This Week in The Journal

● Cellular/Molecular

Counting GABA Release Sites and Active Zones

Ágota A. Biró, Noémi B. Holderith, and Zoltan Nusser

(see pages 12487–12496)

The tradition of quantal analysis of synaptic transmission, which began at the neuromuscular junction, is extended this week to the inhibitory synapse between cholecystokinin-expressing interneurons and hippocampal CA3 pyramidal cells. Biró et al. first determined the quantal amplitude and the number of functional release sites from measurements of unitary IPSCs. Next, they counted the number of boutons and active zones on nerve terminals by light and electron microscopy (EM). The authors report that things don't add up: they found many more functionally determined release sites than anatomically defined active zones as defined by three-dimensional EM reconstructions. Using kinetic modeling, the authors estimated that an approximately fivefold increase in the peak GABA concentration was required for the fivefold enhancement of the postsynaptic response at a single synapse, consistent with multivesicular release at each active zone when release probability is high.

▲ Development/Plasticity/Repair

β-Catenin Signaling in Cortical Precursors

Gregory J. Woodhead, Christopher A. Mutch, Eric C. Olson, and Anjen Chenn

(see pages 12620–12630)

They say that with evolution, us mammals got smarter, thanks to an increase in our cerebral cortex. A clue to the molecules involved in cortical expansion comes from transgenic mice overexpressing β-catenin, a component of the Wnt signaling pathway. These mice have enlarged brains with an increased cortical surface area, presumably because a greater proportion of transgenic cortical precursors reenter the cell cycle after mitosis, thereby enlarging the pool of precursor cells. This week, Woodhead et al. used cre-mediated gene excision *in utero* to knock out β-catenin in the ventricular zone of developing mouse embryos. The loss of β-catenin increased the number of precursors that exited the cell cycle early, differentiated into neurons, and migrated into the developing cortical plate. Inhibition of β-catenin-mediated signaling by expression of two different inhibitors gave similar findings. The results indicate a cell autonomous effect of β-catenin on precursors during cortical neurogenesis.

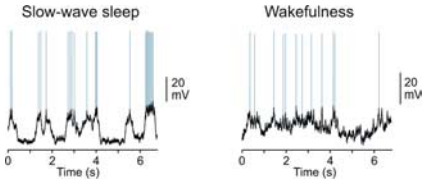
■ Behavioral/Systems/Cognitive

Awake Striatal Spinal Neurons—sans Ups and Downs

Séverine Mahon, Nicolas Vautrelle, Laurent Pezard, Seán J. Slaght, Jean-Michel Deniau, Guy Chouvet, and Stéphane Charpier

(see pages 12587–12595)

Ups and downs are part of daily life, but as Mahon et al. show this week, ups and downs may be mostly a part of nightly life for medium-sized spiny neurons (MSNs) in the striatum. The authors examined the activity of rat MSNs during wakefulness, slow wave sleep, and paradoxical sleep. Previous studies, largely carried out in anesthetized animals, had reported that MSNs undergo rhythmic membrane potential fluctuations between a hyperpolarized quiescent "down" state and a depolarized "up" state associated with action potential discharge. However, by obtaining intracellular recordings from MSNs free of anesthetic, the authors report that these rhythmic up and down shifts only occurred during slow-wave sleep. In the transition from sleep to wakefulness, striatal discharge switched to an irregular firing pattern. Because MSNs are the major input to basal ganglia, such state-dependent changes in firing patterns are likely to have a major influence on basal ganglia function.



The records show spontaneous intracellular activity of a striatal neuron during slow-wave sleep (left) and wakefulness (right). See Mahon et al. for details.

♦ Neurobiology of Disease

A Clue to Gender Influences on Depression

Lisa M. Hines, Paula L. Hoffman, Sanjiv Bhave, Laura Saba, Alan Kaiser, Larry Snell, Igor Goncharov, Lucie LeGault, Maurice Dongier, Bridget Grant, Sergey Pronko, Larry Martinez, Masami Yoshimura, and Boris Tabakoff; World Health Organization/International Society for Biomedical Research on Alcoholism Study on State and Trait Markers of Alcohol Use and Dependence Investigators

(see pages 12609–12619)

Studies have indicated that women are at greater risk for major depression than men. According to Hines et al. this week, a gene encoding a brain-specific adenylyl cyclase may help explain this gender difference. Based on evidence pointing to a role for cAMP signaling in depression, the authors genetically manipulated the AC7 isoform of adenylyl cyclase in the brains of mice, and then assayed the animals for "depression," i.e., immobility on the forced swim test and the tail suspension test. Female, but not male, AC7 transgenic or knockdown mice had respectively more or less depressive-like behavior than controls. But what is true for mice does not always apply to humans. In this case, however, the authors also report an association between polymorphisms in the human AC7 gene and an increased risk in women for "familial depression," defined as a history of depression in a first-degree relative.