This Week in The Journal

● Cellular/Molecular

Carrying the Death Signal in Olfactory Receptor Neurons

Christine Carson, Maya Saleh, France W. Fung, Donald W. Nicholson, and A. Jane Roskams
(see pages 6092–6104)

Apoptosis is the means to a neuron's end in many different situations, ranging from development to ischemia to trauma. This week, Carson et al. examine the signaling pathway that drives the ongoing cell death in olfactory receptor neurons (ORNs). Cell death in these neurons involves retrograde activation of caspase-9 and caspase-3. The authors looked for events upstream of caspase-9 after bulbectomy or an excitotoxic bulb lesion; the latter leaves olfactory nerve terminals intact. Caspase-8 cleavage was detected within hours in a caudorostral pattern from the lesioned target. Within 4 d of target removal, there was also a significant increase in apoptotic ORNs. The p150^{Glued} subunit of dynactin, a required activator of retrograde transport, interacted with caspase-8. Because activation of caspase-8 was reduced in mice lacking the low-affinity nerve growth factor receptor p75, the authors propose that p75 initiates the activation and transport of caspase-8 that leads to ORN cell death.

▲ Development/Plasticity/Repair

EnAbling Dendritic Branching

Eva Marie Yang Moresco, Stephanie Donaldson, Anne Williamson, and Anthony J. Koleske
(see pages 6105–6118)

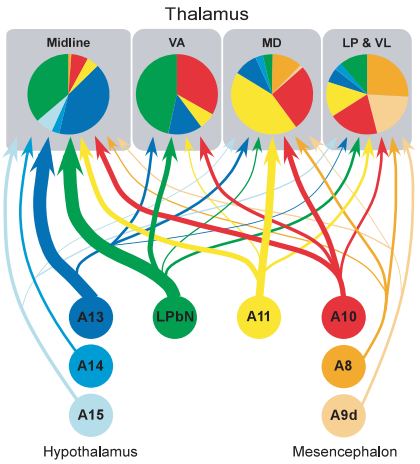
The complexity of dendritic arbors, one of the most distinctive morphological features of neurons, is essential to the operation of neuronal networks. Some of the molecules charged with the task of maintaining dendrites emerge this week in work from Moresco et al. The authors examined Abl and Abl-related gene (Arg), nonreceptor tyrosine kinases that interact with cell surface receptors to shape the cytoskeleton. In brain-specific double knock-out ($abl^{-/-}/arg^{-/-}$) mice, neurons in adult animals were more closely packed and had smaller dendritic arbors, particularly in cortical layers 4 and 5. Dendritic arbors in the double knock-out mice were reduced more than those of either Abl or Arg knock-outs. These deficits only emerged after postnatal day 21, suggesting a role for Abl and Arg in the maintenance of dendrites rather than their initial formation. Overexpression of Arg promoted branching activity of axons and dendrites. Abl and Arg signaling appears to be mediated by integrin receptors activated by adhesion to Semaphorin 7A or laminin-1.

■ Behavioral/Systems/Cognitive

Dopamine in the Primate Thalamus

Miguel Ángel Sánchez-González, Miguel Ángel García-Cabezas, Beatriz Rico, and Carmen Cavada
(see pages 6076–6083)

Making a new discovery in brain anatomy, or even rediscovering an ignored pathway, is no easy task these days. This week, Sánchez-González et al. report a novel thalamic dopamine pathway in humans and primates. Although neurochemical data from the early 1980s indicated that there was dopamine in the thalamus, this fact has received little attention, perhaps because dopaminergic fibers are mostly absent in rodents. Using immunolabeling for tyrosine hydroxylase, dopamine, and the dopamine transporter (DAT), the authors found widely distributed dopaminergic axons in the human and monkey thalamus. The most densely innervated areas were specific association, limbic, and motor nuclei. In the macaque, retrograde tract tracing revealed multiple origins of dopaminergic inputs to the thalamus, including the hypothalamus, periaqueductal gray, ventral mesencephalon, and lateral parabrachial nucleus. Interestingly, some fibers had low DAT content, whereas others were robustly labeled, suggesting possible differences in the spread of dopamine from thalamic release sites.



Summary diagram of the dopamine projection to the macaque monkey thalamus. See the article by Sánchez-González et al. for details.

◆ Neurobiology of Disease

Glucocorticoid Receptor Signaling and Stress Responses

Stephanie Ridder, Sabine Chourbaji, Rainer Hellweg, Alexandre Urani, Christiane Zacher, Wolfgang Schmid, Mathias Zink, Heide Hörtnagl, Herta Flor, Fritz A. Henn, Günther Schütz, and Peter Gass
(see pages 6243–6250)

Alterations in stress responses are common in depression, including increases in plasma cortisol levels, perhaps because of diminished glucocorticoid receptor (GR) expression or function. To explore the role of GRs on behavior in mice, Ridder et al. titrated GR expression at 33% ($GR^{+/-}$ heterozygous mice), 100% (wild-type mice), or 200% (YGR mice that overexpress GR, but with normal promoter elements) of wild type. Although basal levels of corticosterone were similar in heterozygous and wild-type mice, restraint stress caused a greater elevation in the $GR^{+/-}$ mice. Behavior, too, was affected because $GR^{+/-}$ mice had significant coping difficulties in response to unpredictable, repeated footshocks. Similar to patients with depression, $GR^{+/-}$ mice had elevated corticosterone levels in a dexamethasone suppression test. In contrast, the YGR mice were distinctly resistant to the "depression-like" profile in the learned helplessness paradigm. The authors propose that these mice may be useful animal models of depression.