This Week in The Journal

● Cellular/Molecular

Two Distinct Glutamate Signals in Bergmann Glia

Ko Matsui and Craig E. Jahr
(see pages 8932–8939)

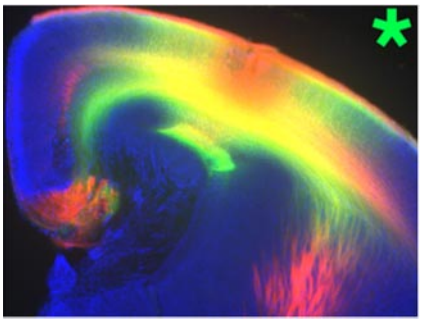
Synaptic transmission used to be simple: transmitter was released from axonal terminals and activated immediately adjacent postsynaptic receptors. Life got more complicated when it became clear that transmitter could be released from some dendrites and glia as well and could spill over to extrasynaptic membranes, to other synapses, or onto glial cells. Recently Matsui and Jahr reported a new form of neuronal–glial glutamate signaling. At the cerebellar climbing fiber synapse, they found that glutamate released from sites outside the active zone, called "ectopic" release, could activate Bergmann glial cells (BGs). This week they further define the features of this rapid neuronal–glial signaling. The ectopic release onto BGs showed marked paired-pulse depression and greater dependence on N-type calcium channels than conventional release onto Purkinje cells. The authors suggest that the local high concentrations of glutamate ectopically released onto BGs regulate the glial encasement of cerebellar synapses. This signal may get BGs in position to use their glutamate transporters to mop up transmitter around conventional synapses.

▲ Development/Plasticity/Repair

Forming Intracortical Projections

Kelly J. Huffman, Sonia Garel, and John L. R. Rubenstein
(see pages 8917–8923)

The neocortex is organized into areas with distinct functions, and this organization requires not only segregation of these areas but appropriate connectivity between and within cortical areas. The areas arise according to instructions from molecules such as FGF8, which is secreted in the rostral telencephalon during development. Although the *Fgf8* hypomorphic mutant mouse displays disordered neocortical patterning, thalamocortical projections are essentially intact, presumably because the latter rely on factors external to the cortex. This week Huffman et al. explore the generation of the intracortical wiring diagram. They used the retrograde-transported dyes DiA and DiI to compare projections from rostral and caudal regions. *Gbx2* mutants lacked thalamocortical projections but had appropriate intracortical projections. In contrast, in *Fgf8* hypomorphic mutants, caudal projections broke out of their intended regions. Thus formation of intracortical and thalamocortical connectivity appears to be under separate developmental control mechanisms.



Fgf8$^{neo/neo}$ mutants showed an abnormal pattern of intracortical projections, indicated by overlap labeling (yellow) of rostral and caudal placement of the dyes DiI (red) and DiA (green), respectively. See the article by Huffman et al. for details.

■ Behavioral/Systems/Cognitive

Hemodynamic Control by Single Cortical Interneurons

Bruno Cauli, Xin-Kang Tong, Armelle Rancillac, Nella Serluca, Bertrand Lambolez, Jean Rossier, and Edith Hamel
(see pages 8940–8949)

It makes sense that neuronal activity should be linked somehow to vascular perfusion, the source of necessary oxygen and glucose. In fact this relationship is the basis of functional neuroimaging. But how does it happen at the cellular level? This week, Cauli et al. use a meticulous combination of techniques to document that GABAergic interneurons locally integrate signals to microvessels. The authors used biocytin labeling and single-cell reverse transcriptase-multiplex PCR in rat cortical slices to characterize the morphology, electrophysiology, and peptide content of neurons contacting blood vessels. Although the cortex contains a diverse mix of interneurons, "vasomotor" neurons aggregated around the microvessels. Action potentials in single interneurons that expressed vasoactive intestinal peptide or nitric oxide synthase caused vessels to dilate, whereas those expressing somatostatin caused contraction. Vasoactive interneurons were innervated by serotonergic or cholinergic afferents, suggesting that the vasomotor interneurons can transduce neural activity into tight temporal and spatial control of cortical microvessels.

♦ Neurobiology of Disease

A Mouse Model of a Childhood Storage Disease

David E. Sleat, Jennifer A. Wiseman, Mukarram El-Banna, Kwi-Hye Kim, Qinwen Mao, Sandy Price, Shannon L. Macauley, Richard L. Sidman, Michael M. Shen, Qi Zhao, Marco A. Passini, Beverly L. Davidson, Gregory R. Stewart, and Peter Lobel
(see pages 9117–9126)

Neurodegenerative disorders are cruel at any age, but when they occur at the beginning of life their impact extends well beyond their relatively rare occurrence. Classical late-infantile neuronal ceroid lipofuscinosis (cLINCL) is one of the inherited lysosomal storage diseases, caused by mutations in the gene for tripeptidyl-peptidase I, a lysosomal serine protease. Autofluorescent material accumulates in neuronal lysosomes; affected children have seizures followed by blindness, ataxia, and death. Sleat et al. targeted the *CLN2* gene to create the first mouse model of cLINCL. The mice appeared healthy at birth, but by 7 weeks of age they developed constant tremors, followed by worsening locomotor abnormalities and premature death at 4–5 months. The cellular histopathology mimicked the human disease, with cytoplasmic autofluorescence inclusions and neurodegeneration in the brain, spinal cord, and periphery. Given the lack of effective treatments for cLINCL, this model may allow testing of future therapeutic strategies.