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SYNAPTIC PLASTICITY

Spinal signals

Activity-dependent changes in the size and shape of individual dendritic spines (known as structural plasticity) are dependent on brain-derived neurotrophic factor (BDNF) and its receptor, tropomyosin-related kinase B (TRKB); however, exactly where or how these proteins act to mediate structural plasticity in dendritic spines is unclear. The findings reported by Harward *et al.* now suggest that BDNF stimulates TRKB activation and structural plasticity in the dendritic spine from which it was released.

To examine the role of BDNF and TRKB in structural plasticity, the authors transfected cultured rat hippocampal slices with a fluorescence resonance energy transfer (FRET)-based sensor of TRKB activation. Using two-photon fluorescence lifetime imaging microscopy, they could detect changes in TRKB activation in individual dendritic spines of transfected CA1 pyramidal neurons. Following the 'uncaging' of glutamate close to single dendritic spines, they observed rapid increases in spine volume and TRKB activation in those spines. This glutamate-evoked TRKB activation was reduced by inhibitors of NMDA receptors (NMDARs) or calcium/calmodulin-dependent protein kinase type II (CaMKII), or an extracellular scavenger of BDNF, suggesting that TRKB activation is triggered by a signalling pathway that is evoked by these factors.

Previous work suggested that BDNF is stored in and released from presynaptic terminals; however, the authors found that the selective removal of BDNF from individual CA1 pyramidal neurons impaired TRKB activation and structural plasticity in the dendritic spines of the same cells, suggesting that the source of BDNF is postsynaptic and that it may act in an autocrine manner. To further examine this possibility, the authors transfected CA1 pyramidal cells with BDNF fused to a fluorophore that increases its fluorescence in response to changes in pH, such as those that accompany exocytosis. They detected transient increases in fluorescence in the spines that were stimulated with uncaged glutamate, indicating that glutamate was released from those spines. They also showed that this release was dependent on activation of both NMDARs and CaMKII.

Structural plasticity of dendritic spines correlates with functional long-term plasticity (fLTP), which can be generated by pairing pre- and postsynaptic stimulation. Here, the authors showed that inhibition of TRKB activation or the scavenging of extracellular BDNF impaired the fLTP that could be induced at Schaffer collateral–CA1 pyramidal neuron synapses in hippocampal slices. Furthermore, the specific elimination of BDNF from individual CA1 pyramidal neurons impaired fLTP in those cells, confirming the importance of autocrine BDNF signalling for this plasticity.

This study provides evidence for dendritic spine-autonomous signalling — through a pathway that involves NMDARs and CaMKII activation, rapid BDNF release and TRKB activation — that contributes to activity-dependent structural and functional plasticity.

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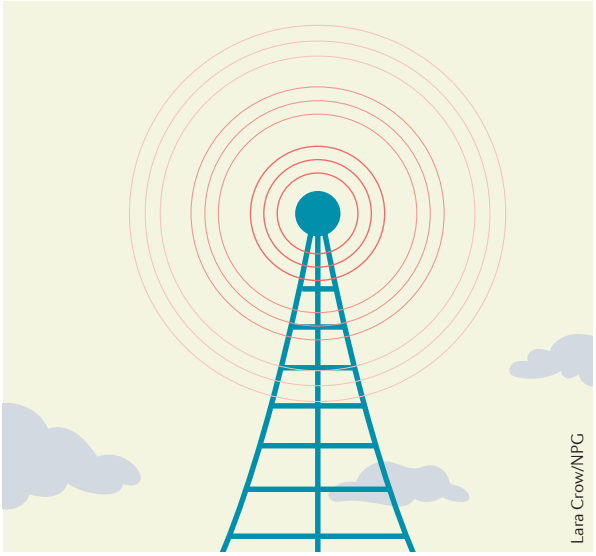

Lara Crow/NPG

> “the selective removal of BDNF from individual CA1 pyramidal neurons impaired TRKB activation and structural plasticity in the dendritic spines of the same cells”

ORIGINAL ARTICLE Harward, S. C. *et al.* Autocrine BDNF–TrkB signalling within a single dendritic spine. *Nature* **538**, 99–103 (2016)