This Week in The Journal

● Cellular/Molecular

Transcriptional Control and the Serotonin Transporter

Elena Klenova, Alison C. Scott, Julian Roberts, Shaharum Shamsuddin, Elizabeth A. Lovejoy, Stephan Bergmann, Vivien J. Bubb, Hans-Dieter Royer, and John P. Quinn
(see pages 5966–5973)

The serotonin transporter (5-HTT) is a molecule of interest in neurological disorders. Although as yet no mutations in coding sequences have been associated with CNS disorders, a tenuous link has been made to two polymorphisms within introns of the human gene for 5-HTT. In this week's *Journal*, Klenova et al. examine transcription factor interactions with the variable nucleotide tandem repeat (VNTR) polymorphism found within intron 2. Three allelic variations have been described, each of which produces differential expression of the 5-HTT *in vitro* and *in vivo*. Using a yeast one-hybrid system, the authors report that the Y-box transcription factor YB-1 binds to VNTR and regulates gene expression *in vitro*. This interaction was modulated by another transcription factor and YB-1 binding partner, CTCF. The authors suggest that the variable VNTR number provides differential YB-1 binding sites, and thus may regulate the expression of 5-HTT.

▲ Development/Plasticity/Repair

GAT-1 and Early Hippocampal Activity

Sampsa Sipilä, Kristiina Huttu, Juha Voipio, and Kai Kaila
(see pages 5877–5880)

Although GAT-1, the primary neuronal GABA transporter expressed in the hippocampus, does not affect synaptic responses mediated by single vesicles (miniature IPSCs), it does regulate GABA spillover when adjacent release sites are simultaneously activated or when multiple axons are stimulated. In early development, GABA responses in hippocampal neurons are depolarizing and underlie the so-called giant depolarizing potentials (GDPs) during the first postnatal week. This spontaneous neural activity is thought to be important in shaping the development of hippocampal networks. In this issue Sipilä et al., using whole-cell voltage clamp and field-potential recordings in postnatal hippocampal slices, report that GAT-1 controls the duration of GABA transients during the coordinated firing of pyramidal neurons and interneurons. The GAT-1-specific uptake blocker NO-711 significantly prolonged the synchronous firing of GDPs. As expected, single evoked IPSPs were not affected by uptake block. Thus GAT-1 is in position to affect even this early phase of hippocampal activity.

■ Behavioral/Systems/Cognitive

Decoding Oscillations in the Locust

Javier Perez-Orive, Maxim Bazhenov, and Gilles Laurent
(see pages 6037–6047)

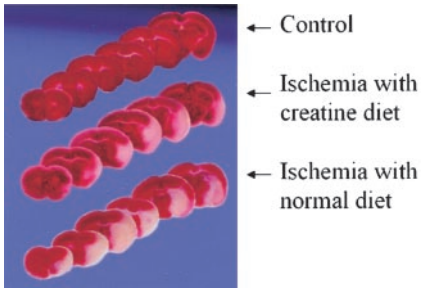
In the locust, excitatory projection neurons (PNs) of the antennal lobe, analogous to the mammalian olfactory bulb, form synapses with Kenyon cells (KCs) in the mushroom body, a structure involved in olfactory memory. Odors evoke firing in specific sets of PNs that in turn activate KC dendrites. But how does the mushroom body decode these combinations to detect odors with high precision? Perez-Orive et al. make the case that KCs use coincidence detection rather than temporal signal integration. The authors combine *in vivo* electrophysiological recordings and computational modeling to show that synchronized oscillatory input from PNs combines with the active membrane properties in KCs to allow supralinear summation of synaptic potentials, thus providing coincidence detector mechanisms (i.e., inputs that arrive together are favored). When the oscillations were blocked, KC neurons were not able to filter noise or distinguish between similar odors.

♦ Neurobiology of Disease

Oral Creatine and Stroke Neuroprotection in Mice

Shan Zhu, Mingwei Li, Bryan E. Figueroa, Aijian Liu, Irina G. Stavrovskaya, Piera Pasinelli, M. Flint Beal, Robert H. Brown Jr, Bruce S. Kristal, Robert J. Ferrante, and Robert M. Friedlander
(see pages 5909–5912)

Creatine has been popularized as a performance enhancer for bodybuilders and athletes. Creatine is also emerging as a protective agent against neurodegenerative diseases as well as acute brain trauma that share the feature of apoptosis. Now Zhu et al. extend the protection to ischemia. Mice received 2 hr of middle cerebral artery (MCA) occlusion followed by 24 hr of reperfusion. Infarcts in mice that were fed a 2% creatine-supplemented diet for the month preceding injury were approximately half the size of controls. Several poststroke biochemical changes accompanied creatine administration, including reduced cytochrome *c* release and caspase-3 activation as well as more stable ATP levels. These results do not determine whether creatine is neuroprotective simply by buffering of ATP levels or whether preserved ATP is a consequence of an independent mechanism of creatine neuroprotection. Treatment required several weeks of pretreatment, because 1 week of pretreatment did not confer protection. It seems that protecting brains, like building muscles, takes time.



Creatine pretreatment reduced ischemic damage attributable to MCA occlusion in mice. The brain sections shown are control (top), ischemic with creatine diet (middle), and ischemia with normal diet (bottom). The pale pink area on the right of sections in the middle and bottom row is the area of damage. See the article by Zhu et al. for details.