# This Week in The Journal

## ● Cellular/Molecular

### *Supralinear Increases in Spine $Ca^{2+}$ Accompany LTD in Striatum*

Tomomi Shindou, Mayumi Ochi-Shindou, and Jeffery R. Wickens

(see pages 13015–13022)

Synaptic plasticity in the striatum is widely believed to underlie motor learning, but where and how the relevant plasticity occurs is controversial. High-frequency stimulation of corticostriatal afferents, which produces long-term synaptic depression (LTD) in slices may not occur *in vivo*. Whether pairing presynaptic stimulation with postsynaptic depolarization produces LTD or long-term potentiation (LTP) appears to depend on the timing of the stimuli and which neurotransmitter receptors are accessible. In the absence of antagonists and evoked dopamine release, Shindou et al. found that pairing glutamate uncaging (producing depolarization equivalent to a single presynaptic spike) with subsequent postsynaptic spiking led to supralinear increases in spine calcium concentrations and induced LTD in mouse striatal slices. Protocols that produced linear calcium increases, including eliciting postsynaptic spiking before uncaging glutamate, elicited neither LTP nor LTD. These results suggest that above-threshold increases in spine calcium concentration underlie LTD. How such calcium elevations are elicited *in vivo* remains uncertain.

## ▲ Development/Plasticity/Repair

### *Sympathetic Axons Stimulate Production of ProNGF*

Anda-Alexandra Calinescu, Tiecheng Liu, Michael M. Wang, and Jimo Borjigin

(see pages 12708–12715)

As developing sympathetic axons innervate their targets, they become dependent on target-derived nerve growth factor (NGF). This dependence ensures that the number of innervating neurons is appropriate for the size of the target, because superfluous neurons die. Production of NGF by target tissue increases as the target grows and after nerve injury, and this stimulates axonal sprouting to increase innervation. Although several studies have indicated that sympathetic neurons become less dependent on NGF as they mature, Calinescu et al. discovered that the neurons and their targets remain interdependent in uninjured adults. Silencing superior cervical ganglion (SCG) activity reduced expression of NGF mRNA in an SCG target, the pineal gland. Innervation of the pineal decreased simultaneously. Mimicking SCG input with β-adrenergic stimulation restored production of proNGF in the pineal and prevented axonal loss. The data suggest that activity of sympathetic axons stimulates target neurotrophin production, which is in turn required for maintenance of sympathetic axons.

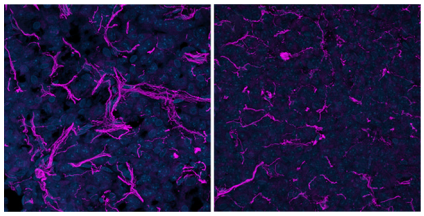
## ■ Behavioral/Systems/Cognitive

### *$D_1$ and $D_2$ Receptors Differentially Regulate Fear and Feeding*

Jocelyn M. Richard and Kent C. Berridge

(see pages 12866–12879)

Neurons in the nucleus accumbens (NAc) receive inputs conveying motivational information from limbic areas, and these synapses are modulated by dopaminergic inputs that convey information about the presence or absence of reward. Plasticity in this circuitry shapes behavioral responses to both appetitive and aversive stimuli. Injection of the AMPA receptor antagonist DNQX into rostral NAc stimulates eating, whereas injection into caudal regions elicits fear responses. At intermediate locations, DNQX elicits eating when administered in dim, quiet environments, but elicits more fear responses when administered in bright, loud environments. Richard and Berridge report that these responses are differentially dependent on activation of $D_1$- and $D_2$-type dopamine receptors (DRs). Although DR antagonists had no effect when administered alone, coinjection of D1DR antagonist prevented DNQX-induced eating or fear responses, depending on the injection location and environment. Coinjection of D2DR reduced DNQX-induced fear responses, increased DNQX-induced eating in loud environments, and did not alter eating in quiet environments.



β-Tubulin staining shows that innervation of the pineal gland was greater under conditions in which SCG neurons were regularly active (left) than after 4 weeks during which SCG activity was suppressed (right). See the article by Calinescu et al. for details.

## ◆ Neurobiology of Disease

### *$CO_2$ Chemoreflex Is Not Required to Maintain Respiration*

Nelina Ramanantsoa, Marie-Rose Hirsch, Muriel Thoby-Brisson, Véronique Dubreuil, Julien Bouvier, et al.

(see pages 12880–12888)

Chemosensors that detect increases in $CO_2$ levels or the accompanying decrease in pH (hypercapnia) stimulate respiration in response to changing environmental conditions and activity. Human mutations in the transcription factor *PHOX2B* slow ventilation and reduce responses to hypercapnia. Mice expressing mutated *PHOX2B* have similar phenotypes, and they die shortly after birth from respiratory failure. The only anatomical defect identified in these mice was loss of brainstem retrotrapezoid nucleus (RTN) neurons, suggesting that RTN neurons are important $CO_2$ chemosensors and that $CO_2$ chemoreflexes are essential for normal respiration. But Ramanantsoa et al. found that restricting expression of mutant *PHOX2B* to the brainstem allowed mice to survive to adulthood, despite lacking RTN neurons. Although respiration was slow and was not stimulated by hypercapnia in newborns, baseline ventilation eventually returned to normal and responses to hypercapnia increased to ~40% of controls. These data suggest other chemosensors become active in adult mice, and that $CO_2$ chemoreflexes are not essential for respiration.