Dynamic Interactions of cAMP Transients and Spontaneous Calcium Spikes

The universally demonstrated functions of cAMP and Ca\textsuperscript{2+} as second messengers in organisms from bacteria to yeast, plants, and animals make it important to experimentally investigate and model the complex signaling network they generate. Previous work has characterized the production and function of Ca\textsuperscript{2+} oscillations, and the physiological significance of the temporal patterns of these transients. Here we report the real-time observation of spontaneous cAMP transients and kinetic interactions between Ca\textsuperscript{2+} and cAMP in embryonic spinal neurons. We find that only specific patterns of Ca\textsuperscript{2+} transients elicit cAMP transients, and that transient elevations of cAMP briefly increase Ca\textsuperscript{2+} spike frequency. Using these data we construct a mathematical model of Ca\textsuperscript{2+}-cAMP crosstalk that reproduces the experimental observations and demonstrates the role of feedback loops in the system. The model predicts that Ca\textsuperscript{2+}-cAMP network is tuned to optimize production of cAMP transients, and defines domains in which stimuli generate distinct temporal patterns of Ca\textsuperscript{2+} and cAMP. Our findings may be relevant to regulation of gene expression by patterns of second messenger oscillations, since similar frequencies of cAMP transients induced by serotonin modify gene expression in the nervous system.

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