This Week in The Journal

● Cellular/Molecular

Neurofilament Turnover and Transport, Revisited

Stéphanie Millecamps, Geneviève Gowing, Olga Corti, Jacques Mallet, and Jean-Pierre Julien

(see pages 4947–4956)

The abundant neurofilaments (NFs) of the cytoskeleton are polymers of light, midsize, and heavy subunits. Although once thought to move unidirectionally, NFs can move bidirectionally along microtubules in a start-and-stop pattern. This week, Millecamps et al. focused on the transport and turnover of light subunits (NF-L). They generated mice that conditionally expressed a transgene encoding human NF-L under the control of doxycycline in mice that were either heterozygous (tTA;hNF-L;NF-L $^{+/-}$) or deficient (tTA;hNF-L;NF-L $^{-/-}$) for endogenous NF-L. Doxycycline treatment reduced hNF-L mRNA within a week, whereas the half-life of the protein was longer, 3 weeks in cerebellum. However, in large-caliber axons in the sciatic nerve, drug treatment did not diminish the existing stationary NF-L network in tTA;hNF-L;NF-L $^{+/-}$ mice. Breakdown of NF-L occurred spontaneously along the entire axon, not just at nerve endings. Accumulation of new hNF-L after cessation of doxycycline in tTA;hNF-L;NF-L $^{-/-}$ mice also appeared synchronously along the nerve, rather than wave-like.

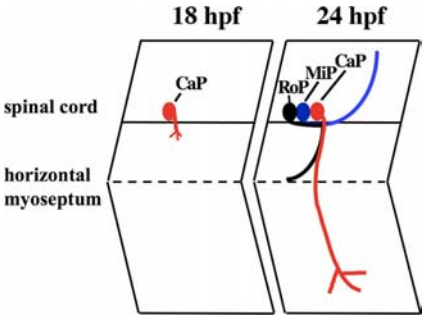
▲ Development/Plasticity/Repair

Zebrafish Pioneer Axons and PlexinA3

Julia Feldner, Michell M. Reimer, Jörn Schweitzer, Björn Wendik, Dirk Meyer, Thomas Becker, and Catherina G. Becker

(see pages 4978–4983)

Plexins, receptors for semaphorin signaling, are among the molecules that guide axon growth and pathfinding. Here, Feldner et al. unveil the molecular niche carved out by plexinA3 in primary motor



The schema shows the outgrowth of primary motor axons (CaP, MiP, and RoP) in embryonic zebrafish spinal cord hemisegments, initiated by the CaP axon at around 18 hours postfertilization. See the article by Feldner et al. for details.

axon guidance. The authors cloned plexinA3 from zebrafish and demonstrate its expression at the ventral edge of the embryonic spinal cord, specifically in the caudal and middle primary motor neurons (CaP and MiP), the axons of which regularly exit the spinal cord. Translation-blocking morpholinos of plexinA3 mRNA caused abnormal axon branching of dorsal and ventral motor nerves, and induced exit from posterior segments of the spinal cord at additional exit points. Overexpression of plexinA3 mRNA, which did not bind the morpholino, rescued the phenotype. Branching and exiting were exacerbated by coinjection of morpholinos that blocked expression of sema3A1 or sema3A2. Sema3A1 in particular appeared to contribute to excess branching, whereas sema3A2 appeared to regulate the increase in exit points.

■ Behavioral/Systems/Cognitive

Financial Gain and Financial Pain

Ben Seymour, Nathaniel Daw, Peter Dayan, Tania Singer, and Ray Dolan

(see pages 4826–4831)

Studies of decision-making and financial gain implicate the striatum in encoding prediction errors. But what about anticipation of financial loss, for example what distinguishes a reward that is greater than expected from a punishment or loss that is less than expected? Seymour et al. used a pavlovian conditioning paradigm in which subjects were shown a series of visual stimuli followed by an indication of personal financial gain or loss. Subjects then made appetitive or aversive predictions, respectively, during functional magnetic resonance imaging. Blood oxygenation level-dependent (BOLD) responses were elevated above baseline, as expected, in the striatum during appetitive predictions. Aversive predictions also elevated BOLD responses, a "positive" (above baseline) response to financial loss. However, the signals were spatially distinct, with gain prediction provoking activation in more anterior and ventral areas and loss prediction associated with more posterior regions.

◆ Neurobiology of Disease

Central Pain and Thalamic Lesions in Humans

Jong H. Kim, Joel D. Greenspan, Robert C. Coghill, Shinji Ohara, and Frederick A. Lenz

(see pages 4995–5005)

Lesions to posterior regions of the thalamus produce poststroke central pain (CPSP), as well as loss or reduction of sensation. This week, Kim et al. mapped the thalamic nuclei in which damage specifically produces allodynia, a painful response to normally innocuous mechanical or cold stimuli. The subjects had experienced small thalamic strokes. The authors used somatosensory testing and atlas-based mapping with positron emission tomography and magnetic resonance imaging. The authors hypothesized that damage to ventral caudal (Vc) and ventral medial posterior (VMpo) nuclei would be necessary to alter cold sensations and produce CPSP. Although all subjects had lesions to the Vc, the VMpo remained intact. Nevertheless, sensitivity to cold and tactile pain was compromised in each case. Unlike other subjects, the patient with the best-preserved Vc had a normal threshold for cold sensation. Heat pain thresholds were unaffected, revealing subnuclear modality specificity within the thalamus.