This Week in The Journal

● Cellular/Molecular

Infiltrating Microglia and Neuropathic Pain

Ji Zhang, Xiang Qun Shi, Stefania Echeverry, Jeffrey S. Mogil, Yves De Koninck, and Serge Rivest

(see pages 12396–12406)

Microglia are everywhere these days. This week, it's neuropathic pain and the spinal cord. Zhang et al. report that resident CNS microglia, as well as those derived from hematogenous macrophages/monocytes that infiltrate the spinal cord, participate in neuropathic pain. The authors tested mice after a partial ligation injury of the sciatic nerve. They tracked the two microglia populations using chimeric mice in which bone marrow stem cells expressing green fluorescent protein were transplanted into irradiated mice. The microglial signaling pathway involved chemokine monocyte chemoattractant protein 1 (MCP-1; also called CCL2) and its receptor, CCR2. MCP-1 is not normally present in the nervous system, but it is induced by injury. The authors report that intrathecal injection of MCP-1 activated microglia in the spinal cord, whereas a neutralizing antibody prevented the injury-induced infiltration of bone marrow-derived microglia. Microglia were not activated in mice lacking CCR2, and these mice did not show mechanical allodynia.

▲ Development/Plasticity/Repair

Spine Shrinkage Does Not Equal LTD

Xiao-bin Wang, Yunlei Yang, and Qiang Zhou

(see pages 12419–12429)

The functional significance of morphological changes that accompany synaptic plasticity has long been debated. Remember "twitching" spines? This week, Wang et al. revisited this issue by examining dendritic spine size after long-term potentiation (LTP) and long-term depression (LTD). Using electrophysiological recordings and simultaneous two-photon time-lapse imaging in rat hippocampal slices, the authors report that spine remodeling and synaptic plasticity are not indelibly linked and can occur independently. Low-frequency stimulation induced LTD and reduced the diameter of dendritic spines. However, a peptide that competes with the endogenous phosphatase substrate p-cofilin inhibited spine shrinkage but did not affect the expression of LTD. Conversely, block of LTD did not prevent spine shrinkage. Pharmacological block of exocytosis prevented the constitutive replacement of internalized AMPA receptors. As a result, synaptic responses were reduced, but spine size was unchanged. Actin remodeling, however, was required for LTD.

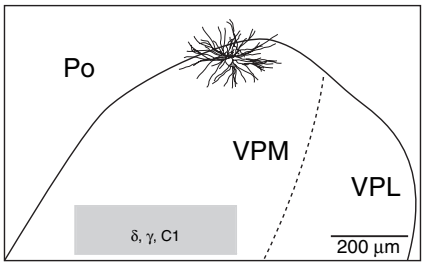
■ Behavioral/Systems/Cognitive

Mapping Vibrissal Pathways in Thalamic Barreloids

Nadia Urbain and Martin Deschênes

(see pages 12407–12412)

What can pass through the head of a barreloid? According to Urbain et al., the answer is a newly discovered pathway for ascending information in the rat vibrissal system. The low-threshold mechanoreceptors on the array of vibrissa on the rodent snout respond only to a single whisker. The afferent fibers from these mechanoreceptors then maintain the array arrangement in sets of cells in the brainstem (barrelettes), thalamus (barreloids), and, of course, in somatosensory cortex (barrels). The authors used extracellular recording to sample whisker-sensitive cells in the thalamus. Cells in the head of barreloids received input from the principal trigeminal nucleus and were sensitive to multiple whiskers. These thalamic cells also received corticothalamic input from the vibrissa motor cortex. The new pathway is thus in position to get those five rows of whiskers in synch during whisking.



The image shows a labeled neuron in the head of a thalamic barreloid. The cell was activated by multiple whiskers and by stimulation of the motor cortex. See the article by Urbain et al. for details.

♦ Neurobiology of Disease

Parkin Rescue of PINK1 Deficiency

Nicole Exner, Bettina Treske, Dominik Paquet, Kira Holmström, Carola Schiesling, Suzana Gispert, Iria Carballo-Carbajal, Daniela Berg, Thomas Gasser, Rejko Krüger, Konstanze F. Winklhofer, Frank Vogel, Andreas S. Reichert, Georg Auburger, Philipp J. Kahle, Bettina Schmid, and Christian Haass

(see pages 12413–12418)

Although most cases of Parkinson's disease (PD) are sporadic, the genes involved in the rare familial cases continue to be instructive. Exner et al. focused on PD-related mitochondrial abnormalities. Mutations in phosphatase and tensin homolog (PTEN)-induced kinase 1 (PINK1) have been linked to juvenile parkinsonism, but the substrates for this kinase remain unknown. PINK1 does contain a mitochondrial targeting sequence, providing a putative link to PD. The authors report that RNAi knockdown of PINK1 in human cell lines resulted in fragmented mitochondria with reduced membrane potential. Low glucose reversibly worsened the condition. Two PINK1 mutations, Q126P and G309D, did not rescue the phenotype. However, expression of wild-type but not mutant parkin overcame the mitochondrial morphological changes. Cultured primary fibroblasts from patients with the two PINK1 mutations also contained fragmented mitochondria. The authors suggest that parkin may act as a stress-protection mechanism in the face of a PINK1 deficiency.