This Week in The Journal

● Cellular/Molecular

Synapsin I and Central Inhibitory Synapses

Pietro Baldelli, Anna Fassio, Flavia Valtorta, and Fabio Benfenati

(see pages 13520-13531)

The phosphoprotein synapsin has long been known for its role in the mobilization of synaptic vesicles. Most of these studies focused on excitatory synapses. However, recent studies suggest that inhibitory synaptic transmission also is reduced in neurons lacking synapsin I (SynI). In this week's *Journal*, Baldelli et al. examined inhibitory synapses in cultured hippocampal neurons from mice lacking SynI. IPSCs were smaller in SynI $^{-/-}$ than in wild-type mice. Although paired-pulse depression was not affected, trains of stimuli caused more synaptic depression in neurons lacking SynI. The loss of SynI reduced the size of the readily releasable pool of synaptic vesicles without affecting release probability or quantal size, consistent with a deficit in recruiting or recycling. The number of inhibitory synaptic contact sites was unchanged in the absence of SynI, but rather fewer synaptic vesicles were released with each action potential.

▲ Development/Plasticity/Repair

NR2B-Dependent Signaling during Synaptogenesis

Benjamin J. Hall, Beth Ripley, and Anirvan Ghosh

(see pages 13446-13458)

During development, there is an increase in AMPA receptors relative to NMDA receptors at most cortical excitatory synapses. NMDA receptor composition also evolves with synaptic maturation, leading to an increase in NR2A-containing receptors. This week, Hall et al. show that the NMDA receptor subunit NR2B influences the synaptic recruitment of AMPA receptors. In cultured neurons, as expected, surface expression of NR1 and NR2B appeared first, with gradually increasing NR2A. In NR2B null mice, AMPA-receptor-mediated synaptic currents were larger than in wild-type mice, suggesting that NR2B might prevent synaptic incorporation of AMPA receptors. The effect was cell autonomous, because it also occurred in neurons in which NR2B was knocked down with a short interfering RNA. Synaptic localization of NR2B was required, but its PDZ domain was not. The increase in AMPA receptors in the absence of NR2B depended on increased levels of its chaperone, TARP (transmembrane AMPA receptor regulatory protein).

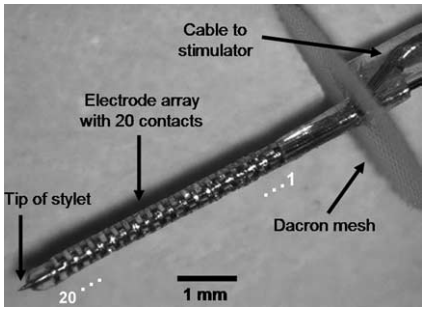
■ Behavioral/Systems/Cognitive

Midbrain Stimulators in Hearing-Impaired Patients

Hubert H. Lim, Thomas Lenarz, Gert Joseph, Rolf-Dieter Battmer, Amir Samii, Madjid Samii, James F. Patrick, and Minoo Lenarz

(see pages 13541-13551)

Cochlear implants (CIs) are perhaps the most successful class of neural prosthetics. However, they are only feasible if the cochlea is implantable and if there is a functional auditory nerve. An alternative, the auditory brainstem implant (ABI), directly stimulates the surface of the cochlear nucleus. Initially used for deafness resulting from acoustic neuromas, ABIs also have been used in some nontumor patients who were not candidates for CIs. This week, Lim et al. report initial results with implants at another site that has a tonotopic organization, the inferior colliculus. The authors implanted three patients with auditory midbrain implants (AMIs) during resection of acoustic neuromas. After implantation, the electrode arrays were stimulated to determine parameters of auditory sensations, including loudness, sound localization, and temporal and direction cues. The patients improved in lip reading, environmental awareness, and speech perception. These are early days for this device, but the results are encouraging.



The image shows the electrode array used in an AMI. The array connected to a microphone, processor, telemetry interface, and current stimulator constitutes the AMI system. See the article by Lim et al. for details.

♦ Neurobiology of Disease

Tobacco Smoke and White Matter Maturation

Leslie K. Jacobsen, Marina R. Picciotto, Christopher J. Heath, Stephen J. Frost, Kristen A. Tsou, Rita A. Dwan, Marcel P. Jackowski, Robert T. Constable, and W. Einar Mencl

(see pages 13491-13498)

"Smoke gets to your white matter" does not sound like a hit tune. But it rings true to Jacobsen et al. The authors examined white matter microstructure in human adolescent smokers and nonsmokers with or without a prenatal exposure to maternal smoking. The authors used diffusion tensor imaging to measure the fractional anisotropy (FA) of white matter. FA measures the directionality of diffusion of water, and for white matter, it increases with age as axon tracts mature. Compared to the other two exposure groups, smokers or those whose mothers smoked during pregnancy had increased FA in anterior cortical areas. Adolescent smokers either with or without a maternal smoking history had increased FA in the internal capsule in the region that contains auditory thalamocortical and cortifugal fibers. FA in the posterior limb of the internal capsule correlated with smokers' reaction time on an auditory attention task.