# Buffer kinetics shape the spatiotemporal patterns of $IP_3$-evoked $Ca^{2+}$ signals in human neuroblastoma cells.

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$Ca^{2+}$ release through $IP_3$Rs plays a diverse role in cellular physiology. High [$IP_3$] gives rise to repetitive, propagating $Ca^{2+}$ waves whereas lower [$IP_3$] evoke transient, localized $Ca^{2+}$ elevations termed puffs. The spatiotemporal properties of $Ca^{2+}$ release enables a high degree of specificity of cellular response. To better understand the physiological functions of local $IP_3$ mediated $Ca^{2+}$ signals in neurons we imaged responses evoked by UV-flash photolysis of membrane-permeant caged $IP_3$ in human neuroblastoma (SH-SY5Y) cells. Photoreleased $IP_3$ resulted in puffs persisting for several minutes, indicating a slow rate of $IP_3$ turnover in these cells. Puff amplitudes were almost independent of [$IP_3$], but puff frequencies increased with increasing photorelease of $IP_3$. Recruitment of puffs differed markedly between sites, suggesting a heterogeneity in their sensitivities. Experiments were performed following loading of cells *via* membrane-permeant ester with intracellular concentrations of tens of μM EGTA so as to 'balkanize' $Ca^{2+}$ waves into discrete localized $Ca^{2+}$ puffs. Surprisingly, puff amplitudes were potentiated (~3-fold) by nanomolar intracellular concentrations of EGTA; though not by similar concentrations of BAPTA. Given that concentrations of EGTA are low as compared to expected concentrations of other endogenous and exogenous $Ca^{2+}$ buffers it seems unlikely that potentiation results from buffering of inhibitory $Ca^{2+}$ feedback on $IP_3$R, but suggests a high-affinity interaction of EGTA with the $IP_3$R.

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