This Week in The Journal

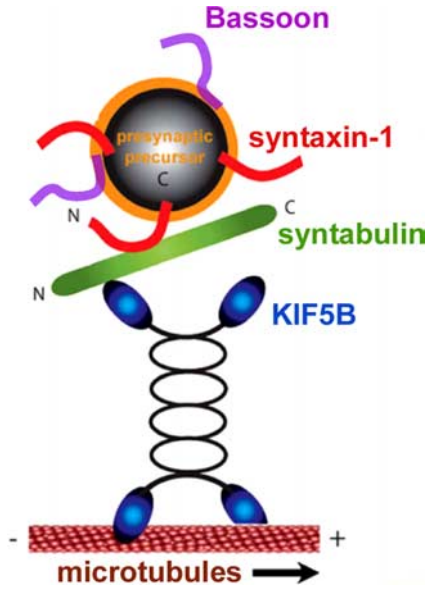
● Cellular/Molecular

Transporting Components to the Active Zone

Qian Cai, Ping-Yue Pan, and Zu-Hang Sheng

(see pages 7284–7296)

If you are planning to ship Piccolo, Bassoon, and a bit of N-cadherin and SNAP-25, you will need some syntabulin, according to Cai et al. this week. Piccolo and its active zone (AZ) compatriots are transported by a complex, which includes syntaxin-1, the kinesin motor KIF5B, and the adaptor protein syntabulin. In fetal rat brains, vesicles containing presynaptic AZ components colocalized with this protein complex. Time-lapse imaging confirmed the colocalization and comovement of these proteins in cultured hippocampal neurons. After RNAi-induced depletion of syntabulin, or use of dominant-negative constructs that interfered with the KIF5B motor complex, GFP (green fluorescent protein)-labeled Bassoon accumulated at the nucleus rather than moving down axons along microtubules. Transport of the AZ precursor vesicles via the syntaxin–syntabulin–KIF5B complex was essential for inclusion of AZ components into functional synapses and the activity-dependent recruitment of new presynaptic boutons.



The schema shows the binding relationships of the syntaxin–syntabulin–KIF5B protein complex, which is necessary to move active zone components to presynaptic terminals. See the article by Cai et al. for details.

▲ Development/Plasticity/Repair

Rats on Ritalin

Jason D. Gray, Michael Punsoni, Nora E. Tabori, Jay T. Melton, Victoria Fanslow, Mary J. Ward, Bojana Zupan, David Menzer, Jackson Rice, Carrie T. Drake, Russell D. Romeo, Wayne G. Brake, Annelyn Torres-Reveron, and Teresa A. Milner

(see pages 7196–7207)

When it comes to drug treatment of children with methylphenidate (MPH; Ritalin) for attention deficit/hyperactivity disorder (ADHD), ongoing debates are everywhere. One question is whether block of monoamine transporters with this drug leads to lasting alterations in the brain. This week, Gray et al. dosed male rats twice weekly between postnatal day 7 (PND7) and PND35 and then tracked immunocytochemical markers out to PND135. In adult rats, the 4 weeks of postnatal treatment decreased anxiety-like behavior on the elevated plus-maze task. At PND35, but not PND135, MPH-treated rats also showed increased tyrosine hydroxylase-immunoreactive fibers in the medial prefrontal cortex as well as changes in several markers in striatum, hippocampus, and hypothalamus. There were no apparent changes in brain structure with MPH treatment. Although the neurochemical changes were mostly short-lived, early MPH exposure in rats did alter at least one measure of adult behavior.

■ Behavioral/Systems/Cognitive

MAPK Signaling in the PVH

Arshad M. Khan, Todd A. Ponzio, Graciela Sanchez-Watts, B. Glenn Stanley, Glenn I. Hatton, and Alan G. Watts

(see pages 7344–7360)

Neuroendocrine neurons in the paraventricular hypothalamic nucleus (PVH) respond to hyperglycemia with synthesis and release of corticotropin-releasing hormone (CRH). This response is driven by inputs from the hindbrain that release catecholamines and neuropeptides onto PVH neurons. This week, Kahn et al. asked whether noradrenaline (NE) was sufficient to trigger the underlying signaling cascade during a glycemic challenge. Intravenous 2-deoxyglucose, a glycolysis blocker, or insulin rapidly increased phosphorylated levels of p44/42 mitogen-activated protein kinases (phospho-ERK1/2) in the PVH. Microinjection of NE into the PVH had a similar effect. Downstream effects included a rise in PVN c-*fos* messenger RNA and plasma levels of corticosterone. *In vitro*, treatment of hypothalamic slices with NE also increased phospho-ERK1/2 in CRH neurons in PVN. This signaling required α_1 adrenoreceptors and MEK (mitogen-activated protein kinase kinase), the kinase that phosphorylates ERK1/2.

♦ Neurobiology of Disease

NO, Peroxynitrite, and Ischemic Tolerance

Alexander Kunz, Laibaik Park, Takato Abe, Eduardo Gallo, Josef Anrather, Ping Zhou, and Costantino Iadecola

(see pages 7083–7093)

Ischemic tolerance is remarkable in that pre-exposure or conditioning to a sublethal injury protects brain tissue against subsequent ischemia. If the phenomenon were better understood, it might be harnessed to treat stroke. Kunz et al. show this week that neuroprotection is two-pronged, affecting the cerebral microvasculature as well as neurons and glia. The authors used the proinflammatory mediator lipopolysaccharide (LPS) to trigger protection. Mice pretreated with LPS had reduced infarct size after middle cerebral artery occlusion and showed improved cerebral blood flow in spared regions. This protection required nitric oxide (NO) produced by inducible NO synthase (iNOS) and superoxide produced by NADPH oxidase (nox2). Peroxynitrite, the product of a reaction between NO and superoxide, was the key to LPS-induced tolerance and vasoprotection. LPS did not protect mice lacking iNOS or nox2. Likewise, protection was reversed by FeTPPS [5,10,15,20-tetrakis(4-sulfonatophenyl)porphyrinato iron (III)], which catalyzes peroxynitrite breakdown. Thus, vasoprotection appears to be an important component of ischemic preconditioning.