This Week in The Journal

● Cellular/Molecular

A Pairing of Transcription Factors

Cross-Repressive Interaction of the Olig2 and Nkx2.2 Transcription Factors in Developing Neural Tube Associated with Formation of a Specific Physical Complex

Tao Sun, Hualing Dong, Lizi Wu, Michael Kane, David H. Rowitch, and Charles D. Stiles
(see pages 9547–9556)

It is a daunting task to sort out the spatiotemporal expression patterns of transcription factors that encode neuronal development. Sun et al. approached this problem for members of two distinct classes of transcription factors, Olig2, a basic helix-loop-helix (bHLH) factor, and Nkx2.2, a homeodomain (HD) factor. Genetic analysis already suggests that these two interact in a cross-repressive manner to delineate the border of the p3 and pMN progenitor domains in the ventral neural tube. Later, they cooperate to promote oligodendrocyte maturation. The authors used two-hybrid and pull-down assays to demonstrate that the two proteins form a complex that requires their bHLH and HD domains. In addition, coexpresssion of the two factors in Cos7 cells allowed translocation of Olig2 from the cytoplasm to the nucleus. Experiments with deletion mutants suggest that the physical interaction, whether direct or indirect, is not sufficient to promote oligodendrocyte differentiation, but appears necessary and sufficient for cross-repression. These results provide further evidence that interactions between these two classes of transcription factors may be a general developmental mechanism.

▲ Development/Plasticity/Repair

Sleepless in the Hippocampus

Sleep Deprivation Causes Behavioral, Synaptic, and Membrane Excitability Alterations in Hippocampal Neurons

Carmel M. McDermott, Gerald J. LaHoste, Chu Chen, Alberto Musto, Nicolas G. Bazan, and Jeffrey C. Magee
(see pages 9687–9695)

The function of sleep remains a mystery, but some speculate that snooze time is necessary to consolidate memories, with neuronal plasticity as the underlying mechanism. A study by McDermott et al. indicates that sleep history in fact affects cellular excitability. Rats were sleep-deprived (SD) for 72 hr in a water bath containing small platforms where they could rest, but not lie down, sort of like a coach seat on a transatlantic flight. This procedure reduced rapid eye movement (REM) sleep. Subsequently, to test memory, a tone (cue) was presented followed by a shock. The next day, SD rats "froze" in the chamber less than control rats, thus indicating a deficit in contextual, hippocampal-dependent memory. There was no difference in a cued memory task; thus amygdala-dependent memory remained intact. In SD animals, the hippocampal CA1 neurons had decreased cell input resistance and enhanced spike frequency adaptation. Excitability of granule cells of the dentate gyrus was unchanged, although long-term potentiation production was reduced in the dentate gyrus and CA1. The authors argue that their results are not a result of immobilization stress but rather a direct consequence of sleep deprivation. The underlying receptors or channels involved in the reduced excitability remain to be determined.

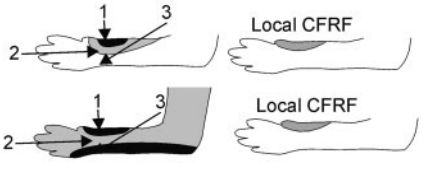
■ Behavioral/Systems/Cognitive

Receptive Field Plasticity in Cerebellar Interneurons

Receptive Field Plasticity Profoundly Alters the Cutaneous Parallel Fiber Synaptic Input to Cerebellar Interneurons *In Vivo*

Henrik Jörntell and Carl-Fredrik Ekerot
(see pages 9620–9631)

Although perhaps not immediately obvious to nonexperts, cerebellum interneurons have distinct cutaneous receptive fields. Inhibitory interneurons (INs) of the molecular layer each receive excitatory input from hundreds of parallel fibers (PFs) and from a single climbing fiber (CF) that determines the receptive field of the interneuron. Thus, only a select few PFs (those with a small receptive field matching that of the adjacent CF) are normally active at IN synapses. The remaining PFs are silent but can be reversibly recruited by coactivation of CFs. Such conjunctive PF–CF stimulation results in a massive expansion of the receptive field of the IN to include the entire forearm in cats. This week, Jörntell and Ekerot examine the underlying synaptic activity *in vivo* using whole-cell patch-clamp recording from interneurons in response to electrical and natural cutaneous stimulation. Their results confirm a long-lasting potentiation of parallel fiber input to interneurons after conjunctive PF and CF activation.



Manual stimulation of the forelimb at three sites (1–3) maps a receptive field of a cerebellar interneuron. Darker shading indicates more synaptic activity. In the bottom panel, note the marked expansion of the receptive field after conjunctive PF–CF stimulation.