The Role of "Mismatch Experience" (Prediction Error) in Updating Maladaptive Memories

1. Introduction

A "mismatch experience" or prediction error—when reality deviates from what is expected based on prior learning—is a critical trigger for updating maladaptive memories. This process is central to both adaptive learning and therapeutic interventions targeting problematic memories, such as those underlying depression, PTSD, and addiction (Ramamurthy & Chen, 2025; Sinclair et al., 2020; Sinclair & Barense, 2019; Sinclair & Barense, 2018; Krawczyk et al., 2017; Fernández et al., 2016; Exton-McGuinness et al., 2015; Das et al., 2015; Sevenster et al., 2013; Das et al., 2018; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Papalini et al., 2020; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023). Prediction error signals prompt the brain to reconsider and potentially revise existing memory traces, making them temporarily malleable and open to modification. This mechanism underpins memory reconsolidation, extinction, and schema revision, and is increasingly leveraged in clinical settings to disrupt or update maladaptive emotional and behavioral patterns (Ramamurthy & Chen, 2025; Sinclair et al., 2020; Sinclair & Barense, 2019; Sinclair & Barense, 2018; Krawczyk et al., 2017; Fernández et al., 2016; Exton-McGuinness et al., 2015; Das et al., 2015; Sevenster et al., 2013; Das et al., 2018; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Papalini et al., 2020; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023).

2. Methods

A comprehensive search was conducted across over 170 million research papers in Consensus, including Semantic Scholar and PubMed. The search strategy targeted foundational theories, neural mechanisms, clinical applications, and methodological diversity related to prediction error and memory updating. In total, 973 papers were identified, 642 were screened, 376 were deemed eligible, and the top 50 most relevant papers were included in this review.

Search Strategy

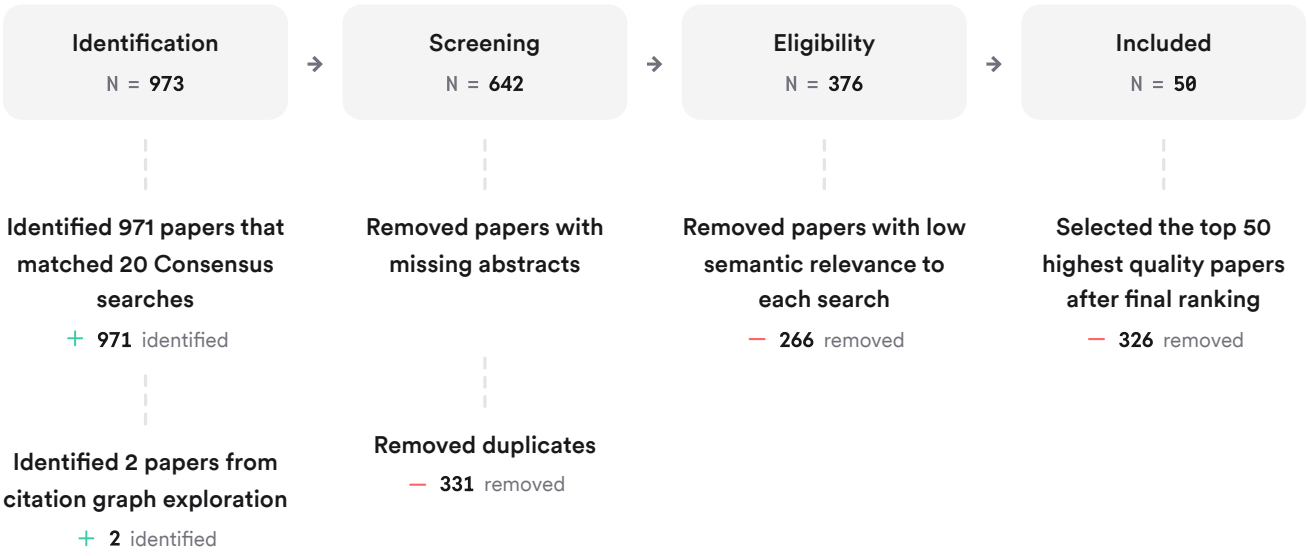

FIGURE 1 Flow of papers through the search and selection process.

Eight unique search groups were used, spanning predictive coding, reconsolidation, clinical interventions, and computational models.

3. Results

3.1 Prediction Error as a Trigger for Memory Updating

Prediction error (PE)—the mismatch between expected and actual outcomes—serves as a signal for the brain to update existing memories (Sinclair et al., 2020; Sinclair & Barense, 2019; Sinclair & Barense, 2018; Krawczyk et al., 2017; Fernández et al., 2016; Exton-McGuinness et al., 2015; Das et al., 2015; Sevenster et al., 2013; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Papalini et al., 2020; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023). When a memory is reactivated and a PE is detected, the memory trace becomes destabilized, entering a labile state where it can be modified or overwritten before reconsolidation (Sinclair et al., 2020; Sinclair & Barense, 2019; Sinclair & Barense, 2018; Krawczyk et al., 2017; Fernández et al., 2016; Exton-McGuinness et al., 2015; Das et al., 2015; Sevenster et al., 2013; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Papalini et al., 2020; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023). This process is observed across species and memory types, including fear, reward, and episodic memories (Sinclair & Barense, 2019; Sinclair & Barense, 2018; Fernández et al., 2016; Exton-McGuinness et al., 2015; Das et al., 2015; Sevenster et al., 2013; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Papalini et al., 2020; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023).

3.2 Neural and Computational Mechanisms

The hippocampus, prefrontal cortex, amygdala, and dopaminergic midbrain are key regions involved in detecting and responding to prediction errors (Sinclair et al., 2020; Sinclair & Barense, 2018; Fernández et al., 2016; Exton-McGuinness et al., 2015; Krawczyk et al., 2021; Das et al., 2015; Sevenster et al., 2013; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Papalini et al., 2020; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023). PE signals can disrupt ongoing neural representations, bias hippocampal states toward encoding new information, and modulate synaptic plasticity (Sinclair et al., 2020; Sinclair & Barense, 2018; Fernández et al., 2016; Bein et al., 2019; Exton-McGuinness et al., 2015; Krawczyk et al., 2021; Das et al., 2015; Sevenster et al., 2013; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Papalini et al., 2020; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023). Computational models, such as predictive coding and reinforcement learning, describe how PE drives belief and memory updating (Ramamurthy & Chen, 2025; Sinclair et al., 2020; Sinclair & Barense, 2018; Fernández et al., 2016; Exton-McGuinness et al., 2015; Heinz et al., 2018; Das et al., 2015; Sevenster et al., 2013; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Sterzer et al., 2018; Papalini et al., 2020; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023; Kumar et al., 2025).

3.3 Clinical and Behavioral Implications

Prediction error is essential for effective memory modification in therapy. Interventions that maximize PE during memory retrieval—such as expectancy violation or incomplete reminders—are more likely to destabilize and update maladaptive memories (Ramamurthy & Chen, 2025; Sinclair & Barense, 2019; Sinclair & Barense, 2018; Exton-McGuinness et al., 2015; Das et al., 2015; Sevenster et al., 2013; Das et al., 2018; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Papalini et al., 2020; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023). This principle is applied in treatments for addiction, PTSD, and depression, where PE-driven procedures can reduce the salience or emotional impact of problematic memories (Ramamurthy & Chen, 2025; Sinclair & Barense, 2019; Sinclair & Barense, 2018; Exton-McGuinness et al., 2015; Das et al., 2015; Sevenster et al., 2013; Das et al., 2018; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Papalini et al., 2020; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023). However, the strength, type, and credibility of the PE, as well as individual differences, influence the likelihood and direction of memory updating (Ramamurthy & Chen, 2025; Liedtke et al., 2025; Gerlicher et al., 2021; Nolden et al., 2025; Kube et al., 2021; Pupillo et al., 2023).

3.4 Boundary Conditions and Limitations

Not all PEs lead to memory updating. The magnitude and type of PE, memory strength, age, and emotional salience, as well as biological and cognitive factors, set boundary conditions for whether reconsolidation and updating occur (Ramamurthy & Chen, 2025; Fernández et al., 2016; Exton-McGuinness et al., 2015; Das et al., 2015; Sevenster et al., 2013; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Gerlicher et al., 2021; Nolden et al., 2025; Kube et al., 2021; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023). Excessively large or implausible PEs may be discounted, while moderate, credible PEs are most effective for updating (Ramamurthy & Chen, 2025; Liedtke et al., 2025; Gerlicher et al., 2021; Nolden et al., 2025; Kube et al., 2021; Pupillo et al., 2023).

Key Papers

Paper	Methodology	Memory Type/Context	Key Results
(Sinclair et al., 2020)	fMRI, behavioral	Episodic memory	PE disrupts hippocampal patterns, enabling memory updating
(Sinclair & Barense, 2019)	Review, human/animal	Episodic, fear, reward	Incomplete reminders (PE) drive reconsolidation and updating
(Sinclair & Barense, 2018)	Behavioral, human	Episodic memory	PE destabilizes memories, drives adaptive updating
(Exton-McGuinness et al., 2015)	Review, animal/human	Appetitive/aversive	Dopaminergic PE necessary for destabilization/reconsolidation
(Sevenster et al., 2013)	Behavioral, human	Fear memory	PE is necessary for reconsolidation and memory labilization

FIGURE 2 Comparison of key studies on prediction error and maladaptive memory updating.

Top Contributors

Type	Name	Papers
Author	Alyssa H. Sinclair	(Sinclair et al., 2020; Sinclair & Barense, 2019; Sinclair & Barense, 2018; Sinclair et al., 2020)
Author	Morgan D. Barense	(Sinclair et al., 2020; Sinclair & Barense, 2019; Sinclair & Barense, 2018; Sinclair et al., 2020)
Author	M. Kindt	(Exton-McGuinness et al., 2015; Sevenster et al., 2013; Gerlicher et al., 2021; Gerlicher et al., 2022; Papalini et al., 2020)
Journal	*Learning & Memory*	(Sinclair & Barense, 2018; Tallot et al., 2017; Bein et al., 2021)
Journal	*Neurobiology of Learning and Memory*	(Krawczyk et al., 2017; Krawczyk et al., 2021)
Journal	*Science*	(Sevenster et al., 2013)

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

4. Discussion

Prediction error is a fundamental mechanism for updating maladaptive memories, with robust evidence from neuroscience, psychology, and clinical research (Sinclair et al., 2020; Sinclair & Barense, 2019; Sinclair & Barense, 2018; Krawczyk et al., 2017; Fernández et al., 2016; Exton-McGuinness et al., 2015; Das et al., 2015; Sevenster et al., 2013; Das et al., 2018; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Papalini et al., 2020; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023). The detection of a mismatch between expectation and reality signals the need for memory revision, making the memory trace labile and open to modification. This process is central to reconsolidation-based therapies and is supported by neural, behavioral, and computational data (Sinclair et al., 2020; Sinclair & Barense, 2019; Sinclair & Barense, 2018; Krawczyk et al., 2017; Fernández et al., 2016; Exton-McGuinness et al., 2015; Das et al., 2015; Sevenster et al., 2013; Das et al., 2018; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Papalini et al., 2020; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023).

However, the effectiveness of PE-driven updating depends on several factors, including the credibility and magnitude of the PE, the strength and age of the memory, and individual biological and cognitive differences (Ramamurthy & Chen, 2025; Fernández et al., 2016; Exton-McGuinness et al., 2015; Das et al., 2015; Sevenster et al., 2013; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Gerlicher et al., 2021; Nolden et al., 2025; Kube et al., 2021; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023). Not all PEs are equally effective, and excessively large or implausible mismatches may be ignored or discounted (Ramamurthy & Chen, 2025; Liedtke et al., 2025; Gerlicher et al., 2021; Nolden et al., 2025; Kube et al., 2021; Pupillo et al., 2023). There are also challenges in reliably inducing PE in clinical settings and translating laboratory findings to real-world therapy (Ramamurthy & Chen, 2025; Liedtke et al., 2025; Gerlicher et al., 2021; Nolden et al., 2025; Kube et al., 2021; Pupillo et al., 2023; Osorio-Gómez et al., 2023).

Claims and Evidence Table

Claim	Evidence Strength	Reasoning	Papers
Prediction error is necessary for destabilizing and updating maladaptive memories	Strong	Strong evidence from animal, human, and clinical studies	(Sinclair et al., 2020; Sinclair & Barense, 2019; Sinclair & Barense, 2018; Krawczyk et al., 2017; Fernández et al., 2016; Exton-McGuinness et al., 2015; Das et al., 2015; Sevenster et al., 2013; Das et al., 2018; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Papalini et al., 2020; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023)
PE triggers memory reconsolidation, making memories labile and modifiable	Strong	Reconsolidation requires PE for labilization	(Sinclair & Barense, 2019; Sinclair & Barense, 2018; Krawczyk et al., 2017; Fernández et al., 2016; Exton-McGuinness et al., 2015; Das et al., 2015; Sevenster et al., 2013; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Papalini et al., 2020; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023)
The magnitude and credibility of PE influence memory updating	Moderate	Moderate, plausible PEs are most effective; large or implausible PEs may be discounted	(Ramamurthy & Chen, 2025; Liedtke et al., 2025; Gerlicher et al., 2021; Nolden et al., 2025; Kube et al., 2021; Pupillo et al., 2023)
Neural mechanisms involve hippocampus, prefrontal cortex, amygdala, and dopamine	Moderate	fMRI, animal, and computational studies support this	(Sinclair et al., 2020; Sinclair & Barense, 2018; Fernández et al., 2016; Exton-McGuinness et al., 2015; Krawczyk et al., 2021; Das et al., 2015; Sevenster et al., 2013; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Papalini et al., 2020; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023)
PE-based interventions can update maladaptive memories in clinical populations	Moderate	Clinical trials show efficacy, but with boundary conditions	(Ramamurthy & Chen, 2025; Sinclair & Barense, 2019; Sinclair & Barense, 2018; Exton-McGuinness et al., 2015; Das et al., 2015; Sevenster et al., 2013; Das et al., 2018; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Papalini et al., 2020; Kennedy et al., 2024; Bein et al.,

Claim	Evidence Strength	Reasoning	Papers
			2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023)
Not all PEs lead to updating; boundary conditions exist	Moderate	Memory strength, age, and emotional salience set limits	(Ramamurthy & Chen, 2025; Fernández et al., 2016; Exton-McGuinness et al., 2015; Das et al., 2015; Sevenster et al., 2013; Felsenberg et al., 2017; Zinn et al., 2020; Tavares et al., 2023; Gerlicher et al., 2021; Nolden et al., 2025; Kube et al., 2021; Kennedy et al., 2024; Bein et al., 2021; Bein et al., 2023; Rouhani et al., 2023; Osorio-Gómez et al., 2023)

FIGURE Key claims and support evidence identified in these papers.

5. Conclusion

Prediction error, or mismatch experience, is a necessary and powerful driver of maladaptive memory updating. It destabilizes existing memories, enabling their modification through reconsolidation or extinction. The effectiveness of this process depends on the nature of the PE, memory characteristics, and individual factors. Harnessing PE in clinical interventions holds promise for treating disorders rooted in maladaptive memories, though challenges remain in optimizing and personalizing these approaches.

5.1 Research Gaps

Key gaps include understanding the optimal parameters for PE induction, individual variability in response, and translating laboratory paradigms to clinical practice.

Research Gaps Matrix

Topic/Attribute	Animal Models	Human Lab Studies	Clinical Trials	Neural Mechanisms	Computational Models
PE and Reconsolidation	10	8	4	7	5
PE Magnitude/Type	5	7	2	3	4
Clinical Application	2	4	7	2	1
Individual Differences	1	2	1	1	1

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

5.2 Open Research Questions

Future research should clarify the optimal conditions for PE-driven memory updating, individualize interventions, and bridge the gap between laboratory and clinical practice.

Question	Why
What are the optimal parameters (magnitude, type, timing) of prediction error for effective maladaptive memory updating?	Determining these will improve the efficacy and reliability of clinical interventions.
How do individual differences (e.g., genetics, neurobiology, psychopathology) affect susceptibility to PE-driven memory updating?	Personalizing interventions could enhance outcomes and reduce relapse.
How can PE-based memory updating protocols be effectively translated from laboratory to real-world clinical settings?	Bridging this gap is essential for widespread therapeutic impact.

FIGURE Key open questions for advancing research on prediction error and memory updating.

In summary, prediction error is a central mechanism for updating maladaptive memories, with strong support from neuroscience and clinical research, but further work is needed to optimize and personalize its application in therapy.

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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