Images in Neuroscience

Carol A. Tamminga, M.D., Editor

Cognition

Confocal microscopic image of a 10-μm segment of a dendrite of a hippocampal pyramidal cell, illustrating the variety in the shapes of dendritic spines.

Long-Term Potentiation

Long-term potentiation is a critical neural process that is likely to underlie learning and memory formation. Long-term potentiation refers to the increase in the amplitude of a glutamatergic excitatory postsynaptic response that is induced by repeated stimulation of that synapse or by coactivation of two sets of synapses in an associative manner. Long-term potentiation is specific to the activated synapses and persists for many hours to days.

Under normal conditions, synaptic excitation is exclusively mediated by glutamate receptors of the so-called AMPA class. Patterns of stimulation that elicit long-term potentiation, however, result in an activation of not only AMPA receptors but also the class of glutamate receptors sensitive to N-methyl-D-aspartic acid (NMDA). These receptors are unique in that they permit a large influx of calcium ions into the postsynaptic cell. The resulting increase in the intracellular calcium concentration activates calcium/calmodulin-dependent and cyclic-AMP-dependent protein kinases that specifically trigger the process of long-term potentiation.

Although the precise nature of the changes in synaptic transmission that ultimately account for the increase in synaptic strength are still the subject of intense interest (and controversy), it is clear that activated protein kinases may affect the AMPA receptors mediating excitatory synaptic transmission in several ways. First, the AMPA receptors may become phosphorylated by one or both kinases, rendering them more sensitive to presynaptically released glutamate. Second, excitatory synapses are located on the ends of small processes known as dendritic spines (figure), and these may be changed in shape or number after induction of long-term potentiation. Finally, clusters of AMPA receptors may be translocated from an intracellular, subsynaptic location and inserted into the postsynaptic membrane at the end of the dendritic spine. The net effect of all three mechanisms is to increase the sensitivity of the postsynaptic cell to glutamate, thereby increasing the chances that activity in the presynaptic cell will successfully elicit action potentials in the postsynaptic cell. Long-term potentiation thus represents a use-dependent strengthening of connections between cells. Because genetic and pharmacological manipulations that prevent induction of long-term potentiation typically block one or more forms of learning and memory in animal experiments, it is likely that the neurobiological changes in glutamatergic synapses underlying long-term potentiation represent the fundamental cellular basis for cognition and the encoding of memories.

SCOTT M. THOMPSON, PH.D.
Baltimore, Md.

Address reprint requests to Dr. Tamminga, Maryland Psychiatric Research Center, University of Maryland, P.O. Box 21247, Baltimore, MD 21228. Image is courtesy of Dr. Thompson.