This Week in The Journal

● Cellular/Molecular

Myrip Facilitates Secretory Vesicle Movement and Tethering

Sébastien Huet, Isabelle Fanget, Ouardane Jouannot, Patricia Meireles, Tim Zeiske, et al.

(see pages 2564–2577)

In neuroendocrine cells, soluble hormones are packaged into secretory granules (SGs) that are transported along microtubules toward release sites in the periphery. Before being exocytosed, SGs must leave the microtubule track, traverse the cortical actin network underlying the membrane, and become tethered to the membrane. Transport across the actin cortex relies on the motor protein myosin Va. Huet et al. investigated the role of Myrip in this process by tracking the movements of SGs in enterochromaffin cells. Normally, SGs were concentrated within the actin cortex and at the plasma membrane. Knocking down Myrip reduced association of myosin Va with SGs; increased the rate of SG movement into, out of, and within the actin cortex; decreased the proportion of immobile SGs; and caused SGs to redistribute away from the periphery. Thus, Myrip appears to help recruit myosin Va to SGs, limit SG diffusion, and facilitate tethering of SGs to the plasma membrane.

▲ Development/Plasticity/Repair

Electroconvulsive Shock Increases Tamalin Expression

Sudhirkumar U. Yanpallewar, Colleen A. Barrick, Mary Ellen Palko, Gianluca Fulgenzi, and Lino Tessarollo

(see pages 2252–2262)

Electroconvulsive shock (ECS) therapy effectively treats major depression, but its potential for negative cognitive side effects reduces its value. Shared actions of ECS and pharmaceutical antidepressants—including increased expression of neurotrophic factors, neurogenesis in the dentate gyrus, and sprouting of granule cells—likely underlie their therapeutic value; unraveling the molecular links between ECS and these downstream effects might lead to the development of new therapeutic options with fewer side effects. Yanpallewar et al. advance this pursuit by showing that hippocampal expression of the scaffolding protein tamalin increases after ECS in mice. Knock-out of tamalin greatly attenuated ECS-induced neurogenesis in the dentate gyrus, as well as reducing ECS-induced stimulation of granule cell axonal and dendritic growth. Despite these effects, tamalin knock-out did not appear to affect development or plasticity under normal conditions. Thus, tamalin, which interacts with metabotropic glutamate receptors and other synaptic proteins, appears to have unique actions in the context of ECS.

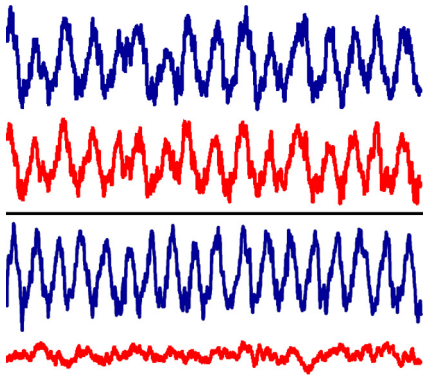
■ Behavioral/Systems/Cognitive

Protein Synthesis Inhibitors Silence Neurons

Arjun V. Sharma, Frank E. Nargang, and Clayton T. Dickson

(see pages 2377–2387)

New memories must be consolidated before they become permanent: disrupting consolidation with additional learning, distracting stimuli, injury, or toxins impairs performance on recall tests. If protein synthesis inhibitors are infused into the hippocampus immediately before or after a learning session, performance is impaired, suggesting memory consolidation requires synthesis of new proteins. Furthermore, previously stored memories appear to transiently reenter a labile state that must undergo protein synthesis-dependent reconsolidation to persist. Although these hypotheses are widely accepted, they rely predominantly on studies in which protein synthesis inhibitors are infused during behavioral experiments. But Sharma et al. report that protein synthesis inhibitors silence both spontaneous and evoked neural activity in hippocampus of anesthetized mice. The effect appeared within 30 min, lasted up to 6 h, and was proportional to the inhibition of protein synthesis. These results suggest that ongoing protein synthesis is required to sustain neural activity, confounding memory studies that use such inhibitors.



Infusion of protein synthesis inhibitors (bottom) suppresses local field potentials in ipsilateral (red) but not contralateral (blue) hippocampus. See the article by Sharma et al. for details.

◆ Neurobiology of Disease

Seizures Follow Depletion of GABA

Z. J. Zhang, J. Koifman, D. S. Shin, H. Ye, C. M. Florez, et al.

(see pages 2499–2512)

Seizures are characterized by sudden onset of synchronized neural activity. Although they are thought to result from an imbalance of excitation and inhibition, mechanisms driving the transition to seizure are unclear. To investigate this question, Zhang et al. studied seizure-like events (SLEs) in intact isolated mouse hippocampus. SLEs were preceded by preictal periods in which GABA-dependent rhythmic discharges occurred at low frequency, and were followed by interictal periods with fewer GABA-dependent discharges. The duration of interictal and preictal periods was reduced—and the frequency of SLEs was thus increased—by GABA receptor antagonists. Glutamatergic currents increased during the preictal period, whereas GABA currents decreased, disappearing at the onset of SLEs. Although sucrose-induced synaptic vesicle release did not induce IPSCs late in the preictal period, GABA agonists continued to produce outward currents. These results suggest that SLEs were triggered by depletion of GABAergic vesicles and maintained by a concurrent increase in excitatory drive.