Presentation Abstract

Program#/Poster#:	240.20/F2
Title:	Intracellular calcium store depletion in rat hippocampal neurons induces long-term increases in the h current
Location:	Hall A-C
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Abstract:	The role of intracellular calcium stores in numerous forms of activity-dependent synaptic plasticity is well established. However, long-term plasticity in voltage-gated ion channel properties mediated by intracellular calcium stores has not been well explored. In this study, employing whole-cell patch-clamp recordings from 4-7 week old male Sprague Dawley rat hippocampal CA1 pyramidal neurons, we report that store depletion induced through ten minute treatment with either 20 μM cyclopiazonic acid (CPA) or 10 μM thapsigargin (TG) led to a long-term increase in the hyperpolarization-activated nonspecific-cation (h) current. This was inferred from the following significant changes at 40 min after baseline: a 35-40% reduction in input resistance, lower action potential firing frequency for given step current injections, a 40-50% increase in resonance frequency, a 300-500% increase in the total inductive phase, a 15-20% increase in resonance strength and a 25% reduction in temporal summation of alpha current injections (CPA: n=7; TG: n=5). We then tested this inference pharmacologically using 20 μM ZD7288, a specific h-channel blocker, in the recording pipette (n=5). We found that CPA-induced reductions in input resistance, action potential firing frequency and temporal summation were all abolished in the presence of ZD7288, while all impedance parameters displayed low-pass characteristics through the entire experimental period. We also found that all CPA-induced changes were blocked by 20 mM BAPTA in the recording pipette (n=6) emphasizing the necessity of postsynaptic calcium in the increase of the h current. Finally, all CPA-induced changes were significantly suppressed in the presence of NMDA receptor antagonists 50 μM D,L-APV and 10 μM (+)MK801 in the bath (n=7), highlighting the possible role for calcium entry through NMDA receptors in this form of plasticity. We are performing additional experiments to explore the mechanisms underlying

this form of plasticity, and to understand the somato-dendritic locus of such plasticity and its relevance to activity-dependent forms of plasticity of the h current. These results suggest an active role for intracellular calcium stores in regulating intrinsic excitability and postsynaptic signal integration in CA1 pyramidal neurons.

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