SYNAPTOGENESIS

Switching to learn

Synaptic plasticity relies on the continuous assembly and disassembly of synapses. Two studies now show that murine β-adducin and its fly homologue HTS, which are actin capping, spectrin binding molecules, have major roles in the coordination of these processes in the hippocampus and neuromuscular junction (NMJ), respectively.

Davis and colleagues found that HTS was located both pre- and postsynaptically at the *Drosophila melanogaster* NMJ, and that flies expressing a truncated form of HTS exhibited a significant loss of presynaptic markers, indicating that an absence of HTS causes the disassembly of synapses. Knocking down presynaptic HTS through RNAi caused similar effects, whereas induction of presynaptic HTS expression in the mutant animals reversed synapse disassembly. Interestingly, further examination of the presynaptic nerve terminals in HTS mutants revealed striking increases in the number of boutons and small calibre, actin-rich membrane protrusions, two hallmarks of enhanced synaptic growth.

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The authors suggest that the loss of HTS's ability to link the dynamic actin cytoskeleton to the more stable spectrin skeleton might have caused the effects that were observed on synapse retraction in the mutant animals. By contrast, the loss of actin capping activity of this protein might have led to an increase in actin polymerization, and hence, the formation of membrane protrusions. The regulation of HTS activity seems to be key in balancing the effects of this protein on new synapse growth versus stability, and the authors showed that HTS phosphorylation at Ser703 was required for localizing the protein to synaptic terminals. However, the precise influence of phoshorylation on the actin capping and spectrin binding activities of HTS remains to be determined.

In another study, Bednarek and Caroni showed that under conditions that enhance plasticity — environmental enrichment — β-adducin is required for the assembly and disassembly of a subpopulation of synapses in the mouse hippocampus, and the subsequent improvement in long-term memory. As in the fly study, the absence of β-adducin led to an increase in spine structures and a decrease in synapse assembly at those spines. Through use of protein synthesis and kinase inhibitors, the authors showed that in mice that were exposed to environmental enrichment, non-phosphorylatable β-adducin maintained synapses in a destabilized state and drove new synapse assembly, whereas protein kinase C (PKC)-phosphorylated β-adducin was necessary for synapse disassembly. Interestingly, improvement in long-term memory formation in mice following exposure to environmental enrichment required both the phosphorylated and dephosphorylated forms of β-adducin, highlighting the functional implications of impaired synapse assembly and disassembly. Future studies of the regulation of β-adducin activity might shed further light on how synapse turnover underlies learning and memory.

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ORIGINAL RESEARCH PAPERS Pielage, J. *et al.* Hts/Adducin controls synaptic elaboration and elimination. *Neuron* **69**, 1114–1131 (2011) | Bednarek, E. & Caroni, P. β-Adducin is required for stable assembly of new synapses and improved memory upon environmental enrichment. *Neuron* **69**, 1132–1146 (2011)