This Week in The Journal

● Cellular/Molecular

Trafficking DAT

Tatiana Sorkina, Manuel Miranda, Kalen R. Dionne, Brian R. Hoover, Nancy R. Zahniser, and Alexander Sorkin

(see pages 8195–8205)

Sorkin et al. set out to track endocytosis of the dopamine transporter (DAT) by creating a mutant transporter with a hemagglutinin (HA) epitope-tag in the large extracellular loop. The authors then followed uptake with an HA antibody in a so-called antibody feeding assay. Although DAT undergoes constitutive and PKC-dependent cycling via clathrin-coated pits, it lacks conventional internalization sequences. The authors tested whether ubiquitination of DAT could serve as an internalization signal. They screened a library of small interfering RNAs (siRNAs) against endocytic proteins in HeLa cells stably expressing YPF-HA-DAT. Not surprisingly, clathrin heavy chain and dynamin emerged from the screen as molecules critical for endocytosis. Knockdown of the ubiquitin ligase Nedd4-2 (neural precursor cell expressed, developmentally downregulated 4-2) also reduced endocytosis, consistent with the idea that PKC-induced DAT ubiquitination by Nedd4-2 accelerates endocytosis.

▲ Development/Plasticity/Repair

Slits in the Retina

Hannah Thompson, Olivier Camand, David Barker, and Lynda Erskine

(see pages 8082–8091)

The Slit family of guidance molecules acts through their Roundabout (Robo) receptors to influence axon pathfinding. This week, Thompson et al. show that Slits help restrict the retinal ganglion cell (RGC) axons to the optic fiber layer (OFL) in the ventral retina, but in dorsal retina they affect the orderly growth of axons within the OFL. RGCs expressed *slit1* and *slit2*, both of which are chemorepellant for RGC axons. In wild-type and *slit1*-deficient embryonic mice, RGC axons were restricted to the OFL, but in mice lacking *slit2* or *slit1* and *slit2*, some axons strayed away from the OFL toward the outer retina. Interestingly, this aberrant patterning was twice as common in axon bundles of the ventral retina compared with the dorsal retina. In mice lacking *slit2*, pathfinding errors occurred within the OFL, but only in the dorsal retina.

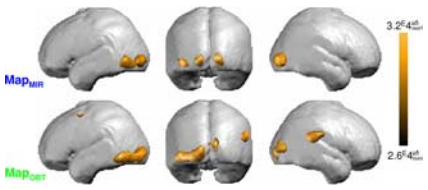
■ Behavioral/Systems/Cognitive

Finding Yourself in Your Own Brain

Shahar Arzy, Gregor Thut, Christine Mohr, Christoph M. Michel, and Olaf Blanke

(see pages 8074–8081)

The feeling of being in one's body requires neural processing in two separate brain areas: the temporoparietal junction (TPJ), which processes the concept of "self," and the extrastriate body area (EBA), dedicated to recognition of human bodies and even body parts. Arzy et al. used evoked potential mapping to examine the tasks performed by each of these areas. Subjects performed an own-body transformation (OBT) task, in which they imagined themselves in the orientation of a schematically presented body, and a mirror (MIR) task in which subjects imagined that the figure was their reflection. The tasks differed subtly in that the OBT task required a disembodied-self location, whereas the MIR task retained their normally embodied position. The sites and timing of activation also differed. Embodied-self location tasks activated the left EBA at 318 ms, which was influenced by whether the subject was seated or supine. The disembodied task activated the right TPJ and left EBA at ~367 ms.



Generators of evoked potentials were localized at the left EBA for the MIR task (top row) but at the right TPJ and left EBA for the OBT task (bottom row). See Arzy et al. for details.

♦ Neurobiology of Disease

The Immune Response in PLP-Overexpressing Mice

Chi Wang Ip, Antje Kroner, Martin Bendszus, Christoph Leder, Igor Kobsar, Stefan Fischer, Heinz Wiendl, Klaus-Armin Nave, and Rudolf Martini

(see pages 8206–8216)

This week, Ip et al. examined mice that overexpress the myelin component proteolipid protein (PLP) and display late-onset demyelination. The authors report that primary glial damage caused a secondary immune response that contributes to the pathology. CD8-expressing T-lymphocytes were upregulated in the PLP transgenic mice, and the T-cells were closely associated with major histocompatibility complex I (MHC-I). The authors surmised that MHC-I+ mutant oligodendrocytes were targeted by T-cells. Flow cytometry experiments confirmed that the brain CD8+ cells were activated mature effector cells. The authors crossed the PLP mice with mice deficient for recombination activating gene-1 (RAG-1) that lack mature T- and B-lymphocytes. Demyelination was reduced in these mice, an effect that was reversed by implantation of CD8+/CD4− bone marrow, indicating that the CD8+ lymphocytes are important to the secondary immune response. The authors suggest that this pattern of secondary, rather than primary, inflammatory/immune response may also underlie some subtypes of multiple sclerosis.