This Week in The Journal

Development/Plasticity/Repair

Versican Guides Nonpeptidergic Nociceptors via NgR2

Bastian E. Bäumer, Antje Kurz, Sarah C. Borrie, Stephan Sickinger, María T. Dours-Zimmermann, et al.

(see pages 1633–1646)

The somata of various somatosensory neurons—including mechanoreceptors, thermoreceptors, and nociceptors—are intermingled in the dorsal root ganglion. These neurons' axons are guided to peripheral targets by different cues. For example, peptidergic nociceptors respond to nerve growth factor and terminate in the stratum spinosum of the epidermis, whereas nonpeptidergic nociceptors respond to glial-derived neurotrophic factor family ligands (GFLs) and terminate in the stratum granulosum. Bäumer et al. report that although subsets of all sensory neuron types express NgR2—a member of the Nogo66 family of guidance receptors—this receptor is especially important for shaping peripheral innervation by nonpeptidergic nociceptors. NgR2 knockout selectively increased the density of nonpeptidergic fibers in the stratum granulosum, resulting in increased sensitivity to noxious mechanical pressure and cool temperatures. Increased peripheral innervation likely stemmed from a failure of nonpeptidergic fibers to be repelled by the extracellular matrix protein versican, which is expressed at the dermal-epidermal border, interacts with NgR2, and repelled wild-type but not NgR2-null axons *in vitro*.

Systems/Circuits

Sex-Specific Neuron and Muscle Properties Shape Locomotion

William R. Mowrey, Jessica R. Bennett, and Douglas S. Portman

(see pages 1579–1591)

Many physical features, including body size, muscle mass, and brain structure, differ between males and females of a species. Males and females also differ in how they perform sex-neutral behaviors such as play, locomotion, and defensive actions. The extent to which such behavioral differences stem from differences in body morphology, muscle physiology, and neural circuitry is largely unexplored. Mowrey et al. investigated this question in *C. elegans*. Male nematodes, which are smaller and more slender than hermaphrodites (modified females), were faster and exhibited greater curvature, longer wavelengths, and greater body-bend frequency during crawling. Masculinizing sensory neurons of hermaphrodites increased the body-bend frequency to that of males, and feminizing males slowed frequency to that of hermaphrodites, but in both cases the body geometry during crawling was unchanged. In contrast, feminizing muscles caused males to exhibit a hermaphodite-like crawling posture without affecting frequency, and masculinizing hermaphrodite muscles masculinized the crawl posture. The results suggest that neurons and muscles change along with body morphology to optimize behaviors.

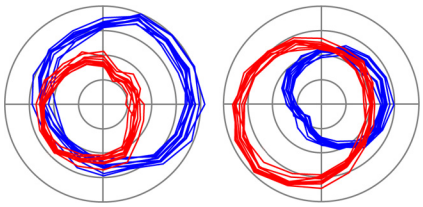
Behavioral/Cognitive

Strength and Variability Guide Force Allocation to Hands

Yousef Salimpour and Reza Shadmehr

(see pages 1806–1818)

Most movements, even simple ones, involve coordinated activation of multiple muscles. To direct these movements, the brain must determine how strongly each muscle should be activated. Although achieving a task such as moving an object can theoretically be accomplished by many different muscle activation patterns, few patterns are used in practice. How does the brain decide which pattern to command? Previous research suggests that the brain chooses strategies that minimize cost, which is determined by muscle strength and variability. Results by Salimpour and Shadmehr support this hypothesis. When people used both arms to move an object to different locations, the dominant arm often contributed more force than the nondominant arm. This was not because the dominant arm was stronger, but because the force it exerted varied less over time. Variability depended on the direction of movement, however, and when the required movement was in directions for which the dominant arm's force was more variable than the nondominant arm's, the arms contributed equal force.



The proportion of force contributed by left (blue) and right (red) arms to move an object in different directions. Results from 10 sessions are shown for a left-handed (left panel) and a right-handed participant. See the article by Salimpour and Shadmehr for details.

Neurobiology of Disease

Spastin Mutations Affect Microtubule Dynamics

Joanna M. Solowska, Mitchell D'Rozario, Daphney C. Jean, Michael W. Davidson, Daniel R. Marenda, et al.

(see pages 1856–1867)

Hereditary spastic paraplegias (HSPs) are a group of adult-onset, progressive neurodegenerative diseases primarily affecting the distal axons of long corticospinal axons, resulting in weakness and stiffness of the lower legs. The most common form of HSP is caused by mutation of spastin, a microtubule-severing protein that likely affects cell shape changes and membrane trafficking. How and why spastin mutations cause axonal degeneration is unknown. Although reduced microtubule severing resulting from haploinsufficiency is often blamed, Solowska et al. argue that such a defect would affect all axons and be most prominent during development. Instead, they propose that accumulation of mutant spastin leads to toxic effects. They show that the M1 isoform, which is less abundant and is expressed only in the spinal cord, accumulated more and was more toxic when mutated than the M87 isoform, which is ubiquitously expressed. Neither mutant isoform reduced microtubule severing when coexpressed with wild-type spastin, but unlike wild-type spastin, mutated M1 spastin associated with microtubules, slowing depolymerization and repolymerization.