This Week in The Journal

● Cellular/Molecular

A Killer Potassium Channel

Christopher B. Fordyce, Ravi Jagasia, Xiaoping Zhu, and Lyanne C. Schlichter
(see pages 7139–7149)

Microglia, the resident immune cells of the brain, are important determinants of CNS inflammation. They play defense in the healthy brain, but microglial activation can also lead to neuronal injury or death. The microglial potassium channel Kv1.3 is involved in microglial proliferation and in the respiratory burst that generates reactive oxygen species such as superoxide; thus Fordyce et al. examined the role of Kv1.3 in microglial-induced neuronal death. The authors used a Transwell culture system in which microglia were activated in a separate chamber and then cocultured with neurons. Expression of microglial Kv1.3 currents increased in activated microglia, whereas block of Kv1.3 reduced the respiratory burst as well as microglia-induced neuronal death. Consistent with an oxidative injury mechanism, peroxynitrite, a toxic product of superoxide and nitric oxide, was involved. However, the Kv1.3-dependent cell-death pathway was independent of the p38 mitogen-activated protein kinase pathway, suggesting that multiple pathways can participate in microglial-induced neurotoxicity.

▲ Development/Plasticity/Repair

Ephrin/Eph Expression in the Human Visual System

Marie-Alexandra Lambot, Fanny Depasse, Jean-Christophe Noel, and Pierre Vanderhaeghen
(see pages 7232–7237)

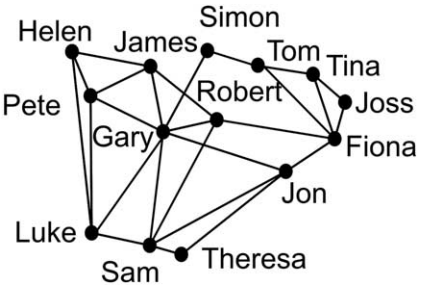
Molecular gradients control retinotopic maps in the primarily monocular visual systems that have been examined. This week, Lambot et al. extend these studies to the human fetal retina, we humans being a binocular species. The authors looked at mRNA expression gradients of ephrin/Eph in the retina and in the dorsal lateral geniculate nucleus (dLGN) when retinal fibers first arrive (week 7) and when ipsilateral and contralateral fibers segregate (week 20). Unlike in the bird or mouse, the developing human retina expressed EphA5 and EphA6 in a bidirectional gradient, with peak expression in the center tapering toward nasal and temporal poles. Ephrin-A5 showed complementary expression. Ephrin-B1, which directs the limited ipsilateral projection in the frog and mouse, was highly expressed throughout the temporal retina but abruptly shifted to low levels in the nasal retina. The dLGN was similar to that of the mouse, with single, complementary gradients of ephrin-A5 and EphA7. The difference in retinal gradients in humans is consistent with binocular organization.

■ Behavioral/Systems/Cognitive

Using Your Hippocampus to Find Your Friends

Dharshan Kumaran and Eleanor A. Maguire
(see pages 7254–7259)

This week, Kumaran and Maguire explore two competing theories of hippocampal function. The cognitive map theory argues that the hippocampus constructs and maintains spatial maps of the environment. In contrast, the relational theory views hippocampal associations as representing nonspatial information. The authors asked subjects to optimize two routes: that between their friends' homes and that between the same friends within their social network. The task was to get a virtual crate of wine from person A to person B, seemingly a critical task for the subjects, male university students in London. When subjects mentally navigated the crate within London, functional magnetic resonance imaging showed that the hippocampus was activated along with parahippocampal, retrosplenial, and posterior parietal areas. In contrast, sending the crate through the social network activated the medial prefrontal cortex, insula, superior temporal sulcus, posterior cingulate cortex, temporoparietal junction, and temporal poles, but not the hippocampus. Thus these data favor the cognitive map theory.



Schematic representation of a subject's network of friends. Lines indicate that two people know each other. The spatial arrangement of names represents their relative location in London. See the article by Kumaran and Maguire for details.

♦ Neurobiology of Disease

A Spine-Free Zone around Amyloid Plaques

Tara L. Spires, Melanie Meyer-Luehmann, Edward A. Stern, Pamela J. McLean, Jesse Skoch, Paul T. Nguyen, Brian J. Bacskai, and Bradley T. Hyman
(see pages 7278–7287)

Whether amyloid plaques themselves play a causal role in Alzheimer's disease is still under debate. One possibility is that plaques themselves affect synaptic function. This week, Spires et al. used multiphoton imaging *in vivo* to look for morphological changes in synapses. They used transgenic mice (Tg2576; 21–24 months of age) overexpressing amyloid precursor protein (APP). To label neurites, they injected an adeno-associated viral green fluorescent protein (GFP) construct into somatosensory cortex. Several weeks later, they imaged GFP-labeled neurites near methoxy-XO4-stained plaques. Although there was no significant decrease in synapses in the region of plaques (i.e. within 100 μm or so), there was an increase in swollen (dystrophic) neurites and a decrease in dendritic spines. Only a few of the dystrophic neurites were spiny dendrites; the vast majority were either axons or aspiny dendrites. Weekly imaging of the same cortical region revealed that the dendrites and plaques were stable for periods of several weeks.