Karolinska Institutet

Department of Clinical Neuroscience

Learning not to fear

Extinction, erasure, and the recovery of fear memories

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ABSTRACT

Much of the progress in understanding the mechanisms underlying the formation and persistence of fear memories comes from studies of Pavlovian conditioning and extinction. Recently, considerable interest has been turn to strategies that facilitate the development and persistence of extinction. This interest has been particularly fueled by the fact that the findings may have important clinical implications by identifying the conditions during which extinction may permanently prevent the recovery of learned fears. The overall aim of this thesis was to identify the temporal factors that drive fear extinction learning (**Study I**) and to investigate different approaches to preventing the return of fear that occurs after extinction (**Study II-IV**). More specifically, we assessed the effects of initiating extinction training within the consolidation (**Study II**) or reconsolidation (**Study III**) time window and the effects of optimizing safety learning during fear extinction through social observation (**Study IV**).

In **Study I**, we evaluated two critical accounts of extinction by separately manipulating the number of non-reinforced trials and the cumulated non-reinforced exposure time during extinction training. Our data did not support that extinction is driven by the cumulative duration of non-reinforced exposure, but rather the number of trials appeared critical. In fact, many extinction trials with a duration shorter than the acquisition trial duration facilitated extinction learning, but this effect did not predict the recovery of fear.

In **Study II**, we found that extinction training initiated within, but not outside, the consolidation time window yielded less extinction of both fear-potentiated startle and shock expectancy ratings, while selectively preventing the return of fear-potentiated startle during a subsequent reinstatement test. Contrary, in **Study III**, extinction training initiated within the reconsolidation time window did not prevent the recovery of fear, as measured by reinstatement of fear-potentiated startle or skin conductance responses, using either fear-relevant or fear-irrelevant stimuli.

Finally, as an alternative approach to preventing the return of fear, in **Study IV**, we capitalized on the fact that much of what we learn about the environment comes through social forms of learning such as through observation of other individuals.
Therefore, we assessed the effects of vicarious safety learning on the decrement of conditioned fear during extinction training and its effects on the subsequent return of fear. We found that vicarious extinction efficiently reduced conditioned fear responses during extinction and blocked the subsequent return of fear, as measured by skin conductance responses during a subsequent reinstatement test.

In sum, the studies in this thesis demonstrate an intricate relation between extinction learning and the return of fear and highlight that extinction represents a highly complex phenomenon that most probably is determined by multiple factors.