This Week in The Journal

● Cellular/Molecular

Single Synapses Uncaged in the Cerebellum

Jun-ichi Tanaka, Masanori Matsuzaki, Etsuko Tarusawa, Akiko Momiyama, Elek Molnar, Haruo Kasai, and Ryuichi Shigemoto
(see pages 799–807)

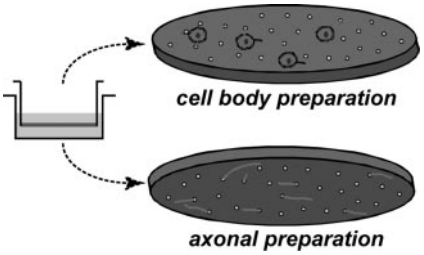
Although single synapses are the functional unit of synaptic transmission, it is understandably difficult to examine the characteristics of any one site. In this issue, Tanaka et al. bring elegance and brute force to the task. They used laser uncaging of photoactivatable glutamate and freeze-fracture replica labeling (FRL) to count AMPA receptors at individual climbing fiber synapses onto Purkinje cells. In slices from postnatal 3- to 4-d-old rats, focal uncaging of glutamate evoked currents through AMPA receptor channels. Using nonstationary fluctuation analysis, they estimated that ~100 channels were activated at well isolated single sites. Subsequently, they reconstructed serial ultrathin sections of the recorded slices to determine the synaptic area. The FRL analysis of immunogold AMPA particles confirmed their calculated synaptic receptor density of 1000–1500 receptors/μm^2. Thus synaptic efficacy of these neonatal climbing fiber synapses is set by the size of the synapse.

▲ Development/Plasticity/Repair

Translation of mRNAs in Axons

Dianna Willis, Ka Wan Li, Jun-Qi Zheng, Jay H. Chang, August Smit, Theresa Kelly, Tanuja T. Merianda, James Sylvester, Jan van Minnen, and Jeffery L. Twiss
(see pages 778–791)

Should proteins be made locally or shipped from the central warehouse? Apparently this choice is available to axons as well as dendrites. In this week's *Journal*, Willis et al. use a proteomics approach to expand the previously short list of proteins produced in axons. They developed a culture method to harvest axons of



DRGs were cultured on a tissue culture insert with 8-μm-diameter pores. The neuron cell bodies and non-neuronal cells remained on the upper membrane surface, whereas axons traversed to the underside of the membrane through the pores. See the article by Willis et al. for details.

injury-conditioned adult rat dorsal root ganglion (DRG) neurons separate from the cell bodies. Newly synthesized proteins metabolically incorporated radioactive cysteine and were then separated by two-dimensional gel electrophoresis and analyzed by mass spectroscopy. The authors identified >100 axonally produced proteins, including cytoskeletal, heat shock, resident endoplasmic reticulum, neurodegenerative disease-related, antioxidant, and metabolic proteins. They used reverse transcription-PCR to confirm that transcripts encoding these proteins were indeed present in the axonal compartment. Nerve growth factor and brain-derived neurotrophic factor selectively increased axonal production of cytoskeletal but not other proteins, by increasing transport of those mRNAs to the axon. The relative contribution of somatic and axonal production for any of these proteins now will be interesting to examine.

■ Behavioral/Systems/Cognitive

Odor Discrimination and High-Frequency Oscillations

Max L. Fletcher, Abigail M. Smith, Aaron R. Best, and Donald A. Wilson
(see pages 792–798)

Oscillatory activity was first reported in the olfactory system >60 years ago. Yet, as is fitting for a good biological problem, its true function in the olfactory system and in other brain regions is still debated. Fast oscillations in the olfactory bulb reflect interactions between the excitatory mitral cells and inhibitory granule and periglomerular interneurons. The oscillations have been postulated to indicate the neural activity underlying odor discrimination. Fletcher et al. test this question by taking advantage of the fact that young rats have not developed their full complement of interneurons in the first few weeks of life. As a result, odor-evoked γ oscillations were not detectable in 7-d-old rat pups. However, the pups showed no discernible deficit in an odor discrimination task compared with their adult, and fully oscillating, comrades. Thus, at least for rat pups, γ oscillations are not an absolute requirement for odor discrimination.

◆ Neurobiology of Disease

Optimizing GDNF Gene Therapy in Parkinsonian Monkeys

Andisheh Eslamboli, Biljana Georgievska, Rosalind M. Ridley, Harry F. Baker, Nicholas Muzyczka, Corinna Burger, Ronald J. Mandel, Lucy Annett, and Deniz Kirik
(see pages 769–777)

Because glial cell line-derived neurotrophic factor (GDNF) promotes the survival of dopamine (DA) neurons, it has been tested, with mixed success, as a therapeutic approach in Parkinson's disease. One problem is the need for continuous delivery of the most effective dose. Eslamboli et al. now undertake this task in monkeys using a recombinant adeno-associated viral vector (rAAV). Their goal was to find a level of GDNF expression that would provide neuroprotection, even regeneration and sprouting of 6-hydroxydopamine (OHDA)-damaged DA neurons, without inducing pharmacological side effects associated with increased dopamine turnover and tyrosine hydroxylase (TH) activity. Unilateral intrastriatal injection of rAAV encoding low levels of GDNF had a minimal effect on dopamine synthesis, whereas high expression caused bilateral increases in TH activity and dopamine turnover. The low dose afforded nearly complete neuroprotection of DA neurons against a 6-OHDA-induced intrastriatal lesion, and improved the monkeys' motor performance.