NEUROSCIENCE June 2004 Vol 5 No 6 HIGHLIGHTS

*Nature Reviews Neuroscience* **5**, 429 (2004); doi:10.1038/nrn1414

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[535K]

**LEARNING AND MEMORY**

# Re-making memories

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There is increasing evidence that stable memories need to be 'reconsolidated' after being retrieved, and that this process has some features in common with the initial consolidation of long-term memories — for example, both require protein synthesis. But now, writing in *Science*, Lee *et al*. have shown that consolidation and reconsolidation in the hippocampus involve different cellular processes

The type of memory that the authors studied is contextual fear conditioning. When a rat is placed in a chamber and given a footshock, it immediately becomes conditioned to associate the chamber with the shock. On a later test, when the rat is placed in the chamber, it will show freezing behaviour, and this can be quantified as a measure of learning. This type of learning depends on the hippocampus, and has been widely used in the study of consolidation and reconsolidation.

Lee and colleagues used antisense oligodeoxynucleotides to investigate the roles of brain-derived neurotrophic factor (BDNF) and the transcription factor Zif268 in the consolidation and reconsolidation of fear conditioning. Antisense oligodeoxynucleotides work by inhibiting the expression of a specific protein at the site of infusion. When BDNF antisense oligodeoxynucleotides were

infused into the hippocampus 90 min before the training session, the rats showed normal freezing behaviour when tested after 3 h, indicating that they had learned the fear conditioning and stored it normally in short-term memory. However, when tested after 24 h, their memory was impaired, showing that the BDNF antisense had prevented the consolidation of the experience into long-term memory.

When the rats are tested by being placed in the chamber but not shocked, their freezing behaviour shows that they are retrieving the memory that was formed after training. Inhibition of protein synthesis at this point prevents the memory from being reconsolidated, so that on subsequent tests the rats show reduced freezing. Infusion of BDNF antisense into the hippocampus before testing did not prevent reconsolidation — unlike the initial consolidation, reconsolidation of the fear memory does not require the generation of BDNF in the hippocampus. However, when the authors infused a Zif268 antisense oligodeoxynucleotide into the hippocampus before testing, reconsolidation was impaired.

In fact, there was a neat double dissociation. Not only was BDNF required for consolidation but not reconsolidation; in addition, Zif268 was required for reconsolidation but not for consolidation. This is a convincing demonstration that the two processes involve different (although potentially overlapping) cellular mechanisms, and should open the way for a clearer understanding of both.

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## References and links

**ORIGINAL RESEARCH PAPER**

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**FURTHER READING**

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