This Week in The Journal

● Cellular/Molecular

Synapse-Specific Expression of Presynaptic NMDA Receptors

Daniel J. Brasier and Daniel E. Feldman

(see pages 2199–2211)

NMDA receptors (NMDARs) are expressed presynaptically in several cortical regions, including at synapses between layer 4 (L4) and L2/3 of rat barrel cortex. This week, Brasier and Feldman report that presynaptic NMDAR expression is restricted to specific subsets of a neuron's synapses in barrel cortex. Using a slice preparation, the authors blocked postsynaptic NMDARs and recorded from L2/3 neurons while stimulating extracellularly in L4 of the underlying barrel or in nearby L2/3. Impressively, they also recorded from pairs of synaptically coupled neurons in L4 and L2/3. They found that blocking presynaptic NMDARs decreased the amplitude of EPSCs and increased the paired-pulse ratio at L4 to L2/3 synapses, suggesting that presynaptic NMDARs increase the probability of neurotransmitter release at these synapses. In contrast, NMDAR blockers had no effect on horizontal L2/3 inputs to the same L2/3 neurons or on L4–L4 synapses, indicating that the modulation is input- and target-specific.

▲ Development/Plasticity/Repair

Activity-Dependent Translational Repression of Sodium Channels

Nara I. Muraro, Andrew J. Weston, Andre P. Gerber, Stefan Luschnig, Kevin G. Moffat, and Richard A. Baines

(see pages 2099–2109)

Regulation of ion channel expression is essential for controlling neuronal excitability and keeping responses within an appropriate range. Neurons frequently respond to hypoactivity or hyperactivity with a change in ion channel expression. In *Drosophila*, for example, increased neuronal activity results in upregulation of the translational repressor Pumilio, which downregulates the voltage-gated Na^+ channel, para. Muraro et al. now show that Pumilio represses translation of para by binding to an open reading frame in para mRNA. The activity of Pumilio was fine-tuned by two cofactors, Brat and Nanos. Brat was necessary for para repression in some but not all neurons, providing cell-type specificity to translational control. Nanos was required for para repression in all neurons, and it was also repressed by Pumilio, providing negative feedback control. Interestingly, overexpression of Pumilio led indirectly to decreases in a K^+ channel (*Shal*) mRNA, suggesting that Na^+ and K^+ conductances are coregulated in *Drosophila* neurons.

■ Behavioral/Systems/Cognitive

Encoding Place and Sequence in the Hippocampus

Timothy J. Senior, John R. Huxter, Kevin Allen, Joseph O'Neill, and Jozsef Csicsvari

(see pages 2274–2286)

Gamma and theta oscillations in the hippocampus are produced by coordinated activity in neural networks and are thought to facilitate learning and memory by regulating the timing of action potentials in pyramidal cells. For example, in rats, the firing of place cells relative to theta is thought to encode a sequence of locations. Because gamma oscillations are sometimes superimposed on theta during exploration, Senior et al. examined how the timing of pyramidal cell action potentials was modulated under these conditions. They discovered that pyramidal cells fell into two categories that differed in when neurons fired relative to gamma and theta oscillations and whether gamma oscillations modified the neurons' spike timing relative to theta. The cells in the two categories also differed in average interspike interval, burst frequency, and spike waveform. These two classes of cells may be differentially suited to encode specific locations versus sequences of locations.

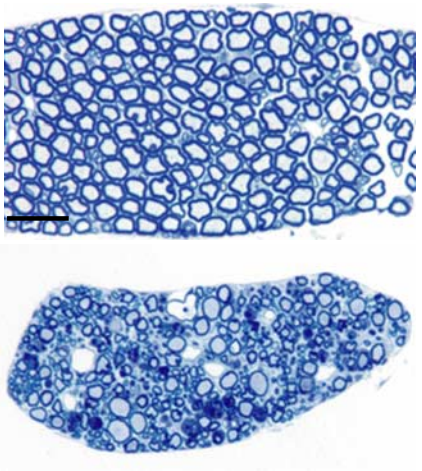
♦ Neurobiology of Disease

Motor Neuron Disease in Dynactin-Mutant Mouse

Fiona M. Laird, Mohamed H. Farah, Steven Ackerley, Ahmet Hoke, Nicholas Maragakis, Jeffrey D. Rothstein, John Griffin, Donald L. Price, Lee J. Martin, and Philip C. Wong

(see pages 1997–2005)

Transgenic mice expressing a mutant form of dynactin in neurons are a useful new model for motor neuron disease, report Laird et al. in this week's *Journal*. As part of a complex with dynein, dynactin is involved in intracellular vesicular transport, and mutations in this gene have been linked to amyotrophic lateral sclerosis (ALS). Dynactin-mutant mice developed many symptoms of ALS: tremors, weakness, and eventual paralysis, accompanied by astrocytic gliosis, accumulation of neurofilaments in proximal axons, motor neuron loss, and muscle atrophy. Before the development of clinical signs (at 5 months), numerous cytoplasmic inclusions, vesicular structures, and autophagosomes appeared in motor neurons. The inclusions contained ubiquitin, a marker of proteolytic degradation. These results are consistent with disruption in vesicular transport being a factor in neurodegeneration in ALS and similar diseases—an appealing hypothesis, because mutations in superoxide dismutase, another gene involved in ALS, are also thought to disrupt intracellular transport.



Ventral roots from control (top) and dynactin-mutant (bottom) mice showing significant loss of large motor axons in the mutant. Scale bar, 50 μm. See the article by Laird et al. for details.