A dendritic switch for synaptic plasticity

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A central tenet of neuroscience is that learning and memory, as well as the refinement of cortical maps during development, are due to changes in the connective strength between individual neurons. In particular, Donald Hebb famously postulated that repeated and persistent correlated activity in pre- and postsynaptic neurons should bring about synaptic strengthening and that this would be a means for storing information at synaptic connections. In recent years, it has been discovered that repeated coincidence of excitatory postsynaptic potentials (EPSPs) and postsynaptic action potentials (APs) results in long-term potentiation (LTP) of synaptic connections, in agreement with the Hebbian postulate. In many cases, backpropagating APs in the dendrites are crucial for triggering such synaptic plasticity, because they help elicit supralinear calcium transients mediated by NMDA receptors and by dendritic voltage-gated ion channels. However, APs typically backpropagate decrementally in distal dendrites of pyramidal neurons. Given the role of APs in triggering coincidence detection, this implies cellular learning rules that rely on backpropagating APs should depend on synapse location.

Neocortical layer 5 (L5) pyramidal neurons constitute an outstanding model system for addressing the issue of location dependence of synaptic plasticity: These neurons have extensive apical dendritic arborizations that, while traversing many hundred microns, cross several cortical layers. In addition, these neurons receive two well-defined inputs which make synapses at relatively distinct dendritic locations: Whereas the vast majority of L5-to-L5 synapses impinge on the proximal, basal dendritic tree, L2/3-to-L5 synapses are found both on the apical and the basal dendrites.

In this study, we explored the plasticity rules of L2/3 and L5 connections onto L5 pyramidal neurons and we investigated the dependence on synapse location as well as on the local excitability of the dendritic arbor. We tested identical plasticity protocols at unitary inputs of different dendritic location, and we concurrently related the resulting plasticity to the location of identified synaptic contacts and to the dendritic calcium signals associated with plasticity induction. To do so, we employed a battery of state-of-the-art techniques, such as quadruple whole-cell recordings, dendritic patch-clamp recordings, two-photon laser-scanning microscopy, and compartmental modelling of neurons reconstructed with Neurolucida.

We discovered that the same AP-EPSP pairing protocol evoked LTP at proximal connections, but LTD at distal inputs, thus resulting in a plasticity gradient along the apical dendrite. We also found that this gradient is due to decremental AP backpropagation into the dendritic tree; dendritic depolarization or cooperative synaptic input could switch plasticity at distal synapses from LTD to LTP but only when strong enough to boost AP backpropagation into the distal dendritic arbor.

Our findings demonstrate a dendritic mechanism by which inputs in deeper cortical layers can regulate plasticity at inputs in more superficial layers. This activity-dependent dendritic switch for synaptic plasticity may enable associative learning across different neocortical layers, which are known to process distinct types of information.