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LOCAL DENDRITIC CALCIUM TRANSIENTS CAUSED BY UNITARY SYNAPTIC EVENTS IN HIPPOCAMPAL NEURONS. V. N. Murthy*, T.J. Sejnowski and C.F. Stevens. Computational Neurobiology, and Molecular Neurobiology Laboratories, Salk Institute, 10010 N. Torrey Pines Rd., La Jolla, CA 92037.

Spontaneous, action potential-independent calcium transients have been observed in dendrites of cortical neurons, and are presumed to be caused by spontaneous transmitter release (Science, 263:529). To determine the mechanisms involved in these presumed miniature synaptic calcium transients (MSCTs), we performed high-temporal resolution confocal imaging of cultured hippocampal neurons filled with 50 μM fluo-3 through a patch pipette. MSCTs were observed at resting membrane potentials in the presence of TTX and no added Mg^{++}, and 100 mosM sucrose to increase spontaneous vesicle release. MSCTs persisted when AMPA receptors were blocked by 10 μM DNQX, and calcium channels were blocked by 50 μM cadmium. MSCTs were blocked reversibly by 100 μM D-APV, an NMDA receptor antagonist. In the presence of 3 mM external Mg^{++}, MSCTs could be suppressed by voltage-clamping the soma at -70 mV; transients reappeared when the membrane was depolarized to -30 mV to remove the Mg^{++} block of NMDA receptors. Taken together, these findings indicate that MSCTs are caused by calcium entry through NMDA receptors when spontaneous vesicle release occurs. MSCTs originate at sites 1 - 2 μm along the dendritic axis, and can spread to 10 μm axially. Preliminary analysis of multiple occurrences of MSCTs at a single site indicates that they can vary considerably in amplitude and duration. These experiments could further the understanding of the causes of response variability at single synapses.
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