This Week in The Journal

Cellular/Molecular

MEF2A Promotes Maturation of Presynaptic Sites

Tomoko Yamada, Yue Yang, Ju Huang, Giovanni Coppola, Daniel H. Geschwind, et al.

(see pages 4726–4740)

Synaptic proteins cluster in developing axons before postsynaptic cells are contacted. As contacts are made, clusters apposing the postsynaptic cell grow larger and orphan clusters disappear. A transcriptional repressor, myocyte enhancer factor 2A (MEF2A), is involved in this process. Yamada et al. found that knocking down MEF2A increased the density of orphan clusters of presynaptic proteins (e.g., synapsin) and orphan vesicle release sites in cultured neurons. Several genes were targeted by MEF2A, including the one encoding synaptotagmin 1 (Syt1), the calcium sensor for synaptic vesicle release. Syt1 was upregulated after MEF2A knockdown, and like MEF2A knockdown, overexpressing Syt1 increased the density of presynaptic orphan sites. Conversely, knocking down Syt1 decreased the density of orphan sites and rescued the effect of MEF2A knockdown. Live imaging revealed that during synaptic maturation, synapsin levels increased in varicosities containing vesicles and active zones as nearby orphan synapsin clusters disappeared. Knocking down MEF2A attenuated this redistribution and reduced the number of synaptic vesicles in varicosities, suggesting that MEF2A promotes synaptic maturation.

Development/Plasticity/Repair

Deafferentation Stimulates Neurogenesis in Dentate Gyrus

Julia V. Perederiy, Bryan W. Luikart, Eric K. Washburn, Eric Schnell, and Gary L. Westbrook

(see pages 4754–4767)

Brain injury often causes deafferentation, followed by sprouting and formation of new synaptic connections. This week, Perederiy et al. demonstrate that deafferentation also stimulates genesis and incorporation of new neurons in mouse dentate gyrus. Unilaterally severing entorhinal projections—which synapse on granule cell apical dendrites in the outer two-thirds of the dentate molecular layer—increased cell proliferation within 2 d and increased the number of newborn neurons in the deafferented dentate gyrus within 14 d. Dendrites of newborn neurons appeared to grow normally at first, but when they reached the denervated zone, growth and branching were reduced relative to growth in the contralateral hemisphere. Although spine density was reduced on distal dendrites of newborn neurons in the deafferented dentate, the spines contained postsynaptic densities. Spine density on newborn neurons was elevated on proximal dendrites, which are innervated by axons from associational cortex, suggesting synaptic reorganization occurred. Dendritic spine density in mature granule cells was unaffected by the lesion, however.

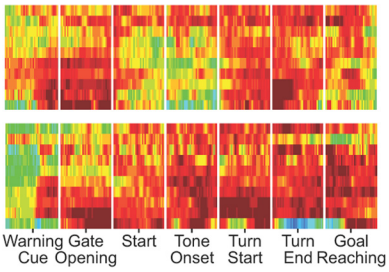
Systems/Circuits

Dopamine Loss Alters Plasticity of Striatal Interneurons

Ledia F. Hernandez, Yasuo Kubota, Dan Hu, Mark W. Howe, Nune Lemaire, et al.

(see pages 4782–4795)

The striatum plays a central role in motor learning and action selection. Thalamic and cortical inputs are integrated by striatal microcircuits that modulate the firing of medium spiny projection neurons (MSNs), which are thought to select appropriate actions and suppress competing actions. During instrumental learning, reward-dependent dopamine release is hypothesized to alter the activity of MSNs and striatal interneurons to promote the execution of appropriate actions. But how dopamine affects different neuron types is poorly understood. To address this, Hernandez et al. created unilateral intrastriatal lesions of dopaminergic projections, then recorded single-unit activity as rats learned and performed a T-maze task. Dopamine depletion increased the spike rate of MSNs, but the neurons exhibited the normal change in firing patterns over the course of learning, firing more during preparation, turning, and goal-reaching periods than during mid-run. In contrast, dopamine depletion greatly attenuated the development of such task-bracketing activity in fast-spiking interneurons: their firing remained strong throughout the task.



As rats learn a maze, the spike rate of fast-spiking interneurons in uninjured striatum (top panels) increases (warmer colors) before run initiation and during turns (panels 2, 5, and 6) and decreases (cooler colors) during mid-run (panels 3 and 4). These training-induced changes do not occur after dopamine depletion (bottom panels). See the article by Hernandez et al. for details.

Behavioral/Cognitive

Deflection of Submandibular Whisker Reflects Speed

Lydia Thé, Michael L. Wallace, Chris Chen, Edith Chorev, and Michael Brecht

(see pages 4815–4824)

When exploring their environments, rats rely heavily on their whiskers. Mystacial whiskers, which rats actively sweep back and forth, are particularly important for discerning shapes, distances, and textures. Because much less is known about the functions of other facial whiskers, Thé et al. investigated a set of three short whiskers—the submandibular whisker trident—aligned in a row on rats' chins. These whiskers pointed to the ground and did not appear to be actively whisked; they rarely contacted anything except when rats were engaged in head-down running while exploring new environments and foraging for food. During this behavior, the central whisker was deflected by contact with the floor, and surprisingly, its deflection angle decreased as the rat's speed increased. Thus, submandibular whiskers may act as a speedometer. Whisker-related activity was detected in the somatosensory cortex in a region where large, isolated barrels were found. Because this region projects to vestibular nuclei, the authors speculate that the whisker trident provides information about heading direction and path integration.