

# The Effects of Psychedelics on Fear Extinction Recall Research from Animal Studies in a Translational Perspective

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The return of fear in patients with post-traumatic stress disorder (PTSD) and anxiety is a major challenge in the treatment of these disorders. Many treatments fail to maintain a fear reduction over the long term. Clinical trials have shown that psychedelic-assisted psychotherapy can achieve a more long-lasting fear reduction than psychotherapy alone. One mechanism contributing to pathological fear and anxiety, which is a therapeutic target of psychedelic-assisted psychotherapy, is the deficiency of fear extinction recall. Since no human studies on this topic exist to date, this review examines the available animal studies investigating the effects of psychedelics on the recall of fear extinction and discusses their relevance to psychedelic-assisted psychotherapy in humans. The results suggest that an enhancement of fear extinction recall through MDMA, Ayahuasca, or DMT in rodents is possible. However, the evidence is limited and, in some cases, contradictory. This review points out relevant aspects for future studies, such as the importance of delayed fear extinction recall tests to evaluate whether long-term fear reduction can be achieved by administering psychedelics. Preclinical and clinical studies will show whether psychedelics can also improve fear extinction recall in humans and whether this is thus one of the mechanisms contributing to fear reduction in anxiety and PTSD patients.

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