This Week in The Journal

Cellular/Molecular
Spontaneous and Evoked Release Activate Different Receptors
Deniz Atasoy, Mert Ertunc, Krista L. Moulder, Justin Blackwell, ChiHyung Chung, Jianzhong Su, and Ege T. Kavalali
(see pages 10151–10166)

In resting neurons, single vesicles spontaneously fuse to the presynaptic membrane, releasing neurotransmitter that produces miniature EPSCs (mEPSCs). mEPSC amplitude is routinely used to estimate the number of vesicles released per action potential and the total number of vesicles per synapse. The validity of these measures depends on the assumption that spontaneous release activates the same postsynaptic receptors as evoked release—an assumption questioned this week by Atasoy et al. The authors applied (+)-5-methyl-10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5,10-imine maleate (MK-801), an antagonist that binds only to activated NMDA receptors, to rat hippocampal neurons in vitro. Applying MK-801 along with tetrodotoxin to block spiking quickly eliminated mEPSCs by blocking all available receptors. Nonetheless, subsequent stimulation evoked EPSCs. Conversely, applying MK-801 during stimulation blocked evoked EPSCs, but not subsequent mEPSCs. Additional experiments and computer models suggested that spontaneous and evoked release activate receptors with different opening probabilities that are distributed in different subregions of the synapse.

Development/Plasticity/Repair
GluR1 Shapes Dendritic Growth
Lei Zhang, Joachim Schessl, Markus Werner, Carsten Bonnemann, Guoxiang Xiong, Jelena Mojsilovic-Petrovic, Weiguo Zhou, Akiva Cohen, Peter Seeburg, Hidemi Misawa, Aditi Jayaram, Kirkwood Personius, Michael Hollmann, Rolf Sprengel, and Robert Kalb
(see pages 9953–9968)

During spinal cord development, motor neuron dendrites grow into neuropil, where they contact axons and form synapses, which leads to additional, activity-dependent arborization. Expression of the GluR1 AMPA receptor subunit in motor neurons is high during dendritic arborization and synaptic development; but expression decreases after connections have formed and dendritic structure stabilizes, suggesting that GluR1 may play a role in this process. In support of this hypothesis, Zhang et al. show that reducing GluR1 expression (via RNA inhibition or knock-out) reduced dendritic growth and branching. In knock-out mice, dendritic changes were accompanied by reductions in the number of premotor interneurons innervating motor neurons, and also in behavioral strength and endurance. Knock-out mice had more type I and fewer type II muscle fibers than controls, possibly resulting from changes in motor neuron firing. Nonetheless, no changes in electrical properties were found, suggesting the changes are subtle or GluR1 effects are activity independent.

Behavioral/Systems/Cognitive
Amygdala Encodes State Value on a Continuous Scale
Marina A. Belova, Joseph J. Paton, and C. Daniel Salzman
(see pages 10023–10030)

One role of the amygdala is to encode the positive or negative value of stimuli or conditions. Some amygdala neurons fire more when presented with positive stimuli, whereas others respond more to negative stimuli. Belova et al. extend this understanding of value coding by showing that individual amygdala neurons provide a continuous representation of value across different stimuli and different task states. They recorded from amygdala neurons in monkeys trained to associate different visual cues with a large liquid reward, a small liquid reward, or an aversive air puff. For all neurons, responses to stimuli associated with small rewards tended to fall between those associated with large rewards and those that signaled punishments. This suggests that amygdala neurons do not use binary coding of positive versus negative value, but rather code a value continuum from positive to negative.

Neurobiology of Disease
CaMKIV Overexpression Enhances Memory
Hotaka Fukushima, Ryouta Maeda, Ryousuke Suzuki, Akinobu Suzuki, Masanori Nomoto, Hiroki Toyoda, Long-Jun Wu, Hui Xu, Ming-Gao Zhao, Kenji Ueda, Aya Kitamoto, Nori Mamiya, Taro Yoshida, Seiichi Homma, Shoichi Masuhige, Min Zhuo, and Satoshi Kida
(see pages 9910–9919)

Local changes in phosphorylation and protein distribution can mediate short-term synaptic changes, but long-lasting changes require gene transcription. One pathway proposed to link synaptic activity to altered gene expression involves calcium/calmodulin-dependent protein kinase IV (CaMKIV). In this model, synaptic activity increases intracellular calcium levels, calcium binds to calmodulin, and the complex activates CaMKIV. CaMKIV then phosphorylates cAMP responsive element-binding protein (CREB), which binds to DNA and promotes transcription of specific plasticity-related genes. In this issue, Fukushima et al. provide strong evidence for a role of CaMKIV in plasticity, by demonstrating that increasing CaMKIV in forebrain of transgenic mice increased CREB activity, improved long-term recognition memory and fear conditioning, and increased long-term potentiation. Like in humans, CaMKIV expression decreased in aged mice, and decreased CaMKIV levels correlated with impaired learning. Intriguingly, memory deficits were erased by overexpression of CaMKIV in aged mice, making them perform similarly to younger wild-type mice.