This Week in The Journal

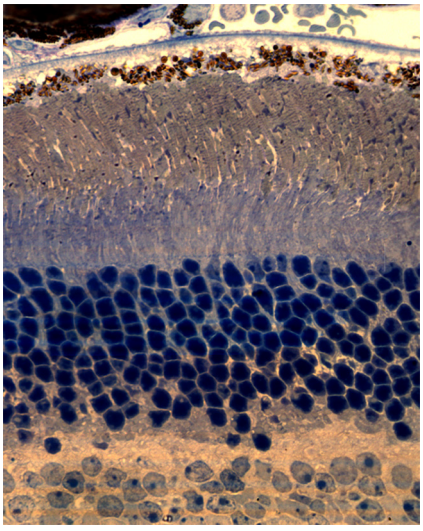
● Cellular/Molecular

Increased Variance in Dark Current Reduces Rod Sensitivity

Alexander V. Kolesnikov, Jie Fan, Rosalie K. Crouch, and Vladimir J. Kefalov

(see pages 11222–11231)

As people age, their visual acuity, night vision, dark adaptation, and contrast sensitivity deteriorate. This decline results partly from loss of rods, but other processes underlying these phenotypes are poorly understood. To determine whether age-related vision loss in mice is similar to that in humans, Kolesnikov et al. compared photoreceptor electrophysiology, morphology, and photopigment levels in old and young mice. Like in humans, visual acuity and contrast sensitivity under bright light were maintained in old mice, indicating that cone function was unimpaired, whereas both measures deteriorated under dim light, indicating rod dysfunction. The number of photoreceptors and the length and width of rod outer segments decreased with age, and responses to light were correspondingly reduced. Increased variance in dark current (reflecting the number of cGMP channels open at rest) in surviving rods accounted for most of their reduced sensitivity. Unlike in humans, however, dark adaptation was unimpaired in old mice; likewise, the visual cycle was unaffected by aging.



Section of retina from 2.5-year-old mouse, stained with toluidine blue. Age-related vision loss in mice exhibits many features of that in humans. See the article by Kolesnikov et al. for details.

▲ Development/Plasticity/Repair

Ectopic Reelin Expression Induces Neuronal Migration

Ken-ichiro Kubo, Takao Honda, Kenji Tomita, Katsutoshi Sekine, Kazuhiro Ishii, et al.

(see pages 10953–10966)

Neocortical projection neurons are generated near the ventricles and migrate outward to form the cortical layers. The first-born neurons form the preplate, which subsequently splits to form the outer Cajal–Retzius layer and the inner subplate. Later-born neurons migrate through the subplate and previously generated neurons, stopping at the marginal zone beneath the Cajal–Retzius layer. This inside-out pattern of development is shaped in part by Reelin, a protein secreted by Cajal–Retzius cells. Loss of Reelin causes inversion of the cortical layers, as later-born neurons do not migrate past previously generated ones. The precise role of Reelin has been unclear, however. Kubo et al. report that ectopic expression of Reelin in developing mouse cortex attracted migrating neurons, causing their somata to aggregate in a sphere around a Reelin-rich, somata-poor center resembling the marginal zone. Furthermore, later-born neurons migrated past earlier-born neurons in these spheres, indicating that Reelin expression can, by itself, reproduce key features of cortical development.

■ Behavioral/Systems/Cognitive

Visual Stimuli Produce Synchronous Activity Across Cortical Areas

Inbal Ayzenshtat, Elhanan Meirovithz, Hadar Edelman, Uri Werner-Reiss, Elie Bienenstock, et al.

(see pages 11232–11245)

As we observe our surroundings, information from across the visual field is carried in parallel streams to separate cortical regions, which process different features such as shape and motion. Despite this distributed processing, we form coherent perceptions of individual objects. Near-synchronous firing across multiple cortical regions has been proposed to underlie binding of features related to each object. Although such synchrony has been recorded, whether it is necessary for binding remains controversial. To bolster the binding-by-synchrony hypothesis, Ayzenshtat et al. used voltage-sensitive dyes to simultaneously measure—with high temporal resolution—the activity of many neuronal populations in areas V1, V2, and V4 of monkey visual cortex. Many pairs and triplets of populations, both within and between cortical areas, repeatedly exhibited correlated activity that occurred at short, fixed time intervals. Together, these patterns contained sufficient information to distinguish whether they were produced in response to coherent or scrambled faces.

♦ Neurobiology of Disease

Memantine Preferentially Blocks Extrasynaptic NMDA Receptors

Peng Xia, H.-S.-Vincent Chen, Dongxian Zhang, and Stuart A. Lipton

(see pages 11246 –11250)

Prolonged activation of NMDA receptors (NMDARs) causes large increases in intracellular calcium, leading to mitochondrial dysfunction, oxidative stress, protease activation, and ultimately cell death. Hyperactivation of NMDARs is thought to underlie cell death in several neuropathological conditions, including stroke and Alzheimer's disease. But normal activation of NMDARs—in addition to being essential for memory and other cognitive functions—activates anti-apoptotic signaling cascades and enhances antioxidant activity, thus promoting cell survival. Therefore, nearly all NMDAR antagonists tested for therapeutic value produce unacceptable side effects, including increased cell death. One exception is memantine, which is used to treat Alzheimer's disease. Memantine binds to open NMDARs with low affinity and rapid off rate, and thus effectively blocks the receptors only during prolonged activation. Normal synaptic transmission is generally spared, likely because glutamate concentration in the synaptic cleft is elevated only briefly. Indeed, Xia et al. now show that memantine preferentially blocks extrasynaptic NMDARs in autaptic cultures of rat hippocampal neurons.