This Week in The Journal

● Cellular/Molecular

Targeting Arc to Synaptic Sites

Fen Huang, Jennifer K. Chotiner, and Oswald Steward

(see pages 9054–9067)

Arc/Arg 3.1 is not only an immediate early gene, but its mRNA is also targeted to dendrites. Thus it has become a focus of studies linking neural activity to changes in synaptic efficacy. This week, Huang et al. further explored the signaling cascade involved in the targeting of Arc mRNA and protein to active synaptic sites. The authors induced long-term potentiation in adult anesthetized rats by stimulating the medial perforant path and recording the response in the dentate gyrus. High-frequency stimulation was continued for periods of up to 90 min. Polymerized actin, measured by phalloidin staining, colocalized with Arc/Arg 3.1 mRNA in the activated dendritic lamina within the molecular layer of the dentate gyrus. This colocalization was blocked by inhibition of Rho kinase or inhibition of actin polymerization with latrunculin B. ERK1 phosphorylation induced by high-frequency stimulation was also required for the targeting of Arc/Arg 3.1 mRNA.

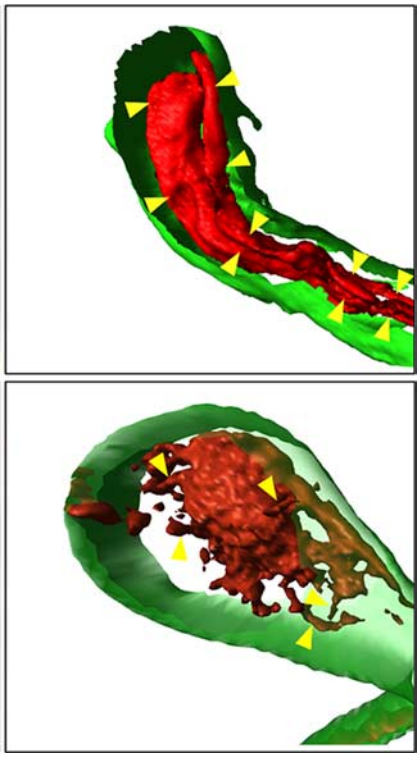
▲ Development/Plasticity/Repair

Retraction Bulbs and Microtubule Networks

Ali Ertürk, Farida Hellal, Joana Enes, and Frank Bradke

(see pages 9169–9180)

It's not altogether clear why injured peripheral axons can regenerate relatively easily, whereas central axons have a much rougher time. This week, Ertürk et al. decided to take a comparative look at microtubules in the business end of the axon: the tip or growth cone. Rather than growth cones, injured central axons have swellings at their tips called retraction bulbs that are the hallmark of a failed growth response. The authors lesioned the dorsal column or the sciatic nerve in 2- to 3-month-old mice and tracked axon tips with a fluorescent reporter. In central axons, retraction bulbs continue to increase in size after injury and contained disorganized microtubule networks compared with the sleek and organized regenerating peripheral axons. Disruption of microtubules with nocodazole caused retraction bulb formation in peripheral axons *in vivo* and in cell culture. In contrast, stabilizing microtubules with taxol prevented retraction bulbs.



A three-dimensional reconstruction of microtubule networks in a growth cone (top) and a retraction bulb (bottom). The yellow arrowheads point to the parallel microtubule bundles in the growth cone compared with the dispersed microtubules in the retraction bulb. See the article by Ertürk et al. for details.

■ Behavioral/Systems/Cognitive

Mapping Fingerpads in S1 with Positive BOLD

Li M. Chen, Gregory H. Turner, Robert M. Friedman, Na Zhang, John C. Gore, Anna W. Roe, and Malcolm J. Avison

(see pages 9181–9191)

Blood oxygenation level-dependent (BOLD) functional magnetic resonance imaging (fMRI) has been widely used to map functional brain activity in humans, whereas optical imaging of intrinsic signals (OIS) has been used for similar purposes in animals. Most BOLD studies use the "positive" signal, rather than the much smaller early negative BOLD that likely corresponds to the signal detected by OIS. OIS is generally regarded as having higher spatial resolution on the order of 100 μm and higher time resolution on the order of 100 ms. This week, Chen et al. compared the two techniques by mapping single distal fingerpad activation in the somatosensory cortex (S1) of anesthetized squirrel monkeys. Using a 9.4 T magnet, the authors report that positive BOLD signals without contrast agents could resolve submillimeter shifts in activation in area 3b, similar to what was detectable with OIS. Coregistration of fMRI and OIS maps in the same monkeys showed close agreement.

♦ Neurobiology of Disease

The Time Course of the Phenotype in HD Mice

Mary Y. Heng, Sara J. Tallaksen-Greene, Peter J. Detloff, and Roger L. Albin

(see pages 8989–8998)

The long latency, measured in decades, before onset of symptoms is a hallmark of adult-onset Huntington's disease (HD). Yet putative treatments would best be tested before overt clinical symptoms emerge in man or in mouse models of the human disease. This week, Heng et al. tracked the time course of changes in behavior and in the striatum of the *Hdh*$^{(CAG)150}$ knock-in mouse model of HD. All mice survived to 100 weeks, but by that point, they had a tremor, unsteady movements, and a staggering gait. A battery of behavioral tested revealed motor abnormalities at 70 and 100 weeks. There were also losses in striatal dopamine D1 and D2 receptors at 70 and 100 weeks and a loss of striatal neuron number at 100 weeks. These longitudinal studies not only validate this mouse model as exhibiting features consistent with HD but also provide a benchmark for its use in studies of pathogenesis and treatment.