This Week in The Journal

● Cellular/Molecular

Fen-1 Endonuclease and Taste Conditioning

Lorena Saavedra-Rodríguez, Adrinel Vázquez, Humberto G. Ortiz-Zuazaga, Nataliya E. Chorna, Fernando A. González, Lissette Andrés, Karen Rodríguez, Fernando Ramírez, Alan Rodríguez, and Sandra Peña de Ortiz

(see pages 5726–5737)

Learning involves changes in synaptic structure mediated by protein modifications and synthesis. Maintenance of these changes is generally thought to underlie memory, and recall is thought to involve reactivation of strengthened synapses. But the lability of synaptic strength and the short lifespan of proteins relative to that of some memories have led Peña de Ortiz and others to question the ability of synaptic changes alone to mediate long-term memory storage: they propose that storage also requires learning-induced genetic changes involving DNA recombination that creates novel proteins, analogous to the generation of diverse antigen receptors by the immune system. Several proteins involved in DNA recombination have been linked to conditioning, and Saavedra-Rodriguez et al. extend this list to include flap structure-specific DNA endoculease-1 (Fen-1). Fen-1 was upregulated specifically in amygdalar neurons during conditioned taste aversion. Knockdown of Fen-1 with antisense oligonucleotides decreased long-term (48 h) taste aversion, but did not affect short-term (2 h) memory.

▲ Development/Plasticity/Repair

Role of GluRδ2 N-Terminus in Synapse Formation

Wataru Kakegawa, Taisuke Miyazaki, Kazuhisa Kohda, Keiko Matsuda, Kyoichi Emi, Junko Motohashi, Masahiko Watanabe, and Michisuke Yuzaki

(see pages 5738–5748)

The δ2 glutamate receptor (GluRD) was named based on its homology with ionotropic glutamate receptors, but it does not bind glutamate and no known ligand activates its ion channel. GluRD is expressed primarily in dendritic spines of cerebellar Purkinje cells (PCs), postsynaptic to parallel fiber (PF) inputs. GluRD knock-out impairs development and long-term depression (LTD) of this synapse, and GluRD-null mice have impaired motor coordination. Kakegawa et al. report that virus-mediated expression of wild-type GluRD in cerebellum of GluRD-null mice increased coordination and the number of PF–PC synapses, whereas expression of GluRD lacking the N-terminal domain did not. Both forms rescued LTD, however. Interestingly, disrupting putative ligand-binding and ion-channel domains did not prevent rescue of the knock-out phenotype, suggesting that these elements are not critical for GluRD function. Previous studies demonstrated that the GluRD C-terminal domain is critical for LTD, but not synapse formation, demonstrating that different GluRD domains serve different functions.

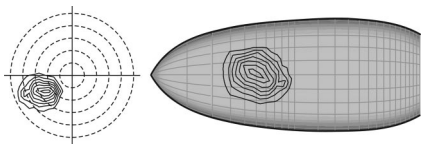
■ Behavioral/Systems/Cognitive

V4 Receptive Fields

Brad C. Motter

(see pages 5749–5757)

Neurons at later stages of cortical visual processing have complex response properties that are derived from inputs from subsets of neurons at earlier stages. Little is known about what defines the input for each higher-order neuron. By precisely mapping spatial receptive fields of neurons in visual area V4, Motter has provided new insights into the relationship between these receptive fields and the visual field map in primary visual cortex (V1). All V4 receptive fields appear to sample from the same amount of V1, whether they represent the central or peripheral visual field. Furthermore, V4 receptive fields are systematically elongated toward the periphery of the visual field because the neurons sample from a circularly symmetric region of the V1 map, in which the representation of more peripheral representations is compressed. These results raise the possibility that other extrastriate visual areas also have a systematic relationship to the map in V1.



The receptive field of a V4 neuron is elongated toward the periphery of the visual field (left), but it samples from a circular area of V1 (right). See the article by Motter for details.

♦ Neurobiology of Disease

Axonal Transport Defects and Tau Hyperphosphorylation

Tomás L. Falzone, Gorazd B. Stokin, Concepción Lillo, Elizabeth M. Rodrigues, Eileen L. Westerman, David S. Williams, and Lawrence S. B. Goldstein

(see pages 5758–5767)

In several neurodegenerative diseases, the microtubule-associated protein tau becomes hyperphosphorylated and accumulates in neurofibrillary tangles, which are believed to disrupt axonal transport of essential proteins, leading to synaptic dysfunction and degeneration. Mutations in tau likely promote hyperphosphorylation in some diseases, but the cause of hyperphosphorylation of normal tau is unknown. Falzone et al. now suggest that impaired axonal transport is not only a result, but also a cause of tau hyperphosphorylation. Mice lacking the anterograde motor protein kinesin light chain 1 (KLC1), showed impaired kinesin-dependent vesicle transport, but axonal development and mitochondrial transport were normal in cultured neurons from newborn animals. Brain structure appeared normal in young mice, but as animals aged, axonal swellings containing accumulated neurofilaments, vesicles, and abnormally phosphorylated tau appeared and increased in number, and axonal degeneration occurred throughout the CNS by 18 months. Abnormal tau phosphorylation was likely mediated by increased activation of stress kinases in axons of knock-out mice.