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SYNAPTIC TRANSMISSION

Keeping calcium contained

The activity of cortical excitatory pyramidal neurons is kept in check by GABAergic interneurons, including those expressing somatostatin (SOM-INs). GABAergic inhibition is known to regulate action potential generation, and it has been proposed that the many dendritic SOM-IN synapses could exert localized control over dendritic electrical or biochemical signalling. Conclusive evidence for this hypothesis has been lacking, but in a new study, Chiu *et al.* show that SOM-INs exert specific, focal regulation of calcium signalling in pyramidal cell dendritic spines.

Chiu *et al.* used a viral vector to selectively express channelrhodopsin 2 in SOM-INs in the prefrontal cortex. The authors optogenetically stimulated cortical SOM-INs and induced an action potential in the pyramidal cell of interest. Using two-photon laser scanning microscopy, they monitored the influence of the SOM-IN-evoked inhibitory postsynaptic currents (IPSCs) on dendritic calcium fluxes in the pyramidal cell. Evoking an IPSC immediately before an action potential resulted in an attenuation of the calcium response in over half of the spines measured. Interestingly, the authors noted that inhibited spines often appeared to be adjacent to uninhibited spines, suggesting that the response was compartmentalized.

To investigate this further, the authors monitored a small dendritic region of a pyramidal cell. Using a spine that showed robust inhibition of the evoked calcium response as a reference, they monitored calcium changes in adjacent spines and the dendritic shaft and found little correlation between them. Mimicking SOM-IN activity pharmacologically by one- or two-photon uncaging of GABA produced similar inhibitory compartmentalization of the calcium signal. The compartmentalization was influenced strongly by the precise diffraction-limited uncaging location, indicating a high degree of spatial precision of IPSC influence on the calcium response. Furthermore, computer modelling of action potential-evoked calcium influx into a single spine indicated that the GABAergic inhibition of calcium transients was localized to the targeted spine and that neither neighbouring spines nor the dendritic branch were affected.

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J. Vallis/NPG

NMDA receptor signalling in apical dendrites is known to be important for the integration of inputs to pyramidal cells. Two-photon uncaging of glutamate (to mimic synaptically evoked calcium influx) evoked NMDA receptor-dependent excitatory postsynaptic potentials (EPSPs). Uncaging of GABA in a reference spine resulted in highly compartmentalized inhibition of both calcium transients and EPSPs. Importantly, GABA uncaging caused a reduction in the summation of glutamatergic responses from adjacent spines, suggesting that it has a potential role in synaptic integration.

These findings reveal a previously unidentified mechanism in which SOM-INs modulate evoked calcium responses in a spine- and synapse-specific manner, and have a role in the induction of plasticity at glutamatergic synapses.

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ORIGINAL RESEARCH PAPER Chiu, C. Q. *et al.* Compartmentalization of GABAergic inhibition by dendritic spines. *Science* **340**, 759–762 (2013)