This Week in The Journal

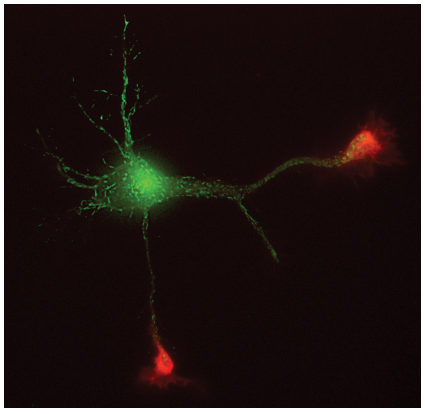
Cellular/Molecular

Dendritic Vesicles Avoid Nascent Axons

Jennifer D. Petersen, Stefanie Kaech, and Gary Banker

(see pages 4135–4147)

The distinct functional properties of axons and dendrites arise from their expression of different proteins. Axon- and dendrite-bound membrane proteins are sorted into separate vesicle populations, which are trafficked differently. Dendritic vesicles are excluded from axons, and although what restricts their movement is unclear, motor proteins that interact selectively with either axonal or dendritic vesicles and with neurite-specific cytoskeletal elements likely are involved. When examining the movement of vesicles carrying fluorescently labeled axonal or dendritic proteins in cultured hippocampal neurons, Petersen et al. saw that dendritic vesicles were excluded from distal axons as soon as the axon was specified. In fact, even before the nascent axon was identifiable, dendritic vesicles moved preferably into neurites that lacked kinesin-1, a motor protein that favors axonal microtubules. This segregation occurred long before the dense actin network underlying the axon initial segment formed and before dendritic microtubules acquired their mature organization, indicating that these cytoskeletal elements are not necessary for selective transport of membrane proteins.



Dendritic vesicles (green) largely avoid neurites favored by the axonal motor protein kinesin-1 (red), even before an axon is established. See the article by Petersen et al. for details.

Systems/Circuits

Locus Ceruleus Can Enhance or Suppress Pain

Louise Hickey, Yong Li, Sarah J. Fyson, Thomas C. Watson, Ray Perrins, et al.

(see pages 4148–4160)

In the 1962 film *Lawrence of Arabia*, Lawrence explains his ability to extinguish a match with his fingers by saying, "The trick. . . is not minding that it hurts." The ability to tolerate pain is thought to be mediated in part by descending analgesic projections from the locus ceruleus (LC), which inhibit nociceptive afferents and second-order projection neurons in the spinal dorsal horn via α2-adrenoceptors. Consistent with this hypothesis, Hickey et al. found that optical activation of ChannelRhodopsin-expressing LC noradrenergic neurons increased the temperature threshold for paw-withdrawal in 11 of 20 rats. Unexpectedly, however, an α2-adrenoceptor antagonist did not block this effect, but instead prolonged it. Furthermore, optical activation reduced withdrawal thresholds in 9 of 20 rats, suggesting that some LC noradrenergic neurons enhance pain responses. Subsequent histological analyses suggested that the antinociceptive effects were mediated predominantly by neurons in the ventral LC and sub-LC, whereas pronociceptive effects were mediated by neurons located more dorsally, in the body of the LC proper.

Behavioral/Cognitive

Opiate Receptor Agonists Differently Affect "Liking" and "Wanting"

Daniel C. Castro and Kent C. Berridge

(see pages 4239–4250)

Animals are motivated to seek out experiences they have found pleasurable. The medial shell of the nucleus accumbens (msNAc) participates in both hedonic experiences ("liking") and motivational responses ("wanting"). Injection of a mu opioid receptor (MOR) agonist into a "hotspot" in the rostrodorsal quadrant of msNAc increases rats' hedonic responses (orofacial movements) and motivational responses (seeking and eating) to sucrose. Castro and Berridge now show that injecting kappa (K) or delta (D) OR agonists into the rostrodorsal hotspot also increased rats' hedonic responses. In contrast, injecting OR agonists into posterior portions of the msNAc reduced hedonic responses. The various agonists had different effects on "wanting", however: MOR agonists increased consumption of sweet food when injected into either rostral or caudal msNAc, whereas DOR agonist increased consumption only when injected into the rostrodorsal hotspot, and KOR agonist had no effect on "wanting." Therefore, liking and wanting are regulated not only by different regions of msNAc, but also by different opiate receptors.

Neurobiology of Disease

Neuronal NMDA Currents Influence Response to Stretch Injury

Tapan P. Patel, Scott C. Ventre, Donna Geddes-Klein, Pallab K. Singh, and David F. Meaney

(see pages 4200–4213)

Mild traumatic brain injury (mTBI) occurs when a force to the head strains brain tissue. The deformation stretches axons, activating stretch-sensitive NMDA receptors (NMDARs) that contain the NR2B subunit. This leads to calcium influx, depolarization, and glutamate release, creating a positive feedback loop that leads to widespread network changes. These network changes cause symptoms such as dizziness, confusion, and visual disturbances. To investigate whether the properties of individual neurons influence how they are affected by mTBI, Patel et al. used an *in vitro* model in which dissociated cortical neurons were grown on stretchable coverslips. Neuronal activity was detected before and after stretch injury via calcium imaging, and the amount of synchronous activity was used to estimate connectivity. The overall level of synchronous activity decreased after stretch injury, but the effects varied across neurons. Neurons whose NMDA currents had a relatively large GluN2B component before stretch were more likely to become uncoupled from other neurons after injury than neurons with a large GluN2A component.