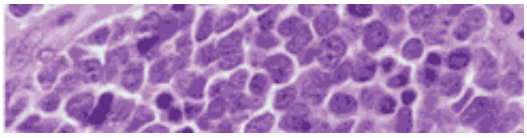
NEUROSCIENCE
September 2002 Vol 3 No 9 HIGHLIGHTS



Nature Reviews Neuroscience **3**, 676 (2002); doi:10.1038/nrn923

printable PDF
[1988K]

LEARNING AND MEMORY

Weeding out memory extinction

Juan Carlos López

Extinction is the reduction of a learned behavioural response on repeated presentations of a conditioned stimulus in the absence of a reinforcer. So, if we train a mouse to fear a tone that is paired with an electric shock, the mouse will freeze the next time it hears the tone, expecting to receive another shock. But if we continue to present the tone in the absence of shock, the association between the two stimuli will gradually become weaker, and the mouse will stop freezing. What are the neural bases of extinction? Reporting in *Nature*, Marsicano *et al*. provide evidence that endocannabinoids are crucially involved. As the extinction of aversive memories might be affected in states such as post-traumatic stress disorder and in certain phobias, the results point to the endocannabinoid system as a possible target for the treatment of these conditions.

Marsicano *et al*. generated mice that lacked the cannabinoid receptor CB1 and trained them in the aversive task that I have just described. $CB1^{-/-}$ mice learned to freeze in response to the tone; however, in contrast to wild-type mice, the CB1-deficient animals failed to extinguish this behavioural response. Moreover, the CB1 antagonist SR141716A had the same effect on extinction if it was administered immediately before the tone.

The amygdala is key to learning the tone–shock association. Marsicano *et al*. therefore predicted that the levels of endogenous cannabinoids should rise in this brain structure immediately after presentation of the tone. Indeed, they confirmed this prediction for two endocannabinoids — anandamide and 2-arachidonoylglycerol. But how might these molecules affect synaptic transmission in the amygdala during extinction? We don't yet know, but the authors made an intriguing finding. In wild-type animals, low-frequency stimulation of inhibitory synapses in the amygdala led to a persistent depression of their efficacy. By contrast, this effect was missing in the amygdala of $CB1^{-/-}$ mice or in the presence of

SR141716A. So, endocannabinoids seem to participate in this synaptic depression, and it will now be important to determine whether and how this effect is related to extinction.

References and links

ORIGINAL RESEARCH PAPER

Marsicano, G. *et al*. The endogenous cannabinoid system controls extinction of aversive memories. *Nature* **418**, 530-534 (2002) | Article | PubMed | ISI | ChemPort |

FURTHER READING

Wilson, R. I. & Nicoll, R. A. Endocannabinoid signalling in the brain. *Science* **296**, 678-682 (2002) | Article | PubMed | ISI | ChemPort |

Medina, J. F. *et al*. Parallels between cerebellum- and amygdala-dependent conditioning. *Nature Rev. Neurosci.* **3**, 122-131 (2002) | Article | PubMed | ISI | ChemPort |
