



## LEARNING AND MEMORY

# Cease or persist?

The establishment of persistent long-term memory (LTM) requires an initial consolidation phase and a subsequent persistence-bestowing phase. It has previously been shown that hippocampal protein synthesis and brain-derived neurotrophic factor (BDNF) expression are necessary for LTM consolidation. Here, Medina and colleagues show that BDNF is sufficient to confer persistence to long-term memories.

Infusion of the protein-synthesis inhibitor anisomycin into the dorsal hippocampus of rats 12 hours after training is known to selectively abrogate the persistence phase of LTM formation: rats that undergo this treatment exhibit consolidated memory of the training after 2 days but the memories do not persist for 7 days. The authors used an inhibitory-avoidance protocol to determine the effect of hippocampal delivery of human recombinant BDNF (hrBDNF) on this deficit. They found that delivery of hrBDNF 15 minutes after anisomycin infusion completely rescued the memory impairment: whereas rats treated with anisomycin alone exhibited reduced latency in encroaching onto a region which they had been trained to associate with an electrical footshock, rats that were also treated with hrBDNF exhibited normal latency.

To reinforce their findings, the authors investigated the interplay

between BDNF and the strength of the applied footshock. Stronger footshocks are known to induce longer-lasting memories. The authors found that a strong footshock that induced LTM formation increased BDNF expression in the dorsal hippocampus, whereas a footshock too weak to induce LTM formation did not. Significantly, infusion of hrBDNF 12 hours after delivery of a weak footshock resulted in the formation of a persistent LTM.

How does BDNF exert its effects on LTM persistence? BDNF is known to phosphorylate and activate ERK protein, and the authors showed that a footshock that increased BDNF levels also induced ERK phosphorylation 12 hours post-shock. Furthermore, infusion of an ERK inhibitor 12 hours post-shock impaired 7-day LTM retention.

Together, these results show that BDNF is necessary and sufficient to induce LTM persistence through its effects on the activity of ERK. These findings might have implications for the treatment of age-related memory impairments, some of which are thought to result from faulty persistence.

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**ORIGINAL RESEARCH PAPER** Bekinschtein, P. *et al.* BDNF is essential to promote persistence of long-term memory storage. *Proc. Natl Acad. Sci. USA* **105**, 2711–2716 (2008)