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Presentation Abstract

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Title: Low ca^{2+} buffering and slow ca^{2+} extrusion in a dendritic inhibitory interneuron of rat hippocampus

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Abstract: Ca^{2+}-mediated excitotoxicity has been proposed to underlie the selective loss of dendritic inhibitory interneurons in epileptic hippocampus. In the present study, we investigated Ca^{2+} buffering and action potential (AP)-evoked Ca^{2+} signaling in the dendrites of oriens lacunosum-moleculare (O-LM) cells in the hippocampal CA1 region, a major type of dendrite-targeting interneurons, using a combination of whole-cell patch-clamp recordings with fast Ca^{2+} imaging in rat brain slices. Cells were loaded with fluorescent Ca^{2+} indicators fura-2 or Oregon Green BAPTA-1 (OGB-1) by patch-clamping the cell bodies and allowing the dyes to diffuse into the dendrites. Ratiometric Ca^{2+} imaging was used to determine the effect of an added Ca^{2+} buffer fura-2 on AP-evoked Ca^{2+} transients. To estimate the AP-mediated Ca^{2+} load and endogenous Ca^{2+}-binding ratio (κ_s) in the proximal dendrites, fluorescence signals were converted into Ca^{2+} concentrations ($[Ca^{2+}]_i$) using isosbestic ratioing method and were analyzed on the basis of the ‘single compartmental model’. The estimated resting $[Ca^{2+}]_i$ was 43 nM and the build-up of $[Ca^{2+}]_i$ during a single AP was up to 613 nM. Analysis of Ca^{2+} transients during fura-2 (150 μM) loading or under different steady-state fura-2 concentrations indicated that O-LM cells have relatively low endogenous Ca^{2+} buffer capacities: the κ_s was 19-23

during fura-2 loading and ~27-58 under steady-state fura-2 concentrations, respectively. The AP-evoked Ca^{2+} signal decays with time constants of about 128-347 ms, corresponding to extrusion rates of 168-258 s^{-1}. To further examine the spatial profile of AP-evoked dendritic Ca^{2+} transients, we measured somatic AP-evoked Ca^{2+} transients along dendrites using the Ca^{2+}-sensitive dye OGB-1. Single APs or AP trains induced by somatic current injection reliably evoked uniform and robust Ca^{2+} accumulations in the dendritic regions up to 150 μm from the soma. The amplitude and decay of Ca^{2+} transients associated with backpropagating APs are relatively independent of distances from the soma. These results show that O-LM cells have low endogenous Ca^{2+}-binding ratios associated with slow Ca^{2+} extrusion that allow large, uniform and prolonged $[Ca^{2+}]_i$ accumulation along somato-dendritic domains. These unique features of Ca^{2+} dynamics may be relevant to synaptic plasticity and the selective vulnerability to excitotoxicity of O-LM cells.

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calcium imaging

Ca2+-binding ratio

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