

This Week in The Journal

● Cellular/Molecular

Tying Ribbons to the Photoreceptor Synapse

Heather A. Van Epps, Mitsuko Hayashi, Louise Lucast, George W. Stearns, James B. Hurley, Pietro De Camilli, and Susan E. Brockerhoff
(see pages 8641–8650)

The constant barrage of sensory information demands continuous release and recycling of synaptic vesicles at synapses in the visual, auditory, and vestibular systems. The ribbon, a characteristic structural feature of these synapses, appears to be built to handle this intense synaptic vesicle traffic. However, the blind zebrafish mutant *nrc* has photoreceptor ribbons that are unanchored and synaptic vesicles that are few and far between. Van Epps et al. set out to determine the gene underlying this mutant. They used positional cloning to identify a premature stop codon in synaptojanin 1 (*Synj1*) as the culprit. This polyphosphoinositide phosphatase normally aids in clathrin-mediated endocytosis and cytoskeleton modeling. Fish with knock-down of *Synj1* by morpholinos displayed a similar phenotype. These actions are presumably attributable to lack of regulation of the *Synj1* substrate PI(4,5)P₂. These results suggest a role for *Synj1* both in anchoring of ribbons and in maintenance of synaptic vesicles at this synapse.

▲ Development/Plasticity/Repair

FGF and Cortical Laminar Development

Hiroshi Hasegawa, Shizuko Ashigaki, Masako Takamatsu, Rika Suzuki-Migishima, Norihiko Ohbayashi, Nobuyuki Itoh, Shinji Takada, and Yasuto Tanabe
(see pages 8711–8719)

The cortex is made up of tightly organized layers of neurons, each with a distinct function. The “inside-out” pattern of radial migration of neocortical cells is well known, but the factors that determine the laminar identity of a cell have defied explanation. Now, Hasegawa et al. outline a scenario in which signaling by fibroblast growth factor (FGF) and the *Pea3* subfamily

of Ets transcription factors mediates the migration of subsequent generations of cortical neurons. Using *in vivo* electroporation, they introduced dominant-negative DNA-binding domains of the transcription factors to determine their influence. Their results indicate that the first generation of neurons expresses FGF, which signals back to FGF receptors in cortical progenitor cells, and the progenitors in turn express temporally regulated *Pea3* transcription factors. Thus, the elusive “environmental factors” present in the ventricular zone get a name. Using knock-out mice, the authors also implicate FGF18 as the specific feedback signal key to neuronal migration in cortical development.

■ Behavioral/Systems/Cognitive

Selecting the Relevant Task

Marcel Brass and D. Yves von Cramon
(see pages 8847–8852)

A monitor babbles news softly over your head. The conversations of other travelers ebb in and out. The loudspeaker blurts out occasional messages, announcing departures, security measures, and smoking areas. Suddenly, your boarding group is announced, and you snap to attention. This familiar airport scene demands that you constantly and unconsciously sort relevant from nonrelevant information as it arrives. Brass and von Cramon this week sought to find the neural substrate for the selection of task-relevant information. Avoiding confounds of more conventional task-relevance measures, they created a new paradigm that separated the task cue from the task itself. Subjects were presented with a series of color- and shape-coded instructions about what kind of information they were to discern from a coming stimulus. Functional MRI revealed that the left lateral prefrontal cortex and part of the left intraparietal sulcus were activated with selection of task-relevant information rather than with selection of the appropriate response.

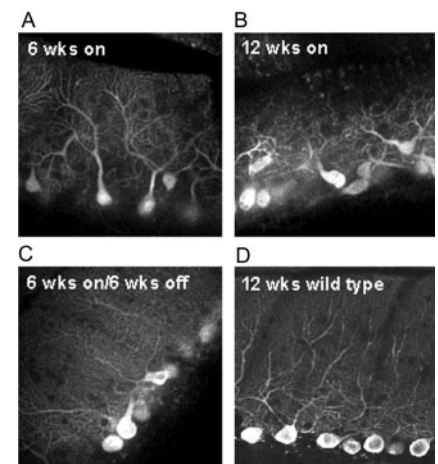
◆ Neurobiology of Disease

Rescuing Mice from Spinocerebellar Ataxia

Tao Zu, Lisa A. Duvick, Michael D. Kaytor, Michael S. Berlinger, Huda Y.

Zoghbi, H. Brent Clark, and Harry T. Orr
(see pages 8853–8861)

The spinocerebellar ataxias (SCAs) are among the handful of triplet-repeat neurological disorders. Type 1 SCA arises from a series of repeated glutamine residues in the ataxin-1 protein, which is encoded by *SCA1* and expressed in Purkinje cerebellar neurons. These neurons eventually degenerate, although motor dysfunction arises well before neuronal death ensues, presumably because of nuclear inclusions of the mutant protein. Could the disease be halted if the wayward protein was removed? This seems plausible given that deletion of *SCA1* has only mild effects in mice. This week, Zu et al. create a tetracycline-regulated conditional mouse model of *SCA1*. They found that when the gene was disabled early in the course of the disease, the pathology was remarkably reversed. Even performance on the complex accelerating rotarod motor task was restored. Smaller gains were made with later adjustments, but the nuclear inclusions of poly-Q protein were reversible even at very late stages. This is good news for these mice and maybe for the therapeutics of these disorders.



For conditional *SCA1*[82Q] mice, 6 weeks with the gene on revealed a detectable degree of Purkinje cell dendritic atrophy that became more severe by 12 weeks (A, B). However, in 6 weeks gene-on/6 weeks gene-off animals, calbindin immunostaining showed essentially normal Purkinje cells, comparable with 12-week-old wild-type mice (C, D). See the article by Zu et al. for details.