This Week in The Journal

● Cellular/Molecular

P2X$_2$ and ACh Receptors, Up Close and Personal

Baljit S. Khakh, James A. Fisher, Raad Nashmi, David N. Bowser, and Henry A. Lester
(see pages 6911–6920)

Functional interactions between receptors or channels are usually attributable to indirect modulatory effects triggered by ion fluxes or second messenger pathways. However, a more direct interaction has been suggested for P2X ATP receptors with nicotinic acetylcholine receptors. This week, Khakh et al. report that the cross-inhibition between $P2X_2$ and $\alpha_4\beta_2$ nicotinic receptor channels likely results from dimer formation between these multisubunit complexes. The authors used two fluorescent methods, fluorescence resonance energy transfer (FRET) and total internal reflection fluorescence (TIRF), to measure the spacing between the two receptors with YFP (yellow fluorescent protein)- and CFP (cyan fluorescent protein)-labeled subunits. They observed FRET between the tagged β_2 nicotinic subunit and tagged $P2X_2$. In neurons, FRET was stronger in hippocampal than ventral midbrain neurons, presumably because of the degree of colocalization of the two receptors in hippocampal neurons. The authors calculate that the distance between $P2X_2$ and α_4 is ~80–100 Å, and even closer (60 Å) for the β_2 subunit.

▲ Development/Plasticity/Repair

Wave Action in the Retinocollicular Pathway

Thomas D. Mrsic-Flogel, Sonja B. Hofer, Claire Creutzfeldt, Isabelle Cloëz-Tayarani, Jean-Pierre Changeux, Tobias Bonhoeffer, and Mark Hübener
(see pages 6921–6928)

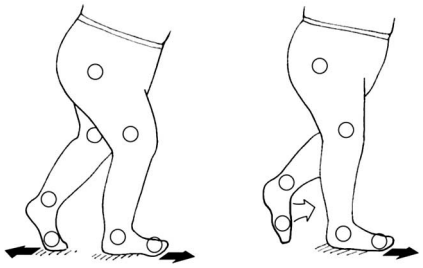
Early waves of activity in the developing retina influence connectivity between retinal ganglion cells and neurons of the superior colliculus (SC) and thereby refine collicular topography. In this week's *Journal*, Mrsic-Flogel et al. set out to visualize the retinotopic map formed in the absence of retinal waves. Whereas the waves are thought to be crucial for fine-tuning of the map, the initial layout relies heavily on axonal guidance molecules. The authors made use of mice lacking the $\beta2$ nicotinic acetylcholine subunit, because early retinal waves are absent in these animals. The mice had significant retinotopic defects as detected in intrinsic optical SC activity evoked by visual stimulation. In $\beta2^{-/-}$ mice, active patches were much larger and had less defined borders compared with wild-type mice. The SC map was also distorted, with anterior elongation and posterior compression. Thus, even the coarse retinotopic map is affected by early retinal activity.

■ Behavioral/Systems/Cognitive

Infants on Treadmills

Jaynie F. Yang, Erin V. Lamont, and Marco Y. C. Pang
(see pages 6869–6876)

Rhythmic locomotor patterning is often studied in beasts ranging from insects to crayfish and on to lampreys and cats. This week, Yang et al. give human infants a first taste of walking while at the same time serving as experimental subjects. The infants kindly allowed their parents to sign the informed consent. Infants (5–11 months), none of whom were yet able to walk independently, were supported under the arms by an adult while their fledgling steps were videotaped on a split-belt treadmill. Most infants were able to step with both belts running the same speed, or even different speeds. In the latter case, the step rate increased on the faster of the two belts. When the belts were running in different directions, one leg stepped forward and the other stepped backward. Although the results are consistent with autonomous pattern generation in each half of the spinal cord, there was also evidence for coordination between limbs.



Sketches from the video frames of an infant stepping on a split treadmill. See the article by Yang et al. for details.

♦ Neurobiology of Disease

Targeting Bcl-x in TH-Positive Neurons

Joseph M. Savitt, Susie S. Jang, Weitong Mu, Valina L. Dawson, and Ted M. Dawson
(see pages 6721–6728)

Bcl-x_L, an antiapoptotic gene product of *Bcl-x*, is upregulated in the surviving dopaminergic neurons in Parkinson's disease, making it of interest as a neuronal survival factor. This week, Savitt et al. used the Cre-lox system to narrow in on the role of Bcl-x in catecholaminergic neurons. The authors deleted Bcl-x selectively from tyrosine hydroxylase (TH)-positive neurons. The transgenic mice were viable but had one-third fewer catecholaminergic neurons, including dopaminergic neurons of the substantia nigra pars compacta and noradrenergic neurons of the locus ceruleus. Thus, the development and survival of catecholaminergic neurons depend on endogenous Bcl-x. Brain levels of dopamine and its metabolites were also reduced, as was overall brain mass. As expected, most surviving dopaminergic neurons expressed Bcl-x_L, but a few TH-positive neurons survived without Bcl-x. Because the TH promoter does not turn on until embryonic day 9, Bcl-x may have been present during a critical early period in those surviving neurons.