

## ***Behavioral blockade of the return of fear in humans***

Daniela Schiller<sup>1,2</sup>, Marie-H. Monfils<sup>2</sup>, David C. Johnson<sup>1</sup>, Candace M. Raio<sup>1</sup>, Joseph E. LeDoux<sup>2</sup>, and Elizabeth A. Phelps<sup>1,2</sup>

<sup>1</sup>Department of Psychology, <sup>2</sup>Center for Neural Science, New York University, New York, NY

A common way to modify fear learning is through extinction. In this process, learned fear responses are no longer expressed after repeated exposure to conditioned stimuli (CSs) that are de-coupled from aversive consequences. Nearly all forms of behavioral therapy rely, at least partially, on extinction learning through exposure to fear arousing stimuli in a safe context. Although extinction provides a relief from fear, this relief might be temporary, as extinguished fear responses often reemerge with the passage of time or with re-exposure to the unconditioned stimulus in the original context. The aim of the present study was to investigate new possible way to prevent the return of fear following extinction.

The fact that extinguished fear can be recovered under certain conditions has been taken to suggest that the fear memory is not erased but rather suppressed. In recent years, there has been abundant research attempting to erase old memories by targeting a particular phase in which memories are labile again, namely, reconsolidation. Specifically, it has been suggested that once an old, fully consolidated, memory is retrieved, this reactivation is followed by an additional phase of consolidation, which is susceptible to interference. There is considerable evidence from animal studies that pharmacological and molecular manipulations at this stage result in inability to retrieve such memories, suggesting they might have been erased.

However, there has yet to be convincing evidence that reconsolidation can be impaired in humans. This is in part due to obvious limitations in the use of invasive manipulations, such as drugs, and the risk of side effects. Thus, there is a critical need to develop drug-free behavioral manipulations to achieve blockade of fear recovery. New evidence reported at the present conference shows that that a single isolated retrieval trial prior to extinction prevents the return of fear in rats (Monfils and colleagues). This suggests that extinction learning interfered with the reconsolidation of the retrieved memory and may have led to its erasure.

To test this hypothesis in humans, we used a fear conditioning paradigm where two CSs were paired with a shock. A day later, subjects received a single presentation of one of the CSs, after which both CSs were extinguished. We tested the recovery of fear following reinstatement and found that only fear to the non-reactivated CS returned. This suggests that retrieval, and hence reconsolidation, helps strengthen extinction. This finding has important implications for the treatment of anxiety disorders, suggesting that the use of drugs might not be required for preventing fear memories from resurfacing.

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