This Week in The Journal

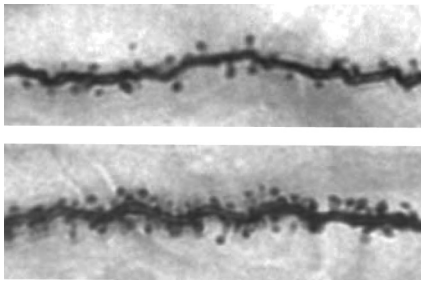
Cellular/Molecular

NrCAM Regulates Spine Density in Cortex

Galina P. Demyanenko, Vishwa Mohan, Xuying Zhang, Leann H. Brennaman, Katherine E.S. Dharbal, et al.

(see pages 11274–11287)

The neuron-glial-related cell adhesion molecule NrCAM is an axon guidance molecule that contributes to the repulsive effects of semaphorin 3F (Sema3F). Expression of NrCAM on rostrally projecting thalamocortical axons, for example, helps steer these axons away from Sema3F in caudal areas. NrCAM expression on thalamocortical axons decreases after the axons reach the cortex, and NrCAM expression then increases in deep cortical layers. Because Sema3F limits the production of dendritic spines in cortical neurons, Demyanenko et al. suspected NrCAM might also have a role in spine regulation. Consistent with this hypothesis, NrCAM was localized in dendritic spines of star pyramidal cells in layer 4 of mouse visual cortex on postnatal day 21, the start of the critical period. Knocking out NrCAM increased spine density on the apical dendrites of these (and other pyramidal) neurons, resulting in an increase in synaptic input as indicated by an increase in miniature EPSC frequency. In addition, NrCAM knockout prevented Sema3F-induced spine retraction in cultured cortical neurons.



Spine density on apical dendrites of star pyramidal cells is greater in NrCAM-null mice (bottom) than in wild-type (top). See the article by Demyanenko et al. for details.

Systems/Circuits

Retinal Capillaries Actively Dilate during Light Stimulation

Tess E. Kornfield and Eric A. Newman

(see pages 11504–11513)

Synaptic activity causes local blood vessels to dilate, thus increasing blood, oxygen, and nutrient supply to the active neurons. The roles of various vessels in this functional hyperemia remain uncertain. To investigate this question, Kornfield and Newman examined changes in vessel diameter and red blood cell (RBC) flux in response to retinal stimulation *in vivo*. Stimulating rat retina with flickering light consistently caused rapid, large dilation of first- and second-order arterioles. Less consistently, smaller, slower dilation occurred in downstream capillaries; venule dilation was smaller and slower still. The extent of capillary dilation varied across the three vascular layers, with the largest increases occurring in the intermediate layer. Here, dilation and RBC flux continued to increase throughout the stimulation period, likely because these capillaries feed the synapses that are most strongly activated by flicker stimulation. The authors conclude that although arterioles are the main drivers of retinal blood flow, capillaries in the intermediate layer may undergo active dilation during visual stimulation.

Behavioral/Cognitive

Dorsomedial Habenula Activity Is Rewarding

Yun-Wei A. Hsu, Si D. Wang, Shirong Wang, Glenn Morton, Hatim A. Zariwala, et al.

(see pages 11366–11384)

The habenula is a part of the epithalamus located on the dorsal posterior surface of the thalamus. By regulating midbrain dopaminergic and serotonergic systems, the habenula is thought to contribute to motivational control of behavior. The lateral habenula indirectly inhibits dopamine neurons, thus signaling the absence of reward and promoting avoidance. Work presented this week by Hsu et al. suggests the dorsal medial habenula (dMHb) has the opposite role. Optical self-stimulation of dMHb acted as a primary reinforcer in mice: the mice ran more on a wheel that triggered dMHb stimulation than on an unrewarded wheel. Conversely, optical inhibition of dMHb output caused acute place aversion. In addition, after dMHb neurons were selectively killed, mice engaged in voluntary wheel running—an intrinsically rewarding activity—less often, and they showed less preference for sucrose solution than controls. These data suggest that dMHb activity contributes to exercise motivation, hedonic states, and positive reinforcement.

Neurobiology of Disease

Lipid Raft Components Play a Role in HAND

Mihyun Bae, Neha Patel, Haoxing Xu, Mingwaoh Lee, Kumiko Tominaga-Yamanaka, et al.

(see pages 11485–11503)

Combinatorial retroviral therapy has greatly increased life expectancy for people infected with HIV, making HIV-associated neurocognitive disorder (HAND) a growing concern. HAND, which is thought to be triggered by the HIV coat protein gp120, shares many characteristics of Alzheimer's disease (AD), including accumulation of β-amyloid (Aβ) peptides. Unlike in AD, however, Aβ accumulates within neurons in HAND. Bae et al. report that mice overexpressing gp120 along with AD-linked versions of amyloid precursor protein (APP) and presenilin 1 develop intraneuronal Aβ deposits, attributable partly to increased activity of the β- and γ-secretases that cleave APP to form Aβ. Increased β-secretase activity required both inhibition of a transcription factor that represses β-secretase transcription and stabilization of lipid rafts where APP is cleaved. Accumulation of sphingomyelin, which stabilizes lipid rafts, also disrupts lysosome function by inhibiting lysosome TRP channels. Intriguingly, an agonist of these channels led to re-acidification of lysosomes and clearance of accumulated sphingomyelin and Aβ in gp120-treated cultured neurons.