Memory reconsolidation in therapy: mechanisms and necessary conditions

1. Introduction

Memory reconsolidation is a neurobiological process whereby reactivated memories become temporarily labile and susceptible to modification before being restabilized. This phenomenon has generated significant interest as a potential mechanism for therapeutic interventions targeting maladaptive memories in conditions such as PTSD, substance use disorders, and anxiety disorders (Lee et al., 2017; Elsey et al., 2018; Elsey & Kindt, 2017; Dunbar & Taylor, 2017; Huang et al., 2024; Milton, 2023; Taylor et al., 2009; Barak & Goltseker, 2021; Chen et al., 2025; Phelps & Hofmann, 2019). Reconsolidation-based therapies aim to disrupt or update problematic memories, offering the possibility of more enduring symptom relief compared to traditional extinction-based approaches, which often leave the original memory intact and susceptible to relapse (Kroes et al., 2016; Elsey & Kindt, 2017; Elsey et al., 2018; Taylor et al., 2009; Barak & Goltseker, 2023; Chen et al., 2025). However, the translation of reconsolidation research from animal models to clinical practice is complex, with several necessary conditions and boundary factors influencing whether reconsolidation can be induced and harnessed therapeutically (Elsey & Kindt, 2017; Treanor et al., 2017; Bolsoni & Zuardi, 2019; Sinclair & Barense, 2019; Wideman et al., 2018). This review synthesizes the current understanding of the mechanisms underlying memory reconsolidation, the conditions required for its induction, and the implications for clinical interventions.

2. Methods

A comprehensive literature search was conducted across over 170 million research papers in Consensus, including sources such as Semantic Scholar and PubMed. The search strategy targeted foundational mechanisms, necessary conditions, therapeutic applications, methodological diversity, and contrasting perspectives on memory reconsolidation in therapy. In total, 934 papers were identified, 313 were screened, 223 were deemed eligible, and the top 50 most relevant papers were included in this review.

Search Strategy

Identification N = 934 → **Screening** N = 313 → **Eligibility** N = 223 → **Included** N = 50

Identification: Identified 934 papers that matched 20 Consensus searches
\+ 934 identified

Screening: Removed papers with missing abstracts
Removed duplicates
— 621 removed

Eligibility: Removed papers with low semantic relevance to each search
— 90 removed

Included: Selected the top 50 highest quality papers after final ranking
— 173 removed

FIGURE 1 Flow of papers through the search and selection process.

Eight unique search groups were used, spanning mechanisms, clinical applications, and methodological considerations to ensure comprehensive coverage of the topic.

3. Results

3.1 Mechanisms of Memory Reconsolidation

Reconsolidation is triggered when a consolidated memory is reactivated, rendering it temporarily labile and open to modification before restabilization (Lee et al., 2017; Elsey et al., 2018; Elsey & Kindt, 2017; Nader, 2015; Chen et al., 2025). This process is dependent on protein synthesis and involves key brain regions such as the amygdala, hippocampus, and prefrontal cortex (Drexler & Wolf, 2017; Wideman et al., 2018; Chen et al., 2025). Neurotransmitter systems, including glutamate, dopamine, noradrenaline, and acetylcholine, play critical roles in both destabilization and restabilization phases (Wideman et al., 2018; Papalini et al., 2020; Drexler & Wolf, 2017). Prediction error—when there is a mismatch between expected and actual outcomes during memory retrieval—is a crucial trigger for reconsolidation, allowing for memory updating or disruption (Sinclair & Barense, 2019; Ecker, 2021; Chen et al., 2025).

3.2 Necessary Conditions and Boundary Factors

Not all memories are equally susceptible to reconsolidation. Boundary conditions include memory age, strength, and the nature of the reactivation procedure (Elsey & Kindt, 2017; Treanor et al., 2017; Bolsoni & Zuardi, 2019; Sinclair & Barense, 2019; Wideman et al., 2018). Stronger or older memories, such as those underlying chronic PTSD or addiction, may be more resistant to reconsolidation, though certain protocols can overcome these barriers (Elsey & Kindt, 2017; Silva & Gräff, 2023; Chen et al., 2025). The presence of prediction error during retrieval is often necessary to induce lability (Sinclair & Barense, 2019; Ecker, 2021). The timing and duration of the reconsolidation window (typically a few hours post-reactivation) are critical for effective intervention, especially for pharmacological approaches (Bolsoni & Zuardi, 2019; Chen et al., 2025).

3.3 Therapeutic Applications and Interventions

Reconsolidation-based interventions have been explored in various clinical contexts, including PTSD, substance use disorders, and depression (Huang et al., 2024; Feduccia & Mithoefer, 2018; Milton, 2023; Meister et al., 2023; Farrell & Mahood, 2022; Fattore et al., 2018; Barak & Goltseker, 2023; Williams et al., 2025; Köhler et al., 2015; Luoma et al., 2021; Kida, 2018; Brewin, 2018; Ross et al., 2017). Both behavioral (e.g., retrieval-extinction, memory updating protocols) and pharmacological (e.g., propranolol, ketamine, MDMA) strategies have shown promise in modifying maladaptive memories (Huang et al., 2024; Feduccia & Mithoefer, 2018; Meister et al., 2023; Fattore et al., 2018; Barak & Goltseker, 2023; Williams et al., 2025; Fattore et al., 2017; Luoma et al., 2021). However, results are mixed, with some studies reporting robust and lasting symptom reduction, while others find limited or no effect, highlighting the importance of protocol specifics and individual differences (Meister et al., 2023; Farrell & Mahood, 2022; Ecker, 2021; Drexler & Wolf, 2018; Phelps & Hofmann, 2019).

3.4 Methodological and Translational Challenges

There is significant methodological heterogeneity in reconsolidation research, including variability in memory types, reactivation procedures, and outcome measures (Treanor et al., 2017; Elsey et al., 2018; Barak & Goltseker, 2021; Barak & Goltseker, 2023; Ecker, 2021; Drexler & Wolf, 2018; Phelps & Hofmann, 2019). Replication failures and inconsistent findings are common, often attributable to differences in prediction error induction, memory characteristics, and intervention timing (Ecker, 2021; Drexler & Wolf, 2018; Phelps & Hofmann, 2019). Translating laboratory protocols to clinical practice remains challenging, and more standardized, systematic research is needed (Treanor et al., 2017; Barak & Goltseker, 2021; Barak & Goltseker, 2023; Ecker, 2021; Phelps & Hofmann, 2019; Gisquet-Verrier & Riccio, 2018).

Key Papers

Paper	Mechanism/Focus	Population/Context	Key Results
(Lee et al., 2017)	Reconsolidation updating, translational studies	Animal & human	Reconsolidation enables memory updating; clinical translation possible but challenging
(Sinclair & Barense, 2019)	Prediction error in reconsolidation	Human & animal	Prediction error is critical for memory lability and updating
(Elsey & Kindt, 2017)	Boundary conditions, strong/old memories	Animal & human	Strong/old memories can be modified with optimized protocols
(Meister et al., 2023)	Pharmacological augmentation in PTSD	Clinical (PTSD)	Mixed results for drugs targeting reconsolidation/extinction
(Ecker, 2021)	Behavioral updating, replication failures	Human	Prediction error and internal experience explain successes/failures

FIGURE 2 Comparison of key studies on memory reconsolidation mechanisms and therapeutic applications.

Top Contributors

Type	Name	Papers
Author	J. Elsey	(Elsey & Kindt, 2017; Elsey et al., 2018)
Author	M. Kindt	(Elsey & Kindt, 2017; Elsey et al., 2018)
Author	S. Barak	(Barak & Goltseker, 2021; Barak & Goltseker, 2023)
Journal	*Neurobiology of Learning and Memory*	(Dunbar & Taylor, 2017; Elsey & Kindt, 2017; Drexler & Wolf, 2017; Wideman et al., 2018)
Journal	*Trends in Cognitive Sciences*	(Lee et al., 2017; Sandrini et al., 2015; Silva & Gräff, 2023)
Journal	*Psychopharmacology*	(Fattore et al., 2018; Fattore et al., 2017; Kida, 2018)

FIGURE 3 Authors & journals that appeared most frequently in the included papers.

4. Discussion

The research on memory reconsolidation in a therapeutic context reveals both significant promise and notable challenges. Mechanistically, reconsolidation offers a unique window for modifying maladaptive memories, with prediction error and memory reactivation as key triggers (Lee et al., 2017; Sinclair & Barense, 2019; Ecker, 2021; Chen et al., 2025). The involvement of specific neurotransmitter systems and brain regions underscores the biological plausibility of targeting reconsolidation for clinical benefit (Drexler & Wolf, 2017; Wideman et al., 2018; Papalini et al., 2020). However, the necessary conditions for reliably inducing reconsolidation—such as memory age, strength, and the precise nature of retrieval—are not always met in clinical populations, limiting the generalizability of laboratory findings (Elsey & Kindt, 2017; Treanor et al., 2017; Bolsoni & Zuardi, 2019; Sinclair & Barense, 2019; Wideman et al., 2018; Silva & Gräff, 2023).

Therapeutic interventions leveraging reconsolidation have shown efficacy in some studies, particularly when protocols are carefully designed to induce prediction error and target the reconsolidation window (Huang et al., 2024; Feduccia & Mithoefer, 2018; Milton, 2023; Meister et al., 2023; Fattore et al., 2018; Barak & Goltseker, 2023; Williams et al., 2025; Fattore et al., 2017; Luoma et al., 2021). Yet, mixed results and replication failures highlight the need for greater methodological rigor and standardization (Treanor et al., 2017; Barak & Goltseker, 2021; Barak & Goltseker, 2023; Ecker, 2021; Drexler & Wolf, 2018; Phelps & Hofmann, 2019; Gisquet-Verrier & Riccio, 2018). The field is also grappling with alternative models, such as memory integration, and the challenge of distinguishing reconsolidation from extinction and other memory processes (Gisquet-Verrier & Riccio, 2018; Chen et al., 2025; Taylor et al., 2009; Barak & Goltseker, 2021).

Claims and Evidence Table

Claim	Evidence Strength	Reasoning	Papers
Reconsolidation can be harnessed to modify maladaptive memories in therapy	Strong	Multiple animal and human studies show memory updating/disruption via reconsolidation-based protocols	(Lee et al., 2017; Elsey & Kindt, 2017; Elsey et al., 2018; Huang et al., 2024; Feduccia & Mithoefer, 2018; Milton, 2023; Barak & Goltseker, 2023; Sinclair & Barense, 2019; Ecker, 2021; Chen et al., 2025)
Prediction error is necessary to trigger reconsolidation and memory lability	Strong	Strong evidence from both animal and human studies; absence of PE often leads to null results	(Sinclair & Barense, 2019; Ecker, 2021; Elsey & Kindt, 2017; Chen et al., 2025)
Strong/old memories are more resistant but can be modified with optimized protocols	Moderate	Experimental and case studies show boundary conditions can be overcome	(Elsey & Kindt, 2017; Silva & Gräff, 2023; Chen et al., 2025; Ecker, 2021)
Pharmacological interventions (e.g., propranolol, ketamine) can augment reconsolidation-based therapy	Moderate	Mixed results in clinical trials; some drugs effective in specific contexts	(Meister et al., 2023; Bolsoni & Zuardi, 2019; Fattore et al., 2018; Fattore et al., 2017; Luoma et al., 2021)
Methodological heterogeneity and protocol specifics explain replication failures	Moderate	Review of successes/failures points to protocol differences, especially in PE induction	(Treanor et al., 2017; Barak & Goltseker, 2021; Barak & Goltseker, 2023; Ecker, 2021; Drexler & Wolf, 2018; Phelps & Hofmann, 2019; Gisquet-Verrier & Riccio, 2018)
Reconsolidation-based interventions are superior to extinction-based approaches for lasting change	Moderate	Some evidence for greater durability, but not consistently replicated in clinical settings	(Kroes et al., 2016; Elsey & Kindt, 2017; Elsey et al., 2018; Taylor et al., 2009; Barak & Goltseker, 2023; Chen et al., 2025; Phelps & Hofmann, 2019)

FIGURE Key claims and support evidence identified in these papers.

5. Conclusion

Memory reconsolidation represents a promising mechanism for therapeutic modification of maladaptive memories, with strong mechanistic support and growing clinical evidence. However, reliably inducing reconsolidation in therapy requires careful attention to necessary conditions such as prediction error, memory characteristics, and intervention timing. Methodological variability and boundary conditions remain significant challenges for clinical translation.

5.1 Research Gaps

Despite advances, gaps remain in understanding the precise triggers for reconsolidation, the optimal protocols for different memory types, and the long-term efficacy of reconsolidation-based interventions in diverse clinical populations.

Research Gaps Matrix

Topic/Attribute	Animal Models	Human Lab Studies	Clinical Trials	Pharmacological	Behavioral
Mechanisms	12	8	2	5	7
Prediction Error	7	6	1	2	5
Boundary Conditions	6	4	1	1	3
Clinical Efficacy	2	3	8	4	6
Long-term Outcomes	1	2	2	1	2

FIGURE Distribution of research across topics and study attributes, highlighting underexplored areas.

5.2 Open Research Questions

Future research should focus on clarifying the triggers and boundary conditions for reconsolidation, optimizing intervention protocols, and evaluating long-term clinical outcomes.

Question	Why
What are the precise neural and psychological triggers required to reliably induce reconsolidation in clinical populations?	Understanding these triggers is essential for developing effective, standardized therapeutic protocols and improving clinical outcomes.
How can reconsolidation-based interventions be optimized for strong, old, or complex maladaptive memories?	Many clinical cases involve entrenched memories; optimizing protocols could expand the applicability and efficacy of reconsolidation therapies.
What are the long-term effects and relapse rates following reconsolidation-based therapy compared to traditional extinction-based approaches?	Assessing durability and relapse is critical for determining the true clinical value of reconsolidation interventions.

FIGURE Key open questions for advancing research on therapeutic memory reconsolidation.

In summary, while memory reconsolidation offers a compelling framework for therapeutic memory modification, further research is needed to overcome translational challenges and fully realize its clinical potential.

These papers were sourced and synthesized using Consensus, an AI-powered search engine for research. Try it at https://consensus.app

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