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Presentation Abstract

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Presentation Title:	Modulation of intrinsic response dynamics by subthreshold inactivating conductances in rat hippocampal pyramidal neurons
Location:	WCC Hall A-C
Presentation time:	Monday, Nov 17, 2014, 8:00 AM -12:00 PM
Presenter at Poster:	Mon, Nov. 17, 2014, 11:00 AM - 12:00 PM
Topic:	++B.04.c. Potassium channels
Authors:	***R. K. RATHOUR**, R. NARAYANAN; Indian Inst. of Sci., Bangalore, India
Abstract:	In a recent modeling study (Rathour and Narayanan, PNAS, 111(17), 2014), we had shown that spatiotemporal interactions among several voltage-gated ion channels, in conjunction with passive membrane properties, could maintain homeostasis in functional maps even in the absence of individual channelostasis. Specifically, we had demonstrated that two subthreshold inactivating conductances (T-type Ca^{++} and A-type K^+) played critical roles in bringing about homeostasis in coexistent functional maps related to intrinsic response dynamics (input resistance, R_{in}; resonance frequency, f_R; resonance strength, Q; total inductive phase, Φ_L; and maximal impedance amplitude, $\|Z\|_{max}$). Assessing the role of the two inactivating conductances in each of these functional maps, we had predicted a previously unknown role for them in regulating impedance-related functional maps. We experimentally tested these theoretical predictions on rat (5[[unable to display character: –]]10 weeks, Sprague Dawley) CA1 pyramidal neurons using whole-cell patch-clamp recordings (at ~33 °C). In doing this, we employed two pharmacological agents each for blocking the A-type K^+ (200 μM $BaCl_2$ or 150 μM 3,4-DAP in the bath) or T-type Ca^{++} (50 μM $NiCl_2$ or 10 μM Mibefradil in the

bath) channels and assessed somatic measurements before and after pharmacological treatment. Consistent with previous literature, blocking *A*-type K^+ channels through either agent increased R_{in} and the action potential firing frequency of these neurons. With reference to impedance-related measurements, whereas treatment with $BaCl_2$ increased $|Z|_{max}$ (32%), reduced f_R (30%) and Φ_L (44%), at [[unable to display character: –]]65 mV, treatment with 3,4-DAP did not significantly alter these measurements although the direction of changes were similar to those of $BaCl_2$. Experiments involving the blockade of *T*-type Ca^{++} conductance showed a significant increase in Q (~4%) and Φ_L (~31%), at [[unable to display character: –]]65 mV, after treatment with $NiCl_2$, but treatment with mibefradil did not alter any measurement significantly. Whereas the differences in the action of $BaCl_2$ and 3,4-DAP could be associated with the blockade of other channels (*e.g.*, inward-rectifying K^+) by $BaCl_2$, the effects of $NiCl_2$ and Mibefradil on all measurements are not very different from each other across a majority of membrane voltages. Despite such dichotomy associated with the specific choice of pharmacological agent, our conclusions are broadly in agreement with our predictions for somatic measurements. We are performing analogous experiments on pyramidal neuron dendrites to fully validate our predictions on the role of these inactivating ion channels in regulating impedance-related functional maps.

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Functional maps

Intrinsic response dynamics

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