Abstract View

ANATOMICAL AND FUNCTIONAL MICRODOMAINS OF CALCIUM AND CALCIUM-DEPENDENT PROTEINS IN DENDRITIC SPINES.

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Intracellular Ca^{2+} concentration is central in regulating synaptic efficacy, but it also has many other effects. The focus of this study is on dendritic spines, which act as specialized compartments for calcium signals. To augment imaging methods that lack the spatiotemporal resolution to explore this compartmentalization, we have combined immunocytochemical data with biophysical modeling. High-resolution immunogold studies reveal that both ligand-gated NMDA receptors and L-type voltage-gated calcium channels concentrate at the synapse in neocortex and hippocampus. In addition, several calcium-binding proteins concentrate at the PSD, as may the phosphatases PP1 and PP2B. Monte Carlo simulations of Ca^{2+} dynamics following different types of neuronal activity result in different Ca^{2+} distributions within the spine, and consequently to differential activation of calcium-dependent proteins. Both CaMKII and PP2B, implicated in the induction of LTP and LTD, respectively, are activated by calmodulin (CaM). When action potentials and EPSPs are paired to induce LTP (EPSP precedes AP) the increase in $[Ca^{2+}]_i$ is 3 times greater than when paired to induce LTD (AP precedes EPSP), but there is a greater than 30-fold difference in the activation of CaM. Moreover, CaM activation is sensitive to its spatial location in the spine relative to the location of calcium sources. This suggests a mechanism for the non-linear transformation of $[Ca^{2+}]_i$ to biochemical activity.

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