This Week in The Journal

Development/Plasticity/Repair

Phasic Firing Increases Bouton Formation in Mesofrontal Axons

Surjeet Mastwal, Yizhou Ye, Ming Ren, Dennisse V. Jimenez, Keri Martinowich, et al.

(see pages 9484–9496)

Midbrain dopaminergic neurons affect numerous processes, including motor control, working memory, learning, reward processing, and motivation, via different projections and firing patterns. For example, neurons in the ventral tegmental area (VTA) fire phasically in response to salient reward-associated or aversive stimuli, and those that project to the medial prefrontal cortex are involved in the control of motivated behavior. Development of these mesofrontal circuits continues into adolescence, and abnormal development of these pathways has been proposed to contribute to several psychiatric disorders. Mastwal et al. now show that this development is influenced by experience. Specifically, wheel running, which stimulates phasic firing in VTA dopaminergic neurons, increased the formation of boutons on mesofrontal axons in adolescent—but not adult—mice, and this effect was mimicked by phasic—but not tonic—optical stimulation of dopaminergic neurons in the VTA. The increase in bouton number was accompanied by prolonged activation of frontal cortex after VTA stimulation and a corresponding suppression of the locomotor response to amphetamine.

Systems/Circuits

Potentiation of Cortical Inputs Prolongs M/T Cell Inhibition

Joy L. Cauthron and Jeffrey S. Stripling

(see pages 9677–9687)

Mitral/tufted (M/T) cells in the olfactory bulb receive inputs from olfactory sensory neurons and project to the piriform cortex, while olfactory bulb granule cells receive input from piriform cortex via association fibers (AFs) and form reciprocal dendrodendritic synapses with M/T cells. Granule cells are thought to have a central role in processing olfactory information. Previous studies indicated that high-frequency stimulation of piriform cortex AFs in rats produced long-lasting potentiation of local field potentials in the olfactory bulb. Investigating the significance of this potentiation, Cauthron and Stripling found that spiking in most presumptive granule cells was primarily driven by a single type of input—either AFs or M/T cells—and cells driven by AF stimulation were found more frequently after high-frequency (potentiating) stimulation of those fibers. Moreover, potentiation of AF inputs increased AF-driven spiking in granule cells, leading to prolonged inhibition of M/T cell firing. Increased inhibition of M/T cells has been found to improve odor discrimination, suggesting a similar role for AF potentiation.

Behavioral/Cognitive

Norepinephrine Induces Hormonal Response to Female Quails

Yasuko Tobari, You Lee Son, Takayoshi Ubuka, Yoshihisa Hasegawa, and Kazuyoshi Tsutsui

(see pages 9803–9811)

The presence of a member of the opposite sex often triggers changes in animals' behaviors. These behavioral changes likely result from changes in the production or secretion of reproductive hormones; however, the molecular pathways linking social encounters to hormonal changes are poorly defined. Tobari et al. now outline one such pathway in sexually active male Japanese quails. Viewing a female increased levels of gonadotropin-inhibitory hormone (GnIH) precursor mRNA in the paraventricular nucleus (PVN) of the hypothalamus, and this was associated with a decrease in plasma levels of luteinizing hormone (LH). Furthermore, viewing a female decreased levels of norepinephrine (NE)—but not other monoamines—in the diencephalon, possibly as a result of increased release. NE increased GnIH release from the hypothalamus *in vitro*, and intracerebroventricular injection of NE reduced plasma levels of LH. The data suggest that viewing a female causes an increase in NE release in the PVN, and this directly stimulates production of GnIH, which inhibits LH secretion from the pituitary.

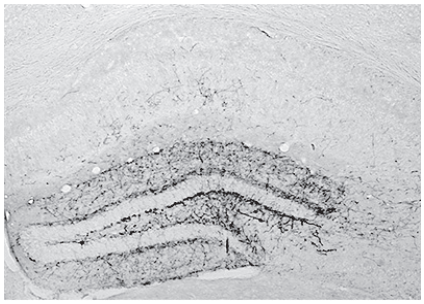
Neurobiology of Disease

Interneuron Grafts Reverse Cognitive Deficits in Old Mice

Leslie M. Tong, Biljana Djukic, Christine Arnold, Anna K. Gillespie, Seo Yeon Yoon, et al.

(see pages 9506–9515)

Cognitive decline during normal aging and in Alzheimer's disease (AD) is associated with a loss of inhibitory neurotransmission in the hippocampus, particularly in the hilus of the dentate gyrus. Possession of the $\epsilon 4$ allele of apolipoprotein E (apoE4)—the strongest genetic risk factor for AD—exacerbates age-related decline of GABA levels in humans, and knocking in this allele in mice leads to loss of hilar interneurons, along with deficits in learning and memory. By grafting immature interneurons and progenitors derived from the medial ganglionic eminence of wild-type mice into the hilar region of aged apoE4 knock-in mice, Tong et al. provide strong evidence linking loss of inhibition to cognitive decline. Grafted neurons survived at least 90 d and became integrated into neuronal circuits, as indicated by increases both in the frequency of spontaneous IPSCs and in inhibitory charge transfer in dentate granule cells. More importantly, interneuron transplantation improved performance of apoE4-expressing mice in the Morris water maze.



Transplanted cells from the medial ganglionic eminence become inhibitory interneurons and integrate into neural circuits in the dentate gyrus, improving memory performance in mice expressing an AD-linked form of ApoE. See the article by Tong et al. for details.