

# This Week in The Journal

## ● Cellular/Molecular

### *Release Probability Is Low At Calyx of Held*

Jeannette A. M. Lorteije, Silviu I. Rusu, Christopher Kushmerick, and J. Gerard G. Borst

(see pages 13770–13784)

The calyx of Held synapse between cochlear nucleus neurons and neurons of the medial nucleus of the trapezoid body is an important relay in the sound localization system. Because its large size makes it possible to record presynaptic and postsynaptic action potentials simultaneously, this synapse is useful for studying synaptic mechanisms. Although the calyx synapse has been considered extremely reliable—presynaptic spikes almost always evoke postsynaptic spikes—some studies in slices have suggested that the synapse is unreliable at high frequencies because the readily releasable pool of vesicles is rapidly depleted, causing short-term depression. Lorteije et al. have compared synaptic properties of calyx synapses *in vivo* and in slices, using whole-cell and extracellular recordings. They found that no significant short-term depression occurred *in vivo*, because the probability of release at individual release sites was much lower *in vivo* than in slices. Nonetheless, failures occurred occasionally *in vivo* because of frequency-independent variability in EPSP size and reductions in postsynaptic excitability.

## ▲ Development/Plasticity/Repair

### *Pain-Related Decreases in Gray Matter Are Reversible*

R. Rodriguez-Raecke, A. Niemeier, K. Ihle, W. Ruether, and A. May

(see pages 13746–13750)

Chronic pain, lasting months or years, is sometimes associated with ongoing disease, such as cancer or arthritis, but it can also arise from nerve or muscle injury and persist after the injury heals, and it sometimes develops without any identifiable cause. Chronic pain causes functional reorganiza-

tion of the cortex, so that cortical responses to painful stimuli differ between pain patients and healthy subjects. Decreases in gray matter volume also occur in central pain-processing areas—including cingulate, insular, and prefrontal cortices—of chronic pain patients. To determine whether these changes are reversible, Rodriguez-Raecke et al. measured gray matter in patients with hip pain resulting from osteoarthritis, which can be eliminated by hip replacement. Before surgery, patients had lower gray matter density than controls in several cortical and brain stem regions, but gray matter density increased in patients within two months of surgery, indicating that brain changes resulting from some forms of chronic pain are reversible.

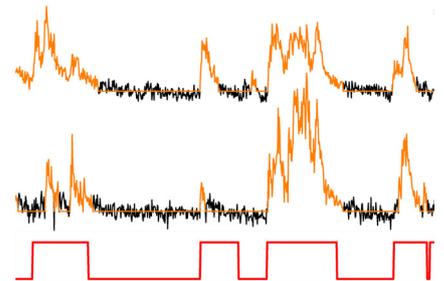
## ■ Behavioral/Systems/Cognitive

### *Functionally Related Neurons Are Clustered in Motor Cortex*

Daniel A. Dombeck, Michael S. Graziano, and David W. Tank

(see pages 13751–13760)

Studying the functional organization of the motor cortex has been limited by the inability to record simultaneously from large numbers of individual neurons in behaving animals. To overcome these problems, Dombeck et al. have developed an apparatus that allows two-photon calcium imaging in head-restrained, unanesthetized mice that can move relatively freely on a spherical treadmill. Using this setup, they recorded the activity of ~80 layer 2/3 motor cortical neurons simultaneously. Segmenting the neuronal population by temporal activity pattern or by correlation with behavior (running or grooming) created similar subsets, and neurons within each subset often were grouped spatially as well as functionally. Moreover, within a given group, neurons with highly correlated activity were likely to be closer to each other than pairs with less correlated activity. These results support the idea of wiring economy, which predicts neurons that are more strongly connected to each other should be positioned close to each other.



Calcium transients (top two traces) in two neurons in mouse motor cortex that were near to each other. Both were active when the mouse was running (bottom trace). See the article by Dombeck et al. for details.

## ◆ Neurobiology of Disease

### *Nanospheres Can Deliver Drugs Across the Blood–Brain Barrier*

H. Karatas, Y. Aktas, Y. Gursoy-Ozdemir, E. Bodur, M. Yemisci, et al.

(see pages 13761–13769)

Many drugs that might be effective in treating neurological diseases have limited clinical use because they do not cross the blood–brain barrier and therefore must be injected intracerebroventricularly. One example is caspase-3 inhibitors, which can decrease secondary damage resulting from ischemia. Karatas et al. have developed a nanoparticle delivery system that efficiently transports caspase-3 inhibitors into the brain. The technique uses nanospheres made of chitosan, a cationic polysaccharide that interacts with negative charges on the brain endothelium. The nanospheres were coated with a specific caspase-3 inhibitor, as well as monoclonal antibodies against a brain-specific transferrin receptor, which facilitates transport across the blood–brain barrier without significant transport into other tissues. When loaded nanoparticles were delivered intravenously to mice, they entered the brain parenchyma within 10 min. Delivery of nanoparticles before or shortly after transient occlusion of the middle cerebral artery significantly reduced the ischemic infarct volume as well as resultant neurological deficits.