This Week in The Journal

Cellular/Molecular

VTA Neurons Coregulate Dopamine and Glutamate Release

Martín F. Adrover, Jung Hoon Shin, and Veronica A. Alvarez

(see pages 3183–3192)

Dopaminergic projections from the ventral tegmental area (VTA) to the nucleus accumbens (NAc) are central in reward processing; most abused drugs facilitate dopamine transmission at these synapses. Some dopaminergic afferents also release glutamate in NAc, thus evoking EPSCs in medium spiny neurons (MSNs). Whether dopamine and glutamate are packaged in the same vesicles and released at the same synapses has been unclear, but experiments by Adrover et al. suggest that they are. Optical stimulation of dopaminergic terminals in NAc both caused dopamine release and evoked glutamatergic EPSCs in MSNs. Like dopamine transients—but unlike EPSCs evoked by stimulating other glutamatergic inputs—optically evoked EPSCs exhibited paired-pulse depression and were inhibited by an agonist of dopamine D2 receptors, which are present on dopaminergic terminals. Thus, glutamate and dopamine release from VTA terminals appears to be coupled. Interestingly, these signaling pathways are uncoupled by cocaine, which inhibits dopamine reuptake: extracellular dopamine continues to modulate MSNs while inhibiting transmitter release from VTA terminals, thus reducing glutamatergic signaling.

Development/Plasticity/Repair

Translational Activators and Repressors Contribute to LTP

Chenghai Dong, Svitlana V. Bach, Kathryn A. Haynes, and Ashok N. Hegde

(see pages 3171–3182)

Cellular levels of a protein are determined by its synthesis and degradation rates, which can be modulated by specific translational activators and repressors and by the activity of the proteasome system. The levels of translational activators and repressors are similarly modulated, adding an extra level of complexity to the regulation of cellular processes such as long-term potentiation (LTP). Inhibiting proteasomal degradation in neurons enhances the early phase (induction) of LTP, but inhibits the late phase (maintenance). Dong et al. propose that these effects stem from proteasomal regulation of translational activators and repressors, respectively. LTP-inducing stimulation initially increased expression of two translational activators, with levels peaking after 45 min. Inhibiting proteasomal degradation before this point increased levels of these activators, whose activity was required for the enhancement of LTP induction. In addition, LTP-inducing stimulation increased expression of two translational repressors, whose levels peaked after 90 min. Inhibiting degradation before this point increased levels of these repressors, which appeared necessary for the reduction of LTP maintenance.

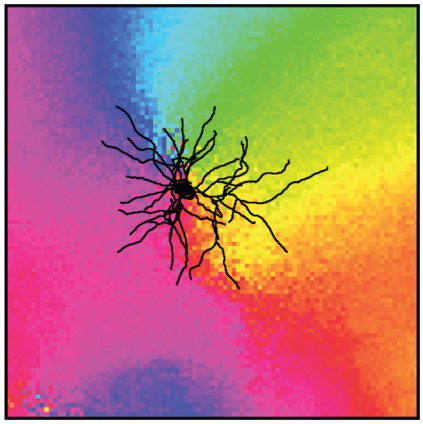
Systems/Circuits

Dendritic Arbor Shape Does Not Vary across Orientation Map

Manuel Levy, Zhongyang Lu, Grace Dion, and Prakash Kara

(see pages 3231–3236)

Across primary visual cortex (V1), neurons that respond preferentially to stimuli of a given orientation are clustered in so-called orientation domains. Domains representing different orientations meet at points called pinwheel centers. Because a neuron's orientation selectivity is shaped by local inputs, one might expect neurons at pinwheel centers—surrounded by neurons with various orientation preferences—to be more broadly tuned than neurons in the center of orientation domains. But several studies have suggested that this is not the case. Neurons at pinwheel centers could theoretically sharpen their tuning by distributing their dendrites in a way that biases their sampling of surrounding domains, but Levy et al. found no evidence for this hypothesis. The size and shape of dendritic arbors of cat layer 2/3 pyramidal cells was independent of soma position relative to the orientation map. Moreover, neurons with somata near pinwheel centers extended dendrites into all surrounding orientation domains. Thus, V1 neurons seem to integrate information from surrounding neurons regardless of their orientation selectivity.



Reconstructed somato-dendritic arbor of a V1 neuron located at a pinwheel center. The neuron's dendrites extend into all surrounding orientation domains (indicated by different colors). See the article by Levy et al. for details.

Neurobiology of Disease

ApoE Peptide Increases Brain Uptake of Therapeutic Enzyme

Annika Böckenhoff, Sandra Cramer, Philipp Wölte, Simeon Knieling, Claudia Wohlenberg, et al.

(see pages 3122–3129)

A major challenge in developing treatments for neurological disorders is ensuring that the therapeutic agent crosses the blood–brain barrier (BBB). Endogenous mechanisms exist for transporting essential molecules across the BBB, however, and these might be exploited to transport therapeutic molecules. This approach might be especially useful for enzyme replacement therapy. Proteins such as insulin bind to specific receptors on the endothelial cells that form the BBB; after binding, the proteins are endocystosed, transported across the cell, and exocytosed into the brain. Böckenhoff et al. fused the receptor-binding domains of several proteins transported in this way to arylsulfatase A (ASA)—a lysosomal enzyme mutated in metachromatic leukodystrophy—and compared their ability to promote brain entry. Of five tested peptides, only one—derived from apolipoprotein E (ApoE)—increased brain delivery of ASA. The ApoE peptide not only increased brain delivery of peripherally injected ASA, but also enabled a greater reduction in lysosomal storage in brains of ASA-null mice than that achieved with wild-type ASA.