Presentation Abstract

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Presentation Title:	Activity dependent modulation of synaptic transmission by presynaptic ryanodine receptors: A dichotomy of short-term depression and facilitation
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Abstract:	Recent studies show extensive presence of Endoplasmic Reticulum (ER) in the presynaptic terminals of CA3-CA1 synapses in the hippocampus. Separately, it has been suggested in that calcium release from intracellular stores plays an important role in various forms of plasticity, however the exact role of presynaptic calcium stores has not been quantified. One of the reasons being the technical difficulty of making any direct measurement of identifying the different sources of calcium in tiny spaces of CA3 axons. Here we propose a detailed computational model of presynaptic terminal that includes all the necessary components that regulate synaptic transmission and, the machinery required for calcium release from intracellular stores (ER, SERCA Pumps, Ryanodine Receptors (RyRs), Inositol Triphosphate Receptors (IP3Rs), Metabotropic Glutamate Receptors (mGluRs) and related G-Protein mediated pathway). Our Monte Carlo simulations in a physiologic geometry of a reconstructed CA3-CA1 synapse show that calcium release from RyRs and IP3Rs can amplify the calcium signal generated by Voltage Dependent Calcium Channels (VDCCs) under conditions of sustained stimulus. The resulting increase in base level calcium can modify the release probability profile. Calcium dynamics regulated by the calcium stores is not tightly temporally correlated with ongoing electrical activity like the calcium release through VDCCs. The enhanced asynchronous activity as a consequence of store release can deplete vesicle resources and lead to prolonged short-term depression. Our model also shows larger paired pulse facilitation ratios for these terminals

compared with presynaptic terminals without ER and these results are in excellent agreement with experimental data. We show that the geometrical arrangement, the distribution, and the interplay between IP3Rs and RyRs dynamically regulate calcium and short-term plasticity.

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IP3R

RyR2

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