This Week in The Journal

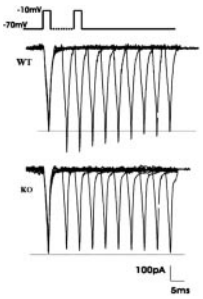
● Cellular/Molecular

Calcium Channel Subtypes and Short-Term Synaptic Plasticity

Carlota González Inchauspe, Francisco J. Martini, Ian D. Forsythe, and Osvaldo D. Uchitel
(see pages 10379–10383)

Anita Scheuber, Richard Miles, and Jean Christophe Poncer
(see pages 10402–10409)

Facilitation of transmitter release occurs with successive calcium channel openings, but the molecules mediating the phenomenon are still unclear. This week, two papers examine the roles of presynaptic calcium channels in facilitation. González Inchauspe et al. measured calcium currents and transmitter release at the giant calyx of Held synapse in mice lacking Cav2.1, the pore-forming subunit of P/Q-type calcium channels. N-type calcium channels (Cav2.2) were able to support vesicle release, but paired-pulse facilitation of synaptic responses and presynaptic calcium currents were absent. The authors suggest that P/Q channels underlie facilitation. Scheuber et al. examine a similar question in the rat CA3/CA1 hippocampal pathway but come to a different conclusion. They pharmacologically separated calcium channel types and found that facilitation was augmented when Cav2.1 was blocked but diminished with Cav2.2 block. Voltage-dependent relief of G-protein-mediated channel inhibition of Cav2.2 channels was responsible for this form of short-term plasticity.



Presynaptic calcium current facilitation evoked by paired-pulse stimulation was present in calyx of Held nerve terminals from wild-type animals (WT), but absent in terminals from mice lacking the Cav2.1 subunit of P/Q-type calcium channels. KO, Knock-out. See the article by González Inchauspe et al. for details.

▲ Development/Plasticity/Repair

Decoying the Nogo-66 Receptor

Shuxin Li, Betty P. Liu, Stephane Budel, Mingwei Li, Benxiu Ji, Lee Walus, Weiwei Li, Adrienna Jirik, Sylvia Rabacchi, Eugene Choi, Dane Worley, Dinah W. Y. Sah, Blake Pepinsky, Daniel Lee, Jane Relton, and Stephen M. Strittmatter
(see pages 10511–10520)

Myelin-derived inhibitory factors limit recovery from spinal cord injury by preventing sprouting and regrowth of axons. These molecules [Nogo, myelin-associated glycoprotein (MAG), and oligodendrocyte myelin glycoprotein (OMgp)] work at the axonal Nogo receptor (NgR). Efforts to block the function of NgR *in vivo* have been moderately successful, and now Li et al. provide more promising results. They created a soluble peptide of the ligand-binding domain of NgR and coupled it to rat IgG1 Fc. They delivered it intrathecally to rats after a spinal cord injury. Axons showed increased sprouting, and rats showed recovery of movement beyond that seen with Nogo antibody treatment, presumably because the peptide disrupts all three receptor–agonist interactions. Electrophysiological measurements showed that improved synapse efficacy accompanied the behavioral improvements. Corticospinal tract neurons and serotonergic, raphespinal neurons contributed to the axonal sprouting. Although NgR–NgR interactions are possible, the authors suggest that the peptide acts like a decoy, sequestering ligand from the endogenous receptor.

■ Behavioral/Systems/Cognitive

Stimulus-Specific Adaptation in the Cat Auditory Cortex

Nachum Ulanovsky, Liora Las, Dina Farkas, and Israel Nelken
(see pages 10440–10453)

Adaptation is one mechanism that the nervous system uses to sort the rare from the common. In neurons from the primary auditory cortex (area A1 in the cat), action potential firing shows strong stimulus-specific adaptation. In this issue, Ulanovsky et al. examine this single-cell adaptation in response to different patterns of pure tones delivered to cats through custom-fitting earphones. These feline musicologists listened to several patterns that the authors called oddball, switching-oddball, and response-curve. Not unexpectedly, adaptation was greater when deviant stimuli in the oddball pattern occurred at a high probability. Overall, the time course of stimulus-specific adaptation spanned a time course from hundreds of milliseconds to tens of seconds. The behavior of the neurons seemed to fit linear models that incorporated both the short- and long-term stimulus history. Adaptation also biased the neurons toward novel or eccentric stimuli. This property appears to be unique to A1 neurons within auditory pathways, because it was not present in auditory thalamic neurons.

♦ Neurobiology of Disease

EtOH, BDNF, and RACK1

Nancy N. H. McGough, Dao-Yao He, Marian L. Logrip, Jerome Jeanblanc, Khanhky Phamluong, Ken Luong, Viktor Kharazia, Patricia H. Janak, and Dorit Ron
(see pages 10542–10552)

How is it that some of us can drink in moderation whereas others fall victim to the physical and psychosocial devastation that is chronic alcoholism? One idea is that chronic excessive alcohol intake results in a series of biochemical adaptations that result in addiction if allowed to proceed unchecked. In this week's *Journal*, McGough et al. identify brain-derived neurotrophic factor (BDNF) as one of the possible brakes on runaway adaptations of this sort. BDNF has already been implicated in control of other drug-addiction pathways. The authors report that BDNF mRNA in neurons *in vitro* increased with acute ethanol exposure and decreased with continuous exposure. Likewise *in vivo*, real-time PCR revealed increases in hippocampal and dorsal striatal BDNF. Purely correlation? Perhaps, but male heterozygous mice lacking one BDNF allele consumed more alcohol than did wild-type controls. The authors traced changes in BDNF expression to the scaffolding protein RACK1 that translocates to the nucleus and regulates BDNF gene expression.