This Week in The Journal

Cellular/Molecular

Amperometry Reveals Release Kinetics at a Ribbon Synapse

Chad P. Grabner and David Zenisek

(see pages 8144–8158)

In amperometry, voltage applied to an electrode oxidizes surrounding molecules, causing a transfer of electrons that produces measurable current. This technique can detect release of oxidizable neurotransmitters, such as catecholamines, revealing the amount of transmitter per vesicle and the kinetics of vesicle fusion. Unfortunately, amperometry cannot detect release of nonoxidizable neurotransmitters, like glutamate. The kinetics of glutamate release are instead inferred either from the shape of postsynaptic EPSCs or from discontinuous capacitance measurements, neither of which is as precise as amperometry. But glutamatergic neurons incubated with catecholamines package these transmitters into vesicles whose release can be monitored with amperometry. Using this technique, Grabner and Zenisek examined exocytosis at ribbon synapses of goldfish retinal bipolar cells. Brief stimulation produced a phase of near-synchronous vesicle fusion within 0.5 ms of Ca^{2+} influx, followed by a trailing phase of desynchronized release, with ~14 vesicles released in 30 ms. A small pause in the rising phase of slow release events suggested pauses occur during fusion pore opening.

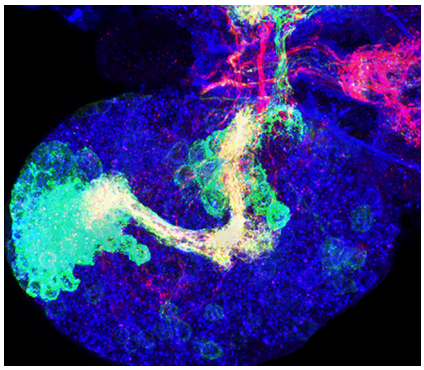
Development/Plasticity/Repair

X11-Dependent Endocytosis Helps Sort Axonal Proteins

Garrett G. Gross, G. Mohiddin Lone, Lok Kwan Leung, Volker Hartenstein, and Ming Guo

(see pages 8575–8586)

Proper neuronal function requires differential distribution of receptors, ion channels, and associated molecules between axons and dendrites. Domain-specific protein expression involves sorting new proteins into appropriate vesicles, transporting vesicles into processes, inserting proteins into the plasma membrane, and anchoring proteins to limit diffusion. Different proteins are sorted at different steps of this process. Most dendritic proteins are sorted into specific vesicles that are excluded from axons; some axonal proteins enter dendrites, but are not inserted into the membrane; and other axonal proteins are inserted but are soon endocytosed and transported to the axon. Gross et al. report that the adaptor protein X11/Mint is involved in the last of these. *Drosophila* X11 binds to the amyloid precursor protein homolog APPL via a cytoplasmic domain that is also required for APPL endocytosis. APPL is normally expressed in axons but not the dendritic calyx of mushroom-body neurons, but silencing X11, mutating the X11-binding domain of APPL, or inhibiting endocytosis caused APPL to appear in the calyx.



Blocking endocytosis in *Drosophila* mushroom body neurons (green) causes APPL (blue) and fasciclin II (red), which are normally restricted to axons in the lobe, to appear in dendrites in the calyx as well. See the article by Gross et al. for details.

Systems/Circuits

Silencing mPFC Increases Firing of Dopamine Neurons

Yong Sang Jo, Jane Lee, and Sheri J. Y. Mizumori

(see pages 8159–8171)

The firing rate of dopamine neurons in the ventral tegmental area (VTA) increases when an unexpected reward is received and decreases when an expected reward is absent. After a cue becomes associated with reward, dopamine neurons spike faster when the cue occurs, but not when the predicted reward is obtained. Neurons in several other brain areas, including the medial prefrontal cortex (mPFC), also respond to reward receipt and omission. Because mPFC projections excite dopaminergic and GABAergic neurons in the VTA, Jo et al. asked how mPFC activity influences reward-related activity of VTA neurons. After rats learned to find food in a radial arm maze, two groups of dopaminergic and non-dopaminergic neurons were examined: before-reward neurons, whose firing increased as a reward was approached, and after-reward neurons, which responded when the reward was consumed. After mPFC was silenced, the responses of before-reward non-dopaminergic neurons were weaker and the responses of before-reward dopaminergic neurons were enhanced, but the responses of after-reward neurons were unaltered.

Neurobiology of Disease

X-Chromosome Imprinting Affects Brain Morphology

Jean-Francois Lepage, David S. Hong, Paul K. Mazaika, Mira Raman, Kristen Sheau, et al.

(see pages 8567–8574)

Epigenetic modification of specific genes in eggs or sperm ("genomic imprinting") prevents expression of maternal or paternal alleles in offspring. Imprinting of X-chromosome genes has sex-specific effects, because only females are affected by imprinting on paternally inherited X chromosomes (X^p) and imprinting on maternally inherited X chromosomes (X^m) only affects half of female cells, because one X chromosome is inactivated in each cell. Whether imprinting of X-linked genes contributes to sexual dimorphism in brain anatomy and cognition is unclear. To address this question, Lepage et al. examined girls with Turner syndrome, in which either X^p or X^m and X inactivation are absent. Differences in cortical thickness, surface area, and volume were found in several regions. For example, cortical thickness in temporal areas was greater in X^p than in X^m girls, whereas gray matter volume in superior frontal regions was greater in X^m than in X^p girls. The results suggest that imprinting of X-chromosome genes can influence sexual dimorphism in the brain.