



A window of opportunity

Although fear is an adaptive response, inappropriate or excessive levels of fear can be maladaptive and lead to anxiety disorders. Consequently, much research has been dedicated to finding strategies for reducing or preventing the formation of fear memories. In a study published in *Nature*, Schiller *et al.* show that fear memories can be blocked in humans by updating them during a window of reconsolidation with new, non-fear-related information.



According to the reconsolidation hypothesis, memories are consolidated every time they are recalled. It is thought that this involves memories becoming unstable (for up to 1 h); this would allow them to be updated. In rodents, pharmacologically blocking the reconsolidation process can prevent the subsequent expression of a fear memory. Schiller *et al.* used a non-pharmacological way to modify fear memories during reconsolidation in humans, using skin conductance responses to determine the level of fear.

Volunteers watched two differently coloured squares (conditioned stimuli (CS)) on a screen, one of which (CS+) was paired with a shock to the wrist. An extinction procedure 24 h later involved repeated presentation of both squares without pairing either with a shock; this resulted in a gradual reduction of the skin conductance response to the CS+. Importantly, some volunteers received a single re-exposure to the CS+ (also without receiving a shock) either 6 h or 10 min before the extinction procedure — outside and within the reconsolidation window, respectively. All subjects underwent another set of stimuli exposures 24 h later.

Normally, re-exposure to a CS+ 24 h after an extinction procedure causes a recovery of the fear response, indicating that extinction has only a temporary effect. Indeed, subjects who were either re-exposed to the CS+ 6 h before the extinction procedure or not re-exposed before extinction showed spontaneous recovery of the fear response on the

first re-exposure trial. By contrast, the volunteers who saw the CS+ 10 min before extinction showed no fear response to the CS+ on the third day. This effect was still apparent a year later, indicating that introducing a reminder of the fearful stimulus before extinction training results in a long-lasting blockade of the fear memory, whereas regular extinction training does not.

To investigate the specificity of the effect the authors used a protocol in which two different squares were paired with a shock. The next day subjects saw one of these squares 10 min before an extinction procedure. During a re-exposure to the stimuli 24 h later, they showed a reduced fear response only to the CS+ of which they had been reminded before the extinction procedure on the previous day. Thus, interfering with the reconsolidation of one stimulus did not affect the memory of another, similar stimulus.

These results confirm those from a recent study in rats showing blockade of fear memory through extinction training during a reconsolidation window and from studies in humans on declarative and motor memory. The specificity and persistence of the findings in the highlighted study suggest that the strategy could be used in the treatment of anxiety disorders, including post-traumatic stress disorder.

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ORIGINAL RESEARCH PAPER Schiller, D. *et al.*
Preventing the return of fear in humans using
reconsolidation update mechanisms. *Nature* 9
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