This Week in The Journal

● Cellular/Molecular

NMDA Receptor Activation Increases Amacrine Cell Coupling

W. Wade Kothmann, E. Brady Trexler, Christopher M. Whitaker, Wei Li, Stephen C. Massey, et al.

(see pages 6747–6759)

AII amacrine cells, part of the rod photoreceptor pathway, can form extensive electrically coupled networks depending on ambient light levels. The cells are relatively uncoupled in total darkness, but coupling increases with light levels until illumination reaches photopic levels, when coupling strength returns to baseline. The increase in coupling parallels phosphorylation of the gap junction protein connexin 36 (Cx36), and dopamine-dependent dephosphorylation of Cx36 in bright light reduces coupling strength. What drives Cx36 phosphorylation in dim light was hitherto unknown, but Kothmann et al. answer this question as well as another: given that NMDA receptors (NMDARs) are not located near glutamatergic synapses in AII amacrines, what do the NMDARs do? It turns out that NMDARs and the calcium-dependent kinase CaMKII colocalize with Cx36 in AII amacrines. Stimulating NMDARs increased Cx36 phosphorylation in dark-adapted rabbit retinas, whereas inhibiting NMDARs or CaMKII in light-adapted retinas caused dephosphorylation, indicating that these proteins regulate amacrine coupling strength.

▲ Development/Plasticity/Repair

Semaphorin and Plexin Confine Horizontal Cell Axons to OPL

Ryota L. Matsuoka, Zheng Jiang, Ivy S. Samuels, Kim T. Nguyen-Ba-Charvet, Lu O. Sun, et al.

(see pages 6859–6868)

In the retina's outer plexiform layer (OPL), photoreceptor terminals form ribbon synapses with bipolar and horizontal cells. Dendrites and axons of horizontal cells are confined to the OPL—the former contacting cones and the latter contacting rods—and they are thought to mediate lateral inhibition. Stratification of the OPL during development depends largely on glutamatergic signaling from photoreceptors: if release is prevented, neurites from rods, and bipolar and horizontal cells grow ectopically in the outer nuclear layer (ONL). Matsuoka et al. show that stratification of mouse horizontal cell neurites also depends on signaling by semaphorin 6A (Sema6a) and its receptor plexin A4 (PlexA4). Knocking out either protein allowed horizontal cell axons to grow through the ONL. As a result, many rod ribbon synapses contained only one horizontal cell axon, instead of the normal two. Although horizontal cell dendrites remained confined to the OPL in mutant mice, they did not exhibit self-avoidance like wild-type dendrites.

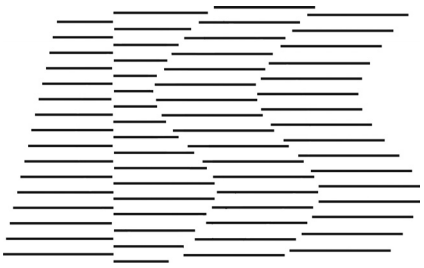
■ Behavioral/Systems/Cognitive

V4 Neurons Respond to Real and Illusory Contours

Yanxia Pan, Minggui Chen, Jiapeng Yin, Xu An, Xian Zhang, et al.

(see pages 6760–6770)

Neurons in visual cortical areas V1, V2, and V4 respond preferentially to lines of particular orientations. The brain represents object contours by combining the responses of many such neurons. Orientation-selective neurons also respond to illusory contours created by some stimuli (Figure). To identify the cortical level at which neurons respond to illusory contours as if they were real, Pan et al. detected responses to real and illusory gratings across V1, V2, and V4 using optical imaging, and then compared orientation maps for each stimulus type. The response profiles for real and illusory gratings precisely overlapped only in V4, remaining closely matched even when the inducing lines were orthogonal to the illusory contours and would thus be expected to preferentially activate a distinct set of orientation-selective neurons. Single-unit recordings confirmed that most cells that responded preferentially to a moving bar of a given orientation responded maximally to illusory contours of the same orientation.



Precise alignment of black lines creates illusory contours across which no actual luminance change exists. Illusory and real contours are detected by the same neurons in V4. See the article by Pan et al. for details.

♦ Neurobiology of Disease

Reduction of PGC-1α Increases Extrasynaptic NMDA Currents

Clare Puddifoot, Marc-Andre Martel, Francesc X. Soriano, Alberto Camacho, Antonio Vidal-Puig, et al.

(see pages 6995–7000)

Mutant huntingtin protein (mHtt) promotes neuronal death in part by reducing expression of the transcriptional coactivator PGC-1α, which regulates transcriptional programs involved in mitochondrial biogenesis. In addition, expression of mHtt enhances extrasynaptic NMDA receptor (eNMDAR) currents, which also suppress PGC-1α. Furthermore, although activation of synaptic NMDARs limits the effects of mHtt by promoting its aggregation in cytoplasmic inclusions, activation of eNMDARs increases mHtt toxicity, partly by inducing disaggregation. Puddifoot et al. now report that suppression of PGC-1α activity further amplifies these effects by increasing eNMDAR current. Knocking down PGC-1α in cultured rat neurons increased eNMDAR currents and NMDA-induced excitotoxicity, whereas expression of exogenous PGC-1α reduced extrasynaptic currents and protected neurons from excitotoxicity. Overexpression of PGC-1α also prevented mHtt-induced increases in eNMDAR currents, suggesting mHtt increases the latter by suppressing the former. PGC-1α is suppressed in Alzheimer's and Parkinson's diseases, so its enhancement of eNMDAR currents might contribute to neurodegeneration in those diseases as well as Huntington's.