High speed two-photon imaging of calcium rise time kinetics and calcium handling in dendritic spines

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Dendritic spines are tiny protrusions located on dendrites which act as biochemically isolated compartments. They are the receiving ends of most of the excitatory synapses in the brain. Calcium signalling in these structures received much attention in recent years because of its central role in synaptic plasticity. So far, calcium handling in spines was studied based on the decay kinetics of calcium transients, either evoked by back propagating action potentials or synaptic stimulation. Rise times of calcium transients were never measured due to technical limitations, but they may be crucial for synaptic plasticity and may reveal important properties of spines and dendrites. With the use of ultra-fast, precisely targeted, two-photon point imaging we were able to measure both rise- and decay kinetics of fast calcium transients in spines and small dendrites of pyramidal cells in mouse visual cortex. We observed that both rise and decay kinetics are at least twice as fast in spines compared to the parent dendrite. To investigate whether differences in calcium kinetics between spines and dendrites were due to morphological differences in surface to volume ratio (SVR) we constructed a one-compartment dynamical model to simulate fast calcium signals. The model included calcium buffering by the dye, endogenous calcium buffering, calcium influx and calcium extrusion and allowed testing of model parameters related to calcium handling and SVR in physiological ranges. Numerical simulations showed that morphological parameters alone are not sufficient to explain differences in calcium handling of dendrites and spines. The model predicts that spines and small dendrites differ in endogenous buffer capacity. In addition, it predicts differential dynamics of free calcium and calmodulin-CAMKII activation in these compartments.

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