Presentation Abstract

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Presentation Title:	The A-type potassium current regulates ER calcium release through inositol triphosphate receptors in a hippocampal pyramidal cell model
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Abstract:

The role of endoplasmic reticulum (ER) Ca^{2+}, released through inositol triphosphate receptors ($InsP_3Rs$), in mediating intraneuronal Ca^{2+} waves and in regulating neural plasticity is well established. An important characteristic of $InsP_3R$ subunits present on the ER of hippocampal pyramidal neurons is that lower cytosolic calcium ($[Ca^{2+}]_c$) co-activates these receptors, while higher $[Ca^{2+}]_c$ inhibits them. Further, the ER runs parallel to the dendritic membrane, which is endowed with several voltage-gated ion channels that can modulate $[Ca^{2+}]_c$. Taking these together, we hypothesized that the dependence of $InsP_3R$ function on $[Ca^{2+}]_c$ would translate into the regulation of ER Ca^{2+} release by active dendrites. In this computational study, based on CA1 pyramidal neurons, we tested this hypothesis by exploring the interactions of a dendritic channel that can modulate $[Ca^{2+}]_c$ -- the *A*-type K^+ channel (*A* channel) -- with $InsP_3Rs$ on the ER membrane. First, we employed experimentally constrained morphology and kinetics for various model constituents to replicate intraneuronal Ca^{2+} waves using two experimentally validated protocols. Next, we confirmed that an increase in *A*-channel density resulted in a decrease in $[Ca^{2+}]_c$ through voltage gated Ca^{2+} channels (VGCC) during action potentials, and through VGCCs and NMDARs during excitatory postsynaptic potentials. In this experimental setup, low *A*-channel density resulted in high $[Ca^{2+}]_c$, which in turn reduced regenerative release of Ca^{2+} through $InsP_3Rs$. On the other hand, increase in *A*-channel density led to increase in both the amplitude and the duration of Ca^{2+} released through $InsP_3Rs$, leading to sustained Ca^{2+} waves. Next, to understand the role of store Ca^{2+} in plasticity frameworks, we employed two different classes of synaptic stimulation protocols (900 pulses of

various stimulus frequencies and theta burst stimulation (TBS)), and incorporated a Ca^{2+}-dependent plasticity rule at a typical AMPAR-NMDAR-mGluR (Group I) containing synapse. Using the 900 pulses protocol, we found that increased mGluR density manifested as a leftward shift in the BCM-like synaptic plasticity curve in a density dependent manner. Finally, increase in dendritic *A*-channel density resulted in increased contribution of ER Ca^{2+} to TBS-induced synaptic plasticity, with the magnitude of this contribution decreasing with an increase in NMDAR:AMPAR ratio at the synapse. Our results suggest that the interactions between active dendrites and ER receptors could regulate the spatio-temporal spread of Ca^{2+} released through $InsP_3Rs$ and influence integration of biochemical signaling involved in various physiological processes.

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Dendritic excitability

Synaptic plasticity

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