This Week in The Journal

● Cellular/Molecular

Activating Transcription Factor 3 and Regeneration

Rhona Seijffers, Charles D. Mills, and Clifford J. Woolf

(see pages 7911–7920)

Injury of peripheral axons results in a regenerative response from the central as well as the peripheral process of a dorsal root ganglion (DRG) neuron. This "conditioning" effect is mediated by altered transcription of multiple genes and involves both enhanced axonal growth and reduced inhibition by myelin. Seijffers et al. concentrated on the transcription factor ATF3 as a candidate mediator of the enhanced growth because ATF3 is expressed after peripheral, but not central, axonal injury. The authors generated transgenic mice that expressed ATF3 constitutively in DRG neurons. After sciatic nerve crush, ATF3 transgenic mice displayed early nerve regeneration similar to wild-type (WT) mice after a preconditioning lesion. Preconditioned WT mice extended axons into the spinal cord after a dorsal column injury, but axons in ATF3 transgenic mice did not. Similarly, ATF3-expressing neurons were unable to overcome myelin inhibition. Thus ATF by itself did not completely recapitulate the benefits of preconditioning.

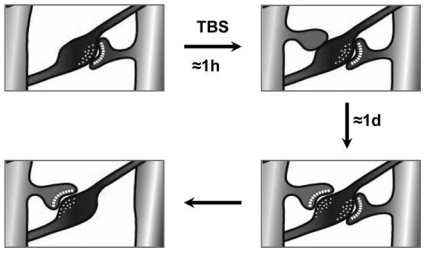
▲ Development/Plasticity/Repair

Making Synapse with New Spines Takes Time

U. Valentin Nägerl, German Köstinger, John C. Anderson, Kevan A. C. Martin, and Tobias Bonhoeffer

(see pages 8149 – 8156)

Sometimes if you want something well made, you have got to allow some time. So it goes it seems with making synapses. Nägerl et al. this week focused on the temporal requirements for the synapse formation at newly formed spines. The authors used two-photon laser-scanning microscopy to image hippocampal slice cultures. After theta-burst stimulation (TBS), CA1 pyramidal neurons generated new dendritic spines that lasted throughout a 19 h imaging period. Spines were visualized in living slices with calcein dye. Most preexisting spines had mature synapses with synaptic clefts and adjacent vesicle-filled boutons. The authors then fixed slices at different time points after TBS for serial section electron microscopy of biocytin-filled neurons. "Young" spines, aged 30 min to 8 h, made physical contact with synaptic boutons but rarely had typical postsynaptic structures. Only older (and wiser?) spines (15–19 h) formed full-fledged synapses.



This schema illustrates a proposed sequence for a newly generated dendritic spine as it contacts a synaptic bouton. Spinogenesis induced by theta-burst stimulation occurs at 1 h (top), followed 1 d later by synapse formation (bottom right). Competition may remove preexisting boutons at a later time (bottom left). See the article by Nägerl et al. for details.

■ Behavioral/Systems/Cognitive

Recognizing Human Bodies, Upright and Inverted

Cosimo Urgesi, Beatriz Calvo-Merino, Patrick Haggard, and Salvatore M. Aglioti

(see pages 8023– 8030)

Visual recognition of the human form is easier when the figure is upright, rather than standing on its head. In fact, it seems there is a cortical region for this task. The extrastriate body area (EBA) in the lateral occipitotemporal cortex prefers bodies upright and can distinguish body parts as well as whole bodies. In this week's *Journal*, Urgesi et al. asked whether body recognition processing is configural, as the "inversion" effect suggests, or local? The authors used repetitive transcranial magnetic stimulation to interfere with premotor, visual, and parietal areas during visual body processing. Disruption of configural processing by ventral premotor cortex stimulation interfered with recognition of upright, but not inverted figures. Stimulation of EBA in contrast interfered with local processing, disrupting recognition of inverted but not upright bodies or body parts. The results pointed to parallel cortical processing pathways for recognition of the human form.

♦ Neurobiology of Disease

A Case for Cytosolic Dopamine Neurotoxicity

W. Michael Caudle, Jason R. Richardson, Min Z. Wang, Tonya N. Taylor, Thomas S. Guillot, Alison L. McCormack, Rebecca E. Colebrooke, Donato A. Di Monte, Piers C. Emson, and Gary W. Miller

(see pages 8138 – 8148)

The vesicular monoamine transporter 2 (VMAT2) packs intracellular vesicles with dopamine for the obvious purpose of neurotransmission. However, this cytosolic scavenging also potentially serves to protect cells from the toxic effects of monoamines. In fact, VMAT is a member of the toxin-extruding antiporter gene family with the interesting acronym TEXAN. Accordingly, Caudle et al. examined whether reduced VMAT2 leads to degeneration of dopamine neurons. The authors examined mice that expressed 5% of the normal protein (VMAT2 LO). These mice showed elevated reactive oxygen species, age-related neurodegeneration in the striatum, reduced striatal dopamine levels, and a corresponding decrease in locomotor behavior. By 18 months, VMAT2 LO mice had lower striatal tyrosine hydroxylase due to loss of DA neurons, and substantia nigral neurons contained levels of α-synuclein associated with Parkinson's disease (PD) pathology. Thus, compromised VMAT2 may increase susceptibility to PD and other neurodegenerative conditions.