This Week in The Journal

● Cellular/Molecular

NCAM Promotes Exocyst-Directed Exocytosis

Yana Chernyshova, Iryna Leshchyns'ka, Shu-Chan Hsu, Melitta Schachner, and Vladimir Sytnyk

(see pages 3522-3535)

Axon growth is directed by extracellular cues that bind to receptors in the growth cone. These receptors are linked to proteins that regulate assembly and disassembly of the axonal cytoskeleton, and thereby regulate neurite extension and turning. Axonal elongation also requires addition of new membrane specifically at the growth cone. This is achieved by targeted exocytosis, which depends on a protein complex called the exocyst that tethers vesicles to specific insertion points. Chernyshova et al. report that the neural cell adhesion molecule (NCAM) directly interacts with components of the exocyst complex and targets them to growth cones. Antibodies that activated NCAM signaling increased exocytosis, phosphorylation of exocyst components, and neurite outgrowth. In contrast, knocking out NCAM or preventing phosphorylation of exocyst proteins reduced membrane insertion at growth cones, association of the exocyst with growth cone membranes, and neurite outgrowth, indicating that NCAM interactions with exocyst components help direct neurite growth.

▲ Development/Plasticity/Repair

Basal Process Imparts Self-Renewability to Cortical Progenitors

Atsunori Shitamukai, Daijiro Konno, and Fumio Matsuzaki

(see pages 3683-3695)

During cortical development, radial glia span the cortical wall, extending one basal and one apical process that attach to the pial and ventricular surfaces, respectively. The nuclei of radial glia move within the cell through the course of the cell cycle, and the cells divide when their nuclei are at the ventricular surface. Sometimes they divide symmetrically, producing two self-renewing daughters that likewise span the cortical wall, and sometimes they divide asymmetrically, producing one radial glia and one daughter that detaches its apical process and migrates basally. These daughters either differentiate into neurons or become self-renewing progenitors in the outer ventricular zone. Shitamukai et al. found that the fate of daughter cells in mice depended on which processes of the mother radial glia it inherited: only daughters that retained the basal process self renewed. Those that also inherited the apical process retained radial glia identity, whereas those that lost the apical process migrated basally and became outer progenitors.

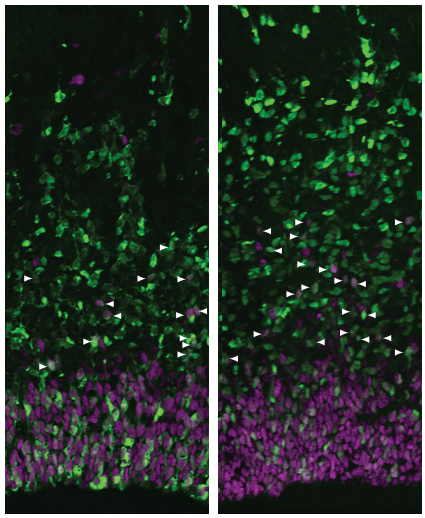
■ Behavioral/Systems/Cognitive

Sleep-Deprived Subjects Alter Gambling Strategy to Maximize Wins

Vinod Venkatraman, Scott A. Huettel, Lisa Y. M. Chuah, John W. Payne, and Michael W. L. Chee

(see pages 3712-3718)

Sleep deprivation impairs many cognitive functions, including vigilance, learning, memory, and decision making. Venkatraman et al. investigated the effects of sleep deprivation on economic decision making by having subjects decide how to modify possible outcomes in a gambling task in order to either minimize losses or maximize gains. To prevent effects on learning from confounding measures of decision making, subjects did not learn the result of gambles until all choices were made. Whereas well rested subjects tended to minimize losses, the same subjects tended to maximize gains after a night of sleep deprivation. These effects were correlated with reduced activation in the insula and increased activation in ventromedial prefrontal cortex (vmPFC). Congruently, when informed of a win, sleep-deprived subjects showed elevated activity in the vmPFC and ventral striatum compared with rested subjects, and when informed of a loss, activity in the insula was lower in sleep-deprived subjects than in rested subjects.



Few undifferentiated progenitor cells (purple) are present outside the ventricular zone (bottom) in developing mouse cortex (left). The number of these progenitors markedly increased when cells were induced to divide asymmetrically such that more daughters received a basal process but no apical process (right). See the article by Shitamukai et al. for details.

♦ Neurobiology of Disease

SMN1 Mutations Disrupt Axonal Transport of mRNA

Claudia Fallini, Honglai Zhang, Yuehang Su, Vincenzo Silani, Robert H. Singer, et al.

(see pages 3914-3925)

Spinal muscular atrophy (SMA) is a degenerative disease that affects motor neurons. It is caused by mutations in SMN1, a protein that associates with components of spliceosomes. Because SMN1 is expressed ubiquitously, why mutations specifically harm motor neurons is unclear. Fallini et al. hypothesized that SMN1 has additional roles in axonal transport or synaptic translation of mRNAs. They visualized interactions between SMN and other proteins by attaching nonfluorescent halves of Venus fluorescent protein (VFP) to SMN1 and potential partners and expressing these fusion proteins in mouse motor neurons. With this technique, fluorescence increases only when two proteins directly interact. SMN1 interacted with HuD, a neuron-specific mRNA-binding protein that regulates axonal transport and translation of growth-associated mRNAs. HuD and SMN1 were cotransported in axons, and knock-down of SMN1 reduced axonal levels of both HuD and mRNA. An SMA-associated mutation in SMN1 reduced interaction between SMN1 and HuD, supporting the hypothesis that SMA results from aberrant mRNA transport.