This Week in The Journal

● Cellular/Molecular

The Consequences of P/Q Channel Splicing

Dipayan Chaudhuri, Siao-Yun Chang, Carla D. DeMaria, Rebecca S. Alvania, Tuck Wah Soong, and David T. Yue
(see pages 6334–6342)

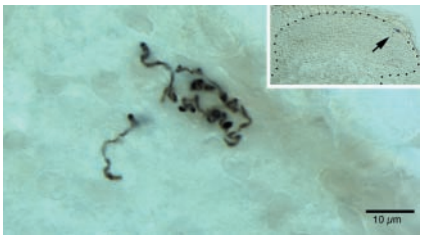
Calcium entry through calcium channels leads to calcium/calmodulin-dependent facilitation (CDF) as well as inactivation (CDI) of these same channels. In this week's *Journal*, Chaudhuri et al. examined how alternative splicing of α_{1A}, the pore-forming subunit of P/Q type calcium channels, affects this process. The C-terminal intracellular tail of α_{1A} contains an alternatively spliced site in exon 37 that results in two variants of an EF-hand-like domain, EFa and EFb. In human embryonic kidney 293 cells expressing α_{1A} with β_{2a} and $\alpha_2\delta$, CDF was manifest as an increase in calcium current during a 50 msec test voltage pulse after a prepulse to facilitate calcium entry. CDI was seen as a gradual decrease in current during longer pulses. The EFb version of the subunit lacked CDF, whereas CDI was unaffected. CDF was also modulated by another splice in the extreme C terminus. The authors suggest that these natural splice variants provide a mechanism to modulate calcium-dependent facilitation dependent on the expression patterns of the splice variants.

▲ Development/Plasticity/Repair

Will the Real Heat Sensor(s) Please Stand Up

C. Jeffery Woodbury, Melissa Zwick, Shuying Wang, Jeffrey J. Lawson, Michael J. Caterina, Martin Koltzenburg, Kathryn M. Albers, H. Richard Koerber, and Brian M. Davis
(see pages 6410–6415)

The TRPV1 receptor/channel is activated by capsaicin (the hot ingredient in chili peppers) and by low pH and heat. Because of its expression in nociceptive sensory neurons, it was thought to be the major sensor of noxious heat in the mammalian sensory system. However, work from Woodbury et al. may force a reassessment of this idea. The authors examined the distribution of TRPV1 in a population of mouse heat-responsive neurons that bind the plant lectin isolectin B4 (IB4). Indeed, unlike in the rat, they found that in the mouse, the IB4-positive population expressed little TRPV1. Furthermore, the heat-sensing neurons of TRPV1-deficient mice still respond to noxious heat in a skin–nerve preparation. These neurons also did not express the related TRPV2 channel. At least for the mouse IB4-expressing nociceptors, the results throw into question the *in vivo* role of the TRPV1 channel and the identity of the primary molecular heat sensor.



This wild-type C-fiber was characterized physiologically and identified immunohistochemically as an IB4-positive and TRPV1-negative polymodal nociceptor. The dorsal horn projection was visualized with Neurobiotin. In the inset, the dotted line indicates the margin of dorsal horn gray matter and shows that this fiber terminates in lamina I. See the article by Woodbury et al. for details.

■ Behavioral/Systems/Cognitive

The Timecourse of Addiction

Anne-Noël Samaha, Nicolas Mallet, Susan M. Ferguson, François Gonon, and Terry E. Robinson
(see pages 6362–6370)

Rapid cocaine delivery, such as smoking "crack" rather than snorting powder, produces an intensely pleasurable and reinforcing high. However, rapid delivery comes with a high price, a greater likelihood of addiction and compulsive drug-seeking behavior. This week, Samaha et al. attack possible adaptations underlying the addictive state, including psychomotor sensitization, dopamine uptake, and induction of immediate early genes (IEGs). Only rats that received rapid cocaine delivery (the same dose given over 5 sec rather than 100 sec) displayed psychomotor sensitization on the second day of drug delivery. In the orbitofrontal and medial prefrontal cortex, nucleus accumbens, and caudate–putamen, c-*fos* and *arc* mRNAs were increased to a greater extent by fast drug delivery. Finally, rapid delivery resulted in a faster onset and larger block of dopamine reuptake. Such kinetic data may also be important in designing anti-addictive treatment strategies.

♦ Neurobiology of Disease

Sizing Up Autism in the Amygdala and Hippocampus

Cynthia Mills Schumann, Julia Hamstra, Beth L. Goodlin-Jones, Linda J. Lotspeich, Hower Kwon, Michael H. Buonocore, Cathy R. Lammers, Allan L. Reiss, and David G. Amaral
(see pages 6392–6401)

Impairments in social interactions as well as language and cognitive deficits define the spectrum of autism. This week, Schumann et al. reexamine a controversial aspect of the underlying neuropathology, the differences in the size of brain structures in male children and adolescents with autism and the related Asperger's syndrome. Using MRI, they measured the volume of the cortex, amygdala, and hippocampus. Although the cortical size was unaffected, the hippocampus was slightly larger in autistic subjects than controls. Interestingly, the amygdala of children, but not adolescents, was larger with autism, regardless of retardation. The comparison confirmed a 40% increase in the amygdala of normal children between age 7.5 and 18.5 that seems to occur prematurely in autism. Although our understanding of these changes is rudimentary, the role of the amygdala in social interactions provides an intriguing possible connection to autism. One thing seems certain: when it comes to the amygdala, bigger is not necessarily better.