This Week in The Journal

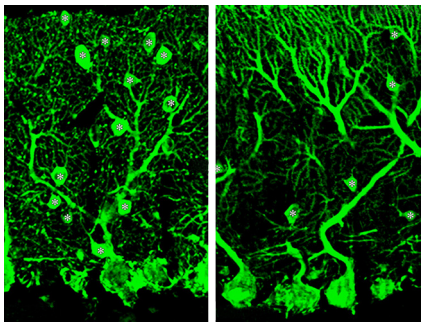
Cellular/Molecular

GluD1 and GluD2 Regulate Different Parallel-Fiber Synapses

Kohtarou Konno, Keiko Matsuda, Chihiro Nakamoto, Motokazu Uchigashima, Taisuke Miyazaki, et al.

(see pages 7412–7424)

Members of the δ subfamily of ionotropic glutamate receptors (GluD1 and GluD2) do not function as conventional glutamate-gated ion channels. Instead, GluD2 is expressed predominantly at synapses between parallel fibers and Purkinje cells, and it is essential for formation, maintenance, and long-term depression of these synapses; mutations in GluD2 cause cerebellar ataxia. Less is known about GluD1, but it induces synaptogenesis *in vitro*; GluD1-null mice have deficits in social behaviors and learning; and it is a candidate gene for schizophrenia, bipolar disease, and autism. Konno et al. report that GluD1 is strongly expressed in excitatory and/or inhibitory neurons in several brain areas, including cerebral cortex, hippocampus, striatum, and cerebellar cortex. In the cerebellum, GluD1 was predominantly expressed at synapses between parallel fibers and interneuron somata. In GludD1-null mice, the number of these synapses per unit of interneuron somatic membrane was approximately halved, and the density of interneurons was reduced by ~36%. Thus, GluD1 and GluD2 have complementary roles at different sets of parallel fiber synapses.



The density and somatic size of molecular layer interneurons (asterisks) was reduced in cerebellar cortex of GluD1-null mice (right) compared to wild-type (left). See the article by Konno et al. for details.

Development/Plasticity/Repair

Mst3 Affects Multipolar-to-Bipolar Transition

Jing Tang, Jacque P.K. Ip, Tao Ye, Yu-Pong Ng, Wing-Ho Yung, et al.

(see pages 7425–7436)

Cortical projection neurons are generated in the ventricular zone and migrate radially to the most superficial layer of the developing cortex. As the neurons pass through the intermediate zone, they extend multiple processes that continually extend and retract. When the neurons reach the cortical subplate, they retract all but their leading and trailing processes and continue their migration along radial glia fibers. The complete journey requires numerous rounds of cytoskeletal assembly and disassembly, which are coordinated by actin- and microtubule-binding molecules regulated by various kinases, phosphatases, and GTPases. Impairing the function of any of these molecules can disrupt migration, resulting in cortical layering defects. For example, Tang et al. discovered that Mst3 phosphorylates RhoA, a GTPase required for actin reorganization during migration. Knocking down Mst3 *in utero*, or preventing its phosphorylation by Cdk5, slowed the transition from multipolar to unipolar morphology. Although neurons eventually entered the cortical plate, they did not populate the correct cortical layer. Knocking down RhoA rescued these defects.

Systems/Circuits

Few Accumbal Neurons Are Required to Reinstate Drug Seeking

Fabio C. Cruz, Klil R. Babin, Rodrigo M. Leao, Evan M. Goldart, Jennifer M. Bossert, et al.

(see pages 7437–7446)

After rehab, addicts often return to their previous surroundings, where contextual cues provoke relapse. Similarly, if a rat is trained to self-administer a drug by pressing a lever in one context and lever-pressing is then extinguished in a new context, returning the rat to the original context will reinstate lever pressing. This reinstatement requires activation of neurons in the nucleus accumbens shell (NAcs). Using Fos expression as a measure, Cruz et al. found that a cocaine-associated context activated only ~3% of NAcs neurons, but these neurons were essential for reinstating drug seeking. To selectively inactivate this population, the prodrug Daun02—which inhibits action potentials after being activated by β-galactosidase—was injected into NAcs of rats in which β-galactosidase expression was driven by the c-fos promoter. This treatment reduced reinstatement of lever-pressing when rats were returned to the cocaine-associated context. In contrast, inactivating a larger subset of neurons after rats were placed in a novel environment did not affect reinstatement in the cocaine-associated context.

Behavioral/Cognitive

Rats Discriminate Salty before Sour or Bitter

Dustin M. Graham, Chengsan Sun, and David L. Hill

(see pages 7398 –7411)

How quickly can an animal discriminate tastes? In most studies of gustation, tastants are injected into the mouth, making it impossible to determine whether different tastes are perceived at different rates. Therefore, Graham et al. developed an apparatus that allowed head-restrained mice to acquire a fixed amount of liquid by licking a spout. Mice then learned to keep licking the spout if sucrose was delivered and to stop licking if NaCl, citric acid, or quinine (bitter) was delivered. The number of times a mouse licked on a stop trial was taken as the time required for discrimination. Mice required half the time (100 ms, or a single lick) to discriminate NaCl from sucrose as to discriminate quinine or acid from sucrose. Reaction times for discriminating NaCl or acid from distilled water were slower, and surprisingly, mice were unable to discriminate quinine from water. Thus, mice appeared to use "not sucrose" to aid discrimination in this task.