This Week in The Journal

● Cellular/Molecular

Short-Term Plasticity Enhances Information Transfer

Ziv Rotman, Pan-Yue Deng, and Vitaly A. Klyachko

(see pages 14800–14809)

Postsynaptic responses at a given synapse vary greatly depending on recent synaptic activity. If vesicle release probability is low, PSP amplitudes generally increase during a spike train, because calcium accumulates in the presynaptic terminal, thus increasing release probability. When release probability is high, however, the pool of readily releasable vesicles becomes depleted during spike trains, and PSP amplitudes successively decrease. Consequently, most synapses exhibit both facilitation and depression, with the balance changing over time. Such short-term plasticity (STP) has been proposed to play important roles in information processing. Using a computational model with release probabilities measured in hippocampal slices, Rotman et al. estimated how well postsynaptic responses reflected presynaptic spike patterns at hippocampal synapses. Information transfer depended on both spike frequency and the number of spikes per burst, and it was enhanced by STP. Based on their calculations, they conclude that STP and burst length combine to optimize information transfer at hippocampal excitatory and inhibitory synapses.

▲ Development/Plasticity/Repair

The Netrin-1 Receptor DCC Interacts with Syntaxin-1

Tiziana Cotrufo, Francesc Pérez-Brangulí, Ashraf Muhaisen, Oriol Ros, Rosa Andrés, et al.

(see pages 14463–14480)

Neurite elongation requires remodeling of the actin cytoskeleton, polymerization and stabilization of microtubules, and insertion of plasma membrane. These steps occur at the tips of growing neurites, where they are regulated by extracellular guidance cues via transmembrane receptors. While much has been learned about intracellular signaling cascades linking guidance molecules to cytoskeletal dynamics, relatively little is known about growth-associated regulation of membrane insertion. Cotrufo et al. now report that the guidance molecule netrin-1 triggers membrane addition by stimulating interaction at the leading edge of growth cones between its receptor, DCC, and syntaxin-1, a protein that facilitates exocytosis. Netrin-1 attracted neurites growing from hippocampal explants, and it stimulated vesicle exocytosis in growth cones. Both effects were blocked by cleaving syntaxin-1. Similarly, syntaxin-1 knockdown in chick spinal commissural axons disrupted netrin-dependent pathfinding *in vivo*. Upon binding netrin-1, DCC may recruit syntaxin-1 to the membrane, promoting asymmetric exocytosis, and thus directing neurite extension.

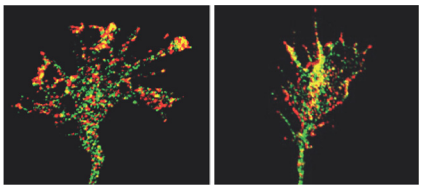
■ Behavioral/Systems/Cognitive

Activation of Accumbal GLP-1 Receptors Reduces Food Intake

Amanda M. Dossat, Nicole Lilly, Kristen Kay, and Diana L. Williams

(see pages 14453–14457)

Glucagon-like peptide 1 (GLP-1) has multiple roles in regulating energy balance: it stimulates insulin secretion, increases insulin sensitivity, regulates blood glucose levels, slows gastric emptying, reduces food intake, and induces taste aversion. After meals, GLP-1 is released both from gut and from neurons in the nucleus of the solitary tract (NTS). Central effects of GLP-1 are likely mediated by NTS projections to various brain areas. Injection of GLP-1 into the hypothalamic paraventricular nucleus suppresses feeding without altering glucose homeostasis, whereas injection into the arcuate nucleus does the opposite; injection into the amygdala induces taste aversion. Dossat et al. examined the role of GLP-1 in rat nucleus accumbens (NAc), an area involved in reward. Injecting GLP-1 into the NAc core, but not into the shell, activated neurons and suppressed eating without producing taste aversion. Furthermore, injecting GLP-1 receptor antagonist into the core increased food intake, supporting a role for NAc in regulating food consumption.



Netrin-1 stimulates association between DCC (red) and syntaxin-1 (green) in growth cones of cultured hippocampal neurons. See the article by Cotrufo et al. for details.

♦ Neurobiology of Disease

MicroRNAs Regulate Ceramide Synthesis in Alzheimer's Disease

Hirosha Geekiyanage and Christina Chan

(see pages 14820–14830)

Sphingolipids are major structural components of cell membranes, and many have signaling functions as well. Several extracellular signals stimulate synthesis of the simplest sphingolipid, ceramide, which directly activates proteins and also promotes formation of signaling microdomains (lipid rafts) in the plasma membrane. Ceramide is elevated in several neurodegenerative diseases, including Alzheimer's (AD). Besides inducing apoptosis, ceramide promotes delivery of secretases to lipid rafts, thus increasing production of β-amyloid (Aβ). The first step in ceramide synthesis requires serine palmitoyltransferase (SPT). Geekiyanage and Chan found that like ceramide, SPT subunits SPTLC1 and SPTLC2 were upregulated in AD cortex, and their levels were correlated with that of Aβ. SPTLC levels appeared to be regulated post-transcriptionally, and several microRNAs decreased levels of SPTLCs, ceramide, and Aβ in cultured mouse astrocytes. These same microRNAs were down-regulated in AD patients. Together, the results suggest that reduced microRNA expression leads to increased ceramide synthesis, and this contributes to increased Aβ production.