This Week in The Journal

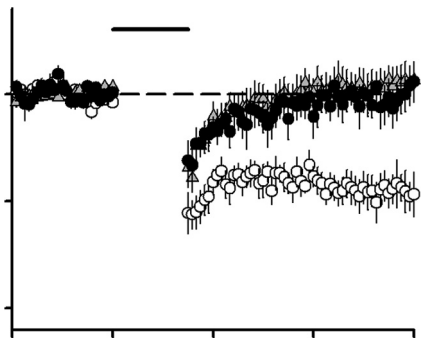
Cellular/Molecular

Noncompetitive NMDA Receptor Antagonist Blocks LTD in Mice

Walter E. Babiec, Ryan Guglietta, Shekib A. Jami, Wade Morishita, Robert C. Malenka, et al.

(see pages 5285–5290)

High-frequency stimulation of rodent hippocampus induces long-term potentiation (LTP) of synaptic strength, whereas low-frequency stimulation induces long-term depression (LTD). Both LTP and LTD require activation of NMDA receptors (NMDARs), and a pervasive view has been that which form of plasticity is produced depends on the amount of Ca^{2+} influx through these receptors. Specifically, large Ca^{2+} influxes are thought to induce LTP, whereas small influxes induce LTD. This hypothesis recently received a major blow when it was reported that MK-801—an NMDAR antagonist that blocks the Ca^{2+} pore without blocking glutamate binding—failed to inhibit LTD in hippocampal slices from young rats, suggesting NMDARs induce LTD through a metabotropic rather than ionotropic mechanism. Wondering whether this phenomenon was limited to young animals, Babiec et al. examined the effect of MK-801 on LTD in adult mice. Unexpectedly, they found that MK-801 blocked LTD not only in adult mice, but also in young mice. Furthermore, MK-801 inhibited NMDAR-induced activation of downstream signaling pathways involved in LTD.



Low-frequency stimulation (during time indicated by bar) caused LTD of the field EPSP slope in mouse hippocampus (open circles). LTD was blocked by MK-801 (filled circles). See the article by Babiec et al. for details.

Development/Plasticity/Repair

Reaching Becomes Bilateral When CST Axons Project Bilaterally

Najet Serradj, Sónia Paixão, Tomasz Sobocki, Mitchell Feinberg, Rüdiger Klein, et al.

(see pages 5211–5221)

EphrinB3, a guidance molecule expressed in the spinal cord midline, repels axons that express EphA4 receptors, including axons of spinal interneurons and axons descending in the corticospinal tract (CST) from primary motor cortex. When EphA4 is knocked out globally, both spinal interneuron and CST axons misproject bilaterally and mice locomote with a hopping rather than alternating-step gait. Locomotion is thought to be driven primarily by central pattern generators in the spinal cord, whereas goal-directed actions such as reaching or stepping over obstacles requires descending control. Therefore, Serradj et al. predicted that restricting EphA4 knockout to CST neurons would cause goal-directed actions to become bilateral, while sparing normal locomotion. This is what they found. In mice lacking EphA4 selectively in CST axons, only these axons projected bilaterally. Motor cortex stimulation often evoked bilateral muscle activation in these mice, and the mice were more likely than controls to hop over obstacles and to reach with both forelimbs rather than with one; but normal walking was unaffected.

Behavioral/Cognitive

Rats May Use Microvibrissae to Discriminate Textures

Praveen Kuruppath, Erez Gugig, and Rony Azouz

(see pages 5115–5120)

Rats have two sets of whiskers that they use for tactile discrimination. The better studied of these are the long macrovibrissae, which project to the barrel cortex. These whiskers actively sweep the environment to discern object shape, distance, and texture. Unlike macrovibrissae, the short microvibrissae present around the nose and mouth are not arranged in a neat grid, and they are relatively stationary—although they brush across surfaces when rats sweep their heads. Previous studies demonstrated that microvibrissae are used to discriminate the shapes of food items. Kuruppath et al. now provide evidence that microvibrissae can also be used to discriminate textures. The authors obtained multiunit recordings from areas of somatosensory cortex that represent the frontobuccal whisker pad while they stimulated rats' microvibrissae with different grades of sandpaper. They found that the firing rates of individual neurons increased along with the paper coarseness to an extent that could support texture discriminations.

Neurobiology of Disease

NMDA Receptor Levels Are Reduced in Down's Syndrome Model

Gurjinder Kaur, Ajay Sharma, Wenjin Xu, Scott Gerum, Melissa J. Alldred, et al.

(see pages 5099–5106)

Down's syndrome (DS) is caused by the presence of an extra copy of chromosome 21. DS phenotypes are thought to result from increased dosage and consequent overexpression of genes and noncoding RNAs present on this chromosome, as well as from epigenetic alterations. These changes have downstream effects on the expression and activity of proteins encoded on other chromosomes. The molecular bases for abnormal brain development and cognitive deficits in DS can be studied in mice in which parts of chromosome 16—which contains many of the same genes as human chromosome 21—are duplicated. Such mice have reduced hippocampal volume, abnormal dendritic spines, altered synaptic plasticity, and learning deficits. Several studies have suggested that an imbalance of inhibitory and excitatory neurotransmission underlies cognitive deficits in these mice. Kaur et al. complement these studies by showing that the Ts2 mouse model of DS has deficits in both learned and innate hippocampus-dependent tasks, along with reductions in hippocampal glutamate levels, NMDA receptor expression, and LTP.