# This Week in The Journal

## ● Cellular/Molecular

### *Orexin Neurons Sense Lactate*

Matthew P. Parsons and Michiru Hirasawa

(see pages 8061–8070)

The brain consumes a large portion of the body's energy, mostly to drive the $Na^+/K^+$ pump that repolarizes neuronal membranes after action potentials. Although neurons, like other cells, use glucose as a fuel source, it has been proposed that active neurons derive most of their energy from lactate that is produced in astrocytes by glycolysis and released into the extracellular space. Parsons and Hirasawa present evidence that supports this controversial hypothesis, and they suggest that hypothalamic orexin neurons, which promote wakefulness and food intake, act as lactate sensors. Blocking lactate transport into cells reduced spontaneous activity in rodent orexin neurons in hypothalamic slices. Removing glucose also reduced activity of orexin neurons, but lactate restored activity and the firing rate depended on lactate concentration. This occurred even after glia were poisoned, whereas reapplying glucose restored neuronal firing only if glia were healthy, suggesting that glucose effects on firing were mediated by glia.

## ▲ Development/Plasticity/Repair

### Gooseberry *Regulates Synaptic Homeostasis*

Bruno Marie, Edward Pym, Sharon Bergquist, and Graeme W. Davis

(see pages 8071–8082)

Neurons keep their excitability within a healthy range through homeostatic mechanisms. For example, knock-out of the nonessential glutamate receptor subunit GluRIIA at *Drosophila* neuromuscular junctions (NMJs) causes a reduction in miniature EPSP amplitude and a compensatory increase in neurotransmitter vesicle release. Conversely, increasing the amount of neurotransmitter per vesicle by expressing the vesicular glutamate transporter (vGluT) causes a compensatory decrease in the number of vesicles released. Marie et al. found that the transcription factor *gooseberry* is required in motor neurons for some, but not all forms of synaptic homeostasis. Reducing *gooseberry* mRNA levels did not affect NMJ miniature EPSP amplitude or quantal content, but it reduced the compensatory increase in vesicle release resulting from GluRIIA knock-out. In contrast, knockdown of *gooseberry* did not reduce the rapid increase in vesicle release that occurs in the presence of nonblocking levels of GluR antagonist, nor did it affect the homeostatic decrease in vesicle release that accompanies expression of vGluT.

## ■ Behavioral/Systems/Cognitive

### *Fat Consumption Reduces Food Intake via Oxytocin*

Silvana Gaetani, Jin Fu, Tommaso Cassano, Pasqua Dipasquale, Adele Romano, et al.

(see pages 8096–8101)

When food enters the intestine, it stimulates the release of satiety signals that act on vagal nerve afferents, which in turn project to brain centers that regulate eating. Consumption of fat, for example, stimulates secretion of oleoylethanolamide (OEA), which activates neurons in the hypothalamus and reduces feeding. Gaetani et al. show that the activated neurons include oxytocin-expressing magnocellular neurons of the paraventricular and supraoptic nuclei. Systemic injection of OEA decreased food consumption and increased *fos* expression in oxytocin neurons, as well as other neurons. Although oxytocin antagonist had no effect on food intake when administered alone, it prevented the reduction in food intake induced by OEA. In contrast, oxytocin antagonist did not alter OEA-induced activation in the nucleus of the solitary tract, an area involved in regulating feeding mediated by the gut hormone cholecystokinin. These data suggest that hypothalamic oxytocin neurons modulate food intake in response to fat consumption.

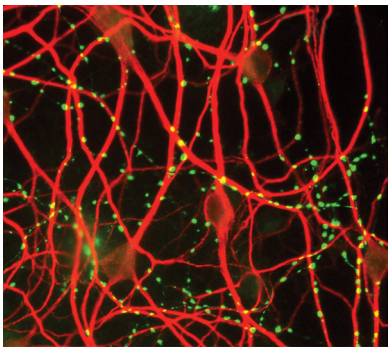
## ♦ Neurobiology of Disease

### *α-Synuclein Pathology Reduces Synaptic Protein Expression*

David A. Scott, Iustin Tabarean, Yong Tang, Anna Cartier, Eliezer Masliah, et al.

(see pages 8083–8095)

α-Synuclein is localized near synaptic vesicles and is thought to modulate synaptic transmission, possibly through interactions with vesicle proteins. In several diseases, including dementia with Lewy bodies (DLB), α-synuclein accumulates in intracellular inclusions in somata, neurites, and synaptic terminals. Formation of these inclusions is correlated with synaptic dysfunction and neurodegeneration. To investigate the cascade of molecular events leading to this dysfunction, Scott et al. cultured hippocampal neurons from mice overexpressing human α-synuclein. Although the number of boutons was similar in transgenic and control cultures, synapses were abnormal: miniature EPSC frequency was reduced in transgenic cultures, and many boutons appeared to be inactive; the number of abnormally large vesicles increased and vesicle density was reduced in boutons expressing human α-synuclein; and levels of every synaptic protein examined—including both endocytic and exocytotic proteins—were reduced at boutons overexpressing α-synuclein. One of these proteins, synapsin, was also reduced in human DLB brains, suggesting that this pathology contributes to human disease.



Human α-synuclein (green) localizes to synaptic boutons along dendrites (red) in hippocampal cultures from transgenic mice. See the article by Scott et al. for details.