produce long-lasting impairments in attention and working memory. In rats, nicotine treatment during adolescence causes attention deficits weeks after nicotine treatment has ceased. This deficit results partly from long-term reduction in the expression of metabotropic glutamate receptors (mGluRs), which presynaptically inhibit glutamate release in the PFC. Goriounova and Mansvelder report that nicotine treatment during adolescence also alters spike timing-dependent long-term potentiation (tLTP) in PFC. A protocol that induced tLTP in control adolescent rats often produced long-term depression (LTD) in those that had received nicotine for 10 days. In contrast, adult rats that had received nicotine as adolescents showed enhanced tLTP compared with controls. Age-dependent effects of mGluR agonists and antagonists suggested the effects of adolescent nicotine exposure resulted from short-term upregulation and long-term downregulation of mGluRs.



PFC neurons that express D1DRs (left) have shorter, less-branched apical dendrites than nearby neurons that do not express these receptors (right). See the article by Seong and Carter for details.

■ Behavioral/Systems/Cognitive

Active Sensing Alters NTS Responses to Tastes

Andre T. Roussin, Alexandra E. D'Agostino, Andrew M. Fooden, Jonathan D. Victor, and Patricia M. Di Lorenzo

(see pages 10494–10506)

In most studies of sensory processing, stimulus presentation is controlled solely by the experimenter. But in real life, animals shape their own sensory experience by actively looking at, touching, or licking objects. Attentional processes and neural circuitry driving these actions feed into sensory circuits and influence stimulus processing. To fully understand sensory processing, therefore, one must examine sensory system activity during active sensing. By recording from the nucleus of the solitary tract (NTS)—the target of the gustatory nerve—in freely licking rats, Roussin et al. discovered that taste-responsive cells were more broadly tuned than was determined previously during passive administration of tastes. In fact, many cells responded to all five basic tastes, and few responded exclusively to a single taste. Furthermore, some cells exhibited inhibitory responses, which were not reported previously. The latency of responses to different tastes varied both within and across cells, suggesting tastes are encoded by spatiotemporal patterns of NTS activity.

♦ Neurobiology of Disease

Nrf2 Reduces Pathological Features of Alexander Disease

Christine M. LaPash Daniels, Elizabeth V. Austin, Danica E. Rockney, Elizabeth M. Jacka, Tracy L. Hagemann, et al.

(see pages 10507–10515)

Mitochondrial respiration generates reactive oxygen species (ROS) that must be disposed of to prevent oxidative damage to DNA, lipids, and proteins, and subsequent cell death. Overproduction or inefficient removal of ROS contributes to many neurodegenerative diseases. The transcription factor Nrf2 regulates several genes involved in synthesizing free-radical scavengers and, although it functions mainly in astrocytes, its activation protects neurons from oxidative stress. Endogenous Nrf2 is upregulated in Alexander disease, a fatal disease caused by gain-of-function mutations in glial fibrillary acidic protein (GFAP) and characterized by formation of Rosenthal fibers in astrocytes, but Daniels et al. asked whether further Nrf2 elevation would be protective in a mouse model of this disease. Indeed it was—overexpression of Nrf2 reduced both GFAP expression and Rosenthal fiber formation across the brain. Surprisingly, however, Nrf2 overexpression did not increase levels of the free-radical scavenger glutathione, which is thought to underlie the neuroprotective effects of Nrf2 in other disease models.