Presentation Abstract

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Authors:	***C. O'DONNELL**[1], T. J. SEJNOWSKI[2,3]; [2]Howard Hughes Med. Inst., [1]Salk Inst. For Biol. Studies, La Jolla, CA; [3]Div. of Biol. Sci., UCSD, La Jolla, CA

Abstract:

The stabilization of long-term synaptic plasticity beyond a few hours requires the synthesis of new proteins. However unlike most other proteins, these plasticity-related proteins (PRPs) are not synthesized in the neuron's cell body but are instead translated in dendrites near the activated synapses. Recent experiments demonstrate that after translation PRPs are restricted to small spatial domains close to the site of synthesis (~100 um), roughly the size of a single dendritic branch (Govindarajan et al., 2011). Despite the crucial role of spatially patterned protein expression in long-term memory, its general function and consequences are not known. We studied this problem using computational modeling at two levels of detail: the biophysical level and the neural circuit level.

Our novel biophysical model of synaptic plasticity in a dendritic neuron was based on data from the rodent hippocampal CA3-CA1 synapse. The model included AMPA receptor dynamics in dendrites, spines and synapses (via trafficking and exo/endocytosis), generic synaptic kinase and phosphotase dynamics and PRP dynamics. Early LTP/LTD occurred through elevation of spine exo/endocytosis rates and up/downregulation of PSD trapping of AMPARs. In contrast, late (PRP-dependent) LTP/LTD was mediated by up/down regulating the number of AMPAR 'slots' in the PSD (Redondo and Morris, 2011). Using the model, we found that each protein synthesis event created a spatio-temporal window within which synaptic strength changes were consolidated. Synaptic changes that occurred outside this window were forgotten within hours.

At the neural circuit level, we derived an expression for the expected persistence of a memory event (a set of synaptic plasticity changes distributed across multiple

neurons) as a function of its spatial overlap with an earlier 'strong' protein-synthesis-inducing memory event. We found that spatially patterned protein synthesis can enable selective consolidation of some memories but forgetting of others, even for simultaneous events that are represented within the same neural population. We then used experimental data on the degree of neural activity pattern overlap in rodent CA3/CA1 (Leutgeb et al., 2004; Vazdarjanova and Guzowski, 2004) to make quantitative predictions on the expected degree of memory consolidation in rodents for events that occur in related environments. Based on these findings we proposed a novel two-step model for selective memory generalization during sleep. The general pattern-matching framework we propose may be broadly applicable to spatial signaling throughout the nervous system.

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Keyword(s): MEMORY

SLEEP

TRANSLATION

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