

Review

Multiple routes to enhanced memory for emotionally relevant events

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Events associated with aversive or rewarding outcomes are prioritized in memory. This memory boost is commonly attributed to the elicited affective response, closely linked to noradrenergic and dopaminergic modulation of hippocampal plasticity. Herein we review and compare this ‘affect’ mechanism to an additional, recently discovered, ‘prediction’ mechanism whereby memories are strengthened by the extent to which outcomes deviate from expectations, that is, by prediction errors (PEs). The mnemonic impact of PEs is separate from the affective outcome itself and has a distinct neural signature. While both routes enhance memory, these mechanisms are linked to different – and sometimes opposing – predictions for memory integration. We discuss new findings that highlight mechanisms by which emotional events strengthen, integrate, and segment memory.

Revisiting emotional memory: remembering the unexpected

While we forget mundane events rapidly, we remember events associated with strong emotions – such as a lottery win or a bear attack – for much longer. Indeed, events linked to rewarding or aversive outcomes are preferentially stored in memory [1–4], adaptively enabling prediction and selection of appropriate actions for similar events in the future. Selective memory enhancement has important consequences for a broad range of contexts, including education, eyewitness testimony, and psychiatry, where disorders such as post-traumatic stress disorder (PTSD) and depression can be marked by crippling reminders of the past.

Better memory for emotionally relevant events is linked to an affective response that increases noradrenergic or dopaminergic modulation of hippocampal neuroplasticity [5–8]. While knowledge about this well-established affect route continues to develop, there is accumulating evidence for an additional ‘prediction’ route, where the PE (see [Glossary](#)) elicited by rewarding or threatening events improves memory. PE is defined as the difference between prediction and actual outcome, whose magnitude [‘unsigned PE’ (UPE)] represents the surprise elicited by that outcome. In **reinforcement learning**, reward- and punishment-related PEs – that is, ‘signed’ PEs (SPEs) defined by affective outcomes – are the canonical signals driving value updating and action selection ([Box 1](#)). The predictive and affective components of an event are often tied, but we can test their distinct contributions. For example, if you were expecting a tax refund of \$1000 but instead owed \$1000 in taxes, the affective outcome of –\$1000 is separate from the outcome’s unexpectedness, that is, the UPE: $|\text{outcome} - \text{prediction}| = \2000 . Of note, the SPE: $\text{outcome} - \text{prediction} = -\2000 , includes both affective and predictive components.

While PEs can elicit affective responses, recent work shows their mnemonic influence to be separate from affect alone. Furthermore, their role in optimizing fundamental computational trade-offs is distinct from the discussed affect route. Namely, the magnitude of PE is thought to determine

Highlights

Memory is enhanced for threatening and rewarding events, which has important implications for psychiatric disorders.

Arousal and motivation (‘affect route’) are driving forces in the encoding and consolidation of emotional memory, shaping the course of systems consolidation.

In addition to this affect route, a ‘prediction route’, governed by reinforcement-learning prediction errors, boosts memory for emotionally relevant events.

Putative dopaminergic and noradrenergic mechanisms both enhance memory; however, they are associated with distinct mnemonic signatures: dopamine (DA) helps integrate, while norepinephrine (NE) segments memory, giving rise to distinct representations of experience.

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Box 1. PE modulation of memory during reinforcement learning

The signed reward prediction error (SPE) is a canonical signal in reinforcement learning that updates the stored values of experiences. SPEs modulate dopaminergic firing from the midbrain, increasing DA when outcomes are better than expected, and decreasing its release to below baseline when outcomes are worse than expected [126,127]. These signals are used to update expectations so that they better align with reality. As learning progresses, the dopaminergic SPE transfers from the outcome event to the predictive cue, a marker of reward anticipation [128]. This SPE may also give rise to stronger memory traces, given that dopamine modulates neural plasticity in the hippocampus, the key structure for episodic memory [4,98]. If memory formation is modulated by the SPE, then we would expect an asymmetric effect on memory, such that a positive PE would improve memory whereas a negative PE would worsen it [95,96]. Indeed, SPEs at the time of predictive cues enhance memory for the cue event, boosting memory for more valued cues [65,95].

Another possibility is that the absolute magnitude of the PE influences memory, enhancing memory for surprising events regardless of whether they were much better or much worse than expected. The locus coeruleus norepinephrine (LC NE) system is thought to mediate the effects of such unsigned prediction errors (UPEs), demonstrating a transient response for unexpected outcomes in both reward and fear learning [87,88]. The LC NE system provides an alternative source of DA to the hippocampus by coreleasing DA with NE, potentially contributing to DA-dependent plasticity in the hippocampus [16–18]. Consistent with this mechanism, UPEs in both reward and threat learning reliably boost memory for associated events in a variety of paradigms [64,66].

Of note, new work has expanded upon and complicated the role of DA from a single, scalar ‘model-free’ value signal to a multiplexed ‘model-based’ prediction signal [129,130], recently suggested to reflect mnemonic, causal inference [131]. Unsigned (nonrewarding) dopaminergic PEs enable broader associative learning of an environment, creating links between two cues, rather than just cue-outcome associations [132]. Unlike striatal DA mechanisms tuned for outcome valence [133], dopaminergic state PEs may indeed have a more direct impact on hippocampal processes.

whether a new experience initiates a distinct memory trace (related to hippocampal ‘pattern separation’ and memory segmentation, given a sufficiently large PE) or, if not, whether the experience is integrated into previous memory (or ‘schema’, related to hippocampal ‘pattern completion’ and memory generalization) [9,10]. Moreover, this affect-prediction division may help distinguish treatment options for memory-related disorders. While the affect route suggests arousal-reduction interventions, the prediction route targets expectation change instead.

Overall, the impact of emotional events on memory is complex, dynamic, and depends, for instance, on its influence at initial encoding, consolidation, or later retrieval [8,11]. Here, we aim to provide an overview of the multiple mechanisms by which aversive or rewarding events shape memory for inherently neutral stimuli that precede or occur at the time of the emotional event. We focus on memory encoding and consolidation, but note that emotion also modulates recall dynamics [12].

We acknowledge that while aversive and appetitive events are associated with ‘opposite’ affect, they may deploy similar mechanisms. For example, while appetitive events are linked to dopaminergic modulation of hippocampal plasticity [4], aversive events also activate mid-brain dopamine to support hippocampal memory [13]. Moreover, historically, paradigms testing aversive events have elicited higher arousal, while those testing appetitive events have elicited higher motivation, leading to different kinds of behavior and memory for those events [14]. Regardless, we consider each described mechanism to contribute to improved emotional memory no matter the valence.

We also distinguish between noradrenergic and dopaminergic memory mechanisms, but memory is contingent on both [15]. To further obfuscate this division, the **locus coeruleus (LC)** coreleases dopamine (DA) along with norepinephrine (NE) to influence hippocampal memory [16–18]. We nevertheless discuss each system separately to highlight their potentially predominant roles in shaping memory, but note that the described mechanisms are unlikely to be selective to DA or NE systems.

Glossary

Event segmentation: a process by which a continuous stream of information is split into separate ‘chunks’ or representations in memory. ‘Event boundaries’ represent the event eliciting segmentation.

Latent state: a hidden generative model that causes events in the environment; a shift in the latent state (‘change point’ event) indicates a change in the statistics governing observed outcomes.

Learning rate: regulates the extent to which new outcomes are integrated into the stored value of an associated event (or action). A high learning rate indicates that a new outcome updates value to a greater extent, diminishing the influence of previous outcomes on that value.

Locus coeruleus (LC): a brainstem nucleus representing the main source of norepinephrine to the brain.

Medial temporal lobe: an anatomically linked system of structures in the brain critical for memory, including the hippocampus and surrounding entorhinal, perirhinal, and parahippocampal cortices.

Prediction error (PE): the difference between expected and actual outcome; signed PEs (‘SPEs’) represent the signed difference (outcome – expectation), whereas unsigned PEs (‘UPEs’) represent the absolute deviation between expectation and outcome.

Reinforcement learning: an associative learning process whereby expectation and behavior are strengthened or weakened by motivationally relevant outcomes (e.g., reward or punishment).

Reinstatement (‘replay’): a mnemonic process whereby the pattern of neural activity present at encoding is repeated after the event.

Salience network: a large-scale neural network that prioritizes the processing of emotionally salient information, including areas such as the insula, the amygdala, and the dorsal cingulate cortex.

Schema network: a large-scale neural network involved in the encoding of information congruent with prior knowledge, including the medial prefrontal cortex, precuneus, and angular gyrus.

Ventral tegmental area (VTA): a midbrain area that is a primary source of dopamine to the brain and the origin of the mesocorticolimbic system, widely implicated in reward processing.

In this review, we first focus on recent insights into how affective state shapes memory. We next discuss new evidence demonstrating that large PEs enhance memory for rewarding and aversive experiences, separate from the effect of the affective outcome itself. We then integrate findings and suggest that PE-driven memory boosts can signal an update of the existing model of the environment, resulting in the reorganization and segmentation of events in memory. Finally, we discuss the application of these findings to psychiatric disorders.

The ‘affect’ route to enhancing memory

We begin by examining new research that validates and extends arousal-based models of memory whereby NE prioritizes emotionally relevant events. We then discuss how reward-based motivation, engaging a dopaminergic circuit, also enhances memory. We nevertheless elaborate upon the mnemonic distinctions between reward-based DA and arousal-based NE, namely in generating more integrated versus disjointed memories, respectively.

Arousal-based noradrenergic mechanism

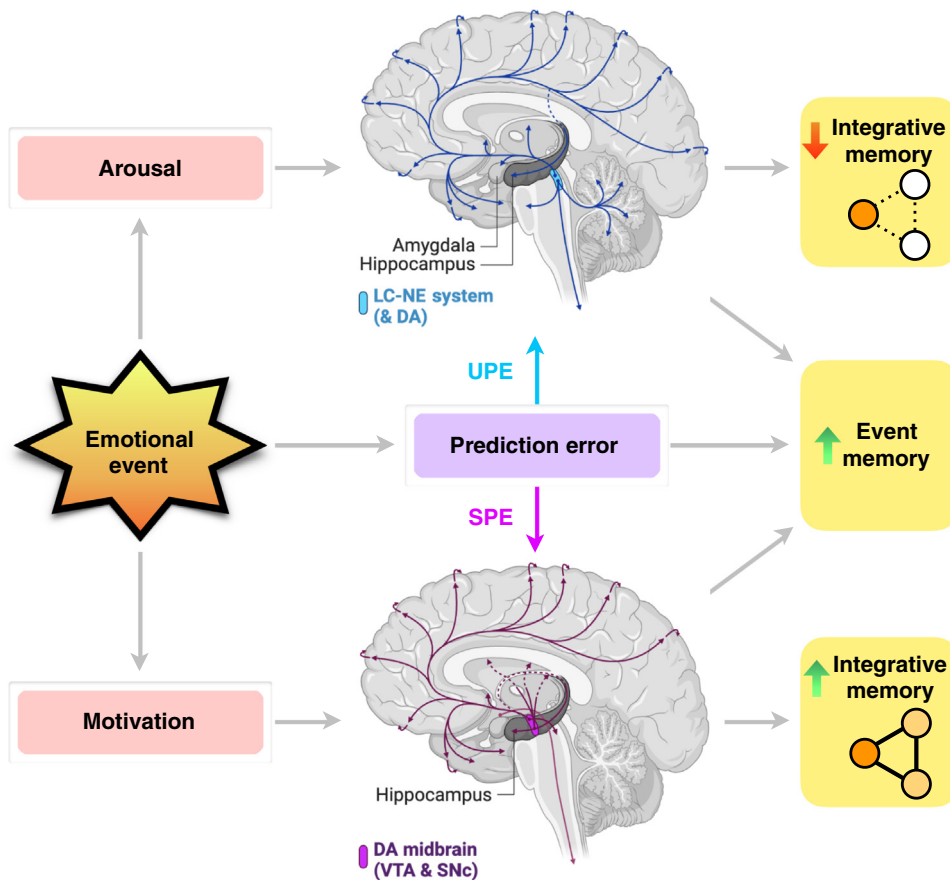
Decades of research establish that better memory for emotional events can be explained by arousal-driven noradrenergic activation of the amygdala. Specifically, the release of NE from the adrenal medulla activates (via the vagal nerve) noradrenergic brainstem nuclei projecting to the amygdala, which then modulates memory consolidation in other brain areas (Box 2) [3,19]. These NE effects can be amplified by glucocorticoids released from the adrenal cortex, which further activate glucose known to enhance memory [20]. Core assumptions of this model receive continuous support. For example, postencoding functional connectivity between the amygdala and neocortical representation areas predict subsequent recognition memory for emotional events [21]. Moreover, a recent study using vagal-nerve stimulation in humans provides causal evidence for the role of vagal activity in memory formation [22]. Similarly, direct electrical stimulation of the human amygdala causes better recognition memory for ongoing neutral events, and does so through the amygdala’s interactions with the hippocampus and perirhinal cortex, consistent with the idea that the amygdala modulates memory in other brain areas [23]. Recent work further highlights that later **reinstatement** of amygdalar–hippocampal patterns [24,25] boosts encoding of ongoing neutral events [26]. Such carry-over effects provide another opportunity to tag events in memory [27,28], creating an extended context for the emotionally arousing event.

Box 2. How noradrenergic arousal helps make emotional memory last

Emotionally arousing events activate a number of physiological systems that help the organism cope with the situation at hand. This orchestrated physiological response includes the release of hormones and neurotransmitters such as catecholamines. These substances, in particular NE, act on the medial temporal lobe and prefrontal areas critically involved in memory formation [3,134,135]. In fact, during emotional arousal, NE is both rapidly released from brainstem nuclei such as the locus coeruleus (LC), and (nor)epinephrine is secreted from the adrenal medulla. This peripheral (nor)epinephrine cannot pass the blood–brain barrier but activates β -adrenergic receptors on vagal afferents projecting to the brainstem nucleus tractus solitarius. Noradrenergic projections from this region project to the amygdala, a key region for emotional memory formation. In particular, lesions of the basolateral part of the amygdala or pharmacological blockade of β -adrenergic activation in this area abolish emotional memory enhancement [136,137]. β -Adrenergic mechanisms of amygdala activation can be further amplified by concurrent activity of glucocorticoids, released during highly stressful events. Simultaneous noradrenergic and glucocorticoid activation of the basolateral amygdala indeed results in especially strong memory for ongoing events [3,138]. Importantly, the amygdala is not the storage site for memories but regulates consolidation in other areas, such as the hippocampus, prefrontal cortex, and dorsal striatum. Moreover, amygdalar modulation is not limited to the emotionally arousing event itself but extends to events preceding the event [138–140].

In sum, decades of research have established that noradrenergic arousal in the basolateral amygdala modulates memory consolidation in other areas, including the hippocampus, to enhance emotional memory. However, recent years have seen exciting new discoveries, including, for example, the specific involvement of the LC, and the long-term vividness of arousal-modulated memory.

New findings further underline the key role of the LC, the primary source of NE in the brain, projecting to virtually all other brain areas (Figure 1) [29], in emotional memory. A recent ultra-high-resolution human fMRI study showed that at encoding, LC activity correlates with the amygdala and arousal to predict emotional memory [30]. This study further revealed that LC connectivity with areas of the **medial temporal lobe** changes dynamically across encoding and consolidation, suggesting distinct roles of the LC during memory encoding and maintenance. Moreover, there is evidence that LC strengthens goal-relevant memory representations in particular, indicating an LC-arousal prioritization mechanism [31]. Intriguingly, we can read from a participant’s eyes which stimuli elicit arousal and are thus selected for long-term storage. Pupil dilation is a biomarker of both arousal and LC activity, and several reports show that it reliably predicts trial-by-trial variability in successful memory encoding [31,32] and retention [33].



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Figure 1. Emotion improves memory through multiple affect and prediction routes. The affect route comprises arousal and motivation. Arousal engages locus coeruleus norepinephrine (LC NE), that also coreleases dopamine (DA) as well as peripheral (nor)epinephrine from the adrenal medulla (Box 2) to modulate amygdala and hippocampal memory. Motivation activates midbrain DA – ventral tegmental area (VTA) and substantia nigra pars compacta (SNc) – to boost memory in the hippocampus. Recent work has identified a prediction-error (PE) route in emotional-memory enhancement, where, in parallel, unsigned prediction errors (UPEs) act on the LC NE system and signed prediction errors (SPEs) act on dopaminergic midbrain neurons to influence hippocampal memory (Box 1). While these routes each give rise to better event memory, they are associated with opposite effects on mnemonic integration. Specifically, DA memory is thought to promote integration of the emotional memory with associated features and events, whereas norepinephrine (NE) memory is thought to disrupt such integration. For a related theoretical framework, see Figure 3 in [14]. Neural pathways constructed with BioRender.com.

Emerging work in this area increasingly focuses on the mechanisms supporting the long-term fate of arousing memories. In addition to synaptic consolidation requiring several hours to complete, a proposed systems-consolidation process can take weeks to months to complete. During systems consolidation, memories become less dependent on the hippocampus and more reliant on neocortical areas [34,35]. This neural reorganization is thought to change memory from a detailed representation to a more gist-like representation [36,37]. Nevertheless, recent evidence demonstrates that noradrenergic arousal can overturn the dynamics of systems consolidation: rats that received NE injection after encoding were able to discriminate a previous threat context from very similar contexts even 28 days after training, indicating that postencoding NE kept memories specific (i.e., episodic) over time. This specificity was accompanied by increased hippocampal involvement in memory over time [38]. In striking parallel, in a human fMRI study, pharmacological increase of noradrenergic arousal after encoding similarly led to more hippocampal involvement after 28 days [39]. These data suggest that postencoding noradrenergic arousal may not only decelerate but even reverse the dynamics of systems consolidation, potentially providing an important mechanism that keeps memories vivid long-term.

Motivation-based dopaminergic mechanism

While arousal certainly plays a part in motivation, the memory boost linked to periods of behavioral invigoration, such as when seeking hedonic rewards, engages a largely separate neural mechanism centered on dopamine (Figure 1). Like arousal, high motivation can enhance memory at all stages of mnemonic processing, although with different consequences. For example, both arousal and motivation enhance attention; however, aversive arousal can narrow attention to the most salient feature (e.g., a gun [40]), whereas reward motivation can broaden attention (e.g., taking in the landscape), which allows for better binding of surrounding features in memory [14].

The **ventral tegmental area (VTA)**, a primary source of DA in the midbrain, is structurally and functionally linked to the hippocampus where long-term potentiation and maintenance is modulated by DA [4,6]. DA further strengthens neutral or weak memories that were temporally close to an emotional event, as in the ‘synaptic tag and capture’ model of synaptic consolidation [41,42]. This plasticity is thought to occur only after a period of consolidation, and indeed, several fMRI studies have observed that reward motivation amplifies activity and connectivity between the midbrain and hippocampus, predicting better postconsolidation memory for reward-motivated events [43–47]. Rewarding memories are additionally bolstered by offline ‘replay’ in the VTA and hippocampus [48], where the relevant neuronal sequences that were active during encoding are repeated and relayed between regions, putatively supporting systems-level consolidation.

Theoretical and empirical work has furthermore distinguished between dopaminergic and noradrenergic memory signatures [14]. DA is thought to integrate experiences across features and events, producing the rich, relational representations characteristic of hippocampal memory [49]. Accordingly, increased postencoding interactions between the VTA and higher-order sensory cortex support better associative memory for reward-motivated events [50]. By contrast, negative events, which engage the amygdalar arousal-based mechanism described earlier, impair integrative and associative memory [51]. Previous work had already highlighted this key difference: while the hippocampus promotes relational encoding, the amygdala disrupts it [49]. Consistent with this, negatively arousing images can engage the amygdala during encoding to strengthen item memory, but reduce hippocampal activity, thereby weakening associative memory [52–54] (although an amygdala–hippocampal phase code is observed to support memory for negative images in intracranial recordings [55]). Highly arousing negative events, such as acute stress, can similarly diminish hippocampal memory [56–59] and impair hippocampus-dependent (contextual) conditioning [60]. Conversely, positive emotion and reward motivation,

putatively relying on dopaminergic–hippocampal modulation, increase item and associative memory as well as the clustering of rewarding events during free recall [54,61,62]. These potentially distinct roles of DA and NE in integrating versus segmenting memories are not limited to ‘affect’ but extend to neural computations at large (discussed later).

The ‘prediction’ route to improving memory

We next present recent evidence of a prediction mechanism which, separate from the effects of affect alone, boosts and organizes memory across aversive and appetitive domains. Aside from triggering an affect response, emotional events can engage fundamental learning mechanisms whereby predictions of the outside world are formed and updated by experience. Given that emotional events can elicit strong expectations and are often unpredictable in nature (with each contributing to arousal [63]), a rapidly developing literature quantifies the effect of emotional expectation, subsequent outcome, and the difference between these (PE), on memory [64–70]. Although mechanisms supporting memory for large PE events likely overlap with those engaged by novel, salient, or oddball events, we focus on PEs for rewarding or aversive (i.e., ‘emotional’) outcomes during incremental learning. These PEs dynamically change with new or more learning (i.e., changes in expectations) and their outcomes are emotionally stimulating.

While appetitive and aversive learning can engage distinct neural systems [71], we next describe shared effects. We moreover characterize how ‘SPEs’ and ‘UPEs’ differentially influence memory for the outcome-predicting cue versus the outcome event itself. After discussing findings in threat and reward learning separately, we summarize results across paradigms (for a list of highlighted findings, see Figure 2).

Threat learning

Recent experiments have examined how PEs influence memory for predictive cues during threat conditioning. In an initial study, participants completed an incidental-encoding Pavlovian-threat-conditioning paradigm where they predicted whether unique exemplars from two different stimulus categories would lead to electric shock [66]. Large UPEs (surprising shock or no shock), and not the expectation of shock nor the outcome itself, boosted recognition memory for the exemplars; this effect was replicated in a second experiment. PEs’ mnemonic influence was moreover spotlighted in another study demonstrating that when the PE associated with a stressful event is reduced by prior information, the well-known memory enhancement of stressful episodes [72,73] can be largely abolished [74].

A subsequent experiment further explored the role of SPEs, and found that large positive PEs (i.e., unexpected shock omission, ‘negative aversive PEs’ in the empirical paper) particularly improved memory [75]. This result is consistent with emerging findings in rodent work demonstrating that unexpected-shock omission activates midbrain dopamine at outcome, suggesting a PE mechanism similar to early reward learning (Box 1 and Figure 3 [76–78]), and one that could support positive-PE (dopamine-dependent) avoidance of threatening outcomes [79,80]. Together, these results suggest that unexpected outcomes, not specifically aversive outcomes, improve memory, and may be responsible for the memory enhancement of stressful episodes.

Given that unpredictability and uncertainty elicit arousal [63,81], these studies have further probed the relationship between PE, arousal, and memory. In line with classic arousal-based models (Box 2), outcome-related arousal indeed improves recognition memory [66,81]. Critically, however, large PEs predict memory independently from arousal, with both predictors explaining recognition memory better than either alone [66,75]. In fact, diminishing the PE associated with a

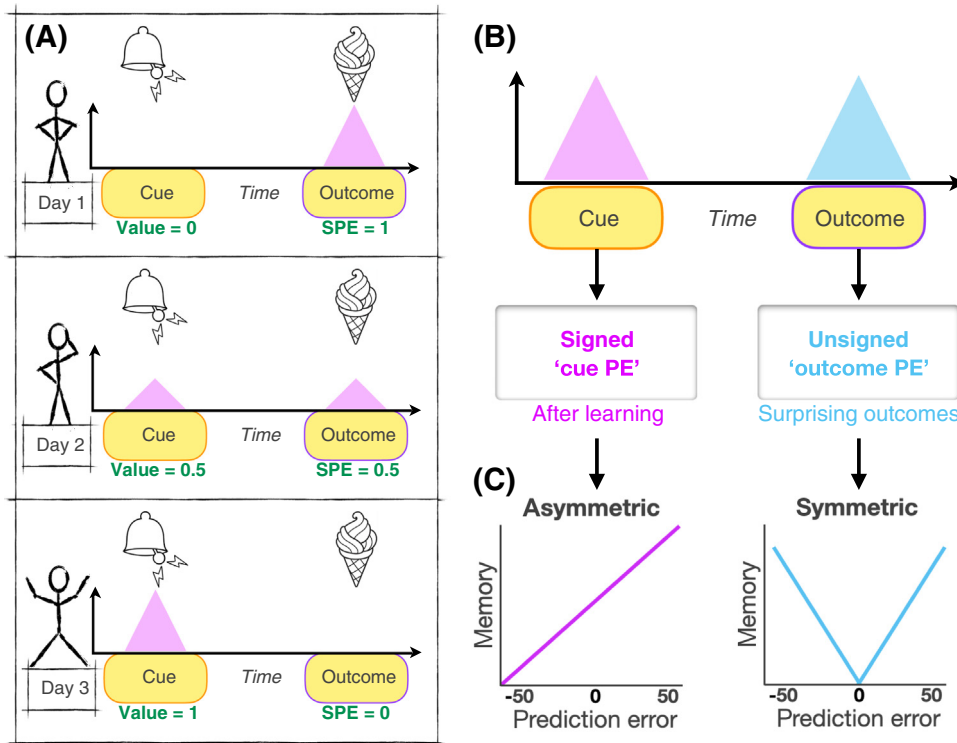
Memory event	Study	Delay	Stimuli	Response	Outcome	# Cats.	PE event	PE type	Result
Cue	R ('21)	sd	s rel.	Prediction 0-100	Reward 0-100	2	Cue	SPE	+
Cue	JN ('19)	sd/nd	a/i rel.	Choice play/pass	Reward/loss -10/1-100	2	Cue	SPE	+
Outcome	R ('18/'21)	sd	s/o rel.	Prediction 0-100	Reward 0-100	2	Outcome	SPE	
Outcome	R ('20)	sd	s rel.	No response	Reward 0-100	1	Outcome	SPE	
Outcome	D ('16)	sd	o irrel.	Choice 2 bandits	Correct/incorrect	2	Outcome	SPE	
Outcome	R ('18/'21)	sd	s/o rel.	Prediction 0-100	Reward 0-100	2	Outcome	UPE	+
Outcome	R ('20)	sd	s rel.	No response	Reward 0-100	1	Outcome	UPE	+
Cue	JN ('19)	sd/nd	a/i rel.	Choice play/pass	Reward/loss -10/1-100	2	Outcome	SPE	
Cue	R ('21)	sd	s rel.	Prediction 0-100	Reward 0-100	2	Outcome	SPE	
Cue	K ('21)	nd	o rel.	Prediction shock slider	Shock/no-shock	3	Outcome	SPE	+
Cue*	W ('14)	nd	o irrel.	Choice 2 bandits	Reward 0/0.25	2	Outcome	SPE	-
Cue	K ('20)	nd	a/i rel.	Prediction shock	Shock/no-shock	2	Outcome	UPE	+
Cue	R ('21)	sd	o rel.	Prediction 0-100	Reward 0-100	1	Outcome	UPE	+
Cue	R ('21)	sd	s rel.	Prediction 0-100	Reward 0-100	2	Outcome	UPE	
Cue	JN ('19)	sd/nd	a/i rel.	Choice play/pass	Reward/loss -10/1-100	2	Outcome	UPE	
Next-trial cue	K ('20)	nd	a/i rel.	Prediction shock	Shock/no-shock	2	Outcome	UPE	
Next-trial cue	R ('18)	sd	s/o rel.	Prediction 0-100	Reward 0-100	2	Outcome	UPE	

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Figure 2. Prediction-error (PE) effects on recognition memory in selected incremental-learning paradigms. 'Memory event' indicates when during learning the memoranda (trial-unique stimulus) occurred; 'cue' is the stimulus representing the outcome-predictive cue (*indicates two cue stimuli presented, otherwise a single cue is presented); 'outcome' is the stimulus occurring during the outcome; 'next-trial cue' is the cue occurring immediately after the tested PE ('proactive' memory). Study abbreviations: D('16), Davidow *et al.*, 2016 [96], reporting adult results; JN('19), Jang *et al.*, 2019 [95]; K('20), Kalbe and Schwabe, 2020 [66]; K('21), Kalbe and Schwabe, 2021 [75]; R('18), Rouhani *et al.*, 2018 [64]; R('20), Rouhani *et al.*, 2020 [86]; R('21), Rouhani and Niv, 2021 [65]; W('14), Wimmer *et al.*, 2014 [101]. 'Delay' means time between encoding (learning task) and recognition (memory task). 'Stimuli' are types of stimuli used and whether they were task relevant. 'Response' means participant action prior to receiving the outcome; 'prediction' or 'no response' refer to Pavlovian-conditioning paradigms and 'choice' to instrumental/operant-conditioning paradigms. 'Outcome' is the type of feedback received. '# Cats.' is the number of categories (or 'bandits') learned about concurrently. 'PE event' indicates when (cue or outcome) the tested PE occurred. 'PE type' indicates whether the tested PE was signed (SPE) or unsigned (UPE). 'Result' indicates whether the tested PE led to memory enhancement ('+' green), decrement ('-' red), or a null result (gray block). Abbreviations: a/i, animate/inanimate items; irrel., irrelevant; nd, next day; o, objects; s, scenes; sd, same day; rel., relevant.

stressful event reduces recognition memory but does not modulate the physiological stress response [74], highlighting the separate effects of arousal and PE on memory.

New fMRI data further show that memory enhancement for large shock-omission PEs is orchestrated by a neural mechanism distinct from arousal [75], and one consistent with pattern separation (giving rise to new, distinct memory traces) versus pattern completion (the integration of experience with prior representations or schemas). Indeed, while recognition memory for expectancy-congruent (low-PE) events is linked to para/hippocampal activity at encoding, memory enhancement for high (shock-omission) PEs is associated with reduced activity and



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Figure 3. Memory predictions for signed prediction error (SPE) and unsigned prediction error (UPE) signals. (A) The reward SPE travels from outcome to the cue predicting reward over the course of learning. Initially (day 1), the cue (sound of the bell) has no value. When it is paired with reward (ice-cream), the unexpected outcome elicits a strong positive prediction error. By day 2, the bell starts to become associated with ice-cream (increased value), activating a small positive PE at the time of the cue and a smaller positive PE at outcome (as the ice-cream is partly predicted and less surprising by now). After the bell has become associated with ice-cream (day 3), a strong positive PE, reflecting high value and expectation of reward, occurs only at cue: the ice-cream event, while (hedonically) appreciated, is no longer unexpected. After learning, the SPE at cue (B) putatively gives rise to an asymmetric effect on memory (C) where increased dopamine enhances memory for cues that predict higher reward (Box 1). Conversely, a UPE signal is thought to activate locus coeruleus norepinephrine (LC/NE) during surprising outcomes throughout learning, symmetrically boosting memory for both positive and negative outcomes that substantially deviate from prior expectation. In line with these predictions, both SPE at cue and UPE at outcome improve memory during reward learning [65].

connectivity both within medial temporal lobe and **schema networks** [82,83]. Instead, shock-omission PEs increase activity in a **salience network**, including the insula and dorsal anterior cingulate cortex, as well as its connectivity with the medial-temporal-lobe network, which predicted better recognition memory for cue events. These neural changes could not be explained by increases in arousal. Together, these data demonstrate that large shock-omission PEs elicit a salience signal that shifts memory mechanisms to encode or ‘pattern separate’ an event rather than integrate it with previous memory. In line with this, recent findings show that PEs not only disrupt sustained memory representations in the hippocampus [84], but also bias it to encode new information [85]. PE’s strengthening and segmenting of memory is further discussed later.

Reward learning

Several recent studies characterize PE’s influence on memory for rewarding events, and like those on threat learning, find that UPE memory modulation is independent of classic ‘affect’ effects, in this case, reward receipt. First, a series of experiments using an incidental-encoding

Pavlovian-reward-conditioning paradigm investigated which features of reward learning impact recognition memory. Consistently and across variations of the paradigm, at reward outcome UPEs, and not SPEs or the reward outcome itself, predict recognition memory for the outcome event [64,86].

This finding is consistent with the classic Pearce–Hall model of associative learning that posits enhanced attention and learning for surprising outcomes (i.e., the learning of values) (Box 1 and Figure 1) [87]. These large UPEs furthermore elicit a phasic response from the LC–NE system [29,88]. Intriguingly, while large UPEs increase both trial-by-trial **learning rate** and event memory, learning rate and memory are consistently uncorrelated, suggesting dissociable effects [64]. In fact, in one paradigm, where reward variance (i.e., ‘risk’) is either high or low (generating frequent large or small PEs, respectively), learning rate is inversely related to variance (i.e., learning rate is higher overall in the low-variance context); this is in line with previous findings [89,90], whereas recognition memory shows the flipped result (i.e., memory is higher overall in the high-variance context). Such findings are reminiscent of the trade-off between rapid adjustment during learning (higher learning rates) and long-term, PE-driven retention of values [91]. Given the rich body of work examining dopaminergic scaling in PEs [92] as well as cholinergic and noradrenergic modulation of expected and unexpected uncertainty, respectively [93], future neuroscientific work is ripe to examine the potentially independent and interacting effects of UPEs on value versus memory updating [94].

Along with the memory-enhancing effects of UPEs during outcomes, new work highlights the additional role of SPEs within [65,95,96] and outside of reinforcement learning [70,97]. Importantly, by contrast to UPEs, SPEs do not seem to influence memory when they occur at the time of the outcome, but improve memory only when they occur at reward cue (results test SPEs and UPEs in the same model, controlling for all potential effects) [65,95] (Figure 2). This mnemonic boost is compatible with the dopaminergic PE signal that transfers from reward outcome to cue over the course of learning (Box 1 and Figure 3), and suggests that, after initial learning, dopamine release at cue could strengthen hippocampal memory [4,98]. The SPE putatively supports another classic associative model, the Mackintosh model [99], where attention and learning increase for cues that reliably predict reward. Interestingly, this model is paradoxical to the aforementioned Pearce–Hall model where unreliable (high-PE) events are predicted to enhance attention and learning.

In fact, a recent experiment indicates that both signals bolster memory, but do so during different phases of learning [65]. In this paradigm, participants learn the values of two stimulus categories and are later tested for recognition memory of trial-unique images occurring at reward cue or outcome. Here, the ‘cue-PE’ (Figure 3) is calculated as the difference between the expected value of the current reward category versus the alternative one. Reinforcement learning models including both cue-SPE and outcome UPE signals to modulate learning rate fit behavior better than models with either component alone. Moreover, the mnemonic boost of the UPE at outcome was again replicated, and in tandem, the SPE at cue was found to improve memory for cue images. In other words, the more participants learn that one category is more rewarding than the other, the more likely they are to remember the cue belonging to the more rewarding category, whereas any surprising outcome, positive or negative, enhances memory for the outcome images. This SPE mechanism at cue could potentially initiate and support memory enhancement during high-reward anticipation [43,44,47,100].

Summary across paradigms

Taken together, PEs improve memory independently of the effects of shock or reward alone. To further compare PE effects on memory, we organized relevant findings from incremental-learning

paradigms (Figure 2). As previously discussed, SPEs at cue consistently enhance memory for a reward-predictive cue, similar to a value signal, and UPEs (but not SPEs) at outcome enhance memory for the outcome event [64,65,86,95,96]. Of note, memory consolidation does not appear to exert a strong influence across paradigms, as PEs influence memory when tested immediately after encoding and 24 h later [95]. Similarly, whether the learning task is operant ('choice') or Pavlovian ('prediction/no response') does not seem to exert an obvious effect across these memory results.

Aside from PE effects on concurrently occurring events, prioritizing cues predictive of important outcomes has great adaptive utility. Studies have thus assessed the retroactive influence of outcome PEs on predictive cues, although with mixed results. During shock learning, outcome PEs enhance memory for their cues [66,75], especially when shock is expected but omitted (a relief, i.e., positive-outcome SPE). By contrast, during reward learning, outcome SPEs do not enhance cue or outcome-event memory [65,95] but do predict later choice [65]. Here, positive-outcome SPEs increase preference for the outcome (over the cue) event of that trial, whereas negative-outcome SPEs increase preference for the cue event, pointing to outcome SPE effects on nondeclarative memory. These different results could be due to task engagement: learning about shocks may be more engaging, potentially bolstering subsequent reactivation of the predictive cue, while outcome SPEs during (online) reward learning may not be salient enough to influence, at least, declarative memory.

Competition between learning and memory signals could also account for inconsistent results across paradigms. For example, during reward learning, outcome UPEs increased cue memory only when there was a single category to learn about; this effect was eliminated when learning about two categories which elicit additional, potentially competing, PEs at cue [65]. Moreover, in a paradigm that presented two choices at once and where the two trial-unique stimuli were task-irrelevant, the outcome SPE competed with and decreased memory for those events [101]. Future work could test how task manipulations – specifically those modulating engagement, competition, and relevance – govern whether PEs enhance or diminish memory for predictive cues.

Finally, given that memory-boosting signals can spill over to adjacent events [102], threat and reward-learning paradigms have assessed 'proactive' memory for the cue following the PE-eliciting outcome, but have not found an effect [64,66]. Of note, although we previously discussed retroactive memory for preceding predictive cues, these results may not be generalizable to preceding nonpredictive events and should be evaluated separately.

PEs organize memories

In previous sections we discussed that while 'affect' and 'prediction' mechanisms both contribute to emotional-memory enhancement, they may differentially organize memories. For example, mnemonic structure formed through the affect route may rely more on consolidation mechanisms [103], whereas it emerges without delay through the prediction route, suggesting stronger reliance on encoding processes [86]. Moreover, different putative neuromodulators – namely mid-brain DA and LC NE (and DA) – are linked to integrating across versus segmenting memories, respectively [14,104]. **Event segmentation**, associated with hippocampal pattern separation, can occur after detecting an external (or potentially internal) change. This change can lead to an 'event boundary' in memory, which divides events that came before the change from those that followed, giving rise to distinct representations or 'chunks' of past experience [9,105–108]. Although memory for the event boundary itself is boosted, temporal-order memory for events spanning it is worse, demonstrating a mnemonic trade-off between the distinct event and the temporal integration of adjacent events [109].

Large-reward PEs have recently been shown to act like event boundaries in memory, improving recognition memory for the event itself but diminishing temporal memory for events across them [86]. Relatedly, in the threat-learning study described above [75], high-magnitude PEs upregulate a neural salience network and downregulate a schema network, which was associated with better cue memory. These neural dynamics further suggest that large PEs disrupt integration of continuous events in memory.

Nevertheless, whether high-magnitude PEs strengthen and/or segment memory depends on whether they (are inferred to) represent an event boundary or not. For example, an environment marked by frequent surprising changes (high-outcome variance), such as gambling in Las Vegas, may be segmented differently in memory than a single surprising event ushering in a lasting change (change-point), such as the coronavirus disease 2019 (COVID-19) pandemic (for an ecological and longitudinal examination of memory across the pandemic, see [110]). In fact, two separate experiments investigated the mnemonic effects of large PEs generated by either high-outcome variance [64] or by a change-point in the mean of the underlying reward distribution [86]. High-magnitude PEs boost recognition memory in both tasks. When these PEs are generated by high-outcome variance (e.g., gambling events), they additionally improve overall temporal memory for items in the high-(vs. low)-variance context [64]. However, when large PEs signal a change-point (e.g., events before and after the pandemic), they disrupt temporal memory for items across the boundary [86]. These two seemingly contradictory results indicate that high-magnitude PEs alone do not create event boundaries in memory, they need to further reflect a (meaningful) change in the **latent state** [111].

New work demonstrates that increased pupil dilation, a marker of LC NE release and arousal, predicts segmentation between events spanning boundaries [112]. How the LC NE system helps strengthen and/or segment events in memory is still unclear, but research suggests that each process could occur at different time-points. For example, a surprising event leads to an early increase in pupil dilation, whereas a change-point leads to a late decrease in pupil dilation [113]. Potentially, a surprising change-point event could first increase noradrenergic firing, thereby strengthening that event in memory, and then decrease it to engage memory segmentation. Consistent with this hypothesis/idea, the observed segmentation for large change-point PEs [86] does not occur between the high-PE event and its predecessor, but rather sometime during the high-PE event, sparing the connection of that event to its predecessor while segmenting events that cross it. Accordingly, in the computational model developed to reproduce these results (a variant of the context, maintenance and retrieval model [114]), segmentation in the mental (or 'temporal') context occurs after the high-PE event. The high-PE event itself is strongly stamped in temporal context, demonstrating intact associations with both preceding and subsequent contexts, thereby representing a junction between them.

Memory strengthening and segmenting could additionally, or alternatively, be orchestrated by distinct mechanisms. Event segmentation across change-points indeed predicts shifting state representations or pattern separation in the orbitofrontal cortex [115] and the hippocampus [116,117]. Large PEs experienced within a latent state (e.g., a high-variance context) are not expected to induce representational changes. In fact, a recent theoretical model proposes that similar sequences of PEs may be later clustered (or desegmented) in memory to form an abstract representation of that state. This (nonepisodic) abstraction can then be applied to new, relevant situations, enabling useful generalization [118]. Future work could characterize how PEs (within and across latent states) may differentially deploy mnemonic integration and segmentation to support adaptive behavior.

In short, a consistently growing literature shows that PEs are a fundamental modulator of memory by enhancing memory for emotional events and by further structuring those memories into distinct representations (Figure 4). The extent to which PEs may act independently or interactively with more ‘affective’ mechanisms is a promising direction for future work. For example, SPEs, associated with DA release, and UPEs, associated with activation of the LC NE system, are strong candidates for modulating the integration versus separation of emotional events in memory. While large SPEs may help integrate rewarding cues with their outcomes, potentially giving rise to reward schemas, large UPEs may help divide those schemas (e.g., rewarding vs. punishing schemas) in memory.

Applications of PE memory enhancement

Research on emotional-memory mechanisms aims to develop novel approaches to modifying unwanted and debilitating memory. While the affect route suggests pharmacological or psychological (emotion-focused) treatment targeting arousal processes, the prediction route emphasizes interventions that update patients’ prior expectation and beliefs (e.g., cognitive-behavioral therapy). Within the affect route, the classic arousal-based mechanism inspired several pharmacological interventions that targeted NE or glucocorticoid signaling to disrupt overly strong emotional memory in anxiety disorders and PTSD [119,120]. However, although such pharmacological treatments may be effective, they risk side effects. PE-based modification offers a less invasive approach to modifying unwanted memories. One potential application relates to the finding that stress-induced memory boost is diminished when people receive prior information about the stressful event [66]. Of course, many emotional events occur without warning. However, some can be predictable to an extent (e.g., in emergency units, fire services, or combat situations), where detailed information of what could occur might help attenuate the strength of potentially traumatic memory.

PE-based memory mechanisms might also be biased in psychiatric disorders. For instance, individuals with depressive symptoms are more likely to remember events associated with high-magnitude negatively valenced PEs, whereas those without depressive symptoms preferentially remember events associated with large positively valenced PEs [121]. These findings may contribute to the reported memory bias for negative versus positive events in depression and vice versa in healthy individuals (memory bias is demonstrated for low or matched arousal events [122–124]). Attentional interventions may help reorient depressed patients towards surprising positive outcomes during encoding. Moreover, along with weakening of unwanted memories, therapeutic interventions can leverage PE-based mechanisms to strengthen positively surprising outcomes that challenge patient expectations and prior beliefs. Indeed, learning from expectancy violations is a key mechanism predicting success in exposure-based therapy for anxiety disorders [125].

Concluding remarks

Accumulating evidence shows that high-magnitude PEs associated with aversive or rewarding events boost memory for neutral events that predict or co-occur with the emotional outcome. This PE-driven mechanism can further update and structure our mnemonic representation of the world, enabling better prediction of future rewards and threats. Crucially, PE-based memory enhancement is separate from the well-described ‘affect’ mechanism governed by arousal and motivational state. We therefore suggest that two routes – affect and prediction – enhance memory and implicate different strategies in tackling aberrant emotional memory.

While the described PE-based mechanism broadens our perspective on the components driving memory enhancement, several key questions remain (see [Outstanding questions](#)). Addressing

Outstanding questions

If both affect-driven and PE-driven memory mechanisms are linked to noradrenergic and dopaminergic action, how do these mechanisms differ? What neural processes make PE effects on memory distinct from affect (and vice versa)?

How do dopaminergic and noradrenergic systems interact to balance the strengthening, integration, and segmentation of memory (e.g., between PEs that reflect a change in the latent state vs. not)?

While unsigned PEs increase both learning rate and memory, these effects are uncorrelated; which mechanisms differentiate value (outcome) and memory (outcome-event) updating as well as long-term retention of values?

How do value and surprise signals interact to modulate memory in the brain?

Do positively valenced PEs across threat and reward learning (e.g., a reward PE and a shock-omission PE) act similarly or differently on neural memory mechanisms?

Is PE-memory enhancement selective for predictive information, or is there a similar enhancement for nonpredictive stimuli present in temporal proximity to the PE?

Is PE-memory enhancement dependent on the temporal distance of a stimulus to the outcome PE?

Do affect and prediction routes produce different mnemonic signatures and dynamics at retrieval?

Does the deployment of affect versus prediction mechanisms vary depending on age? For instance, is emotional-memory enhancement in young children driven primarily by arousal mechanisms, while PE mechanisms become more relevant when the hippocampus and the prefrontal cortex are fully developed?

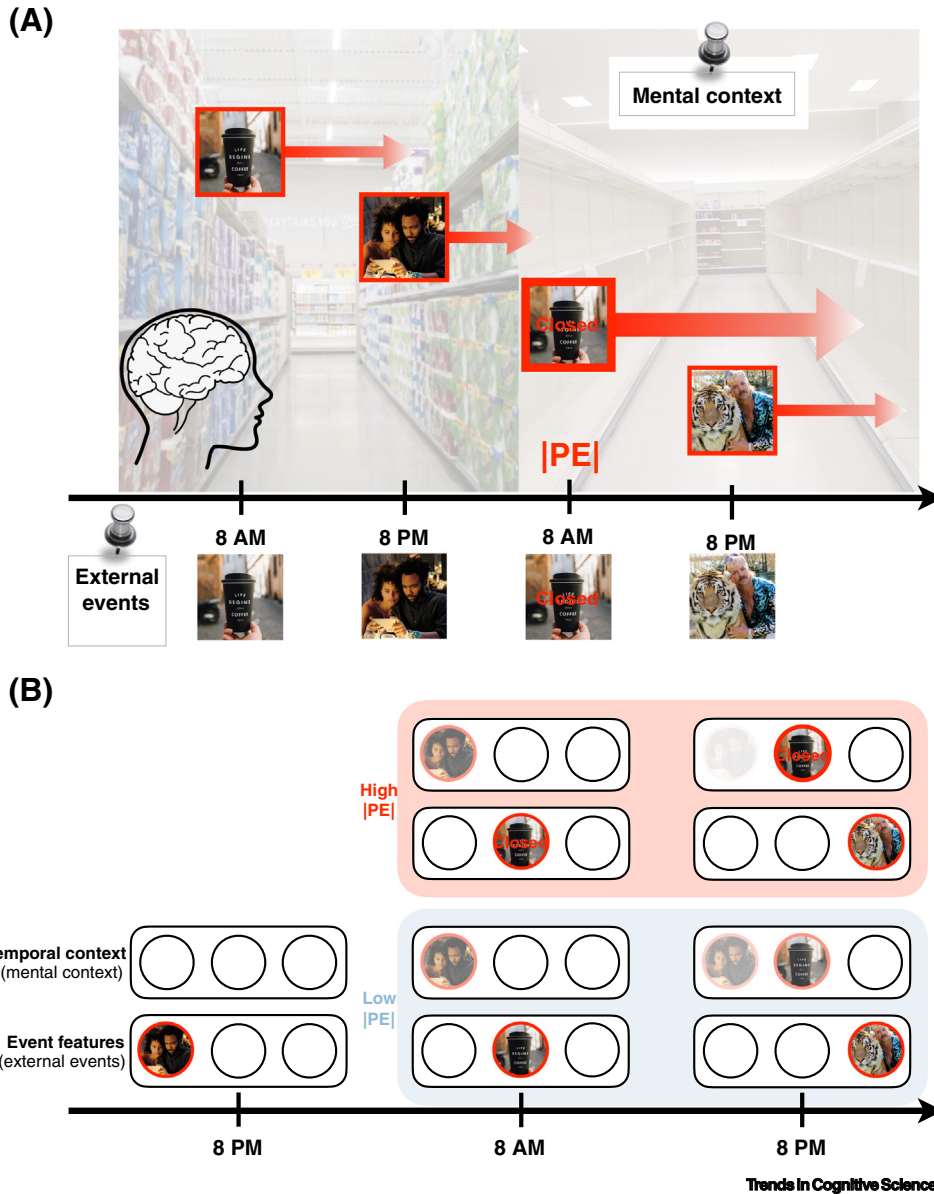


Figure 4. Prediction-error (PE) segmentation of events in memory [86, 114]. (A) External events activate and linger in the brain (mental or temporal context) to create associations with new events experienced in temporal proximity (overlap between red arrows indicates associative binding between events). The pictured individual has a routine of coffee at 8 a.m. and television at 8 p.m. If each event elicits the same amount of activation, events are uniformly associated with previous ones in memory. However, a high-magnitude PE can disrupt integration, splitting events that came before it from those that came after. Here, the individual learns of coronavirus disease 2019 (COVID-19) when noticing their coffee-shop is closed. This surprising event enters temporal context with higher drift rate, meaning it is stamped strongly in memory and clears out previously active events, leading to the formation of two distinct contexts: one prepandemic (stocked aisles) and one postpandemic (empty aisles). (B) Similarly, within the computational model [86], external events (event features) enter into (the next event's) temporal context with a stable drift rate. PEs increase this drift rate, consequently enhancing event activation at the expense of other active events in temporal context. The temporal context of the next event, in turn, is strongly associated with the high-PE event, but not with events that came before it (compare 'high IPEI' vs. 'low IPEI' in the figure). The high-PE event itself is still associated with the previous and subsequent context, but impairs integration across it, as supported by empirical evidence [86]. Image source: Atlanta (FX), 2018; Tiger King (Netflix), 2020.

these and related questions may not only further our understanding of how emotional events shape memory but may also offer more effective interventions to diminish disruptive memory in psychiatric disorders.

Acknowledgments

We gratefully acknowledge funding from the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) – Project number 449640848, GRK 2753/1 to L.S.

Declaration of interests

No interests are declared.

References

- Hamann, S. (2001) Cognitive and neural mechanisms of emotional memory. *Trends Cogn. Sci.* 5, 394–400
- LaBar, K.S. and Cabeza, R. (2006) Cognitive neuroscience of emotional memory. *Nat. Rev. Neurosci.* 7, 54–64
- McGaugh, J.L. (2006) Make mild moments memorable: add a little arousal. *Trends Cogn. Sci.* 10, 345–347
- Shohamy, D. and Adcock, R.A. (2010) Dopamine and adaptive memory. *Trends Cogn. Sci.* 14, 464–472
- Li, S. *et al.* (2003) Dopamine-dependent facilitation of LTP induction in hippocampal CA1 by exposure to spatial novelty. *Nat. Neurosci.* 6, 526–531
- Lisman, J. *et al.* (2011) A neo-Hebbian framework for episodic memory; role of dopamine-dependent late LTP. *Trends Neurosci.* 34, 536–547
- Gray, R. and Johnston, D. (1987) Noradrenaline and beta-adrenoceptor agonists increase activity of voltage-dependent calcium channels in hippocampal neurons. *Nature* 327, 620–622
- Joëls, M. *et al.* (2011) Stress and emotional memory: a matter of timing. *Trends Cogn. Sci.* 15, 280–288
- Shin, Y.S. and DuBrow, S. (2021) Structuring memory through inference-based event segmentation. *Top. Cogn. Sci.* 13, 106–127
- McClelland, J.L. *et al.* (1995) Why there are complementary learning systems in the hippocampus and neocortex: insights from the successes and failures of connectionist models of learning and memory. *Psychol. Rev.* 102, 419–457
- Mather, M. and Sutherland, M.R. (2011) Arousal-biased competition in perception and memory. *Perspect. Psychol. Sci.* 6, 114–133
- Talmi, D. *et al.* (2019) A retrieved context model of the emotional modulation of memory. *Psychol. Rev.* 126, 455–485
- Tsetsenis, T. *et al.* (2021) Midbrain dopaminergic innervation of the hippocampus is sufficient to modulate formation of aversive memories. *Proc. Natl. Acad. Sci. U. S. A.* 118, e2111069118
- Cleworth, D. and Murty, V.P. (2019) Echoes of emotions past: how neuromodulators determine what we recollect. *eNeuro* 6 ENEURO.0108-18.2019
- Hauser, T.U. *et al.* (2019) Distinct roles of dopamine and noradrenaline in incidental memory. *J. Neurosci.* 39, 7715–7721
- Kempadoo, K.A. *et al.* (2016) Dopamine release from the locus coeruleus to the dorsal hippocampus promotes spatial learning and memory. *Proc. Natl. Acad. Sci. U. S. A.* 113, 14835–14840
- Takeuchi, T. *et al.* (2016) Locus coeruleus and dopaminergic consolidation of everyday memory. *Nature* 537, 357–362
- Wagatsuma, A. *et al.* (2018) Locus coeruleus input to hippocampal CA3 drives single-trial learning of a novel context. *Proc. Natl. Acad. Sci. U. S. A.* 115, E310–E316
- Rozenzwaal, B. *et al.* (2009) Stress, memory and the amygdala. *Nat. Rev. Neurosci.* 10, 423–433
- Smith, M.A. *et al.* (2011) Glucose enhancement of human memory: a comprehensive research review of the glucose memory facilitation effect. *Neurosci. Biobehav. Rev.* 35, 770–783
- Kark, S.M. and Kensinger, E.A. (2019) Post-encoding amygdala-visuosensory coupling is associated with negative memory bias in healthy young adults. *J. Neurosci.* 39, 3130–3143
- Ventura-Bort, C. *et al.* (2021) Establishment of emotional memories is mediated by vagal nerve activation: evidence from non-invasive taVNS. *J. Neurosci.* 41, 7636–7648
- Inman, C.S. *et al.* (2018) Direct electrical stimulation of the amygdala enhances declarative memory in humans. *Proc. Natl. Acad. Sci. U. S. A.* 115, 98–103
- de Voogd, L.D. *et al.* (2016) Awake reactivation of emotional memory traces through hippocampal-neocortical interactions. *NeuroImage* 134, 563–572
- Hermans, E.J. *et al.* (2016) Persistence of amygdala-hippocampal connectivity and multi-voxel correlation structures during awake rest after fear learning predicts long-term expression of fear. *Cereb. Cortex* 27, 3028–3041
- Tambini, A. *et al.* (2017) Emotional brain states carry over and enhance future memory formation. *Nat. Neurosci.* 20, 271–278
- Dunsmoor, J.E. *et al.* (2015) Emotional learning selectively and retroactively strengthens memories for related events. *Nature* 520, 345–348
- Kalbe, F. and Schwabe, L. (2022) On the search for a selective and retroactive strengthening of memory: is there evidence for category-specific behavioral tagging? *J. Exp. Psychol. Gen.* 151, 263–284
- Sara, S.J. (2009) The locus coeruleus and noradrenergic modulation of cognition. *Nat. Rev. Neurosci.* 10, 211–223
- Jacobs, H.I. *et al.* (2020) Dynamic behavior of the locus coeruleus during arousal-related memory processing in a multi-modal 7T fMRI paradigm. *eLife* 9, e52059
- Cleworth, D.V. *et al.* (2018) Locus coeruleus activity strengthens prioritized memories under arousal. *J. Neurosci.* 38, 1558–1574
- Bergt, A. *et al.* (2018) Reading memory formation from the eyes. *Eur. J. Neurosci.* 47, 1525–1533
- de Gee, J.W. *et al.* (2020) Pupil-linked phasic arousal predicts a reduction of choice bias across species and decision domains. *eLife* 9, e54014
- Alvarez, P. and Squire, L.R. (1994) Memory consolidation and the medial temporal lobe: a simple network model. *Proc. Natl. Acad. Sci. U. S. A.* 91, 7041–7045
- Kitamura, T. *et al.* (2017) Engrams and circuits crucial for systems consolidation of a memory. *Science* 356, 73–78
- Winocur, G. *et al.* (2007) Memory consolidation or transformation: context manipulation and hippocampal representations of memory. *Nat. Neurosci.* 10, 555–557
- Dandolo, L.C. and Schwabe, L. (2018) Time-dependent memory transformation along the hippocampal anterior–posterior axis. *Nat. Commun.* 9, 1–11
- Atucha, E. *et al.* (2017) Noradrenergic activation of the basolateral amygdala maintains hippocampus-dependent accuracy of remote memory. *Proc. Natl. Acad. Sci. U. S. A.* 114, 9176–9181
- Krenz, V. *et al.* (2021) Noradrenergic arousal after encoding reverses the course of systems consolidation in humans. *Nat. Commun.* 12, 1–11
- Kensinger, E.A. (2009) Remembering the details: effects of emotion. *Emot. Rev.* 1, 99–113
- Dunsmoor, J.E. *et al.* (2022) Tag and capture: how salient experiences target and rescue nearby events in memory. *Trends Cogn. Sci.* 26, 782–795
- Frey, U. and Morris, R.G.M. (1997) Synaptic tagging and long-term potentiation. *Nature* 385, 533–536
- Adcock, R.A. *et al.* (2006) Reward-motivated learning: mesolimbic activation precedes memory formation. *Neuron* 50, 507–517

44. Wittmann, B.C. *et al.* (2005) Reward-related fMRI activation of dopaminergic midbrain is associated with enhanced hippocampus-dependent long-term memory formation. *Neuron* 45, 459–467
45. Murty, V.P. and Adcock, R.A. (2014) Enriched encoding: reward motivation organizes cortical networks for hippocampal detection of unexpected events. *Cereb. Cortex* 24, 2160–2168
46. Braun, E.K. *et al.* (2018) Retroactive and graded prioritization of memory by reward. *Nat. Commun.* 9, 4886
47. Stanek, J.K. *et al.* (2019) Expected reward value and reward uncertainty have temporally dissociable effects on memory formation. *J. Cogn. Neurosci.* 31, 1443–1454
48. Gomperts, S.N. *et al.* (2015) VTA neurons coordinate with the hippocampal reactivation of spatial memory. *eLife* 4, e05360
49. Murty, V.P. and Alison Adcock, R. (2017) Distinct medial temporal lobe network states as neural contexts for motivated memory formation. In *The Hippocampus from Cells to Systems: Structure, Connectivity, and Functional Contributions to Memory and Flexible Cognition* (Hannula, D.E. and Duff, M.C., eds), pp. 467–501, Springer
50. Murty, V.P. *et al.* (2017) Selectivity in postencoding connectivity with high-level visual cortex is associated with reward-motivated memory. *J. Neurosci.* 37, 537–545
51. Bisby, J.A. and Burgess, N. (2017) Differential effects of negative emotion on memory for items and associations, and their relationship to intrusive imagery. *Curr. Opin. Behav. Sci.* 17, 124–132
52. Bisby, J.A. *et al.* (2016) Opposing effects of negative emotion on amygdalar and hippocampal memory for items and associations. *Soc. Cogn. Affect. Neurosci.* 11, 981–990
53. Madan, C.R. *et al.* (2017) Emotional arousal impairs association-memory: roles of amygdala and hippocampus. *Neuroimage* 156, 14–28
54. Williams, S.E. *et al.* (2022) The power of negative and positive episodic memories. *Cogn. Affect. Behav. Neurosci.* 22, 869–903
55. Costa, M. *et al.* (2022) Aversive memory formation in humans involves an amygdala–hippocampus phase code. *Nat. Commun.* 13, 6403
56. Goldfarb, E.V. and Phelps, E.A. (2017) Stress and the trade-off between hippocampal and striatal memory. *Curr. Opin. Behav. Sci.* 14, 47–53
57. Schwabe, L. and Wolf, O.T. (2012) Stress modulates the engagement of multiple memory systems in classification learning. *J. Neurosci.* 32, 11042–11049
58. Vogel, S. *et al.* (2018) Stress leads to aberrant hippocampal involvement when processing schema-related information. *Learn. Mem.* 25, 21–30
59. Grob, A.-M. *et al.* (2022) Stress disrupts insight-driven mnemonic reconfiguration in the medial temporal lobe. *Neuroimage* 265, 119804
60. Simon-Kutschner, K. *et al.* (2019) Fear without context: acute stress modulates the balance of cue-dependent and contextual fear learning. *Psychol. Sci.* 30, 1123–1135
61. Madan, C.R. *et al.* (2019) Positive emotion enhances association-memory. *Emotion* 19, 733–740
62. Horwath, E.A. *et al.* (2023) Value restructures the organization of free recall. *Cognition* 231, 105315
63. de Berker, A.O. *et al.* (2016) Computations of uncertainty mediate acute stress responses in humans. *Nat. Commun.* 7, 10996
64. Rouhani, N. *et al.* (2018) Dissociable effects of surprising rewards on learning and memory. *J. Exp. Psychol. Learn. Mem. Cogn.* 44, 1430–1443
65. Rouhani, N. and Niv, Y. (2021) Signed and unsigned reward prediction errors dynamically enhance learning and memory. *eLife* 10, e61077
66. Kalbe, F. and Schwabe, L. (2020) Beyond arousal: prediction error related to aversive events promotes episodic memory formation. *J. Exp. Psychol. Learn. Mem. Cogn.* 46, 234–246
67. Bein, O. *et al.* (2021) Mnemonic prediction errors promote detailed memories. *Learn. Mem.* 28, 422–434
68. Antony, J.W. *et al.* (2020) Behavioral, physiological, and neural signatures of surprise during naturalistic sports viewing. *Neuron* 109, 377–390.e7
69. Greve, A. *et al.* (2017) Does prediction error drive one-shot declarative learning? *J. Mem. Lang.* 94, 149–165
70. Ergo, K. *et al.* (2020) Reward prediction error and declarative memory. *Trends Cogn. Sci.* 24, 388–397
71. Iordanova, M.D. *et al.* (2021) Neural substrates of appetitive and aversive prediction error. *Neurosci. Biobehav. Rev.* 123, 337–351
72. Sandi, C. *et al.* (1997) Experience-dependent facilitating effect of corticosterone on spatial memory formation in the water maze. *Eur. J. Neurosci.* 9, 637–642
73. Vogel, S. and Schwabe, L. (2016) Stress in the zoo: tracking the impact of stress on memory formation over time. *Psychoneuroendocrinology* 71, 64–72
74. Kalbe, F. *et al.* (2020) Expectancy violation drives memory boost for stressful events. *Psychol. Sci.* 31, 1409–1421
75. Kalbe, F. and Schwabe, L. (2022) Prediction errors for aversive events shape long-term memory formation through a distinct neural mechanism. *Cereb. Cortex* 32, 3081–3097
76. Yau, J.O.-Y. and McNally, G.P. (2022) The activity of ventral tegmental area dopamine neurons during shock omission predicts safety learning. *Behav. Neurosci.* 136, 276–284
77. Salinas-Hernández, X.I. *et al.* (2018) Dopamine neurons drive fear extinction learning by signaling the omission of expected aversive outcomes. *eLife* 7, e38818
78. Stelly, C.E. *et al.* (2019) Pattern of dopamine signaling during aversive events predicts active avoidance learning. *Proc. Natl. Acad. Sci. U. S. A.* 116, 13641–13650
79. Maia, T.V. (2010) Two-factor theory, the actor-critic model, and conditioned avoidance. *Learn. Behav.* 38, 50–67
80. Wietzikoski, E.C. *et al.* (2012) Roles of D1-like dopamine receptors in the nucleus accumbens and dorsolateral striatum in conditioned avoidance responses. *Psychopharmacology* 219, 159–169
81. Spoormaker, V.I. *et al.* (2012) Additional support for the existence of skin conductance responses at unconditioned stimulus omission. *NeuroImage* 63, 1404–1407
82. van Kesteren, M.T.R. *et al.* (2012) How schema and novelty augment memory formation. *Trends Neurosci.* 35, 211–219
83. Vogel, S. *et al.* (2018) Stress affects the neural ensemble for integrating new information and prior knowledge. *NeuroImage* 173, 176–187
84. Sinclair, A.H. *et al.* (2021) Prediction errors disrupt hippocampal representations and update episodic memories. *Proc. Natl. Acad. Sci. U. S. A.* 118, e2117625118
85. Bein, O. *et al.* (2020) Mnemonic prediction errors bias hippocampal states. *Nat. Commun.* 11, 3451
86. Rouhani, N. *et al.* (2020) Reward prediction errors create event boundaries in memory. *Cognition* 203, 104269
87. Pearce, J.M. and Hall, G. (1980) A model for Pavlovian learning: variations in the effectiveness of conditioned but not of unconditioned stimuli. *Psychol. Rev.* 87, 532–552
88. Nassar, M.R. *et al.* (2012) Rational regulation of learning dynamics by pupil-linked arousal systems. *Nat. Neurosci.* 15, 1040–1046
89. Diederer, K.M.J. and Schultz, W. (2015) Scaling prediction errors to reward variability benefits error-driven learning in humans. *J. Neurophysiol.* 114, 1628–1640
90. Nassar, M.R. *et al.* (2010) An approximately Bayesian delta-rule model explains the dynamics of belief updating in a changing environment. *J. Neurosci.* 30, 12366–12378
91. Collins, A.G.E. *et al.* (2017) Working memory load strengthens reward prediction errors. *J. Neurosci.* 37, 4332–4342
92. Tobler, P.N. *et al.* (2005) Adaptive coding of reward value by dopamine neurons. *Science* 307, 1642–1645
93. Yu, A.J. and Dayan, P. (2005) Uncertainty, neuromodulation, and attention. *Neuron* 46, 681–692
94. Monosov, I.E. (2020) How outcome uncertainty mediates attention, learning, and decision-making. *Trends Neurosci.* 43, 795–809
95. Jang, A.I. *et al.* (2019) Positive reward prediction errors during decision-making strengthen memory encoding. *Nat. Hum. Behav.* 3, 719–732
96. Davidow, J.Y. *et al.* (2016) An upside to reward sensitivity: the hippocampus supports enhanced reinforcement learning in adolescence. *Neuron* 92, 93–99
97. Calderon, C.B. *et al.* (2020) Signed reward prediction errors in the ventral striatum drive episodic memory. *J. Neurosci.* 41, 1716–1726

98. Lisman, J.E. and Grace, A.A. (2005) The hippocampal-VTA loop: controlling the entry of information into long-term memory. *Neuron* 46, 703–713
99. Mackintosh, N.J. (1975) A theory of attention: variations in the associability of stimuli with reinforcement. *Psychol. Rev.* 82, 276–298
100. Iigaya, K. *et al.* (2020) The value of what's to come: neural mechanisms coupling prediction error and the utility of anticipation. *Sci. Adv.* 6, eaba3828
101. Wimmer, G.E. *et al.* (2014) Episodic memory encoding interferes with reward learning and decreases striatal prediction errors. *J. Neurosci.* 34, 14901–14912
102. Duncan, K.D. and Schlichting, M.L. (2018) Hippocampal representations as a function of time, subregion, and brain state. *Neurobiol. Learn. Mem.* 153, 40–56
103. Dunsmoor, J.E. *et al.* (2018) Event segmentation protects emotional memories from competing experiences encoded close in time. *Nat. Hum. Behav.* 2, 291–299
104. Duszakiewicz, A.J. *et al.* (2019) Novelty and dopaminergic modulation of memory persistence: a tale of two systems. *Trends Neurosci.* 42, 102–114
105. DuBrow, S. *et al.* (2017) Does mental context drift or shift? *Curr. Opin. Behav. Sci.* 17, 141–146
106. Davachi, L. and DuBrow, S. (2015) How the hippocampus preserves order: the role of prediction and context. *Trends Cogn. Sci.* 19, 92–99
107. Gershman, S.J. *et al.* (2014) Statistical computations underlying the dynamics of memory updating. *PLoS Comput. Biol.* 10, e1003939
108. Reynolds, J.R. *et al.* (2007) A computational model of event segmentation from perceptual prediction. *Cogn. Sci.* 31, 613–643
109. Heusser, A.C. *et al.* (2018) Perceptual boundaries cause mnemonic trade-offs between local boundary processing and across-trial associative binding. *J. Exp. Psychol. Learn. Mem. Cogn.* 44, 1075–1090
110. Rouhani, N. *et al.* (2023) Collective events and individual affect shape autobiographical memory. *Proc. Natl. Acad. Sci. U. S. A.* 120, e2221919120
111. Yu, L.Q. *et al.* (2021) Adaptive learning is structure learning in time. *Neurosci. Biobehav. Rev.* 128, 270–281
112. Clewett, D. *et al.* (2020) Pupil-linked arousal signals track the temporal organization of events in memory. *Nat. Commun.* 11, 4007
113. O'Reilly, J.X. *et al.* (2013) Dissociable effects of surprise and model update in parietal and anterior cingulate cortex. *Proc. Natl. Acad. Sci. U. S. A.* 110, E3660–E3669
114. Polyn, S.M. *et al.* (2009) A context maintenance and retrieval model of organizational processes in free recall. *Psychol. Rev.* 116, 129–156
115. Nassar, M.R. *et al.* (2019) Dissociable forms of uncertainty-driven representational change across the human brain. *J. Neurosci.* 39, 1688–1698
116. DuBrow, S. and Davachi, L. (2014) Temporal memory is shaped by encoding stability and intervening item reactivation. *J. Neurosci.* 34, 13998–14005
117. Ezzyat, Y. and Davachi, L. (2014) Similarity breeds proximity: pattern similarity within and across contexts is related to later mnemonic judgments of temporal proximity. *Neuron* 81, 1179–1189
118. Lehnert, L. *et al.* (2020) Reward-predictive representations generalize across tasks in reinforcement learning. *PLoS Comput. Biol.* 16, e1008317
119. de Quervain, D. *et al.* (2017) Stress, glucocorticoids and memory: implications for treating fear-related disorders. *Nat. Rev. Neurosci.* 18, 7–19
120. Pigeon, S. *et al.* (2022) Impairing memory reconsolidation with propranolol in healthy and clinical samples: a meta-analysis. *J. Psychiatry Neurosci.* 47, E109–E122
121. Rouhani, N. and Niv, Y. (2019) Depressive symptoms bias the prediction-error enhancement of memory towards negative events in reinforcement learning. *Psychopharmacology* 236, 2425–2435
122. Bradley, B.P. *et al.* (1995) Implicit and explicit memory for emotion-congruent information in clinical depression and anxiety. *Behav. Res. Ther.* 33, 755–770
123. Dillon, D.G. and Pizzagalli, D.A. (2018) Mechanisms of memory disruption in depression. *Trends Neurosci.* 41, 137–149
124. Cataldo, A.M. *et al.* (2022) Abnormal evidence accumulation underlies the positive memory deficit in depression. *J. Exp. Psychol. Gen.* 152, 139–156
125. Pittig, A. *et al.* (2022) Change of threat expectancy as mechanism of exposure-based psychotherapy for anxiety disorders: evidence from 8484 exposure exercises of 605 patients. *Clin. Psychol. Sci.* 11, 199–217
126. Barto, A.G. (1995) Adaptive critic and the basal ganglia. In *Models of Information Processing in the Basal Ganglia* (Houk, J.C. *et al.*, eds), pp. 215, MIT press
127. Montague, P.R. *et al.* (1996) A framework for mesencephalic dopamine systems based on predictive Hebbian learning. *J. Neurosci.* 16, 1936–1947
128. Schultz, W. *et al.* (1997) A neural substrate of prediction and reward. *Science* 275, 1593–1599
129. Langdon, A.J. *et al.* (2018) Model-based predictions for dopamine. *Curr. Opin. Neurobiol.* 49, 1–7
130. Hamid, A.A. *et al.* (2021) Wave-like dopamine dynamics as a mechanism for spatiotemporal credit assignment. *Cell* 184, 2733–2749.e16
131. Jeong, H. *et al.* (2022) Mesolimbic dopamine release conveys causal associations. *Science* 378, eabq6740
132. Sharpe, M.J. *et al.* (2017) Dopamine transients are sufficient and necessary for acquisition of model-based associations. *Nat. Neurosci.* 20, 735–742
133. Jaskir, A. and Frank, M.J. (2023) On the normative advantages of dopamine and striatal opponency for learning and choice. *eLife* 12, e85107
134. Cahill, L. *et al.* (1994) Beta-adrenergic activation and memory for emotional events. *Nature* 371, 702–704
135. Strange, B.A. and Dolan, R.J. (2004) β -Adrenergic modulation of emotional memory-evoked human amygdala and hippocampal responses. *Proc. Natl. Acad. Sci. U. S. A.* 101, 11454–11458
136. Cahill, L. *et al.* (1995) The amygdala and emotional memory. *Nature* 377, 295–296
137. McGaugh, J.L. *et al.* (1996) Involvement of the amygdala in memory storage: interaction with other brain systems. *Proc. Natl. Acad. Sci. U. S. A.* 93, 13508–13514
138. Roozendaal, B. *et al.* (2006) Glucocorticoid enhancement of memory requires arousal-induced noradrenergic activation in the basolateral amygdala. *Proc. Natl. Acad. Sci. U. S. A.* 103, 6741–6746
139. Cahill, L. *et al.* (2003) Enhanced human memory consolidation with post-learning stress: interaction with the degree of arousal at encoding. *Learn. Mem.* 10, 270–274
140. Anderson, A.K. *et al.* (2006) Emotion enhances remembrance of neutral events past. *Proc. Natl. Acad. Sci. U. S. A.* 103, 1599–1604