This Week in The Journal

● Cellular/Molecular

Voltage-Sensitive Dyes Can Enhance GABA Currents

Steven Mennerick, Mariangela Chisari, Hong-Jin Shu, Amanda Taylor, Michael Vasek, *et al.*

(see pages 2871–2879)

Voltage-sensitive dyes are powerful tools for studying neuronal activity, allowing researchers to record interactions between many individual neurons in a network, as well as measure changes in voltage across compartments of single cells. The value of voltage-sensitive dyes, however, has been limited by several factors, including low signal-to-noise ratio, which often necessitates averaging across trials to detect activity; slow kinetics, which limits the ability to resolve individual spikes in a burst; difficulty in loading dyes into tissue; and toxicity at high concentrations. Mennerick et al. now report an additional limitation that must be considered when choosing and designing voltage-sensitive dyes. They found that several such dyes potentiate $GABA_A$ receptor currents. Specifically, Di-4-ANEPPS and DiBAC4(3) potentiated baseline currents in transfected oocytes and cultured hippocampal neurons. Other dyes—Di-8-ANEPPS and ANNINE 6plus—did not potentiate baseline GABA responses but did enhance responses upon excitation with light. Such potentiation could alter spiking patterns in neuronal networks.

▲ Development/Plasticity/Repair

Zebrafish Lack an External Germinal Layer

Natalie Chaplin, Christian Tendeng, and Richard J. T. Wingate

(see pages 3048–3057)

In the earliest stages of cerebellar development in mice, granule cell precursors are generated at the edges of an opening on the dorsal surface of the neural tube, called the rhombic lip. Unlike other neuronal precursors, primary granule cell precursors migrate along the outer surface of the neural tube, forming the external germinal layer. Later, these cells undergo extensive proliferation on the surface of the brain and migrate inward to form the granule cell layer, which helps define the basic organization of the cerebellum. Similar patterns of cerebellar development occur in birds and reptiles. As demonstrated by Chaplin et al., however, an external germinal layer does not form in zebrafish or sharks. Instead, the expression pattern of a specific marker of granule cell precursors suggests that a population of these cells is maintained along the cerebellar midline during development in fish, and granule cells migrate tangentially from this region.

■ Behavioral/Systems/Cognitive

Fatty Acid Binding Protein Modulates D_2 Dopamine Receptors

Norifumi Shioda, Yui Yamamoto, Masahiko Watanabe, Bert Binas, Yuji Owada, and Kohji Fukunaga

(see pages 3146–3155)

Fatty acid binding proteins (FABPs) are cytoplasmic proteins that bind long-chain fatty acids to facilitate transport through the aqueous intracellular environment. Unlike proteins that transport other lipids, FABPs comprise a family of tissue-specific homologs suggesting that they have tissue-specific functions. Although originally identified in heart, heart-type FABP (H-FABP) is also highly expressed in neurons, where it is important for incorporation of arachidonic acid into membranes. Shioda et al. found that H-FABP bound to D_2 dopamine receptors (D2Rs) in brain extracts and that the proteins were colocalized in cholinergic neurons and glutamatergic terminals in the dorsal striatum of mice. Overexpression of H-FABP increased activation of downstream effectors of D2Rs in transfected neuroblastoma cells, suggesting H-FABP enhances D2R function. In striatal cholinergic neurons, D2R activation reduces acetylcholine release whereas blocking D2Rs increases acetylcholine release. This effect was greater in mice lacking H-FABP, consistent with a role for H-FABP in D2R function.

♦ Neurobiology of Disease

Mid1 *Knock-out Models Cerebellar Defect of Opitz BBB/G Syndrome*

Alessio Lancioni, Mariateresa Pizzo, Bianca Fontanella, Rosa Ferrentino, Luisa M. R. Napolitano, *et al.*

(see pages 2880–2887)

Opitz BBB/G syndrome results from abnormal development of ventral midline structures and is generally characterized by wide-spaced eyes, defects in larynx, trachea and/or esophagus, and sometimes by cleft lip and malformation of the cerebellar vermis. An X-linked form of the disease results from loss of function of midin, a ubiquitin ligase encoded by *MID1*. Midin is thought to tag microtubule-associated protein phosphatase 2A for degradation, thereby regulating the activity of other microtubule-associated proteins and thus microtubule dynamics. To study how defects in MID1 cause developmental defects, Lancioni et al. knocked out *Mid1* in mice. *Mid1* knock-out resulted in hypoplasia of the anterior portion of the cerebellar vermis, as well as diminished motor coordination, delayed motor learning, and reduced habituation of the startle reflex. The cerebellar defects arose embryonically and may have resulted from rostral displacement of the midbrain–hindbrain border and reduced expression of a fibroblast growth factor in this region.

Sagittal section through vermis shows defect (arrow) in anterior portion of mice lacking *Mid1* (right). See the article by Lancioni *et al.* for details.