On the Mechanism of Synaptic Depression Induced by CaMKIIN, an Endogenous Inhibitor of CaMKII

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Activity-dependent synaptic plasticity underlies, at least in part, learning and memory processes. NMDA receptor (NMDAR)-dependent long-term potentiation (LTP) is a major synaptic plasticity model. During LTP induction, Ca2+/calmodulin-dependent protein kinase II (CaMKII) is activated, autophosphorylated and persistently translocated to the postsynaptic density, where it binds to the NMDAR. If any of these steps is inhibited, LTP is disrupted. The endogenous CaMKII inhibitor proteins CaMKIIN?,? are rapidly upregulated in specific brain regions after learning. We recently showed that transient application of peptides derived from CaMKIIN? (CN peptides) persistently depresses synaptic strength and reverses LTP saturation, as it allows further LTP induction in previously saturated pathways. The treatment disrupts basal CaMKII-NMDAR interaction and decreases bound CaMKII fraction in spines. To unravel CaMKIIN function and to further understand CaMKII role in synaptic strength maintenance,