Keep CALM and Mind the Synapse

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Calcium is a ubiquitous second messenger, and at synapses it is essential for the release of neurotransmitter. However, changes in the local calcium concentration also affect the morphology of the synapse, which can significantly change the dynamic of transmission. We have previously described a phenomenon of developmental synapse addition in the neuromuscular system of C. elegans. During this addition, synapses elongate and divide to form new synapses from existing ones. We also found a genetic pathway by which this addition occurs. This pathway includes a calcium channel that is resident at the synapse, the calcium-dependent kinase (CaMKII) and a calcium binding protein named calmyrin in vertebrates. Loss of function in these genes results in synapses that begin to elongate, but then fail continue. We also have identified structural proteins at the synapse that are required for inhibition of elongation in order to promote division. Here I will discuss how loss of function mutations in the calmyrin ortholog, calm-1, can suppress defects that are induced by other proteins involved in this pathway, and thus may be a critical effector in this pathway. Mutations in human calmyrins are linked to a number of inherited disorders, including Usher Syndrome, Autism and Alzheimer's disease, thus it is important to understand how this protein works in the development and maintenance of neural networks.