Inactivation of T-type calcium channels in the apical proximal dendrites of CA3 neurons; A role for the mossy fibre-CA3 synapse

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A significant proportion of the low-threshold T-type Ca^{2+} channels are inactivated at around resting membrane potentials. Little is known about the inactivation profile of T-type channels in different dendritic compartments. Here we map T-type Ca^{2+} channel inactivation on individual CA3 pyramidal neurons. Methods: Sharp electrode (tip filled with Oregon Green BAPTA-1) recordings were made from CA3 pyramidal neurons in organotypic hippocampal cultures. Ca^{2+} transients elicited by back propagating action potentials were monitored using confocal microscopy. Transients in the soma, proximal and distal apical dendrites were measured. Results: Block of T-type channel activity with the antagonist Ni^{2+} (100Î¼M) was significantly different in the peri-somatic and proximal apical dendritic compartments (Ni^{2+} block; 25.6 ± 7.5%(soma) vs. 0.07 ± 8.6% (proximal dendrite), n=15, $p \leq 0.05$). Ni^{2+} block in distal apical dendrites was 49 ±5.3%, n=7. T-type Ca^{2+}channels can be de-inactivated by hyperpolarizing potentials. The injection of a constant current, shifting the membrane potential by –20mV, revealed a Ni^{2+}-sensitive component of the transient in the proximal apical dendrite (Ni^{2+} block; 19% ±9, n=6, p = 0.1). This argues that T-type Ca^{2+} channels are present, but normally inactivated in this compartment. Mossy fibres originating from dentate granule cells form synapses almost exclusively onto the proximal apical dendrite of CA3 pyramidal neurons. To test if release of glutamate from these unusual synapses was involved we applied the AMPA/kainate receptor antagonist, CNQX (20Î¼M). CNQX revealed a significant increase in the Ca^{2+} transient (105 ±46%, n=12), a component of which was Ni^{2+} sensitive (Ni^{2+} block in CNQX= 31± 11%, n=12). Conclusion: These results demonstrate a proximal apical dendrite specific T-type channel inactivation on CA3 pyramidal neurons. This inactivation depends on the release of glutamate from mossy fibre-CA3 pyramidal neuron synapses.