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Models of Signaling Mechanisms in LTP

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Much of what we know, or suspect we know, about learning and memory comes from the study of long-term potentiation (LTP). LTP is an increase in the strength or weight of synapses that can be induced by strong high frequency trains of action potentials. Despite years of study, it is still not known precisely how action potentials arriving al synapses in particular temporal patterns can generate cellular signals that trigger the biochemical reactions within dendritic spines that lead to long-term modifications of synaptic strength. This project will provide an understanding of this process by combining modeling and experimental studies to characterize the cellular signaling processes that occur with the development of long-term potentiation. Specific aims are: 1) To quantify how much of a change at individual synapses is necessary to account for the amount of potentiation observed in LTP, 2) To determine systematically stimulation protocols that are successful in eliciting LTP to allow identification of signaling cascades that particular protocols may activate, 3) To characterize the role of synaptic failures in initiating or hindering signaling processes, 4) To identify the differences in signaling mechanisms involved in NMDA-dependent and NMDA-independent forms of LTP in hippocampal area CA1, 5) To understand how molecular signaling complexes develop and function in dendritic spines. The combined modeling and experimental studies will provide critical insights into some of the outstanding questions about the mechanisms of cellular signaling in long-term potentiation. This knowledge can be used to understand mechanisms involved both in normal learning and memory and in the prevention or disruption of learning and memory that occurs with alcohol abuse.

Project (or PI) Website

http://cneuro.zool.ohiou.edu/holmes

Publications

1. Holmes, W.R. and Grover L.M. 2006. Quantifying the magnitude of changes in synaptic level parameters with long-term potentiation. *J. Neurophysiol.* (in press)

2. Holmes, W.R., Ambros-Ingerson, J. and Grover L.M. 2006. Fitting experimental data to models that use morphological data from public databases. *J. Comput. Neurosci.* 20:349-365.

3. Ambros-Ingerson, J. and Holmes, W.R. 2005. Analysis and comparison of morphological reconstructions of hippocampal field CA1 pyramidal cells. *Hippocampus* 15:302-315.