Interactions between memory and reward systems

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Key points

- Information and events that are relevant for goal attainment are preferentially remembered over mundane experiences.
- Neural systems underlying reward and motivation signal the value of information, resulting in release of neuromodulatory neurotransmitters.
- Dopamine is a neuromodulator that is both central to reward and motivation and essential for stable long term memory formation.
- Understanding interactions between memory and reward systems can provide a pathway for understanding how 'valuable' information is prioritized.
- Studies in both humans and non-human animals suggest that dopaminergic midbrain modulates hippocampal function to shape memory contents and form.
- We review empirical studies for evidence of midbrain-hippocampal interaction as a neural mechanism of adaptive memory formation, relating it to theoretical frameworks and translational implications.

1 Introduction

We draw on memories of our past experience to guide future decisions and behaviors. To enable effective access to relevant memories, our brain needs to adaptively prioritize information that may be important for attaining future goals. How does the brain decide what experiences are transformed into enduring memory traces? What mechanisms determine the form of memories to support future adaptive behavior? A key to addressing these questions is to understand how the brain assigns 'value' to information, and how this value signal is subsequently translated into a signal for learning. Research in neuroscience has generated a substantial body of work regarding reward, motivation, and memory systems in the brain. In the present chapter we explore their interactions, focusing on the interaction between the ventral tegmental area (VTA) as implementing a "reward value" system and its impact on

the hippocampus, an exemplary memory system. The goal of the current chapter is to provide an overview of an adaptive memory system in which motivationally relevant information is prioritized and available to guide future behavior.

In the first section we examine **neurobiological systems implicated in representing and predicting rewards and in motivation**, focusing on the role of VTA dopamine. In the second section, we discuss how **anatomical properties of the hippocampus may determine dopaminergic influences on its function.** In the third, we review **theoretical accounts of how VTA-Hippocampal interactions can influence learning**, how these relate to reward, and other potential mechanisms to be considered. In the fourth, we summarize the **human evidence of reward effects on different stages of memory processing**, focusing on encoding, consolidation and retrieval of episodic memories. In the fifth, we discuss the **clinical relevance of dysfunction in reward systems as it relates to memory and other brain and behavioral disorders**. In the sixth, we consider potential therapeutic interventions, and finally, we identify **future directions and open questions** to be resolved.

2   Reward and motivation in the brain

The ventral tegmental area (VTA) is a midbrain nucleus containing dopamine neurons that project widely across the brain. Dopaminergic projections from the VTA can be broadly separated along two pathways—the mesocortical pathway which projects to prefrontal, motor and sensory regions, and the mesolimbic pathway which projects to the striatum and hippocampus.

Dopaminergic projections from the mesolimbic circuits play a pivotal role in supporting reward and motivation. Often referred to as the 'pleasure molecule' in popular media, dopamine has long been identified for its role in supporting reward processing and motivated behavior. While accumulating evidence over the past decade has further illuminated the importance of dopamine for learning and memory formation, a gap remains to be bridged—how is the mnemonic role of dopamine related to its role in reward and motivation? Here, we discuss how the dopaminergic midbrain is implicated in motivation and reward processing, and consequently, how this can further support adaptive learning and memory formation.

While early work on dopamine largely focused on its role in supporting motor functions, later work implied that dopamine may be more important for supporting the motivation to initiate action, rather than the actual execution of action (Wise, 2004). Causal evidence for the role of dopamine in supporting motivation has been shown using pharmacological suppression of dopamine, with multiple studies demonstrating that dopamine antagonists reduce the initiation of goal-directed action, but do not impair the motor capacity for action (Berridge and Robinson, 1998; Wise, 2004). This was further supported by recordings of dopamine neurons in monkeys, showing that action initiation was preceded by phasic firing of dopamine neurons, suggestive of its role in behavioral activation (Schultz, 1986; Schultz and Romo, 1990).

Because these phasic responses changed over time, it was proposed that the initially observed dopaminergic regulation of motivated behavior may be one facet of a more generalized role for dopamine in reward learning and the reinforcement of actions leading to reward (Salamone and Correa, 2012; Schultz, 1998; Walton and Bouret, 2019). According to this account of reinforcement and reward learning, phasic dopamine bursts function as a neurobiological equivalent of a reward prediction error (RPE) signal that represents the deviation between the actual and an expected outcome (refer to Section 4 for further discussions of RPE as a canonical learning signal). This proposal was based upon observations during associative learning in which the firing properties of dopamine neurons change as a cue-reward pairing is learned (Fig. 1). Prior to learning, dopamine neurons in the VTA show a transient burst of increased firing following the receipt of reward, consistent with a role as a reward processing signal. However, as the reward becomes more predictable, dopamine neurons no longer respond to the presentation of an expected reward, but instead
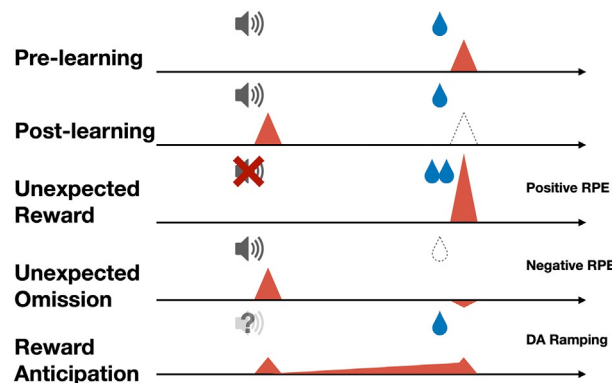
Fig. 1   Schematic depiction of VTA dopamine firing related to reward anticipation and prediction errors. Prior to learning (Pre-learning), phasic firing of VTA dopamine neurons is observed during reward receipt. When the predictive association of the cue-reward pairing is acquired, phasic firing of dopamine neurons is observed during cue presentation, rather than during the receipt of an expected reward. Phasic firing of dopamine neurons is also sensitive to the magnitude of reward, increasing when reward is greater than expected (positive reward prediction error) and decreasing (relative to baseline) when reward is smaller than expected or omitted (negative reward prediction error). Recent work has also identified ramping activity, where dopamine neurons exhibit increase in firing with increasing proximity to an anticipated reward. This may be most prominently observed when there is uncertainty in reward expectations.

show increased bursting to the reward predicting cue (Schultz et al., 1997). Such a shift in firing, from after outcomes to after cues, has been proposed to reflect a reinforcement learning mechanism that strengthens behaviors leading to rewards. These dopamine neurons have also been shown to exhibit sensitivity to the magnitude of rewards, increasing their firing when a reward is larger than expected, and conversely, decreasing their firing (relative to baseline) when an expected reward is omitted (Bayer and Glimcher, 2005; Schultz et al., 1997). A causal role for dopamine in associative learning (supporting the anticipation of reward), including computation of its expected value, has been shown using pharmacology and optogenetics. In particular, the disruption of phasic dopamine firing can impair the acquisition of stimulus associations (Flagel et al., 2011; Tang et al., 2020), while the stimulation of phasic firing may be sufficient for the acquisition of associations (Sharpe et al., 2017, 2020; Steinberg et al., 2013; Tsai et al., 2009). While here we primarily focus on the role of dopamine in reward processing, dopamine has also been implicated in avoidance of aversive stimuli (e.g., Fadok et al., 2009; Salamone, 1994; for detailed discussion refer to Bromberg-Martin et al., 2010; Salamone and Correa, 2012).

While the burst firing following surprising rewards and other events proved compelling for researchers, dopamine neuronal activity fluctuates over different timescales. The increased burst firing described above is referred to as a **Phasic** response. It has been argued that higher likelihood of reward in the environment and thus frequency of phasic responses, should cumulatively result in increased background or residual dopamine availability, (Niv, 2007; Niv et al., 2005), which may signal the value of effort in the current context (Cagniard et al., 2006; Hamid et al., 2016); "*tonic dopamine*" is sometimes used to refer to this residual dopamine availability. In addition, dopamine neurons have a baseline level of spontaneous firing, often referred to as **Tonic** activity (Grace and Bunney, 1984; Niv et al., 2007). When they are released from their baseline inhibition, they increase their tonic activity and increase their likelihood of bursting (such disinhibition occurs following hippocampal activity, for example in response to novelty). Phasic and tonic activity have been shown to be dissociable and their selective disruption produces dissociable behavioral outcomes (e.g. Grieder et al., 2012; Zweifel et al., 2009). Beyond phasic and tonic activity, recent works have also identified **Ramping** activity, in which dopamine neurons exhibit a gradual increase in firing with increasing spatial or temporal proximity to reward (Farrell et al., 2022; Howe et al., 2013; Mohebi et al., 2019). Such ramping activity has been attributed with various potential functions, including tracking of estimated value (Kim et al., 2020), state uncertainty (Mikhael et al., 2022), gain control (Lloyd and Dayan, 2015), and motivation (Sarno et al., 2022). The mechanisms of ramping activity continue to be debated and further studies are required to clarify its behavioral significance (Gershman, 2014; Kim et al., 2020; Lerner et al., 2021; Lloyd and Dayan, 2015; Song and Lee, 2020).

Dopamine receptors are broadly classified into two subtypes: D1-like (D1/D5) and D2-like (D2/D3/D4) receptor families. Based on their coupling to second messenger systems, they are associated with mainly increasing and decreasing neural activity, respectively (Seamans et al., 2001; Trantham-Davidson et al., 2004; but see Leonard et al., 2003; Undieh, 2010). These subtypes also show different affinity for dopamine, which has been thought to contribute to differential effects of tonic and phasic VTA activity. Affinity for dopamine is orders of magnitude higher for D2-like than D1-like receptors, suggesting differential sensitivity to extracellular dopamine concentrations and thus the dynamics of VTA activity. While occupancy of high-affinity D2-like receptors would reflect increased tonic activity, it was thought that low-affinity D1-like receptors would be insensitive to these differences and register only phasic activity (Dreyer et al., 2010). However, recent evidence that incorporates the slow unbinding rates seen by both receptors suggests that D1 receptors are similarly affected by fluctuations in tonic dopamine and by dopamine ramps (Hunger et al., 2020).

Accruing evidence continues to reveal the complexities of dopaminergic signaling, with dopamine neurons signaling a diverse range of motivationally significant events, e.g. saliency (Horvitz, 2000), sensory prediction errors (Stalnaker et al., 2019; Takahashi et al., 2017), and also to unexpected omission of rewards (Ishino et al., 2023). As a result, the evidence supports moving beyond a simplistic view of dopamine as signaling reward, or even reward prediction error. It remains clear, nonetheless, that dopamine sits at a nexus linking reward, motivation and learning. In the following section, we discuss the anatomy of midbrain projections, and consider their significance for the modulation of learning and memory in the hippocampus.

3   Dopamine in the hippocampus

The medial temporal lobe (MTL), encompassing the hippocampus proper and its surrounding neocortex (including the parahippocampal cortex, perirhinal cortex, entorhinal cortex and subiculum) is well-documented to be critical for episodic memory, although the exact role it plays remains in question (Davachi, 2006; Eichenbaum, 2017; Simons and Spiers, 2003; Squire et al., 2004). Regions across the MTL are thought to support different forms of memory representation. The parahippocampal and perirhinal cortices of the neocortical MTL are thought to support representations of context and item respectively, while the hippocampus is theorized to support relational information, binding discrete representations into integrated representations (Brown and Aggleton, 2001; Davachi et al., 2003; Davachi and Wagner, 2002; Diana et al., 2007; Eichenbaum, 2000; Ranganath and Ritchey, 2012). While there is evidence that dopamine influences memory processes across the entire MTL, the following section will focus primarily on the hippocampus, given the limited investigation to date of dopaminergic influence in the neocortical MTL.

Converging evidence from humans and animals supports a role for dopamine as a critical modulator of hippocampal functions (Edelmann and Lessmann, 2018; Jay, 2003; Lisman et al., 2011; Lisman and Otmakhova, 2001; Shohamy and Adcock, 2010). Anatomical studies have shown that dopamine receptors are present in the hippocampus (Beaulieu and Gainetdinov, 2011;

Gasbarri et al., 1997; Yu et al., 2019), and dopaminergic neurons from the midbrain project directly to the hippocampus (Gasbarri et al., 1994a; Gasbarri et al., 1994b; Samson et al., 1990). Indeed, dopamine has been shown to be a necessary precursor for synaptic plasticity in the hippocampus (Frey et al., 1990, 1991; Li et al., 2003; Otmakhova and Lisman, 1996, 1998) and to be necessary for the persistence of long-term memories (Frey et al., 1990; Frey and Morris, 1997; Huang and Kandel, 1995; Rossato et al., 2009; Sajikumar and Frey, 2004; Swanson-Park et al., 1999). While the sparsity of midbrain projections to the hippocampus (contrasting with the dense projections to the striatum), has led to ongoing contentions regarding the primary source of hippocampal dopamine (McNamara and Dupret, 2017), stimulation of the VTA alters transmission in the Schaeffer collaterals between CA3 and CA1 (Rosen et al., 2015), and lesion studies have shown that levels of dopamine in the hippocampus are reduced following ablation of VTA projections (Scatton et al., 1980). Despite recent evidence for the locus coeruleus (LC) as an alternate source of hippocampal dopamine (Kempadoo et al., 2016; Takeuchi et al., 2016), other recent studies have continued to demonstrate the significance of VTA-hippocampal pathways for memory formation (Tsetsenis et al., 2021). Further work is required to clarify the conditions promoting dopaminergic modulation of hippocampus by the LC or the VTA and their dissociable contributions to memory formation.

Further contributing to this complexity, the hippocampus is not a homogenous structure, and dopaminergic modulation from the midbrain likely varies across its extent due to anatomical variation over subfields and along its longitudinal axis. Anatomical tracing in rodents has shown that VTA neurons might project more strongly to the ventral hippocampus, which is most analogous to the anterior hippocampus in humans (Oades and Halliday, 1987; but see Edelmann and Lessmann, 2018). While the innervation and relative receptor distribution vary significantly across species (Shohamy and Adcock, 2010), suggesting caution in extrapolating rodent data, neuroimaging studies in humans have also shown preferential anatomical (Elliott et al., 2023) and functional (Kahn and Shohamy, 2012) connectivity between the VTA and the anterior hippocampus. Notably, the distribution of dopamine receptor types has been shown to vary across hippocampal subfields and across the longitudinal axis of the hippocampus (Edelmann and Lessmann, 2018; Wei et al., 2018). As previously discussed, differences in dopamine binding affinity for receptor subtypes has been thought to influence sensitivity to different concentrations of dopamine and thus timescales of dopamine activity, but recent modeling that incorporates the slow unbinding rates seen by both receptors suggests that both receptor families would be affected by fluctuations in tonic dopamine and by dopamine ramps as well as phasic responses (Hunger et al., 2020). The striatum, where dopamine receptors are closely apposed to the abundant dopaminergic projection terminals, is set up to rapidly detect the transients associated with phasic activity (Edelmann and Lessmann, 2018). In contrast, the hippocampus and other cortical regions may not be able to resolve the timing of transients because their sparse VTA innervation offers terminals that are more distant from receptors. This anatomical constraint implies that even though its receptors are predominantly D1 receptors, slower changes in extracellular dopamine would be the primary meaningful signals from VTA to the hippocampus, implying mechanisms for memory modulation over longer timescales.

In the following section, we briefly examine the role of dopamine in the regulation of synaptic plasticity, focusing on its influence on long-term potentiation (LTP), the cellular mechanism thought to underlie learning and long-term memory.

3.1   Dopaminergic modulation of neural plasticity

At the cellular level, traces of learning are primarily observed as changes in synaptic strength in the form of long-term potentiation (LTP) and long-term depression (LTD). Dopamine has been shown to be essential for both LTP and LTD. Since the relation of LTD and memory formation is not well understood (refer to Stacho and Manahan-Vaughan, 2022 for a review on the potential role of LTD in learning and memory formation), we focus the following discussion on LTP.

Dopamine can exert significant influence on both early- (Otmakhova and Lisman, 1996) and late-LTP (Frey et al., 1993). Both processes are thought to underlie long-term memory formation in the hippocampus. Studies in animals have shown that the activation of D1 dopamine receptors in the CA1 subfield can lower the threshold for LTP induction (Li et al., 2003; Swant and Wagner, 2006), increase the magnitude of LTP (Otmakhova and Lisman, 1996), inhibit depotentiation (Otmakhova and Lisman, 1998), and induce protein synthesis required for late-LTP (Huang and Kandel, 1995). Indeed, stabilization of LTP for long-term memory has been shown to require activation of D1 receptors in the hippocampus (Frey et al., 1990; Frey and Morris, 1997; Huang and Kandel, 1995; Rossato et al., 2009; Sajikumar and Frey, 2004; Swanson-Park et al., 1999). While these studies have primarily focused on the CA1, this is not the only region influenced by dopaminergic modulation, and similar effects have been observed in the dentate gyrus (Kulla and Manahan-Vaughan, 2000; Kusuki et al., 1997).

Beyond a direct influence on LTP, dopamine can also influence neural plasticity through the modulation of "metaplasticity"—mechanisms that regulate the likelihood of LTP formation (Abraham, 2008; Edelmann and Lessmann, 2013; Sheynikhovich et al., 2013). One way in which dopamine can influence metaplasticity is through synaptic tagging (Frey and Morris, 1997, 1998). In the 'synaptic tag and capture' account, strong stimulation resulting in dopamine release can increase the likelihood of LTP for weak stimulation occurring in close temporal proximity, resulting in long term plasticity from both the strong and the weak stimulation (for extended discussions see Dunsmoor et al., 2022; Frey and Morris, 1998; Redondo and Morris, 2011; Rogerson et al., 2014). These findings highlight a temporally extended influence of dopamine on learning and memory formation, which we will further discuss in the later section on *Memory Consolidation* (Section 5.2).

3.2   Dopaminergic modulation is evident in activity-dependent representations

Information representation in the hippocampus has been shown to exhibit sensitivity to motivation and reward expectation, and the influence of dopaminergic modulation. This modulation is evident from changes in representation of the information coded in neural activity, specifically in the activity of 'place cells' (Moser et al., 2008; O'Keefe, 1976; O'Keefe and Dostrovsky, 1971). Place cells are neurons in the hippocampus which have been shown to exhibit selective firing to specific locations in the environment, i.e. their 'place fields' (Best et al., 2001; Eichenbaum et al., 1999). Place cells in the hippocampus exhibit greater sensitivity to locations that have greater motivational significance, including those relevant for attaining task goals and rewards. More place cells have place fields for those locations, amplifying their representation in memory (Hollup et al., 2001; Krishnan et al., 2022; Mamad et al., 2017). Recent work has shown that such enhanced representation for motivationally significant places is supported by ramping activity of VTA dopamine neurons prior to expected rewards. (Krishnan et al., 2022), demonstrating modulation of hippocampal states by reward anticipation.

The stability of hippocampal place fields over time has also been used to indicate memory representation. Place fields for a given cell change over time; they can represent more than one place as animals move to new environments (O'Keefe and Conway, 1978). Within the same environmental context, the long term stability of a place field has been considered as an indication of memory representation, in that place field stability has been shown to correlate with spatial memory performance (Kentros et al., 2004; Kinsky et al., 2018; Muzzio et al., 2009). Place field stability has also been shown to be dopamine-dependent. In particular, place field stability was disrupted following the application of D1/D5 receptor antagonists and enhanced by agonists (Kentros et al., 2004), and also when neural activity in the VTA was disrupted (Martig and Mizumori, 2011).

To summarize, reward anticipation, VTA inputs, and dopamine D1-like receptors have been shown to influence place field sensitivity and stability in the hippocampus. Together, these findings set the stage for understanding how dopamine can modulate hippocampal functioning, and how this might provide a basis for adaptive episodic memory formation in humans. Moving beyond local neurobiological mechanisms, the following section reviews systems-level theoretical frameworks, discussing how different contexts and events can modulate dopaminergic response to support adaptive memory formation for motivationally salient experiences.

4   Modulation of memory circuits by dopaminergic reward systems

The diverse projections of the midbrain dopaminergic circuitry enable modulation of learning via the concurrent engagement of distinct mechanisms that can operate across multiple timescales. In the following, we discuss theoretical models and frameworks regarding how the mesolimbic reward circuits can modulate learning and memory formation in the MTL.

4.1   Reward prediction errors: A signal for learning and episodic memory?

Despite prolific investigations on the role of dopamine in both reinforcement learning and episodic memory, in early work these were seen as depending on distinct memory systems that relied on dissociable brain circuits, and as a result, their study remained largely independent. The recent confluence of research on episodic memory and reinforcement learning includes studies attempting to draw a connection between dopamine-eliciting reward prediction errors and memory formation (Jang et al., 2019; Rouhani et al., 2023; Sinclair et al., 2023; Sinclair and Barense, 2019; Wimmer et al., 2014); however, findings thus far have been mixed.

Reward prediction error (RPE), defined as the difference between the magnitude of a predicted reward and an actual outcome, is the canonical learning signal in reinforcement learning models. By signaling the deviation from expectations, RPE can be thought of as a feedback signal for the preceding action, enabling association of the action with its subsequent outcome. Reward prediction errors can be distinguished based on whether they are 'signed' or 'unsigned'. While a signed RPE indicates whether the outcome is better (positive) or worse (negative) than predicted, an unsigned RPE represents the absolute deviation from expectation without the valence (positive or negative), and can be indicative of surprise. This can be used to learn the value of actions in a given situation or '*state*', enabling the selection of optimal actions (Sutton and Barto, 1998). Dopamine neurons in the VTA have been proposed as the neurobiological basis for RPEs following the work of Schultz and colleagues (Schultz et al., 1997), who showed that firing rates of dopamine neurons were proportional to the signed deviation from an expected reward, paralleling theoretical expectations of a RPE signal (but see Ishino et al., 2023 for recent findings showing dopamine signaling of negative RPE).

While postulation of dopamine as the neurobiological proxy substrate for RPE has propelled investigation on the role of dopamine in learning, early interest was largely focused on striatal-mediated reward learning. This focus can be largely attributed to reinforcement learning models being primarily designed for continuous incremental learning (rather than episodic and single-shot learning), which was thought to depend on the striatum. The ventral striatum is the major projection target of VTA dopamine neurons (Beckstead et al., 1979; Beier et al., 2015; Lammel et al., 2008, 2011; Swanson, 1982). Indeed, findings in both humans and animals support the presence of RPE signals in the ventral striatum (e.g. Garrison et al., 2013; Keiflin and Janak, 2015; Shohamy, 2011), and Parkinson's patients with impaired dopaminergic transmission also show impairment in reward learning tasks (Foerde and Shohamy, 2011).

In the same way that RPE constitutes a signal for updating in continuous associative learning models, there is also a growing interest in the investigation of RPE as a learning signal for episodic memory formation (e.g. Rouhani et al., 2023). In early attempts

to bridge the links between continuous associative learning and episodic memory formation, Wimmer et al. (2014) had participants perform a reward learning task, with incidental encoding of trial-unique objects. Given the importance of dopamine for hippocampal synaptic plasticity, it was predicted that high RPE, associated with phasic dopamine release, should lead to the formation of stronger memories for the temporally coincident stimulus. However, rather than such a synergistic effect, Wimmer and colleagues found a negative correlation, whereby higher RPE was associated with poorer memory for the trial-unique object. This finding was taken as indicative of a potential trade-off between the two forms of learning, and supportive of distinct learning systems (Poldrack et al., 2001).

Building on the predictions of associative learning models (Esber and Haselgrove, 2011; Mackintosh, 1975; Pearce and Hall, 1980), recent experiments have further attempted to dissociate the effects of signed and unsigned prediction error across the different phases of learning. In the Mackintosh model (Mackintosh, 1975), it is proposed that attention is increased for cues that *reliably* predict rewards and, therefore, it should be expected that a positive prediction error will enhance memory for the *reward-predictive* cues. Contrasting with the Mackintosh model, the Pearce-Hall model (Pearce and Hall, 1980) proposes that cues preceding *unexpected* outcomes would receive greater attention, and so it should be expected that an unsigned prediction error (i.e. Surprise) would enhance memory formation for cues associated with greater *uncertainty*. Supporting the predictions of the Mackintosh model, it was demonstrated that while positive RPE at outcome did not enhance memory for the outcome item, positive RPE at cue presentation enhanced episodic memory for the cue item (Jang et al., 2019; Rouhani and Niv, 2021). Contrasting the effects observed during reward cueing, recent work has also shown support for the Pearce-Hall model, whereby unsigned RPE at outcome was found to enhance memory for the outcome item (Rouhani and Niv, 2021). While these findings do support a potential role of RPE in modulating memory formation, the dissociation across different phases (at cue versus outcome) is inconsistent with a simple account of modulation by phasic dopamine RPEs, and in particular, it is unclear why signed and unsigned PE would differentially influence memory at different timepoints.

Further complicating the interpretation of potential effects of RPE on memory, probabilistic reward cues are now thought to evoke a combination of phasic PE-like VTA firing after a cue and ramping firing during anticipation of the outcome they predict. A recent behavioral study provides evidence that these distinct responses may differentially influence memory based on the timing of the event to be encoded relative to the occurrence of the cue and thus relative to these VTA response components (Stanek et al., 2019).

Furthermore, it should also be noted that there is currently no evidence of direct transmission of phasic dopaminergic RPE signals from the VTA to the hippocampus. Indeed, the architecture of sparse VTA innervation to the hippocampus, which contrasts with its density in the striatum, is not consistent with detection of transient dopamine signals with precise temporal resolution, as would be required for detection and attribution of error signaling.

4.2   The Hippocampal-VTA loop: Novelty, reward, or the anticipation of change?

A prominent account of dopaminergic enhancement of memory, the Hippocampal-VTA loop account (Lisman and Grace, 2005), proposes a functional circuit whereby novelty signals in the hippocampus are relayed to the VTA, engaging its mesolimbic projections to release dopamine in the hippocampus and modulate hippocampal memory. While this account was proposed as a mechanism for enhanced encoding of novel events and information, it has often been generalized in the research literature as a mechanistic pathway for the enhanced encoding of other motivationally-salient events beyond novelty, including those associated with reward.

In the Hippocampal-VTA loop model, the hippocampus serves as a novelty detector comparing incoming information with existing long-term memories (Knight, 1996). This is proposed to be accomplished through a mismatch detection mechanism in the CA1, via the comparison of predictions from CA3 inputs, and actual percepts coming from the entorhinal cortices (Lisman and Grace, 2005; for detailed mechanistic discussion of how novelty detection can occur in the hippocampus, refer to Kafkas and Montaldi, 2018; Kumaran and Maguire, 2007; Lisman and Otmakhova, 2001). The detection of novelty leads to the conveyance of a novelty signal from the hippocampus to the VTA via a polysynaptic pathway: excitatory signals to the nucleus accumbens, which inhibits the ventral pallidum, decreasing pallidum inhibition of the VTA dopamine neurons (Floresco et al., 2001, 2003; Lodge and Grace, 2006; Luo et al., 2011). This VTA disinhibition increases dopamine release within the hippocampus, and thus facilitates memory formation for the novel events (Lisman and Grace, 2005; Otmakhova et al., 2013).

Because the detection of novelty relies on a mismatch between internal predictions and sensory inputs, parallels have often been drawn between novelty detection and prediction errors (Wessel et al., 2012). To provide a unifying account of the response of dopamine neurons to RPEs and to novelty, theoretical models have proposed that novelty may increase reward value (i.e. novelty bonus), so that novel events elicit positive RPEs (Kakade and Dayan, 2002). This account would suggest that RPEs and novelty should both modulate memory via phasic burst firing of dopamine neurons. The expected dynamics of dopaminergic modulation are left open in the Hippocampal-VTA loop model, but the neural circuit mechanisms it does specify, yield disinhibition of VTA dopamine neurons (Grace et al., 2007), rather than directly producing the phasic bursts of VTA firing thought to implement RPEs. As formulated, the Hippocampal-VTA loop provides an account for observations of temporally extended memory modulation after novel experience and a mechanism for how phasic PE responses to behaviorally relevant events would be enhanced by novel contexts, and metaplastic tagging offers a mechanism for memory enhancement to also extend backward in time. However, it does not include a candidate mechanism for understanding how a PE in response to a novel or salient event selectively enhances memory for that event.

Nevertheless, studies in humans have shown general support for the engagement of hippocampus and the midbrain VTA during both the anticipation and the experience of novelty (Bunzeck et al., 2012; Bunzeck and Düzel, 2006; Krebs et al., 2011; Schott et al., 2004; Wittmann et al., 2007). Experiments investigating the Hippocampal-VTA loop account have often demonstrated a temporally extended influence of novelty exposure on subsequent memory formation (e.g. Humans: Ballarini et al., 2013; Cen et al., 2021; Fenker et al., 2008; Schomaker et al., 2014; Rodents: Li et al., 2003; Straube et al., 2003; Takeuchi et al., 2016). Not all studies report this novelty enhancement, however (see Biel and Bunzeck, 2019; Quent and Henson, 2022 for recent work showing no memory benefits from pre- or post- learning exposure to novelty). Taking into account such temporal dynamics, it appears unlikely that novelty-driven dopaminergic modulation of memory formation is supported by mechanisms relating to temporally precise RPE signals from the midbrain VTA. Furthermore, recent studies in rodents have suggested that in some contexts, novelty-related enhancement of memory does not depend on the VTA, but may instead be dependent on the co-release of dopamine by the noradrenergic locus coeruleus (Kempadoo et al., 2016; Takeuchi et al., 2016). These limits on the role of VTA in novelty modulation of the hippocampus argue for recognizing limits on the generalizability of the VTA-Hippocampal loop account. They also raise interesting questions about precisely when and how the VTA is important to memory formation and whether considering reward anticipation and other motivational states can help clarify these relationships.

In a recent proposal, it was suggested that distinct forms of novelty may differentially engage dopaminergic modulation by the VTA and the LC (Duszkiewicz et al., 2018). 'Common novelty', defined as novel experiences that share commonality with past experiences, was proposed to activate the VTA to promote integration of the new memory with existing memories. 'Distinct novelty', defined as novel experience with minimal relations to past experiences, is proposed to activate the LC to support detailed and distinctive episodic memory. These memory effects are argued to occur by enhancing or suppressing systems consolidation via gene expression (Genzel et al., 2017). While this account requires further empirical support and does not distinguish between novelty prediction error signals versus anticipation or other dynamic features, it exemplifies for future investigations: (i) the consideration of different sources of dopamine, (ii) the dissociable mnemonic influence of VTA and LC modulation, (iii) the context in which they are elicited, and (iv) the relationships between novelty signals in different behavioral or motivational contexts, including reward prediction.

4.3 Neuromodulatory regulation of the medial temporal lobe for memory formation: Neuromodulation-MTL frameworks

Recent frameworks proposed by the present authors and others have focused on the anticipation and experience of motivationally salient events as neuromodulatory states that bias memory outcomes by selectively engaging regions of the medial temporal lobe in memory formation (Chiew and Adcock, 2019; Clewett and Murty, 2019; Murty and Adcock, 2017; Murty and Dickerson, 2016). While these frameworks differ in their focus on the mnemonic influence of affective (Clewett and Murty, 2019) and motivational states (Chiew and Adcock, 2019; Murty and Adcock, 2017; Murty and Dickerson, 2016), they share a common emphasis on neuromodulation of the medial temporal lobe by dopaminergic and noradrenergic systems, and as such, will be discussed collectively as *Neuromodulation-MTL* frameworks.

These frameworks were initially developed based on findings of differences in memory outcomes under valenced (i.e., positive and negative) motivational or affective states. While negative emotions have been shown to enhance memory for details of isolated target items (Bisby and Burgess, 2017; Bowen et al., 2018; Kensinger, 2007; Mather and Sutherland, 2011; Yonelinas and Ritchey, 2015), positive affect has been argued to broaden the scope of information processing (Ashby et al., 1999; Fredrickson, 2001; but see Harmon-Jones et al., 2013). This broadened processing has been argued to promote integrated memory representations of the item and its associated context (Madan et al., 2019; Murty et al., 2011; Murty et al., 2017b; Shigemune et al., 2014; Talarico et al., 2009; Wittmann et al., 2005; Wolosin et al., 2012, 2013).

Broadly, the *Neuromodulation-MTL* frameworks propose that these affective and motivational states correspond to states of activation of dopaminergic VTA or the noradrenergic LC. Building on the known differences in representational content across the medial temporal lobe, Neuromodulation-MTL frameworks propose that these distinct neuromodulatory states bias memory by selectively engaging different medial temporal circuitry and regions. In particular, while activation of mesolimbic dopaminergic projection systems from VTA would promote integration of multiple features through engagement of the hippocampus proper and its networks, activation of the noradrenergic projections systems from LC would instead drive selective prioritization of salient features through interactions with the amygdala and neocortical medial temporal lobe (entorhinal, parahippocampal, and perirhinal cortices). While initially drawing on experimental findings elicited by positive (e.g. reward approach) and negative (e.g. punishment avoidance) motivation, it should be highlighted that the framework does not assume one-to-one mapping whereby VTA is engaged by positive motivations while the LC is engaged by negative motivations. Rather, it is proposed that attributes commonly associated with each motivational state reflect the typical preferential engagement of distinct neuromodulatory nuclei.

Similar to the previously discussed frameworks, under the Neuromodulation-MTL framework, enhanced memory formation in the hippocampus is thought to depend on dopaminergic modulation from the VTA. However, rather than a temporally specific response to an external trigger (e.g. novelty, surprise or prediction error) that enhances memory for that trigger event, the Neuromodulation-MTL framework proposes a temporally-extended state in which information-processing mode and memory formation are biased by modulation from the VTA or the LC. In support of this account, it has been shown that encoding for incidental information can be enhanced during the anticipation of motivationally relevant events (Gruber et al., 2014; Murty and
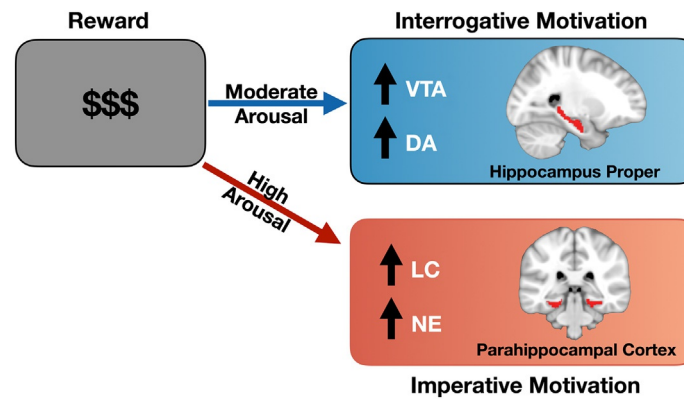
Fig. 2   Schematic depiction of reward modulation of memory based on the Neuromodulation-MTL framework. Activation of the VTA during reward anticipation can promote an Interrogative motivational state associated with high dopaminergic (DA) tone and the engagement of hippocampus to enhance associative memory formation. However, activation of the LC, such as when arousal is high, can instead promote an Imperative motivational state associated with high noradrenergic (NE) tone and the engagement of surrounding parahippocampal cortex to enhance memory formation for discrete items. Whether reward enhances or impairs memory is thus predicted to depend on the specific modulatory and mnemonic circuitry engaged by the reward context, as well as on whether task performance is dependent on hippocampus proper. In particular, high arousal in reward incentive contexts is predicted to disrupt enhancement of hippocampal memory.

Adcock, 2014). Recent work using fMRI has revealed how anticipatory VTA activation may support hippocampal patterns of activation conducive to memory formation; strikingly, this modulation of hippocampal states during high VTA activity explained the relationship between VTA and successful memory formation (Poh et al., 2022). While there is some evidence for analogous engagement of noradrenergic circuits and neocortical MTL regions during enhanced encoding of salient information (Clewett et al., 2014, 2018; Lee et al., 2018), the nature of their interaction and its role in memory remains to be clarified. Full demonstration of dissociable memory outcomes supported by distinct neuromodulatory nuclei, as predicted by the Neuromodulation-MTL accounts, awaits further study.

The Neuromodulation-MTL models offer explanations not only for motivated memory more broadly (Murty and Adcock, 2017), but also for variable experiences of reward and their memory impacts, including predictions about how and when reward enhancement of memory may be disrupted. If reward anticipation is accompanied by high VTA dopaminergic tone, an individual will experience an *Interrogative* motivational state that biases exploratory information seeking and engagement of the hippocampus during encoding. Alternatively, an individual may experience *Imperative* motivation during reward anticipation (Fig. 2). Although Imperative motivation is typical under threat of punishment or during avoidance of aversive stimuli, it may also emerge in pursuit of reward because of perceived high stakes (as in choking), subjective time pressure (Sinclair et al., 2023), or other cognitive or affective biases. Imperative motivation biases restricted information-seeking in support of achieving salient, urgent goals. Imperative motivation corresponds to increased LC tone and arousal, and engages amygdala and cortical MTL during encoding, reducing hippocampal involvement in memory formation (Clewett and Murty, 2019; Murty and Adcock, 2017). These findings highlight a limit on computational models using objective value of incentives to predict learning, and point to the need to consider the specific neuromodulatory systems engaged by incentives or other motivators in order to understand their impact on learning and thus behavior.

Finally, while the *Neuromodulation-MTL* framework draws contrasts between states that typically preferentially involve either the VTA or the LC (with the consequent modulation of downstream MTL regions), it should be highlighted that external stimulus events that elicit dopamine and norepinephrine release tend to overlap, and that LC activity can modulate the excitability of VTA neurons (Isingrini et al., 2016; Mejias-Aponte, 2016). Coupled with findings crucially implicating dopamine from LC in hippocampal memory formation under some circumstances, future investigations should consider interactions between LC and VTA in supporting distinct brain states for action, information processing, and memory formation.

4.4   Summary

In this section, we reviewed three theoretical frameworks that aim to explain how VTA-Hippocampal interactions can support adaptive memory formation for motivationally salient experiences. These frameworks are built upon the neurobiological properties of dopamine neurons, focusing on the neural response to prediction errors, novelty, and reward anticipation. While these accounts may each focus on different mechanisms, they are not necessarily in conflict, but could instead reflect mechanisms that operate at multiple timescales to enhance memory formation. Drawing from behavioral and neuroimaging studies in humans, the next section reviews evidence for reward modulation across different stages of memory processing.

5   Reward modulation of memory processing in humans

Over the past decade, there has been an accumulating body of work investigating how reward motivation can influence memory formation in humans. Building on different theoretical foundations (refer to Section 4), these studies have examined how reward systems can be engaged in different motivational contexts across the different stages of memory processing. In this section, we organize our review based on these stages, from initial encoding, to post-learning consolidation, and finally retrieval. While most of these studies rely on blood oxygenation level dependent (BOLD) signal measured using fMRI in humans, and as such, are not direct measures of dopamine release, there is complementary evidence that BOLD responses in the midbrain are correlated with dopamine release (Schott et al., 2008) and that stimulation of the VTA (in rodents) is associated with increased BOLD signal in regions innervated by the VTA (Lohani et al., 2017). Finally, we consider the dynamic nature of memory, and discuss how dopaminergic modulation can influence the transformation of memory representations over time.

5.1   Motivational influence on memory encoding

The use of extrinsic reward incentives has been central to our understanding of motivational influence on memory formation. One commonly used experimental procedure for the study of reward-motivated memory in humans is the Monetary Incentivized encoding (MIE) task (Adcock et al., 2006). In a typical MIE task, participants are presented with a reward cue which indicates the value of an upcoming stimulus, which is a neutral image (Fig. 3). Participants can earn the associated value if they successfully remember the stimulus on a subsequent memory test. In line with the expectation that reward systems are involved in motivated learning, fMRI studies using the MIE have consistently shown that greater BOLD activation in the midbrain VTA following cues signaling a high reward, but preceding stimulus presentation, predicts memory for the upcoming stimulus (Adcock et al., 2006; Duan et al., 2020; Wolosin et al., 2012). Importantly, there is also evidence that reward-related memory enhancement is associated with greater VTA-Hippocampal functional connectivity during the anticipatory period (preceding stimulus presentation) (Adcock et al., 2006), consistent with theoretical expectations for VTA modulation of the hippocampus during the anticipation of motivationally relevant events. Another commonly used task that uses extrinsic reward value to study motivated learning is the *Value-directed Remembering task* (VDR; refer to Chiew and Bowen, 2022; Knowlton and Castel, 2021 for discussion of its applications). Rather than temporally isolating anticipatory or modulatory intervals for mechanistic investigation, the VDR task is optimized to investigate strategic reward-based prioritization and behavioral efficiency in memory formation; the VDR task is well suited to characterizing individual differences in strategic encoding behaviors due to disorders or over development and aging.

Apart from extrinsic rewards, intrinsic motivations, such as curiosity, can similarly engage the reward system to enhance memory formation. Using a trivia quiz task (Fig. 3), studies have shown that trivia questions eliciting relatively high curiosity evoke greater anticipatory activation in reward circuitry (Duan et al., 2020; Gruber et al., 2014; Kang et al., 2009; Poh et al., 2022). Similar to that seen during the anticipation of monetary rewards, this activation was also associated with better memory for the subsequently presented trivia answers (Duan et al., 2020; Gruber et al., 2014; Kang et al., 2009; Poh et al., 2022). Further providing support for VTA modulation of the hippocampus, work by Gruber and colleagues showed that increased VTA-Hippocampal connectivity was not only associated with memory benefits for the trivia answers, but was also associated with memory benefits for an irrelevant face image that was presented during anticipation of the trivia answers. Recent work using multivoxel pattern analysis to characterize neural states in the hippocampus has offered a candidate mechanism: BOLD activation magnitude in the VTA was associated with
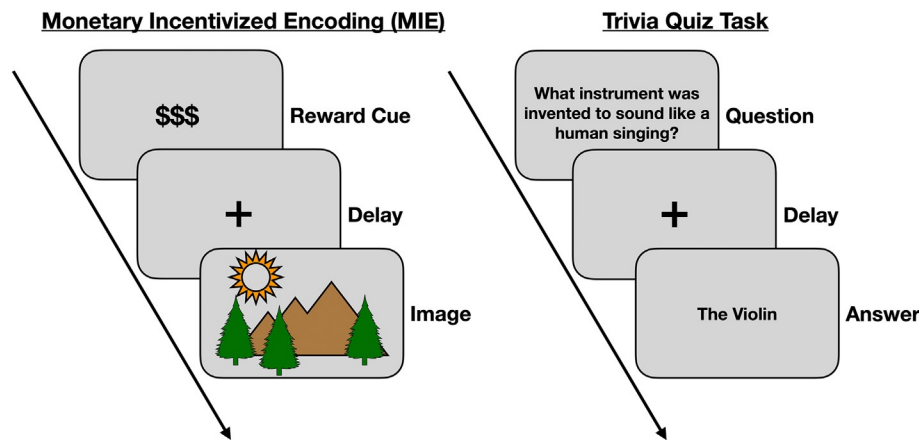
Fig. 3 Examples of tasks used in the study of motivated encoding in humans. In the Monetary Incentive Encoding (MIE) task, participants are motivated by extrinsic monetary rewards to encode the upcoming memoranda (e.g. a valence-neutral image, image-pairs, or words). Variations of the MIE have also examined the effects of motivation on retrieval by pairing high rewards with a specific stimulus category (rather than a unique exemplar). In the Trivia Quiz task, participants are motivated by intrinsic curiosity to learn the answer for the trivia question. These studies have consistently shown that anticipatory VTA activation (preceding the memoranda) was predictive of subsequent learning and memory formation.

the manifestation of a 'learning state' in the hippocampus, predictive of successful memory formation (Poh et al., 2022). The higher the VTA activation, the more similar the hippocampal pattern of activation was to its most typical state, and the greater the likelihood that the upcoming information would be remembered.

While we focus here on the medial temporal lobe for mechanistic investigation, there is of course considerable evidence that motivated memory involves neural circuitry beyond the medial temporal lobe. The prefrontal cortex (PFC), which has been consistently implicated during reward motivated learning (Braver et al., 2014; Chiew and Adcock, 2019; Knowlton and Castel, 2021), both projects to and receives projections from the VTA (Morales and Margolis, 2017; Oades and Halliday, 1987; Sawaguchi and Goldman-Rakic, 1994; Sesack and Pickel, 1992; Swanson, 1982). Evidence from anatomical and functional studies suggest that the VTA, PFC, and hippocampus constitute a functional circuit that enables dopaminergic signaling across multiple timescales, with the PFC regulating phasic activity and the HPC regulating tonic activity (Murty et al., 2017a). Stimulation of PFC projections to dopamine neurons in the VTA has been shown to regulate phasic firing in rodents (Gariano and Groves, 1988; Murase et al., 1993), and fMRI evidence in humans indicates that VTA BOLD responses to rewards may be gated by the dorsolateral PFC (Ballard et al., 2011). While hippocampal activity has been shown to reduce the inhibition of VTA dopamine neurons, thus increasing tonic activity, as reviewed above in Section 4 (Floresco et al., 2001, 2003; Lodge and Grace, 2006; Luo et al., 2011), there are no known direct excitatory inputs from the hippocampus to VTA neurons. PFC direct excitatory projections to VTA, on the other hand, are well-positioned to actively maintain increases in VTA activity, such as the anticipatory ramping profile (Howe et al., 2013; Totah et al., 2013). Beyond the regulation of VTA, it has also been proposed that PFC activation during motivated learning could reflect greater engagement of strategic encoding (Cohen et al., 2014, 2019), or the appraisal of prediction errors (Gruber and Ranganath, 2019). PFC is also implicated in sustaining hippocampal representations to allow their elaboration and integration into memory (reviewed in Preston and Eichenbaum, 2013). Further taking into account the involvement of the medial PFC in reward processing (Kahnt, 2018; O'Doherty, 2004), and also in schema formation (Gilboa and Marlatte, 2017; van Kesteren et al., 2012), future studies should consider how efferents from the VTA to the PFC and hippocampus may support the formation of integrated representations.

While we have primarily focused on enhancement of memory during reward motivation, there is evidence that motivation does not necessarily lead to better memory performance. Individual differences in anxiety have been shown to modulate reward-related memory benefits (Callan and Schweighofer, 2008). High physiological arousal during reward motivation has also been associated with reward impairment of memory performance (Murty et al., 2011). These exceptions to reward enhancements of hippocampal memory are examples of *imperative* motivational states proposed to be dominated by norepinephrine, rather than dopamine, in our *Neuromodulation-MTL framework*. The imposition of extrinsic rewards can also have counterproductive effects when intrinsic motivation for learning is already high; this *undermining effect* has been well documented in educational psychology research (Deci et al., 2001; Kuhbandner et al., 2016; Murayama et al., 2010; Wehe et al., 2015). Thus, in examining the influence of reward motivation on learning, it is important to consider not only the objectively observable incentives but also—and more importantly for predicting memory impacts—the learner's subjective experience of those incentives within the broader motivational context. As discussed above, the *Neuromodulation-MTL framework* proposes that the motivational contexts correspond to neural contexts: specific neuromodulatory states that selectively engage MTL neural circuitries for encoding. It is not the valence of incentives or reinforcers per se but rather these neuromodulatory states which influence the form and content of memories.

5.2   Reward modulation of post-learning consolidation

A key prediction based on cellular studies of the time course of dopaminergic modulation on synaptic plasticity is that dopaminergic influence on memory formation should extend beyond the encoding event, and hence influence post-learning consolidation. Consolidation broadly refers to the stabilization of memory representations following learning, and encompasses both cellular consolidation and systems consolidation. Cellular consolidation primarily involves the strengthening of representations at local synapses, whereas systems consolidation is thought to involve the 'transfer' of memory representations from the hippocampus to the neocortex (Frankland and Bontempi, 2005; McClelland et al., 1995; Wang and Morris, 2010). While the neurophysiological evidence for dopaminergic modulation of consolidation primarily relates to cellular consolidation, there is also evidence suggestive of a role in systems consolidation. As behavioral evidence may not be sufficient in differentiating the two forms of consolidation, the subsequent interpretation of behavioral effects in humans largely refers to consolidation without explicit differentiation between these two mechanisms.

Consolidation effects on memory are often examined by comparing performance between an immediate and a delayed memory test. As consolidation effects are delay-dependent, memory benefits that manifest only at delayed testing, but not during the immediate test, are considered to represent the effects of memory consolidation. Early evidence for reward-modulation of consolidation in humans comes from the work of Wittmann et al. (2005). In this study, the authors examined memory performance for object drawings that indicated whether participants would receive a monetary reward for their performance on a speeded reaction-time task. Comparing memory performance during immediate test and a delayed-test (3 weeks later), it was observed that recognition for reward-predicting images was better in the delayed-test, but not during the immediate test. In addition, reward predicting images also evoked greater BOLD activation in the hippocampus and the midbrain, consistent with expectations that dopaminergic modulation of the hippocampus during encoding may facilitate subsequent consolidation.

Building on the framework of synaptic tag-and-capture, studies in humans have also demonstrated reward-related consolidation effects by examining retroactive effects from behavioral tagging. These paradigms typically involve three distinct

phases – (i) Pre-association, (ii) Associative learning, and (iii) Post-association (Fig. 4). In an example of one such paradigm, participants are shown images from two different categories during the 'Pre-association' phase, without reinforcement of either categories. Following a brief interval, participants are shown new images from the same categories during the 'Associative learning' phase, but one of the categories acquires motivational significance through associative pairing with positive (Patil et al., 2016) or negative reinforcements (Dunsmoor et al., 2015). Following the acquisition of associative pairings, new images from the same categories are presented in the 'Post-association' phase without any additional reinforcements. Consistent with a temporally extended influence of synaptic-tagging, memory was enhanced for the reinforced image category. However this enhancement was observed not only for images presented during and after the reinforcement, but was also retroactively observed for images that were presented prior to reinforcement (Dunsmoor et al., 2015; Patil et al., 2016). In addition, this effect appeared to be stronger in a delayed-memory test than during an immediate test, suggestive of retroactive, delay-dependent consolidation effects. It should however be noted that in a study using a similar task structure, retroactive memory enhancement was not observed when the reward was not performance-dependent (Oyarzún et al., 2016), and more work is required to clarify the conditions in which retroactive memory enhancement is manifested. While studies such as these primarily demonstrate a lingering mnemonic effect that appears to be sustained over minutes across different task blocks, recent work have also demonstrated such reward-related retroactive effects on a trial-by-trial level (Braun et al., 2018), suggesting the possibility of multiple distinct timescale at which 'tagging' effects may occur.

While synaptic tag-and-capture provides a mechanism for cellular consolidation, there is also evidence for dopaminergic modulation of systems consolidation. A key mechanism thought to underlie the 'transfer' of hippocampal memory traces to the neocortex is memory replay (Chen and Wilson, 2023; Káli and Dayan, 2004). By reactivating patterns of neural activity from prior experiences, memory replay enables the integration of new information into the neocortex gradually, avoiding catastrophic interference (Kumaran et al., 2016; McClelland et al., 1995; O'Reilly and Norman, 2002). In rodents, it has been shown that memory replay co-occurs with the firing of VTA neurons (Gomperts et al., 2015), and can increase following the receipt of rewards (Ambrose et al., 2016; Bhattarai et al., 2020; Michon et al., 2019). While non-invasive imaging modalities in humans may preclude high-fidelity analysis of memory replay due to their spatial and temporal resolution limits (but see Liu et al., 2019, 2021; McFadyen et al., 2023; Schuck and Niv, 2019 for detection of rapid replay in humans with non-invasive MEG), these effects can also manifest at scales that are observable with fMRI (Schuck and Niv, 2019; Staresina et al., 2013; Tambini et al., 2010; Tambini and Davachi,
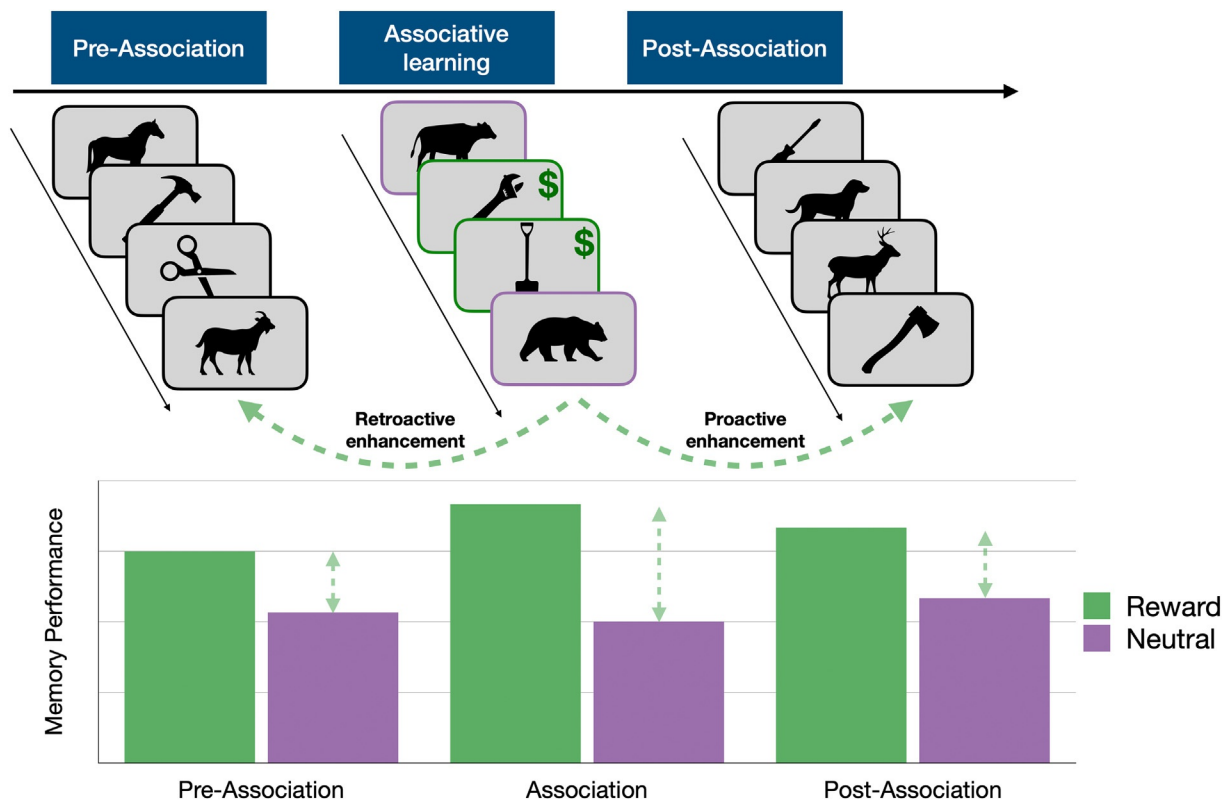
Fig. 4 Schematic depiction of a behavioral tagging experiment in humans. Participants are shown images from two different categories (e.g. Animals and Tools) across three phases. In the Pre-association phase, all images are presented without any reinforcement. During the Association phase, one of the image categories (e.g. Tools) would acquire motivational significance through pairing with reinforcers (e.g. rewards, as illustrated here, or mild static shocks for negative reinforcers). Following associative learning, participants would once again be presented with images in the absence of additional reinforcements. These studies have often shown enhanced memory for the reinforced image category, not only during Associative learning, but also in the Pre-association and in the Post-association phase, suggestive of both retroactive and proactive enhancement for images in the same category.

2013; Wittkuhn and Schuck, 2021). Examining co-fluctuations in BOLD activity during post-learning rest (i.e. 'Functional connectivity'), Gruber et al. (2016) showed that post-learning increases in functional connectivity between the VTA and the hippocampus were associated with reward-related memory enhancement (refer to Frank et al., 2019 for discussions on individual differences in functional connectivity between hippocampus and reward centers and Cohen et al., 2022 for discussions on developmental changes in post-learning functional connectivity). In addition, multivoxel patterns in the hippocampus showed a preferential 'reactivation' of high-reward context, and this was similarly associated with reward-related memory benefits (Gruber et al., 2016). Beyond the hippocampus, reward-related changes in functional connectivity with the VTA have also been observed in category-selective visual cortices. By pairing an image category with monetary reward, Murty et al. (2017b) were able to show selective increases in functional connectivity between the VTA and visual processing regions responsive to the rewarded image category, suggesting that reward-modulation of consolidation may also involve the reinstatement or stabilization of representation in perceptual processing regions.

In conjunction, these studies demonstrate that engagement of the mesolimbic reward system can facilitate not only memory encoding, but also memory consolidation. This enhanced consolidation may be supported by the prioritized 'reactivation' of reward-related information, enabling its stabilization and integration into the neocortex.

5.3   Reward circuits and motivated retrieval

While motivational influence on encoding and consolidation can increase the accessibility of information during retrieval, there is also evidence that reward motivation can modulate decision processes during memory retrieval. In a modified Monetary Incentivized Encoding (MIE) task where a stimulus category (rather than unique exemplars) was associated with high reward during encoding, participants showed a shift in response bias, increasing the tendency to respond 'Old' to images belonging to the high-reward category (Bowen et al., 2020). When reward incentives were presented both during encoding and retrieval, recognition accuracy was greatest for faces that were paired with a reward on both occasions (Marini et al., 2011). In addition, when rewards were paired with specific responses (either correct judgment of 'Old' or 'New') during recognition, the choice for a rewarded response was associated with greater BOLD activation in striatal regions, regardless of reward outcome (Han et al., 2010; but see Elward et al., 2015; King et al., 2018 for an alternative interpretation of striatal engagement during memory retrieval). Further supporting a causal role for dopaminergic reward circuitry in modulation of retrieval, the use of a D2-receptor antagonist has been shown to enhance recognition accuracy, and this effect was associated with greater activation in the VTA and hippocampus during retrieval (Clos et al., 2019b). These findings suggest that reward motivation can engage reward circuitry to modulate retrieval; however, the mechanisms by which this occurs remains to be clarified (for a review of striatal engagement during memory retrieval refer to Scimeca and Badre, 2012).

Apart from strategic shifts in decision thresholds (Bowen et al., 2020), the engagement of dopaminergic reward circuitry may also increase the value of cognitive effort (Westbrook et al., 2020; Westbrook and Braver, 2016), potentially influencing strategic control and the allocation of cognitive resources toward memory search (for detailed review, refer to Chiew and Bowen, 2022). Another potential mechanism is the modulation of hippocampal processing via dopaminergic modulation. Pattern completion, which supports retrieval based on partial cues, have been shown to be disrupted in dopamine transporter knockout mice (Li et al., 2010), suggesting a role for dopamine regulation in pattern completion. How dopamine modulates pattern completion, and thus retrieval, remains to be investigated.

5.4   Dopaminergic modulation of memory updating—Integration, differentiation and forgetting

While broadly delineated based on processes of encoding, consolidation, and retrieval, memory is dynamic and also encompasses multiple processes involved in the updating and modification of memory traces. Here we briefly discuss how dopaminergic modulation has been implicated in memory updating processes, focusing on integration, differentiation and forgetting.

Integration and differentiation. The assimilation of newly learned information with existing knowledge requires the reorganization and updating of older memories, particularly when the new experiences are related to prior knowledge. As learning occurs, neural representations of different memories can transform, becoming more similar to each other through *integration*, or becoming more dissimilar to each other through *differentiation*. While the mechanisms underlying such transformations remain an active area of investigation, there is evidence that dopamine may be implicated in both integration and differentiation of memory representations.

Integration of related experiences via the abstraction of their common relational structures linking memory elements has been proposed to enable generalization and representational flexibility common across experiences. Experimentally, the co-activation of the midbrain and the hippocampus during associative learning has been shown to relate to subsequent ability to generalize the learned relationship to newly encountered information (e.g. Upon learning that Group X prefers both Items A and B, and Group Y prefers Items C and D, one may infer that someone who likes Item A would be more likely to prefer Item B over Item D) (Shohamy and Wagner, 2008). In addition, the use of reward motivation has been shown to constitute a 'shared context' through which discrete pieces of information may be embedded. Through the analysis of BOLD activity patterns in the hippocampus, it has been shown that the patterns of activity are more similar for items encoded under motivational contexts associated with the same levels of monetary reward than for contexts associated with different levels of reward (Wolosin et al., 2013; Zeithamova et al., 2018), and behaviorally, the use of free-recall has shown that memories can be adaptively reorganized based on the reward context, such that

items associated with high rewards were more likely to be clustered during recall (Horwath et al., 2023). While the role of dopamine in supporting the formation of integrated representations has not been definitively demonstrated, one mechanism that may facilitate integration is the regulation of neural excitability, because excitability has been shown to increase overlap between the neural ensembles recruited during the encoding of different events, meaning that these ensembles would be more likely to reactivate one event when the other is activated in memory (Cai et al., 2016; Chowdhury et al., 2022; Delamare et al., 2023; Mau et al., 2020). Furthermore, while we have focused on integration during learning, it has been shown that abstraction and integration may predominantly happen during 'offline' consolidation. While the importance of dopamine for memory consolidation is further suggestive of its potential role in supporting memory integration, this remains to be demonstrated in future investigations.

Whereas integration can facilitate abstraction, minimizing representational overlap through differentiation can reduce interference and thus support detailed memories. The potential role of dopaminergic modulation in differentiation was suggested in early work of event perception. In particular, it was proposed that a change in context can elicit prediction error and trigger phasic dopamine release. Such prediction errors elicited at event boundaries could serve as a neural signal for global updating (Zacks et al., 2007, 2011). Behaviorally, reward prediction errors have been shown to create event boundaries that can disrupt the integration of cross-boundary events (Rouhani et al., 2020). Studies using fMRI have shown greater BOLD activation in the dopaminergic midbrain during anticipation of event boundaries (Zacks et al., 2011), and during surprising events (Antony et al., 2021). Similarly, representations in the hippocampus exhibit greater dissimilarity across boundaries than within a boundary (Ezzyat and Davachi, 2014). Apart from the hippocampus, patterns of activity across distributed brain regions have been shown to exhibit abrupt change following an event boundary (Baldassano et al., 2017). However, it should be noted that these studies have not directly examined whether activation in the midbrain is related to representational differentiation.

A recent theoretical model proposed that prediction errors can support both integration and differentiation based on the consistency of new information with existing knowledge (Bein et al., 2023). In addition, the non-monotonic plasticity hypothesis suggests that the transformation of memory representations may be dependent on the degree of memory reinstatement, such that moderate reinstatement supports differentiation, while strong reinstatement supports integration (Detre et al., 2013; Newman and Norman, 2010; Ritvo et al., 2019). As such, investigation of dopaminergic influences on memory transformation may require further consideration of the activated representational content.

Forgetting. The influence of reward systems on the selectivity of memory can be considered as selectivity of 'forgetting', and recent work has established a role for dopamine in the regulation of forgetting (Castillo Díaz et al., 2021). While forgetting is often viewed as a decay or the 'absence' of a memory, there is a growing body of work emphasizing the adaptive role of forgetting in facilitating new learning, increasing accessibility of competing memories, and in the flexible updating of prior memories (Anderson and Hulbert, 2021; Bjork and Bjork, 2019; Hardt et al., 2013; Ryan and Frankland, 2022; Storm, 2011). Retrieval-induced forgetting, whereby memory retrieval can lead to the forgetting of associated items, has been considered to reflect an adaptive mechanism whereby competing information is inhibited to facilitate access of relevant memory traces (Anderson et al., 1994; Anderson and Hulbert, 2021; Norman et al., 2007). In rodents, retrieval-induced forgetting has been shown to be inhibited following inactivation of the VTA, and this is mediated via D1-receptors in the prefrontal cortex (Gallo et al., 2022), suggesting a causal role for dopamine in regulating the active forgetting of competing memories. However, in a study where human participants were given juice rewards during successful memory retrieval, retrieval-induced forgetting was not increased, but was instead eliminated (Imai et al., 2014), suggesting that the presentation of reward during retrieval may also strengthen or preserve memories for competing items. As neuroimaging was not performed in this study, it is unclear if this reduction in retrieval-induced forgetting was mediated via dopaminergic reward circuitries.

5.5   Summary

While there is considerable evidence that reward modulation can influence memory processing across different stages via multiple mechanisms, these mechanisms have often been considered in isolation. A thorough understanding of the neural basis of adaptive memory requires further consideration of how distinct mechanisms can interact to modulate memory formation across different timescales. In this section, we focused our discussion on work in healthy young adults, and in the next section, we will review evidence for impaired learning and memory when dopaminergic functioning is disrupted.

6   Dysfunction of the dopaminergic systems and implication for learning and memory

The dysregulation of dopaminergic circuitry has been observed in various psychiatric and neurodegenerative conditions. Having detailed the importance of dopamine in learning and memory formation, it would be expected that the disruption of dopaminergic functions may constitute a key factor underlying learning and memory deficits that are common in diverse clinical populations. In the following section, we review evidence for the disruption of dopaminergic circuits in healthy aging and across different clinical populations. We consider how impairments of learning and memory might not only be the consequence of clinical disorders but could potentially constitute a transdiagnostic process leading to disordered cognition and behavior. We follow up with a discussion regarding how dopaminergic pathways could be a mechanistic target for therapeutic interventions, and discuss the potential for using non-invasive modulation of dopaminergic pathways as a low-risk early intervention.

6.1   Disordered cognition as an outcome of learning dysfunctions

As dopamine is postulated to play a central role in reinforcement learning, there has been growing interest in explaining disordered cognition and behavior using reinforcement learning models, particularly in disorders with strong dopaminergic associations (Maia and Frank, 2011). In this formulation, cognitive deficits can be seen as an outcome of alterations in learning from rewards or punishments, stemming from dopamine dysregulation. The use of reward-learning tasks in conjunction with reinforcement learning models hence provides a means for characterizing the processes that may be implicated. Here, we consider how dysregulation of dopamine not only influences reinforcement learning but may also implicate hippocampal-dependent learning mechanisms.

Addiction. Building on the role of dopamine in reinforcing learned behaviors, one of the earliest applications of reinforcement learning models in psychiatry was toward understanding drug addiction and addictive behaviors (Redish, 2004). In the initial formulation of these ideas, it was proposed that compulsive drug behavior may arise from a self-perpetuating cycle, whereby the value of an action leading to drug receipt is constantly increasing due to the absence of normal bounds on positive prediction errors during reward consumption (Redish, 2004). This growing value thus serves to reinforce drug seeking behaviors. While subsequent behavioral experiments do not support the predictions of an 'unbounded' prediction error (Panlilio and Goldberg, 2007), this initial application of reinforcement learning facilitated the development of more sophisticated models that are better able to account for the maladaptive behaviors observed in addiction (Gueguen et al., 2021; Huys et al., 2016; Liu et al., 2020; Mollick and Kober, 2020).

Hippocampal-dependent learning mechanisms have also been implicated in the development and behavioral expression of addiction (Belujon and Grace, 2011; Koob and Volkow, 2010; Kutlu and Gould, 2016; Robbins et al., 2008). By forming an association between neutral stimuli in the environment and the experience of substance use, the neutral stimulus could become a 'cue' that drives the reinstatement of craving behaviors (Crombag et al., 2008; Di Chiara et al., 1999) personal smoking versus personal non-smoking contexts has been shown to activate hippocampus together with insula, which predicted the number of puffs on a cigarette obtained after the session (McClernon et al., 2016) There have been ongoing investigations into whether learned associations could be weakened after learning through reactivation, which renders memories labile, followed by the disruption of their 'reconsolidation' (Exton-McGuinness and Milton, 2018; Sorg, 2012; Taylor et al., 2009; Torregrossa and Taylor, 2013). While the evidence for reconsolidation-based therapy for addiction in humans has been mixed thus far (Exton-McGuinness and Milton, 2018), there are multiple mechanistic pathways that offer targets for weakening the learned associations that create cues for drug use. As interactions between the VTA and hippocampus have been implicated in post-learning consolidation, future investigations should examine if the suppression of dopaminergic reward circuitry can serve as a target for disrupting the reconsolidation of dysfunctional associations in addiction.

Schizophrenia. Schizophrenia is a complex disorder characterized by a combination of positive symptoms of psychosis, negative symptoms including avolition, and cognitive impairments, including impairments of learning and memory (Andreasen and Flaum, 1991; Guo et al., 2019). Dysfunction of the dopaminergic system has been proposed to play a major role in schizophrenia pathogenesis (Howes and Kapur, 2009). The dopamine hypothesis followed observations of the effects of D2-blocking drugs, and "psychotomimetic" effects of amphetamine (Angrist et al., 1974; Carlsson, 1988; Snyder, 1976). The original hypotheses posited excessive dopaminergic signaling, with variants specifying that hyperfunction in the mesolimbic pathway caused positive symptoms, while reduced signaling in the mesocortical pathway caused negative symptoms.

Much recent evidence implicates other neurotransmitters and pathways in the pathophysiology of psychosis. However, a key question for models of schizophrenia is to explain not only the physiology of the acute state of psychosis, but also how psychosis stabilizes and becomes chronic. This stabilization implies either development, neurodegeneration, or learning. Candidate mechanisms underpinning the transition to chronic psychosis include plasticity in cortex, striatum, and medial temporal lobe memory systems.

Dopamine dysregulation in schizophrenia has been proposed to give rise to distortions in prediction errors, resulting in the formation of inaccurate associations, failure to habituate, and the misattribution of salience to events. The question remains whether these changes are due to disease effects on dopaminergic projection neurons themselves, changes in dopamine receptors, or from inputs to midbrain dopamine nuclei, for example inputs from the prefrontal cortex or hippocampus.

Hippocampal signals have been shown to increase the activation of VTA neurons in rodents (Floresco et al., 2001), a relationship that has also been demonstrated in humans using fMRI (Murty et al., 2017a). This increased hippocampal signaling thus offers a potential explanation for the sustained hyperdopaminergic state hypothesized in schizophrenia (Lodge and Grace, 2011). Patients with Schizophrenia indeed show memory deficits (Aleman et al., 1999; Ranganath et al., 2008), including less updating and stronger priors. Whether these hippocampal deficits in schizophrenia are dopamine dependent is a question under active investigation.

Aging and neurodegeneration. The disruption of dopamine function has been prominently implicated in various neurodegenerative diseases including Parkinson's disease and Alzheimer's disease (Morgan et al., 1987; Rangel-Barajas et al., 2015). However, as dopamine functioning also decreases in normative aging (Bäckman et al., 2006, 2010), it remains an open question how changes in the dopaminergic systems contribute to memory decline in either healthy aging or neurodegeneration.

There is accumulating evidence that the degeneration of VTA dopaminergic neurons may contribute to memory deficits in Alzheimer's disease (D'Amelio et al., 2018). Using rodent models, the degeneration of dopamine neurons have been shown to precede the formation of amyloid plaques and neuronal loss in the hippocampus (Nobili et al., 2017), suggesting that deficits in

hippocampal-dependent memory may arise as an outcome of VTA neuron degeneration. In humans, patients with Alzheimer's disease have been shown to exhibit reduced functional connectivity between the VTA and medial temporal lobe regions (Serra et al., 2018), and structural findings also showed that smaller VTA volume in Alzheimer's patients was associated with poorer episodic memory function (De Marco and Venneri, 2018). While administration of dopaminergic drugs have shown successes in modulating synaptic plasticity (as measured by motor-evoked potentials) in patients with Alzheimer's disease (Koch et al., 2011, 2014), its influence on cognitive outcomes has been less apparent (Koch et al., 2020).

Work in healthy aging has suggested that, beyond a direct influence on cognitive functioning, decrease in dopamine may also impact cognition by increasing the cost of cognitive effort and decreasing intrinsic motivation (Hess, 2014). In line with this account, it has been demonstrated that older adults show a better ability to retain memory for information that they were curious about (Castel, 2023; McGillivray et al., 2015), and the elicitation of curiosity also enhanced older adults' ability to learn task-irrelevant information (Galli et al., 2018). These findings suggest that beyond the regulation of dopaminergic functioning via pharmaceutics, the regulation of motivation may also be crucial for preventing the exacerbation of memory decline in aging and neurodegeneration.

Major Depressive Disorder. The lack of motivation and anhedonia in patients with depression have been suggested to reflect a reduction in sensitivity to rewards (Eshel and Roiser, 2010; Pizzagalli, 2014; Treadway and Zald, 2013). Consistent with this account, depressed patients have been shown to exhibit reduced learning from rewarding outcomes and are less likely to encode new positive information (Rupprechter et al., 2020). In addition, episodic memories have been shown to exhibit similar affective bias against positive information during major depressive disorders (Burt et al., 1995). Building on the relation between prediction errors to episodic encoding, it was shown that while patients with depression exhibited better episodic encoding following prediction error, this was only observed during negative prediction errors, but not following positive prediction errors (Rouhani and Niv, 2019). While none of the above studies have shown a direct link between dopamine dysregulation and impaired encoding of positive information, pharmacological enhancement of dopaminergic function in healthy adults has shown an increased weighting of positive information during decision making (Pessiglione et al., 2006). The study hints at a potential mechanistic pathway whereby affective bias may be alleviated through the upregulation of dopamine functions.

In addition to an affective bias in the encoding of new memories, positive memories are less accessible for recall in individuals with depression (Gaddy and Ingram, 2014). In a clinical trial that aimed to increase the accessibility of positive memories through the upregulation of amygdala activity, it was shown that real-time fMRI neurofeedback training can increase the recall of positive autobiographical memory, and also decrease associated depressive symptoms (Young et al., 2017). While the study focused on the role of the amygdala in the enhanced encoding of salient events, the amygdala receives substantial dopaminergic projection from the VTA, and it is possible that upregulation of amygdala activation during neurofeedback would also implicate broader network level changes involving the dopaminergic circuits, which could contribute to learning in these paradigms.

7   Modulation of dopaminergic function and motivation for learning enhancement and clinical interventions

With the broad influence of dopamine across a range of cognitive functions and clinical disorders, the modulation of dopaminergic function has been a key target for enhancing cognitive functions and for the alleviation of clinical symptoms. While the complex dynamics of dopaminergic influence can make it difficult for precise targeting, there is evidence for the successful regulation of dopaminergic functioning pertaining to learning and memory. Here, we briefly discuss evidence for pharmacological manipulation of dopamine in the context of learning and memory, and we consider recent developments of real-time fMRI neurofeedback as a potential tool for more targeted, non-invasive intervention.

Pharmacological manipulation of dopamine for learning and memory. Based on the evidence that dopamine is essential to long term plasticity and memory formation, it might be expected that simply increasing dopamine levels should enhance learning and memory. Across studies on mnemonic effects of pharmacological augmentation of dopamine levels in humans, however, findings have painted a more complex picture, perhaps less surprising in view of the multiple mechanisms reviewed here.

In populations with diminished dopaminergic functioning, evidence suggests that the pharmacological increase of dopamine can produce mnemonic benefits, such as in patients with Parkinson's disease (Thurm et al., 2016) or in healthy older adults (Baeuchl et al., 2023; Morcom et al., 2010). Healthy older adults with poorer memory performance, suggestive of lower baseline dopamine levels, have been shown to demonstrate memory benefits following administration of the dopamine agonist bromo-criptine (Abdulrahman et al., 2017). Baseline dopamine levels is an important consideration in identifying mechanisms through which distinct processes may be influenced by pharmacological manipulation. It has been proposed that working memory and prefrontal functions may be impaired when dopamine is either insufficient or excessive (Cools and D'Esposito, 2011; Seamans and Yang, 2004; Williams and Goldman-Rakic, 1995). By characterizing a non-monotonic inverted U-shaped relationship between dopamine levels and cognitive functions that contributes to long-term memory formation, these findings suggest that baseline dopamine levels may similarly determine the mnemonic effects of dopaminergic drugs. Future work examining the mnemonic effects of dopamine pharmacology would require a more precise consideration of baseline dopamine levels and dose-dependent effects (e.g. Chowdhury et al., 2012; Monte-Silva et al., 2009) to characterize an optimum range of dopamine for long-term memory.

In addition to consideration of an individual's baseline dopamine availability, predicting dopaminergic pharmacological effects on memory may also need to account for the multiple mechanisms and their interactions modulated by dopaminergic

pharmacology. In contrast to populations with reduced dopamine availability, pharmacologic manipulation of dopamine in healthy young adults has been equivocal, with results showing both enhanced (Clos et al., 2019a, 2019b; Knecht et al., 2004; Ripollés et al., 2018) and impaired memory performance (Apitz and Bunzeck, 2013; Baeuchl et al., 2023; Gönner et al., 2023). This mixed picture may stem partly from the way in which dopamine levels have typically been experimentally manipulated in humans (both patients and healthy participants) via the use of L-dopa, which is a dopamine precursor and is thus not selective to any dopamine receptor subtype or anatomical distribution (see above sections for discussion of D1- and D2-like receptor subtypes and their distributions and cognitive effects). This non-selectivity implies that a behavioral effect of L-dopa will depend on the interaction of multiple concurrent mechanisms. While some studies in older adults have investigated the D2 agonist bromocriptine in aging, it is also a D1 antagonist. While D1 agonists would potentially be more relevant for hippocampal function, the only agents that have been available are investigational and have significant side effects that limit their use. Even in populations with diminished dopaminergic functions, the mnemonic effects of dopamine manipulation can vary based on task demands (Sharp et al., 2020), and can also evolve across time (Chowdhury et al., 2012; Grogan et al., 2017; Isotalus et al., 2023). Like arousal and motivational states, accounting for baseline cognitive performance and dopamine availability will likely be important for predicting the effects of L-dopa and other agents in healthy young participants.

To summarize, while better understanding of potential mnemonic benefits of dopamine drugs on both healthy and clinical populations will benefit from studies with more precise spatial and temporal targeting, for example via increasing receptor specificity (e.g. Abdulrahman et al., 2017; Clos et al., 2019b; Hauser et al., 2019; Morcom et al., 2010), rationales for pharmacological enhancement will remain complex and irreducibly constrained by the need to characterize of an individual's baseline dopamine status at the time of a pharmacological challenge. The *Neuromodulation-MTL framework* would also argue for a need to consider shorter-term state changes as important contexts for drug effects. All in all, these limitations together point to a need for methods more dynamic than orally administered drugs for regulating dopamine function.

Endogenous self-regulation of reward systems with neurofeedback. Beyond the augmentation of brain activity through pharmaceutical manipulation, there has also been immense interest in understanding how individuals can learn to endogenously regulate their brain activity. One way in which this has been examined is through neurofeedback, where brain activity is recorded and converted into signals which can then be used as a feedback signal for learning (deCharms, 2008; Hampson, 2021; LaConte, 2011; Sitaram et al., 2016; Weiskopf, 2012). Using real-time fMRI, it has been shown that human participants are able to upregulate activity in the dopaminergic VTA when presented with visual feedback informative of BOLD activity in their VTA (Sulzer et al., 2013). More recently, in a study emphasizing the use of motivational strategies during neurofeedback training, it was demonstrated that human participants are able to develop the ability for upregulation of VTA BOLD activation, even in the absence of feedback (MacInnes et al., 2016).

As would be expected based on the evidence reviewed above, the successful upregulation of BOLD activity in the VTA was accompanied by increased post-training functional connectivity between the VTA and the hippocampus (MacInnes et al., 2016), as well as the accumbens. Whether this increased functional coupling translates to changes in associated cognitive processing, such as enhanced learning, as observed in studies of motivated memory (e.g. Adcock et al., 2006; Murty and Adcock, 2014; Wolosin et al., 2012), or the regulation of hippocampal states supporting memory formation (Poh et al., 2022) remains to be investigated.

Because neurofeedback provides a non-invasive tool that enables precise targeting of specific brain structures, connections, and even activation patterns (Ramot and Martin, 2022; Taschereau-Dumouchel et al., 2022; Watanabe et al., 2017) there is an immense potential for translational application, particularly in prevention or the early stages of clinical disorders, where the use of drugs may be considered premature or too risky. As work continues to progress in the domain of neurofeedback, it is important to demonstrate the functional and behavioral significance of endogenous regulation (e.g. Rance et al., 2018; Thibault et al., 2018; Tursic et al., 2020), and to further identify individual differences that may prevent learning from neurofeedback (Haugg et al., 2020, 2021; Hellrung et al., 2022).

Regulation of motivation for learning-based interventions. Neurofeedback is a technique that aims to train individuals to regulate their own brain function, but we are already extracting important lessons from the use of neurofeedback techniques about the potential applications of self-regulation skills more broadly. The findings reviewed above imply that self-regulation of motivation is a skill that can be learned, and moreover, used to enhance memory and learning in education and therapeutic settings. Many psychotherapies leverage the ability to perceive contingencies, to abstract rules from specific events (Johnson and Redish, 2007) for new decisions, to prospect future outcomes (Addis et al., 2007; Hassabis and Maguire, 2009), and to generalize insights from the clinician's office to daily life. All these cognitive functions are associated with the hippocampus and medial temporal lobe memory system function. Understanding how motivation may enhance adaptive memory formation offers potential tools to understand and improve learning and learning-based therapies.

Beyond the argument that self-regulation of motivation is a potentially powerful tool for enhancing adaptive learning, it is worth noting that human social behavior already includes tools for regulating the same affective and neuromodulatory states that are the target of neurofeedback-based training. For example, a technique common in Motivational Interviewing therapy (Miller, 1983; Miller and Rollnick, 2009) involves a preparatory, conditional cue to set up an opportunity for learning: "I have some information that may be useful to you. Would you like me to share it?" This approach of eliciting another person's "appetite for information" may, via the anticipation and motivational state it engenders, enhance memory formation for the knowledge being communicated. Recent work has shown that instructed motivational states can bias information seeking choice behaviors and influence learning.

By using different cover stories for an identical reinforcement learning task (pretending to be a thief (i) executing or (ii) planning a heist), it was shown that the induction of different motivational states led to decisions that prioritized either reward or the reduction of uncertainty, despite identical reinforcement and incentives (Sinclair et al., 2023). Considering the mechanistic insights provided by neurofeedback and other experimental studies in the context of behavioral interventions, both current and novel, will help rationalize, assess, and integrate a broad repertoire of tools for helping people achieve states conducive to adaptive learning.

8 Open questions for future research

8.1 How do reward effects on memory translate to actions, decisions, and future behavior?

A central feature of an adaptive memory system is the flexible application of memories to inform future behavior and decisions. While recent investigations have progressively examined how episodic memory can influence decision making, it remains unclear how motivational bias in memory formation would translate to future behavior, and whether this is mediated by similar reward circuitries.

Prior work has shown that the retrieval of memoranda encoded in a rewarding context is associated with BOLD activation in the reward circuits, suggesting that value information can be reinstated during memory retrieval (Elward et al., 2015; Kuhl et al., 2010). Further suggestive of a potential value 'transfer', it has been shown that when a motivationally-neutral image acquires value through reward-learning, the reward can increase the value of other associated images, even when the images have never been paired with a reward (Wimmer and Shohamy, 2012). These findings hint at a potential mechanism whereby motivational significance experienced in an encoding context can be transferred and generalized to a novel context through memory retrieval.

Consistent with a role of memory retrieval in decision-making, the induction of a 'retrieval state', primed by presentation of familiar images, has been shown to increase the weight given to past experiences during decision-making (Duncan and Shohamy, 2016). The successful retrieval of reward outcomes from prior experiences can also bias subsequent choice preference for images that were previously associated with high rewards (Murty et al., 2016). More directly implicating memory retrieval in the decision process, recent work has shown how the neural reinstatement of previous contexts can bias ongoing choices (Bornstein and Norman, 2017), and that a reminder of a specific episodic event can bias value estimation during decision-making (Bornstein et al., 2017). While these studies demonstrate how past memories can influence future decisions, open questions remain as to: (i) whether engagement of reward circuits during learning is associated with subsequent reinstatement in novel contexts, and (ii) whether maladaptive decision-making may be in part driven by disruption of the adaptive encoding and retrieval of episodic experiences.

On the flip side, our actions and choices can also influence the memories that we form. Rather than being passive recipients of information, humans are active information-seekers, and the ways in which we seek information can be biased by ongoing mood (Lydon-Staley et al., 2021) and motivational state (Hsiung et al., 2023; Sinclair et al., 2023). Even in the absence of differences in informational content, it has been shown that the subjective experience of choice (DuBrow et al., 2019; Murty et al., 2015), agency (Hon and Yeo, 2021; Ruiz et al., 2023), or the engagement of motor processing (Kinder and Buss, 2021; Yebra et al., 2019) may be sufficient to enhance memory formation. As dopamine is also implicated in driving action and goal-directed behavior, it is possible that engagement of dopaminergic circuits during the anticipation (of action or choice) may suffice for enhanced learning of temporally coincident information. Dissecting this influence will, however, require disentangling from other modulatory influences associated with actions and intentions, including sensory experience, planning, and motor behavior.

9 Concluding remarks

Investigating the interactions between reward and memory systems has enabled a deeper understanding of the links between individual motivational states and memory formation, providing a neurobiological basis for an adaptive memory system. Here, we reviewed theoretical frameworks and empirical evidence, highlighting how rewards and their anticipation can modulate different stages of memory processing across distinct timescales. We also considered how pathological outcomes could arise from disruptions to reward circuits and their impact on memory systems, and how remediation via dopaminergic modulation could serve as potential intervention for learning and memory disorders. More work will be needed to investigate the precise mnemonic benefits associated with dopaminergic manipulations, while limitations on pharmacological development argue for additional behavioral investigations.

As reviewed in this chapter, while the precise underlying mechanisms of motivated memory remain under active investigation in multiple fields, there is strong and convergent evidence that modulation of memory circuits by dopamine originating in the ventral tegmental area plays a central role in the adaptive prioritization of motivationally-relevant memories, with substantial roles for other neurotransmitters and projection systems, including norepinephrine and the amygdala. In contrast to the once canonical view that the hippocampus and medial temporal lobes are automatic recorders of attended novel experience, it is now abundantly clear that rewards and motivational states act at multiple spatial and temporal scales and via multiple synergistic mechanisms to shape memory for adaptive behavior.

References

Abdulrahman H, Fletcher PC, Bullmore E, and Morcom AM (2017) Dopamine and memory dedifferentiation in aging. *NeuroImage* 153: 211–220.

Abraham WC (2008) Metaplasticity: Tuning synapses and networks for plasticity. *Nature Reviews. Neuroscience* 9(5): 387.

Adcock RA, Thangavel A, Whitfield-Gabrieli S, Knutson B, and Gabrieli JDE (2006) Reward-motivated learning: Mesolimbic activation precedes memory formation. *Neuron* 50(3): 507–517.

Addis DR, Wong AT, and Schacter DL (2007) Remembering the past and imagining the future: Common and distinct neural substrates during event construction and elaboration. *Neuropsychologia* 45(7): 1363–1377.

Aleman A, Hijman R, de Haan EH, and Kahn RS (1999) Memory impairment in schizophrenia: A meta-analysis. *The American Journal of Psychiatry* 156(9): 1358–1366.

Ambrose RE, Pfeiffer BE, and Foster DJ (2016) Reverse replay of hippocampal place cells is uniquely modulated by changing reward. *Neuron* 91(5): 1124–1136.

Anderson MC and Hulbert JC (2021) Active forgetting: Adaptation of memory by prefrontal control. *Annual Review of Psychology* 72: 1–36.

Anderson MC, Bjork RA, and Bjork EL (1994) Remembering can cause forgetting: Retrieval dynamics in long-term memory. *Journal of Experimental Psychology. Learning, Memory, and Cognition* 20(5): 1063–1087.

Andreasen NC and Flaum M (1991) Schizophrenia: The characteristic symptoms. *Schizophrenia Bulletin* 17(1): 27–49.

Angrist B, Sathananthan G, Wilk S, and Gershon S (1974) Amphetamine psychosis: Behavioral and biochemical aspects. *Journal of Psychiatric Research* 11: 13–23.

Antony JW, Hartshorne TH, Pomeroy K, Gureckis TM, Hasson U, McDougle SD, and Norman KA (2021) Behavioral, physiological, and neural signatures of surprise during naturalistic sports viewing. *Neuron* 109(2): 377–390.e7.

Apitz T and Bunzeck N (2013) Dopamine controls the neural dynamics of memory signals and retrieval accuracy. *Neuropsychopharmacology* 38(12): 2409–2417.

Ashby FG, Isen AM, and Turken AU (1999) A neuropsychological theory of positive affect and its influence on cognition. *Psychological Review* 106(3): 529–550.

Bäckman L, Nyberg L, Lindenberger U, Li S-C, and Farde L (2006) The correlative triad among aging, dopamine, and cognition: Current status and future prospects. *Neuroscience and Biobehavioral Reviews* 30(6): 791–807.

Bäckman L, Lindenberger U, Li S-C, and Nyberg L (2010) Linking cognitive aging to alterations in dopamine neurotransmitter functioning: Recent data and future avenues. *Neuroscience and Biobehavioral Reviews* 34(5): 670–677.

Baeuchl C, Glöckner F, Koch C, Petzold J, Schuck NW, Smolka MN, and Li S-C (2023) Dopamine differentially modulates medial temporal lobe activity and behavior during spatial navigation in young and older adults. *NeuroImage* 273: 120099.

Baldassano C, Chen J, Zadbood A, Pillow JW, Hasson U, and Norman KA (2017) Discovering event structure in continuous narrative perception and memory. *Neuron* 95(3): 709–721.e5.

Ballard IC, Murty VP, and Carter RMK (2011) Dorsolateral prefrontal cortex drives mesolimbic dopaminergic regions to initiate motivated behavior. *The Journal of Neuroscience* 31(28): 10340–10346.

Ballarini F, Martínez MC, Díaz Perez M, Moncada D, and Viola H (2013) Memory in elementary school children is improved by an unrelated novel experience. *PLoS One* 8(6): e66875.

Bayer HM and Glimcher PW (2005) Midbrain dopamine neurons encode a quantitative reward prediction error signal. *Neuron* 47(1): 129–141.

Beaulieu J-M and Gainetdinov RR (2011) The physiology, signaling, and pharmacology of dopamine receptors. *Pharmacological Reviews* 63(1): 182–217.

Beckstead RM, Domesick VB, and Nauta WJ (1979) Efferent connections of the substantia nigra and ventral tegmental area in the rat. *Brain Research* 175(2): 191–217.

Beier KT, Steinberg EE, DeLoach KE, Xie S, Miyamichi K, Schwarz L, Gao XJ, Kremer EJ, Malenka RC, and Luo L (2015) Circuit architecture of VTA dopamine neurons revealed by systematic input-output mapping. *Cell* 162(3): 622–634.

Bein O, Gasser C, Amer T, Maril A, and Davachi L (2023) Predictions transform memories: How expected versus unexpected events are integrated or separated in memory. *Neuroscience and Biobehavioral Reviews*: 105368.

Belujon P and Grace AA (2011) Hippocampus, amygdala, and stress: Interacting systems that affect susceptibility to addiction. *Annals of the New York Academy of Sciences* 1216: 114–121.

Berridge KC and Robinson TE (1998) What is the role of dopamine in reward: Hedonic impact, reward learning, or incentive salience? *Brain Research. Brain Research Reviews* 28(3): 309–369.

Best PJ, White AM, and Minai A (2001) Spatial processing in the brain: The activity of hippocampal place cells. *Annual Review of Neuroscience* 24: 459–486.

Bhattarai B, Lee JW, and Jung MW (2020) Distinct effects of reward and navigation history on hippocampal forward and reverse replays. *Proceedings of the National Academy of Sciences* 117(1): 689–697.

Biel D and Bunzeck N (2019) Novelty before or after word learning does not affect subsequent memory performance. *Frontiers in Psychology* 10: 1379.

Bisby JA and Burgess N (2017) Differential effects of negative emotion on memory for items and associations, and their relationship to intrusive imagery. *Current Opinion in Behavioral Sciences* 17: 124–132.

Bjork RA and Bjork EL (2019) Forgetting as the friend of learning: Implications for teaching and self-regulated learning. *Advances in Physiology Education* 43(2): 164–167.

Bornstein AM and Norman KA (2017) Reinstated episodic context guides sampling-based decisions for reward. *Nature Neuroscience* 20(7): 997–1003.

Bornstein AM, Khaw MW, Shohamy D, and Daw ND (2017) Reminders of past choices bias decisions for reward in humans. *Nature Communications* 8: 15958.

Bowen HJ, Kark SM, and Kensinger EA (2018) NEVER forget: Negative emotional valence enhances recapitulation. *Psychonomic Bulletin & Review* 25(3): 870–891.

Bowen HJ, Marchesi ML, and Kensinger EA (2020) Reward motivation influences response bias on a recognition memory task. *Cognition* 203: 104337.

Braun EK, Wimmer GE, and Shohamy D (2018) Retroactive and graded prioritization of memory by reward. *Nature Communications* 9: 4886.

Braver TS, Krug MK, Chiew KS, Kool W, Westbrook JA, Clement NJ, Adcock RA, Barch DM, Botvinick MM, Carver CS, Cools R, Custers R, Dickinson A, Dweck CS, Fishbach A, Gollwitzer PM, Hess TM, Isaacowitz DM, et al. (2014) Mechanisms of motivation–cognition interaction: Challenges and opportunities. *Cognitive, Affective, & Behavioral Neuroscience* 14(2): 443–472.

Bromberg-Martin ES, Matsumoto M, and Hikosaka O (2010) Dopamine in motivational control: Rewarding, aversive, and alerting. *Neuron* 68(5): 815–834.

Brown MW and Aggleton JP (2001) Recognition memory: What are the roles of the perirhinal cortex and hippocampus? *Nature Reviews. Neuroscience* 2(1): 51–61.

Bunzeck N and Düzel E (2006) Absolute coding of stimulus novelty in the human substantia nigra/VTA. *Neuron* 51(3): 369–379.

Bunzeck N, Doeller CF, Dolan RJ, and Duzel E (2012) Contextual interaction between novelty and reward processing within the mesolimbic system. *Human Brain Mapping* 33(6): 1309–1324.

Burt DB, Zembar MJ, and Niederehe G (1995) Depression and memory impairment: A meta-analysis of the association, its pattern, and specificity. *Psychological Bulletin* 117(2): 285–305.

Cagniard B, Beeler JA, Britt JP, McGehee DS, Marinelli M, and Zhuang X (2006) Dopamine scales performance in the absence of new learning. *Neuron* 51(5): 541–547.

Cai DJ, Aharoni D, Shuman T, Shobe J, Biane J, Song W, Wei B, Veshkini M, La-Vu M, Lou J, Flores SE, Kim I, Sano Y, Zhou M, Baumgaertel K, Lavi A, Kamata M, Tuszynski M, Mayford M, et al. (2016) A shared neural ensemble links distinct contextual memories encoded close in time. *Nature* 534(7605): 115–118.

Callan DE and Schweighofer N (2008) Positive and negative modulation of word learning by reward anticipation. *Human Brain Mapping* 29(2): 237–249.

Carlsson A (1988) The current status of the dopamine hypothesis of schizophrenia. *Neuropsychopharmacology* 1(3): 179–186.

Castel AD (2023) Memory selectivity in older age. *Current Opinion in Psychology* 55: 101744.

Castillo Díaz F, Caffino L, and Fumagalli F (2021) Bidirectional role of dopamine in learning and memory-active forgetting. *Neuroscience and Biobehavioral Reviews* 131: 953–963.

Cen D, Gkoumas C, and Gruber MJ (2021) Anticipation of novel environments enhances memory for incidental information. *Learning & Memory* 28(8): 254–259.

Chen ZS and Wilson MA (2023) Now and then: How our understanding of memory replay evolves. *Journal of Neurophysiology*. https://doi.org/10.1152/jn.00454.2022.

Chiew KS and Adcock RA (2019) Motivated memory. In: *The Cambridge Handbook of Motivation and Learning*, pp. 517–546. Cambridge University Press.

Chiew KS and Bowen HJ (2022) Chapter Three: Neurobiological mechanisms of selectivity in motivated memory. In: Elliot AJ (ed.) *Advances in Motivation Science*, vol. 9, pp. 57–87. Elsevier.

Chowdhury R, Guitart-Masip M, Bunzeck N, Dolan RJ, and Düzel E (2012) Dopamine modulates episodic memory persistence in old age. *The Journal of Neuroscience* 32(41): 14193–14204.

Chowdhury A, Luchetti A, Fernandes G, Filho DA, Kastellakis G, Tzilivaki A, Ramirez EM, Tran MY, Poirazi P, and Silva AJ (2022) A locus coeruleus-dorsal CA1 dopaminergic circuit modulates memory linking. *Neuron*. https://doi.org/10.1016/j.neuron.2022.08.001.

Clewett D and Murty VP (2019) Echoes of emotions past: How neuromodulators determine what we recollect. *eNeuro* 6(2). https://doi.org/10.1523/ENEURO.0108-18.2019.

Clewett D, Schoeke A, and Mather M (2014) Locus coeruleus neuromodulation of memories encoded during negative or unexpected action outcomes. *Neurobiology of Learning and Memory* 111: 65–70.

Clewett D, Huang R, Velasco R, Lee T-H, and Mather M (2018) Locus coeruleus activity strengthens prioritized memories under arousal. *The Journal of Neuroscience* 38(6): 1558–1574.

Clos M, Bunzeck N, and Sommer T (2019a) Dopamine enhances item novelty detection via hippocampal and associative recall via left lateral prefrontal cortex mechanisms. *The Journal of Neuroscience* 39(40): 7920–7933.

Clos M, Bunzeck N, and Sommer T (2019b) Dopamine is a double-edged sword: Dopaminergic modulation enhances memory retrieval performance but impairs metacognition. *Neuropsychopharmacology* 44(3): 555–563.

Cohen MS, Rissman J, Suthana NA, Castel AD, and Knowlton BJ (2014) Value-based modulation of memory encoding involves strategic engagement of fronto-temporal semantic processing regions. *Cognitive, Affective, & Behavioral Neuroscience* 14(2): 578–592.

Cohen MS, Cheng LY, Paller KA, and Reber PJ (2019) Separate memory-enhancing effects of reward and strategic encoding. *Journal of Cognitive Neuroscience* 31(11): 1658–1673.

Cohen AO, Glover MM, Shen X, Phaneuf CV, Avallone KN, Davachi L, and Hartley CA (2022) Reward enhances memory via age-varying online and offline neural mechanisms across development. *The Journal of Neuroscience* 42(33): 6424–6434.

Cools R and D'Esposito M (2011) Inverted-U–shaped dopamine actions on human working memory and cognitive control. *Biological Psychiatry* 69(12): e113–e125.

Crombag HS, Bossert JM, Koya E, and Shaham Y (2008) Context-induced relapse to drug seeking: A review. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences* 363(1507): 3233–3243.

D'Amelio M, Puglisi-Allegra S, and Mercuri N (2018) The role of dopaminergic midbrain in Alzheimer's disease: Translating basic science into clinical practice. *Pharmacological Research* 130: 414–419.

Davachi L (2006) Item, context and relational episodic encoding in humans. *Current Opinion in Neurobiology* 16(6): 693–700.

Davachi L and Wagner AD (2002) Hippocampal contributions to episodic encoding: Insights from relational and item-based learning. *Journal of Neurophysiology*. https://doi.org/10.1152/jn.00046.2002.

Davachi L, Mitchell JP, and Wagner AD (2003) Multiple routes to memory: Distinct medial temporal lobe processes build item and source memories. *Proceedings of the National Academy of Sciences of the United States of America* 100(4): 2157–2162.

De Marco M and Venneri A (2018) Volume and connectivity of the ventral tegmental area are linked to neurocognitive signatures of Alzheimer's disease in humans. *Journal of Alzheimer's Disease* 63(1): 167–180.

deCharms RC (2008) Applications of real-time fMRI. *Nature Reviews. Neuroscience* 9(9): 720–729.

Deci EL, Koestner R, and Ryan RM (2001) Extrinsic rewards and intrinsic motivation in education: Reconsidered once again. *Review of Educational Research* 71(1): 1–27.

Delamare G, Zaki Y, Cai DJ, and Clopath C (2023) Drift of neural ensembles driven by slow fluctuations of intrinsic excitability. *eLife*. https://doi.org/10.7554/elife.88053.2.

Detre GJ, Natarajan A, Gershman SJ, and Norman KA (2013) Moderate levels of activation lead to forgetting in the think/no-think paradigm. *Neuropsychologia* 51(12): 2371–2388.

Di Chiara G, Tanda G, Bassareo V, Pontieri F, Acquas E, Fenu S, Cadoni C, and Carboni E (1999) Drug addiction as a disorder of associative learning. Role of nucleus accumbens shell/extended amygdala dopamine. *Annals of the New York Academy of Sciences* 877: 461–485.

Diana RA, Yonelinas AP, and Ranganath C (2007) Imaging recollection and familiarity in the medial temporal lobe: A three-component model. *Trends in Cognitive Sciences* 11(9): 379–386.

Dreyer JK, Herrik KF, Berg RW, and Hounsgaard JD (2010) Influence of phasic and tonic dopamine release on receptor activation. *Journal of Neuroscience* 30(42): 14273–14283.

Duan H, Fernández G, van Dongen E, and Kohn N (2020) The effect of intrinsic and extrinsic motivation on memory formation: Insight from behavioral and imaging study. *Brain Structure & Function* 225(5): 1561–1574.

DuBrow S, Eberts EA, and Murty VP (2019) A common mechanism underlying choice's influence on preference and memory. *Psychonomic Bulletin & Review*. https://doi.org/10.3758/s13423-019-01650-5.

Duncan KD and Shohamy D (2016) Memory states influence value-based decisions. *Journal of Experimental Psychology. General* 145(11): 1420–1426.

Dunsmoor JE, Murty VP, Davachi L, and Phelps EA (2015) Emotional learning selectively and retroactively strengthens memories for related events. *Nature* 520: 345–348.

Dunsmoor JE, Murty VP, Clewett D, Phelps EA, and Davachi L (2022) Tag and capture: How salient experiences target and rescue nearby events in memory. *Trends in Cognitive Sciences* 26(9): 782–795.

Duszkiewicz AJ, McNamara CG, Takeuchi T, and Genzel L (2018) Novelty and dopaminergic modulation of memory persistence: A tale of two systems. *Trends in Neurosciences* 42(2): 102–114.

Edelmann E and Lessmann V (2013) Dopamine regulates intrinsic excitability thereby gating successful induction of spike timing-dependent plasticity in CA1 of the hippocampus. *Frontiers in Neuroscience* 7: 25.

Edelmann E and Lessmann V (2018) Dopaminergic innervation and modulation of hippocampal networks. *Cell and Tissue Research* 373(3): 711–727.

Eichenbaum H (2000) A cortical-hippocampal system for declarative memory. *Nature Reviews. Neuroscience* 1(1): 41–50.

Eichenbaum H (2017) Prefrontal–hippocampal interactions in episodic memory. *Nature Publishing Group* 18(9): 547–558.

Eichenbaum H, Dudchenko P, Wood E, Shapiro M, and Tanila H (1999) The hippocampus, memory, and place cells: Is it spatial memory or a memory space? *Neuron* 23(2): 209–226.

Elliott BL, Mohyee R, Ballard IC, Olson IR, Ellman LM and Murty VP (2023) In Vivo Structural Connectivity of the Reward System Along the Hippocampal Long-Axis. In: *bioRxiv*. p. 2023.09.11.556537. doi: 10.1101/2023.09.11.556537.

Elward RL, Vilberg KL, and Rugg MD (2015) Motivated memories: Effects of reward and recollection in the core recollection network and beyond. *Cerebral Cortex* 25(9): 3159–3166.

Esber GR and Haselgrove M (2011) Reconciling the influence of predictiveness and uncertainty on stimulus salience: A model of attention in associative learning. *Proceedings of the Royal Society B* 278(1718): 2553–2561.

Eshel N and Roiser JP (2010) Reward and punishment processing in depression. *Biological Psychiatry* 68(2): 118–124.

Exton-McGuinness MTJ and Milton AL (2018) Reconsolidation blockade for the treatment of addiction: Challenges, new targets, and opportunities. *Learning & Memory* 25(9): 492–500.

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(5): 1179–1189.

Fadok JP, Dickerson TMK, and Palmiter RD (2009) Dopamine is necessary for cue-dependent fear conditioning. *The Journal of Neuroscience* 29(36): 11089–11097.

Farrell K, Lak A, and Saleem AB (2022) Midbrain dopamine neurons signal phasic and ramping reward prediction error during goal-directed navigation. *Cell Reports* 41(2): 111470.

Fenker DB, Frey JU, Schuetze H, Heipertz D, Heinze H-J, and Düzel E (2008) Novel scenes improve recollection and recall of words. *Journal of Cognitive Neuroscience* 20(7): 1250–1265.

Flagel SB, Clark JJ, Robinson TE, Mayo L, Czuj A, Willuhn I, Akers CA, Clinton SM, Phillips PEM, and Akil H (2011) A selective role for dopamine in stimulus-reward learning. *Nature* 469(7328): 53–57.

Floresco SB, Todd CL, and Grace AA (2001) Glutamatergic afferents from the hippocampus to the nucleus accumbens regulate activity of ventral tegmental area dopamine neurons. *The Journal of Neuroscience* 21(13): 4915–4922.

Floresco SB, West AR, Ash B, Moore H, and Grace AA (2003) Afferent modulation of dopamine neuron firing differentially regulates tonic and phasic dopamine transmission. *Nature Neuroscience* 6(9): 968–973.

Foerde K and Shohamy D (2011) The role of the basal ganglia in learning and memory: Insight from Parkinson's disease. *Neurobiology of Learning and Memory* 96(4): 624–636.

Frank LE, Preston AR, and Zeithamova D (2019) Functional connectivity between memory and reward centers across task and rest track memory sensitivity to reward. *Cognitive, Affective, & Behavioral Neuroscience*. https://doi.org/10.3758/s13415-019-00700-8.

Frankland PW and Bontempi B (2005) The organization of recent and remote memories. *Nature Reviews. Neuroscience* 6(2): 119–130.

Fredrickson BL (2001) The role of positive emotions in positive psychology: The broaden-and-build theory of positive emotions. *The American Psychologist* 56(3): 218–226.

Frey U and Morris RG (1997) Synaptic tagging and long-term potentiation. *Nature* 385(6616): 533–536.

Frey U and Morris RG (1998) Synaptic tagging: Implications for late maintenance of hippocampal long-term potentiation. *Trends in Neurosciences* 21(5): 181–188.

Frey U, Schroeder H, and Matthies H (1990) Dopaminergic antagonists prevent long-term maintenance of posttetanic LTP in the CA1 region of rat hippocampal slices. *Brain Research* 522(1): 69–75.

Frey U, Matthies H, Reymann KG, and Matthies H (1991) The effect of dopaminergic D1 receptor blockade during tetanization on the expression of long-term potentiation in the rat CA1 region in vitro. *Neuroscience Letters* 129(1): 111–114.

Frey U, Huang YY, and Kandel ER (1993) Effects of cAMP simulate a late stage of LTP in hippocampal CA1 neurons. *Science* 260(5114): 1661–1664.

Gaddy MA and Ingram RE (2014) A meta-analytic review of mood-congruent implicit memory in depressed mood. *Clinical Psychology Review* 34(5): 402–416.

Galli G, Sirota M, Gruber MJ, Ivanof BE, Ganesh J, Materassi M, Thorpe A, Loaiza V, Cappelletti M, and Craik FIM (2018) Learning facts during aging: The benefits of curiosity. *Experimental Aging Research* 44(4): 311–328.

Gallo FT, Zanoni Saad MB, Silva A, Morici JF, Miranda M, Anderson MC, Weisstaub NV, and Bekinschtein P (2022) Dopamine modulates adaptive forgetting in medial prefrontal cortex. *The Journal of Neuroscience* 42(34): 6620–6636.

Gariano RF and Groves PM (1988) Burst firing induced in midbrain dopamine neurons by stimulation of the medial prefrontal and anterior cingulate cortices. *Brain Research* 462(1): 194–198.

Garrison J, Erdeniz B, and Done J (2013) Prediction error in reinforcement learning: A meta-analysis of neuroimaging studies. *Neuroscience and Biobehavioral Reviews* 37(7): 1297–1310.

Gasbarri A, Packard MG, Campana E, and Pacitti C (1994a) Anterograde and retrograde tracing of projections from the ventral tegmental area to the hippocampal formation in the rat. *Brain Research Bulletin* 33(4): 445–452.

Gasbarri A, Verney C, Innocenzi R, Campana E, and Pacitti C (1994b) Mesolimbic dopaminergic neurons innervating the hippocampal formation in the rat: A combined retrograde tracing and immunohistochemical study. *Brain Research* 668(1-2): 71–79.

Gasbarri A, Sulli A, and Packard MG (1997) The dopaminergic mesencephalic projections to the hippocampal formation in the rat. *Progress in Neuro-Psychopharmacology & Biological Psychiatry* 21(1): 1–22.

Genzel L, Rossato JI, Jacobse J, Grieves RM, Spooner PA, Battaglia FP, Fernández G, and Morris RGM (2017) The Yin and Yang of memory consolidation: Hippocampal and neocortical. *PLoS Biology* 15(1): e2000531.

Gershman SJ (2014) Dopamine ramps are a consequence of reward prediction errors. *Neural Computation* 26(3): 467–471.

Gilboa A and Marlatte H (2017) Neurobiology of schemas and schema-mediated memory. *Trends in Cognitive Sciences* 21(8): 618–631.

Gomperts SN, Kloosterman F, and Wilson MA (2015) VTA neurons coordinate with the hippocampal reactivation of spatial experience. *eLife* 4. https://doi.org/10.7554/eLife.05360.

Gönner L, Baeuchl C, Glöckner F, Riedel P, Smolka MN, and Li S-C (2023) Levodopa suppresses grid-like activity and impairs spatial learning in novel environments in healthy young adults. *Cerebral Cortex* 33(23): 11247–11256.

Grace AA and Bunney BS (1984) The control of firing pattern in nigral dopamine neurons: Single spike firing. *The Journal of Neuroscience* 4(11): 2866–2876.

Grace AA, Floresco SB, Goto Y, and Lodge DJ (2007) Regulation of firing of dopaminergic neurons and control of goal-directed behaviors. *Trends in Neurosciences* 30(5): 220–227.

Grieder TE, George O, Tan H, George SR, Le Foll B, Laviolette SR, and van der Kooy D (2012) Phasic D1 and tonic D2 dopamine receptor signaling double dissociate the motivational effects of acute nicotine and chronic nicotine withdrawal. *Proceedings of the National Academy of Sciences of the United States of America* 109(8): 3101–3106.

Grogan JP, Tsivos D, Smith L, Knight BE, Bogacz R, Whone A, and Coulthard EJ (2017) Effects of dopamine on reinforcement learning and consolidation in Parkinson's disease. *eLife* 6. https://doi.org/10.7554/eLife.26801.

Gruber MJ and Ranganath C (2019) How curiosity enhances hippocampus-dependent memory: The prediction, appraisal, curiosity, and exploration (PACE) framework. *Trends in Cognitive Sciences* 23(12): 1014–1025.

Gruber MJ, Gelman BD, and Ranganath C (2014) States of curiosity modulate hippocampus-dependent learning via the dopaminergic circuit. *Neuron* 84(2): 486–496.

Gruber MJ, Ritchey M, Wang S-F, Doss MK, and Ranganath C (2016) Post-learning hippocampal dynamics promote preferential retention of rewarding events. *Neuron* 89(5): 1110–1120.

Gueguen MCM, Schweitzer EM, and Konova AB (2021) Computational theory-driven studies of reinforcement learning and decision-making in addiction: What have we learned? *Current Opinion in Behavioral Sciences* 38: 40–48.

Guo JY, Ragland JD, and Carter CS (2019) Memory and cognition in schizophrenia. *Molecular Psychiatry* 24(5): 633–642.

Hamid AA, Pettibone JR, Mabrouk OS, Hetrick VL, Schmidt R, Vander Weele CM, Kennedy RT, Aragona BJ, and Berke JD (2016) Mesolimbic dopamine signals the value of work. *Nature Neuroscience* 19(1): 117–126.

Hampson M (2021) *fMRI Neurofeedback*. Academic Press.

Han S, Huettel SA, Raposo A, Adcock RA, and Dobbins IG (2010) Functional significance of striatal responses during episodic decisions: Recovery or goal attainment? *The Journal of Neuroscience* 30(13): 4767–4775.

Hardt O, Nader K, and Nadel L (2013) Decay happens: The role of active forgetting in memory. *Trends in Cognitive Sciences* 17(3): 111–120.

Harmon-Jones E, Gable PA, and Price TF (2013) Does negative affect always narrow and positive affect always broaden the mind? Considering the influence of motivational intensity on cognitive scope. *Current Directions in Psychological Science* 22(4): 301–307.

Hassabis D and Maguire EA (2009) The construction system of the brain. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences* 364(1521): 1263–1271.

Haugg A, Sladky R, Skouras S, McDonald A, Craddock C, Kirschner M, Herdener M, Koush Y, Papoutsi M, Keynan JN, Hendler T, Cohen Kadosh K, Zich C, MacInnes J, Adcock A, Dickerson K, Chen N, Young K, Bodurka J, et al. (2020) Can we predict real-time fMRI neurofeedback learning success from pretraining brain activity? *Human Brain Mapping* 41(14): 3839–3854.

Haugg A, Renz FM, Nicholson AA, Lor C, Götzendorfer SJ, Sladky R, Skouras S, McDonald A, Craddock C, Hellrung L, Kirschner M, Herdener M, Koush Y, Papoutsi M, Keynan J, Hendler T, Cohen Kadosh K, Zich C, Kohl SH, et al. (2021) Predictors of real-time fMRI neurofeedback performance and improvement—A machine learning mega-analysis. *NeuroImage* 237: 118207.

Hauser TU, Eldar E, Purg N, Moutoussis M, and Dolan RJ (2019) Distinct roles of dopamine and noradrenaline in incidental memory. *The Journal of Neuroscience* 39(39): 7715–7721.

Hellrung L, Kirschner M, Sulzer J, Sladky R, Scharnowski F, Herdener M, and Tobler PN (2022) Analysis of individual differences in neurofeedback training illuminates successful self-regulation of the dopaminergic midbrain. *Communications Biology* 5(1): 845.

Hess TM (2014) Selective engagement of cognitive resources: Motivational influences on older adults' cognitive functioning. *Perspectives on Psychological Science* 9(4): 388–407.

Hollup SA, Molden S, Donnett JG, Moser MB, and Moser EI (2001) Accumulation of hippocampal place fields at the goal location in an annular watermaze task. *The Journal of Neuroscience* 21(5): 1635–1644.

Hon N and Yeo N (2021) Having a sense of agency can improve memory. *Psychonomic Bulletin & Review*. https://doi.org/10.3758/s13423-020-01849-x.

Horvitz JC (2000) Mesolimbocortical and nigrostriatal dopamine responses to salient non-reward events. *Neuroscience* 96(4): 651–656.

Horwath EA, Rouhani N, DuBrow S, and Murty VP (2023) Value restructures the organization of free recall. *Cognition* 231: 105315.

Howe MW, Tierney PL, Sandberg SG, Phillips PEM, and Graybiel AM (2013) Prolonged dopamine signalling in striatum signals proximity and value of distant rewards. *Nature* 500(7464): 575–579.

Howes OD and Kapur S (2009) The dopamine hypothesis of schizophrenia: Version III—The final common pathway. *Schizophrenia Bulletin* 35(3): 549–562.

Hsiung A, Poh J-H, Huettel SA, and Adcock RA (2023) Curiosity evolves as information unfolds. *Proceedings of the National Academy of Sciences of the United States of America* 120(43): e2301974120.

Huang YY and Kandel ER (1995) D1/D5 receptor agonists induce a protein synthesis-dependent late potentiation in the CA1 region of the hippocampus [Review of D1/D5 receptor agonists induce a protein synthesis-dependent late potentiation in the CA1 region of the hippocampus]. *Proceedings of the National Academy of Sciences of the United States of America* 92(7): 2446–2450.

Hunger L, Kumar A, and Schmidt R (2020) Abundance compensates kinetics: Similar effect of dopamine signals on D1 and D2 receptor populations. *The Journal of Neuroscience* 40(14): 2868–2881.

Huys QJM, Maia TV, and Frank MJ (2016) Computational psychiatry as a bridge from neuroscience to clinical applications. *Nature Neuroscience* 19(3): 404–413.

Imai H, Kim D, Sasaki Y, and Watanabe T (2014) Reward eliminates retrieval-induced forgetting. *Proceedings of the National Academy of Sciences* 111(48): 17326–17329.

Ishino S, Kamada T, Sarpong GA, Kitano J, Tsukasa R, Mukohira H, Sun F, Li Y, Kobayashi K, Naoki H, Oishi N, and Ogawa M (2023) Dopamine error signal to actively cope with lack of expected reward. *Science Advances* 9(10): eade5420.

Isingrini E, Perret L, Rainer Q, Amilhon B, Guma E, Tanti A, Martin G, Robinson J, Moquin L, Marti F, Mechawar N, Williams S, Gratton A, and Giros B (2016) Resilience to chronic stress is mediated by noradrenergic regulation of dopamine neurons. *Nature Neuroscience* 19(4): 560–563.

Isotalus HK, Carr WJ, Blackman J, Averill GG, Radtke O, Selwood J, Williams R, Ford E, McCullagh L, McErlane J, O'Donnell C, Durant C, Bartsch U, Jones MW, Muñoz-Neira C, Wearn AR, Grogan JP, and Coulthard EJ (2023) L-DOPA increases slow-wave sleep duration and selectively modulates memory persistence in older adults. *Frontiers in Behavioral Neuroscience* 17: 1096720.

Jang AI, Nassar MR, Dillon DG, and Frank MJ (2019) Positive reward prediction errors during decision-making strengthen memory encoding. *Nature Human Behaviour*. https://doi.org/10.1038/s41562-019-0597-3.

Jay TM (2003) Dopamine: A potential substrate for synaptic plasticity and memory mechanisms. *Progress in Neurobiology* 69(6): 375–390.

Johnson A and Redish AD (2007) Neural ensembles in CA3 transiently encode paths forward of the animal at a decision point. *The Journal of Neuroscience* 27(45): 12176–12189.

Kafkas A and Montaldi D (2018) How do memory systems detect and respond to novelty? *Neuroscience Letters* 680: 60–68.

Kahn I and Shohamy D (2012) Intrinsic connectivity between the hippocampus, nucleus accumbens, and ventral tegmental area in humans. *Hippocampus* 23(3): 187–192.

Kahnt T (2018) A decade of decoding reward-related fMRI signals and where we go from here. *NeuroImage* 180(Pt A): 324–333.

Kakade S and Dayan P (2002) Dopamine: Generalization and bonuses. *Neural Networks* 15(4-6): 549–559.

Káli S and Dayan P (2004) Off-line replay maintains declarative memories in a model of hippocampal-neocortical interactions. *Nature Neuroscience* 7(3): 286–294.

Kang MJ, Hsu M, Krajbich IM, Loewenstein G, McClure SM, Wang JT-Y, and Camerer CF (2009) The wick in the candle of learning: Epistemic curiosity activates reward circuitry and enhances memory. *Psychological Science* 20(8): 963–973.

Keiflin R and Janak PH (2015) Dopamine prediction errors in reward learning and addiction: From theory to neural circuitry. *Neuron* 88(2): 247–263.

Kempadoo KA, Mosharov EV, Choi SJ, Sulzer D, and Kandel ER (2016) Dopamine release from the locus coeruleus to the dorsal hippocampus promotes spatial learning and memory. *Proceedings of the National Academy of Sciences* 113(51): 14835–14840.

Kensinger EA (2007) Negative emotion enhances memory accuracy: Behavioral and neuroimaging evidence. *Current Directions in Psychological Science* 16(4): 213–218.

Kentros CG, Agnihotri NT, Streater S, Hawkins RD, and Kandel ER (2004) Increased attention to spatial context increases both place field stability and spatial memory. *Neuron* 42(2): 283–295.

Kim HR, Malik AN, Mikhael JG, Bech P, Tsutsui-Kimura I, Sun F, Zhang Y, Li Y, Watabe-Uchida M, Gershman SJ, and Uchida N (2020) A unified framework for dopamine signals across timescales. *Cell* 183(6): 1600–1616.e25.

Kinder KT and Buss AT (2021) The effect of motor engagement on memory: Testing a motor-induced encoding account. *Memory & Cognition* 49(3): 586–599.

King DR, de Chastelaine M, Elward RL, Wang TH, and Rugg MD (2018) Dissociation between the neural correlates of recollection and familiarity in the striatum and hippocampus: Across-study convergence. *Behavioural Brain Research* 354: 1–7.

Kinsky NR, Sullivan DW, Mau W, Hasselmo ME, and Eichenbaum HB (2018) Hippocampal place fields maintain a coherent and flexible map across long timescales. *Current Biology: CB* 28(22): 3578–3588.e6.

Knecht S, Breitenstein C, Bushuven S, Wailke S, Kamping S, Flöel A, Zwitserlood P, and Ringelstein EB (2004) Levodopa: Faster and better word learning in normal humans. *Annals of Neurology* 56(1): 20–26.

Knight R (1996) Contribution of human hippocampal region to novelty detection. *Nature* 383(6597): 256–259.

Knowlton BJ and Castel AD (2021) Memory and reward-based learning: A value-directed remembering perspective. *Annual Review of Psychology*. https://doi.org/10.1146/annurev-psych-032921-050951.

Koch G, Esposito Z, Codecà C, Mori F, Kusayanagi H, Monteleone F, Di Lorenzo F, Bernardi G, and Martorana A (2011) Altered dopamine modulation of LTD-like plasticity in Alzheimer's disease patients. *Clinical Neurophysiology* 122(4): 703–707.

Koch G, Di Lorenzo F, Bonnì S, Giacobbe V, Bozzali M, Caltagirone C, and Martorana A (2014) Dopaminergic modulation of cortical plasticity in Alzheimer's disease patients. *Neuropsychopharmacology* 39(11): 2654–2661.

Koch G, Motta C, Bonnì S, Pellicciari MC, Picazio S, Casula EP, Maiella M, Di Lorenzo F, Ponzo V, Ferrari C, Scaricamazza E, Caltagirone C, and Martorana A (2020) Effect of rotigotine vs placebo on cognitive functions among patients with mild to moderate Alzheimer disease: A randomized clinical trial. *JAMA Network Open* 3(7): e2010372.

Koob GF and Volkow ND (2010) Neurocircuitry of addiction. *Neuropsychopharmacology* 35(1): 217–238.

Krebs RM, Heipertz D, Schuetze H, and Duzel E (2011) Novelty increases the mesolimbic functional connectivity of the substantia nigra/ventral tegmental area (SN/VTA) during reward anticipation: Evidence from high-resolution fMRI. *NeuroImage* 58(2): 647–655.

Krishnan S, Heer C, Cherian C, and Sheffield MEJ (2022) Reward expectation extinction restructures and degrades CA1 spatial maps through loss of a dopaminergic reward proximity signal. *Nature Communications* 13(1): 6662.

Kuhbandner C, Aslan A, Emmerdinger K, and Murayama K (2016) Providing extrinsic reward for test performance undermines long-term memory acquisition. *Frontiers in Psychology* 7: 79.

Kuhl BA, Shah AT, DuBrow S, and Wagner AD (2010) Resistance to forgetting associated with hippocampus-mediated reactivation during new learning. *Nature Neuroscience*. http://www.nature.com/neuro/journal/v13/n4/abs/nn.2498.html.

Kulla A and Manahan-Vaughan D (2000) Depotentiation in the dentate gyrus of freely moving rats is modulated by D1/D5 dopamine receptors. *Cerebral Cortex* 10(6): 614–620.

Kumaran D and Maguire EA (2007) Which computational mechanisms operate in the hippocampus during novelty detection? *Hippocampus* 17(9): 735–748.

Kumaran D, Hassabis D, and McClelland JL (2016) What learning systems do intelligent agents need? Complementary learning systems theory updated. *Trends in Cognitive Sciences* 20(7): 512–534.

Kusuki T, Imahori Y, Ueda S, and Inokuchi K (1997) Dopaminergic modulation of LTP induction in the dentate gyrus of intact brain. *Neuroreport* 8(8): 2037–2040.

Kutlu MG and Gould TJ (2016) Effects of drugs of abuse on hippocampal plasticity and hippocampus-dependent learning and memory: Contributions to development and maintenance of addiction. *Learning & Memory* 23(10): 515–533.

LaConte SM (2011) Decoding fMRI brain states in real-time. *NeuroImage* 56(2): 440–454.

Lammel S, Hetzel A, Häckel O, Jones I, Liss B, and Roeper J (2008) Unique properties of mesoprefrontal neurons within a dual mesocorticolimbic dopamine system. *Neuron* 57(5): 760–773.

Lammel S, Ion DI, Roeper J, and Malenka RC (2011) Projection-specific modulation of dopamine neuron synapses by aversive and rewarding stimuli. *Neuron* 70(5): 855–862.

Lee T-H, Greening SG, Ueno T, Clewett D, Ponzio A, Sakaki M, and Mather M (2018) Arousal increases neural gain via the locus coeruleus-norepinephrine system in younger adults but not in older adults. *Nature Human Behaviour* 2(5): 356–366.

Leonard SK, Petitto JM, Anderson CM, Mooney DH, Lachowicz JE, Schulz DW, Kilts CD, and Mailman RB (2003) D1 dopamine receptors in the amygdala exhibit unique properties. *Annals of the New York Academy of Sciences* 985(1): 536–539.

Lerner TN, Holloway AL, and Seiler JL (2021) Dopamine, updated: Reward prediction error and beyond. *Current Opinion in Neurobiology* 67: 123–130.

Li S, Cullen WK, Anwyl R, and Rowan MJ (2003) Dopamine-dependent facilitation of LTP induction in hippocampal CA1 by exposure to spatial novelty. *Nature Neuroscience* 6(5): 526–531.

Li F, Wang LP, Shen X, and Tsien JZ (2010) Balanced dopamine is critical for pattern completion during associative memory recall. *PLoS One* 5(10): e15401.

Lisman JE and Grace AA (2005) The Hippocampal-VTA loop: Controlling the entry of information into long-term memory. *Neuron* 46(5): 703–713.

Lisman JE and Otmakhova NA (2001) Storage, recall, and novelty detection of sequences by the hippocampus: Elaborating on the SOCRATIC model to account for normal and aberrant effects of dopamine. *Hippocampus* 11(5): 551–568.

Lisman JE, Grace AA, and Duzel E (2011) A neoHebbian framework for episodic memory; role of dopamine-dependent late LTP. *Trends in Neurosciences* 34(10): 536–547.

Liu Y, Dolan RJ, Kurth-Nelson Z, and Behrens TEJ (2019) Human replay spontaneously reorganizes experience. *Cell* 178(3): 640–652.e14.

Liu S, Dolan RJ, and Heinz A (2020) Translation of computational psychiatry in the context of addiction. *JAMA Psychiatry* 77(11): 1099–1100.

Liu Y, Mattar MG, Behrens TEJ, Daw ND, and Dolan RJ (2021) Experience replay is associated with efficient nonlocal learning. *Science* 372(6544). https://doi.org/10.1126/science.abf1357.

Lloyd K and Dayan P (2015) Tamping ramping: Algorithmic, implementational, and computational explanations of phasic dopamine signals in the accumbens. *PLoS Computational Biology* 11(12): e1004622.

Lodge DJ and Grace AA (2006) The hippocampus modulates dopamine neuron responsivity by regulating the intensity of phasic neuron activation. *Neuropsychopharmacology* 31(7): 1356–1361.

Lodge DJ and Grace AA (2011) Hippocampal dysregulation of dopamine system function and the pathophysiology of schizophrenia. *Trends in Pharmacological Sciences* 32(9): 507–513.

Lohani S, Poplawsky AJ, Kim S-G, and Moghaddam B (2017) Unexpected global impact of VTA dopamine neuron activation as measured by opto-fMRI. *Molecular Psychiatry* 22(4): 585–594.

Luo AH, Tahsili-Fahadan P, Wise RA, Lupica CR, and Aston-Jones G (2011) Linking context with reward: A functional circuit from hippocampal CA3 to ventral tegmental area. *Science* 333(6040): 353–357.

Lydon-Staley DM, Zhou D, Blevins AS, Zurn P, and Bassett DS (2021) Hunters, busybodies and the knowledge network building associated with deprivation curiosity. *Nature Human Behaviour* 5(3): 327–336.

MacInnes JJ, Dickerson KC, Chen N-K, and Adcock RA (2016) Cognitive neurostimulation: Learning to volitionally sustain ventral tegmental area activation. *Neuron* 89(6): 1331–1342.

Mackintosh NJ (1975) A theory of attention: Variations in the associability of stimuli with reinforcement. *Psychological Review* 82(4): 276–298.

Madan CR, Scott SME, and Kensinger EA (2019) Positive emotion enhances association-memory. *Emotion* 19(4): 733–740.

Maia TV and Frank MJ (2011) From reinforcement learning models to psychiatric and neurological disorders. *Nature Neuroscience* 14(2): 154–162.

Mamad O, Stumpp L, McNamara HM, Ramakrishnan C, Deisseroth K, Reilly RB, and Tsanov M (2017) Place field assembly distribution encodes preferred locations. *PLoS Biology* 15(9): e2002365.

Marini F, Marzi T, and Viggiano MP (2011) "Wanted!" The effects of reward on face recognition: Electrophysiological correlates. *Cognitive, Affective, & Behavioral Neuroscience* 11(4): 627–643.

Martig AK and Mizumori SJY (2011) Ventral tegmental area disruption selectively affects CA1/CA2 but not CA3 place fields during a differential reward working memory task. *Hippocampus* 21(2): 172–184.

Mather M and Sutherland MR (2011) Arousal-biased competition in perception and memory. *Perspectives on Psychological Science* 6(2): 114–133.

Mau W, Hasselmo ME, and Cai DJ (2020) The brain in motion: How ensemble fluidity drives memory-updating and flexibility. *eLife* 9. https://doi.org/10.7554/eLife.63550.

McClelland JL, McNaughton BL, and O'Reilly RC (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. *Psychological Review* 102(3): 419.

McClernon FJ, Conklin CA, Kozink RV, Adcock RA, Sweitzer MM, Addicott MA, Chou Y-H, Chen N-K, Hallyburton MB, and DeVito AM (2016) Hippocampal and insular response to smoking-related environments: Neuroimaging evidence for drug-context effects in nicotine dependence. *Neuropsychopharmacology* 41(3): 877–885.

McFadyen J, Liu Y, and Dolan RJ (2023) Differential replay of reward and punishment paths predicts approach and avoidance. *Nature Neuroscience* 26(4): 627–637.

McGillivray S, Murayama K, and Castel AD (2015) Thirst for knowledge: The effects of curiosity and interest on memory in younger and older adults. *Psychology and Aging* 30(4): 835–841.

McNamara CG and Dupret D (2017) Two sources of dopamine for the hippocampus [Review of Two sources of dopamine for the hippocampus]. *Trends in Neurosciences* 40(7): 383–384.

Mejias-Aponte CA (2016) Specificity and impact of adrenergic projections to the midbrain dopamine system. *Brain Research* 1641(Pt B): 258–273.

Michon F, Sun J-J, Kim CY, Ciliberti D, and Kloosterman F (2019) Post-learning hippocampal replay selectively reinforces spatial memory for highly rewarded locations. *Current Biology* 29(9): 1436–1444.e5.

Mikhael JG, Kim HR, Uchida N, and Gershman SJ (2022) The role of state uncertainty in the dynamics of dopamine. *Current Biology*. https://doi.org/10.1016/j.cub.2022.01.025.

Miller WR (1983) Motivational interviewing with problem drinkers. *Behavioural and Cognitive Psychotherapy* 11(2): 147–172.

Miller WR and Rollnick S (2009) Ten things that motivational interviewing is not. *Behavioural and Cognitive Psychotherapy* 37(2): 129–140.

Mohebi A, Pettibone JR, Hamid AA, Wong J-MT, Vinson LT, Patriarchi T, Tian L, Kennedy RT, and Berke JD (2019) Dissociable dopamine dynamics for learning and motivation. *Nature*. https://doi.org/10.1038/s41586-019-1235-y.

Mollick JA and Kober H (2020) Computational models of drug use and addiction: A review. *Journal of Abnormal Psychology* 129(6): 544–555.

Monte-Silva K, Kuo M-F, Thirugnanasambandam N, Liebetanz D, Paulus W, and Nitsche MA (2009) Dose-dependent inverted U-shaped effect of dopamine (D2-like) receptor activation on focal and nonfocal plasticity in humans. *The Journal of Neuroscience* 29(19): 6124–6131.

Morales M and Margolis EB (2017) Ventral tegmental area: Cellular heterogeneity, connectivity and behaviour. *Nature Reviews. Neuroscience* 18(2): 73–85.

Morcom AM, Bullmore ET, Huppert FA, Lennox B, Praseedom A, Linnington H, and Fletcher PC (2010) Memory encoding and dopamine in the aging brain: A psychopharmacological neuroimaging study. *Cerebral Cortex* 20(3): 743–757.

Morgan DG, May PC, and Finch CE (1987) Dopamine and serotonin systems in human and rodent brain: Effects of age and neurodegenerative disease. *Journal of the American Geriatrics Society* 35(4): 334–345.

Moser EI, Kropff E, and Moser M-B (2008) Place cells, grid cells, and the brain's spatial representation system. *Annual Review of Neuroscience* 31: 69–89.

Murase S, Grenhoff J, Chouvet G, Gonon FG, and Svensson TH (1993) Prefrontal cortex regulates burst firing and transmitter release in rat mesolimbic dopamine neurons studied in vivo. *Neuroscience Letters* 157(1): 53–56.

Murayama K, Matsumoto M, Izuma K, and Matsumoto K (2010) Neural basis of the undermining effect of monetary reward on intrinsic motivation. *Proceedings of the National Academy of Sciences of the United States of America* 107(49): 20911–20916.

Murty VP and Adcock RA (2014) Enriched encoding: Reward motivation organizes cortical networks for hippocampal detection of unexpected events. *Cerebral Cortex* 24(8): 2160–2168.

Murty VP and Adcock RA (2017) Distinct medial temporal lobe network states as neural contexts for motivated memory formation. In: Hannula DE and Duff MC (eds.) *The Hippocampus from Cells to Systems: Structure, Connectivity, and Functional Contributions to Memory and Flexible Cognition*, pp. 467–501. Springer International Publishing.

Murty VP and Dickerson KC (2016) Motivational influences on memory. In: Kim S-I, Reeve J, and Bong M (eds.) *Advances in Motivation and Achievement*, vol. 19, pp. 203–227. Emerald Group Publishing Limited.

Murty VP, LaBar KS, Hamilton DA, and Adcock RA (2011) Is all motivation good for learning? Dissociable influences of approach and avoidance motivation in declarative memory. *Learning & Memory* 18(11): 712–717.

Murty VP, DuBrow S, and Davachi L (2015) The simple act of choosing influences declarative memory. *The Journal of Neuroscience* 35(16): 6255–6264.

Murty VP, FeldmanHall O, Hunter LE, Phelps EA, and Davachi L (2016) Episodic memories predict adaptive value-based decision-making. *Journal of Experimental Psychology. General* 145(5): 548–558.

Murty VP, Ballard IC, and Adcock RA (2017a) Hippocampus and prefrontal cortex predict distinct timescales of activation in the human ventral tegmental area. *Cerebral Cortex* 27(2): 1660–1669.

Murty VP, Tompary A, Adcock RA, and Davachi L (2017b) Selectivity in postencoding connectivity with high-level visual cortex is associated with reward-motivated memory. *The Journal of Neuroscience* 37(3): 537–545.

Muzzio IA, Kentros C, and Kandel E (2009) What is remembered? Role of attention on the encoding and retrieval of hippocampal representations. *The Journal of Physiology* 587(Pt 12): 2837–2854.

Newman EL and Norman KA (2010) Moderate excitation leads to weakening of perceptual representations. *Cerebral Cortex* 20(11): 2760–2770.

Niv Y (2007) Cost, benefit, tonic, phasic: What do response rates tell us about dopamine and motivation? *Annals of the New York Academy of Sciences* 1104(1): 357–376.

Niv Y, Daw N, and Dayan P (2005) How fast to work: Response vigor, motivation and tonic dopamine. *Advances in Neural Information Processing Systems* 18. https://proceedings.neurips.cc/paper_files/paper/2005/hash/3812f9a59b634c2a9c574610eaba5bed-Abstract.html.

Niv Y, Daw ND, Joel D, and Dayan P (2007) Tonic dopamine: Opportunity costs and the control of response vigor. *Psychopharmacology* 191(3): 507–520.

Nobili A, Latagliata EC, Viscomi MT, Cavallucci V, Cutuli D, Giacovazzo G, Krashia P, Rizzo FR, Marino R, Federici M, De Bartolo P, Aversa D, Dell'Acqua MC, Cordella A, Sancandi M, Keller F, Petrosini L, Puglisi-Allegra S, Mercuri NB, et al. (2017) Dopamine neuronal loss contributes to memory and reward dysfunction in a model of Alzheimer's disease. *Nature Communications* 8: 14727.

Norman KA, Newman EL, and Detre G (2007) A neural network model of retrieval-induced forgetting. *Psychological Review* 114(4): 887–953.

O'Doherty JP (2004) Reward representations and reward-related learning in the human brain: Insights from neuroimaging. *Current Opinion in Neurobiology* 14(6): 769–776.

O'Keefe J (1976) Place units in the hippocampus of the freely moving rat. *Experimental Neurology* 51(1): 78–109.

O'Keefe J and Conway DH (1978) Hippocampal place units in the freely moving rat: Why they fire where they fire. *Experimental Brain Research* 31(4): 573–590.

O'Keefe J and Dostrovsky J (1971) The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Research* 34(1): 171–175.

O'Reilly RC and Norman KA (2002) Hippocampal and neocortical contributions to memory: Advances in the complementary learning systems framework. *Trends in Cognitive Sciences* 6(12): 505–510.

Oades RD and Halliday GM (1987) Ventral tegmental (A10) system: Neurobiology. 1. Anatomy and connectivity. *Brain Research* 434(2): 117–165.

Otmakhova NA and Lisman JE (1996) D1/D5 dopamine receptor activation increases the magnitude of early long-term potentiation at CA1 hippocampal synapses. *The Journal of Neuroscience* 16(23): 7478–7486.

Otmakhova NA and Lisman JE (1998) D1/D5 dopamine receptors inhibit depotentiation at CA1 synapses via cAMP-dependent mechanism. *The Journal of Neuroscience* 18(4): 1270–1279.

Otmakhova NA, Duzel E, Deutch AY, and Lisman J (2013) The Hippocampal-VTA loop: The role of novelty and motivation in controlling the entry of information into long-term memory. In: Baldassarre G and Mirolli M (eds.) *Intrinsically Motivated Learning in Natural and Artificial Systems*, pp. 235–254. Berlin Heidelberg: Springer.

Oyarzún JP, Packard PA, de Diego-Balaguer R, and Fuentemilla L (2016) Motivated encoding selectively promotes memory for future inconsequential semantically-related events. *Neurobiology of Learning and Memory* 133: 1–6.

Panlilio LV and Goldberg SR (2007) Self-administration of drugs in animals and humans as a model and an investigative tool. *Addiction* 102(12): 1863–1870.

Patil A, Murty VP, Dunsmoor JE, Phelps EA, and Davachi L (2016) Reward retroactively enhances memory consolidation for related items. *Learning & Memory* 24(1): 65–69.

Pearce JM and Hall G (1980) A model for Pavlovian learning: Variations in the effectiveness of conditioned but not of unconditioned stimuli. *Psychological Review* 87(6): 532–552.

Pessiglione M, Seymour B, Flandin G, Dolan RJ, and Frith CD (2006) Dopamine-dependent prediction errors underpin reward-seeking behaviour in humans. *Nature* 442(7106): 1042–1045.

Pizzagalli DA (2014) Depression, stress, and anhedonia: Toward a synthesis and integrated model. *Annual Review of Clinical Psychology* 10: 393–423.

Poh J-H, Vu M-AT, Stanek JK, Hsiung A, Egner T, and Adcock RA (2022) Hippocampal convergence during anticipatory midbrain activation promotes subsequent memory formation. *Nature Communications* 13(1): 6729.

Poldrack RA, Clark J, Pare-Blagoev EJ, and Shohamy D (2001) Interactive memory systems in the human brain. *Nature* 414(6863): 546–550.

Preston AR and Eichenbaum H (2013) Interplay of hippocampus and prefrontal review cortex in memory. *CURBIO* 23(17): R764–R773.

Quent JA and Henson RN (2022) Novel immersive virtual reality experiences do not produce retroactive memory benefits for unrelated material. *Quarterly Journal of Experimental Psychology* 75(12): 2197–2210.

Ramot M and Martin A (2022) Closed-loop neuromodulation for studying spontaneous activity and causality. *Trends in Cognitive Sciences* 26(4): 290–299.

Rance M, Walsh C, Sukhodolsky DG, Pittman B, Qiu M, Kichuk SA, Wasylink S, Koller WN, Bloch M, Gruner P, Scheinost D, Pittenger C, and Hampson M (2018) Time course of clinical change following neurofeedback. *NeuroImage* 181: 807–813.

Ranganath C and Ritchey M (2012) Two cortical systems for memory- guided behaviour. *Nature Reviews. Neuroscience* 13(10): 1–14.

Ranganath C, Minzenberg MJ, and Ragland JD (2008) The cognitive neuroscience of memory function and dysfunction in schizophrenia. *Biological Psychiatry* 64(1): 18–25.

Rangel-Barajas C, Coronel I, and Florán B (2015) Dopamine receptors and neurodegeneration. *Aging and Disease* 6(5): 349–368.

Redish AD (2004) Addiction as a computational process gone awry. *Science* 306(5703): 1944–1947.

Redondo RL and Morris RGM (2011) Making memories last: The synaptic tagging and capture hypothesis. *Nature Reviews. Neuroscience* 12(1): 17–30.

Ripollés P, Ferreri L, Mas-Herrero E, Alicart H, Gómez-Andrés A, Marco-Pallares J, Antonijoan RM, Noesselt T, Valle M, Riba J, and Rodriguez-Fornells A (2018) Intrinsically regulated learning is modulated by synaptic dopamine signaling. *eLife* 7. https://doi.org/10.7554/eLife.38113.

Ritvo VJH, Turk-Browne NB, and Norman KA (2019) Nonmonotonic plasticity: How memory retrieval drives learning. *Trends in Cognitive Sciences* 23(9): 726–742.

Robbins TW, Ersche KD, and Everitt BJ (2008) Drug addiction and the memory systems of the brain. *Annals of the New York Academy of Sciences* 1141: 1–21.

Rogerson T, Cai DJ, Frank A, Sano Y, Shobe J, Lopez-Aranda MF, and Silva AJ (2014) Synaptic tagging during memory allocation. *Nature Reviews. Neuroscience* 15(3): 157–169.

Rosen ZB, Cheung S, and Siegelbaum SA (2015) Midbrain dopamine neurons bidirectionally regulate CA3-CA1 synaptic drive. *Nature Neuroscience* 18(12): 1763–1771.

Rossato JI, Bevilaqua LRM, Izquierdo I, Medina JH, and Cammarota M (2009) Dopamine controls persistence of long-term memory storage. *Science* 325(5943): 1017–1020.

Rouhani N and Niv Y (2019) Depressive symptoms bias the prediction-error enhancement of memory towards negative events in reinforcement learning. *Psychopharmacology* 236(8): 2425–2435.

Rouhani N and Niv Y (2021) Signed and unsigned reward prediction errors dynamically enhance learning and memory. *eLife* 10. https://doi.org/10.7554/eLife.61077.

Rouhani N, Norman KA, Niv Y, and Bornstein AM (2020) Reward prediction errors create event boundaries in memory. *Cognition* 203: 104269.

Rouhani N, Niv Y, Frank MJ, and Schwabe L (2023) Multiple routes to enhanced memory for emotionally relevant events. *Trends in Cognitive Sciences*. https://doi.org/10.1016/j.tics.2023.06.006.

Ruiz NA, DuBrow S, and Murty VP (2023) Agency as a bridge to form associative memories. *Journal of Experimental Psychology. General* 152(6): 1797–1813.

Rupprechter S, Romaniuk L, Series P, Hirose Y, Hawkins E, Sandu AL, and Steele JD (2020) Blunted medial prefrontal cortico-limbic reward-related effective connectivity and depression. *Brain* 143(6): 1946–1956.

Ryan TJ and Frankland PW (2022) Forgetting as a form of adaptive engram cell plasticity. *Nature Reviews. Neuroscience* 23(3): 173–186.

Sajikumar S and Frey JU (2004) Late-associativity, synaptic tagging, and the role of dopamine during LTP and LTD. *Neurobiology of Learning and Memory* 82(1): 12–25.

Salamone JD (1994) The involvement of nucleus accumbens dopamine in appetitive and aversive motivation. *Behavioural Brain Research* 61(2): 117–133.

Salamone JD and Correa M (2012) The mysterious motivational functions of mesolimbic dopamine. *Neuron* 76(3): 470–485.

Samson Y, Wu JJ, Friedman AH, and Davis JN (1990) Catecholaminergic innervation of the hippocampus in the cynomolgus monkey. *The Journal of Comparative Neurology* 298(2): 250–263.

Sarno S, Beirán M, Falcó-Roget J, Diaz-deLeon G, Rossi-Pool R, Romo R, and Parga N (2022) Dopamine firing plays a dual role in coding reward prediction errors and signaling motivation in a working memory task. *Proceedings of the National Academy of Sciences of the United States of America* 119(2). https://doi.org/10.1073/pnas.2113311119.

Sawaguchi T and Goldman-Rakic PS (1994) The role of D1-dopamine receptor in working memory: Local injections of dopamine antagonists into the prefrontal cortex of rhesus monkeys performing an oculomotor delayed-response task. *Journal of Neurophysiology* 71(2): 515–528.

Scatton B, Simon H, Le Moal M, and Bischoff S (1980) Origin of dopaminergic innervation of the rat hippocampal formation. *Neuroscience Letters* 18(2): 125–131.

Schomaker J, van Bronkhorst MLV, and Meeter M (2014) Exploring a novel environment improves motivation and promotes recall of words. *Frontiers in Psychology* 5: 918.

Schott BH, Sellner DB, Lauer C-J, Habib R, Frey JU, Guderian S, Heinze H-J, and Düzel E (2004) Activation of midbrain structures by associative novelty and the formation of explicit memory in humans. *Learning & Memory* 11(4): 383–387.

Schott BH, Minuzzi L, Krebs RM, Elmenhorst D, Lang M, Winz OH, Seidenbecher CI, Coenen HH, Heinze H-J, Zilles K, Düzel E, and Bauer A (2008) Mesolimbic functional magnetic resonance imaging activations during reward anticipation correlate with reward-related ventral striatal dopamine release. *The Journal of Neuroscience* 28(52): 14311–14319.

Schuck NW and Niv Y (2019) Sequential replay of nonspatial task states in the human hippocampus. *Science* 364(6447): eaaw5181.

Schultz W (1986) Responses of midbrain dopamine neurons to behavioral trigger stimuli in the monkey. *Journal of Neurophysiology* 56(5): 1439–1461.

Schultz W (1998) Predictive reward signal of dopamine neurons. *Journal of Neurophysiology* 80(1): 1–27.

Schultz W and Romo R (1990) Dopamine neurons of the monkey midbrain: Contingencies of responses to stimuli eliciting immediate behavioral reactions. *Journal of Neurophysiology* 63(3): 607–624.

Schultz W, Dayan P, and Montague PR (1997) A neural substrate of prediction and reward. *Science* 275(5306): 1593–1599.

Scimeca JM and Badre D (2012) Striatal contributions to declarative memory retrieval. *Neuron* 75(3): 380–392.

Seamans JK and Yang CR (2004) The principal features and mechanisms of dopamine modulation in the prefrontal cortex. *Progress in Neurobiology* 74(1): 1–58.

Seamans JK, Gorelova N, Durstewitz D, and Yang CR (2001) Bidirectional dopamine modulation of GABAergic inhibition in prefrontal cortical pyramidal neurons. *The Journal of Neuroscience* 21(10): 3628–3638.

Serra L, D'Amelio M, Di Domenico C, Dipasquale O, Marra C, Mercuri NB, Caltagirone C, Cercignani M, and Bozzali M (2018) In vivo mapping of brainstem nuclei functional connectivity disruption in Alzheimer's disease. *Neurobiology of Aging* 72: 72–82.

Sesack SR and Pickel VM (1992) Prefrontal cortical efferents in the rat synapse on unlabeled neuronal targets of catecholamine terminals in the nucleus accumbens septi and on dopamine neurons in the ventral tegmental area. *The Journal of Comparative Neurology* 320(2): 145–160.

Sharp ME, Duncan K, Foerde K, and Shohamy D (2020) Dopamine is associated with prioritization of reward-associated memories in Parkinson's disease. *Brain: A Journal of Neurology* 143(8): 2519–2531.

Sharpe MJ, Chang CY, Liu MA, Batchelor HM, Mueller LE, Jones JL, Niv Y, and Schoenbaum G (2017) Dopamine transients are sufficient and necessary for acquisition of model-based associations. *Nature Neuroscience* 20(5): 735–742.

Sharpe MJ, Batchelor HM, Mueller LE, Yun Chang C, Maes EJP, Niv Y, and Schoenbaum G (2020) Dopamine transients do not act as model-free prediction errors during associative learning. *Nature Communications* 11(1): 106.

Sheynikhovich D, Otani S, and Arleo A (2013) Dopaminergic control of long-term depression/long-term potentiation threshold in prefrontal cortex. *The Journal of Neuroscience* 33(34): 13914–13926.

Shigemune Y, Tsukiura T, Kambara T, and Kawashima R (2014) Remembering with gains and losses: Effects of monetary reward and punishment on successful encoding activation of source memories. *Cerebral Cortex* 24(5): 1319–1331.

Shohamy D (2011) Learning and motivation in the human striatum. *Current Opinion in Neurobiology* 21(3): 408–414.

Shohamy D and Adcock RA (2010) Dopamine and adaptive memory. *Trends in Cognitive Sciences* 14(10): 464–472.

Shohamy D and Wagner AD (2008) Integrating memories in the human brain: Hippocampal-midbrain encoding of overlapping events. *Neuron*. http://www.sciencedirect.com/science/article/pii/S0896627308008052.

Simons JS and Spiers HJ (2003) Prefrontal and medial temporal lobe interactions in long-term memory. *Nature Reviews. Neuroscience* 4(8): 637–648.

Sinclair AH and Barense MD (2019) Prediction error and memory reactivation: How incomplete reminders drive reconsolidation. *Trends in Neurosciences* 42(10): 727–739.

Sinclair AH, Wang YC, and Adcock RA (2023) Instructed motivational states bias reinforcement learning and memory formation. *Proceedings of the National Academy of Sciences of the United States of America* 120(31): e2304881120.

Sitaram R, Ros T, Stoeckel L, Haller S, Scharnowski F, Lewis-Peacock J, Weiskopf N, Blefari ML, Rana M, Oblak E, Birbaumer N, and Sulzer J (2016) Closed-loop brain training: The science of neurofeedback. *Nature Publishing Group* 18(2): 1–16.

Snyder SH (1976) The dopamine hypothesis of schizophrenia: Focus on the dopamine receptor. *The American Journal of Psychiatry* 133(2): 197–202.

Song MR and Lee SW (2020) Dynamic resource allocation during reinforcement learning accounts for ramping and phasic dopamine activity. *Neural Networks* 126: 95–107.

Sorg BA (2012) Reconsolidation of drug memories. *Neuroscience and Biobehavioral Reviews* 36(5): 1400–1417.

Squire LR, Stark CEL, and Clark RE (2004) The medial temporal lobe. *Annual Review of Neuroscience* 27(1): 279–306.

Stacho M and Manahan-Vaughan D (2022) The intriguing contribution of hippocampal long-term depression to spatial learning and long-term memory. *Frontiers in Behavioral Neuroscience* 16: 806356.

Stalnaker TA, Howard JD, Takahashi YK, Gershman SJ, Kahnt T, and Schoenbaum G (2019) Dopamine neuron ensembles signal the content of sensory prediction errors. *eLife* 8: 16.

Stanek JK, Dickerson KC, Chiew KS, Clement NJ, and Adcock RA (2019) Expected reward value and reward uncertainty have temporally dissociable effects on memory formation. *Journal of Cognitive Neuroscience* 31(10): 1443–1454.

Staresina BP, Alink A, Kriegeskorte N, and Henson RN (2013) Awake reactivation predicts memory in humans. *Proceedings of the National Academy of Sciences* 110(52): 21159–21164.

Steinberg EE, Keiflin R, Boivin JR, Witten IB, Deisseroth K, and Janak PH (2013) A causal link between prediction errors, dopamine neurons and learning. *Nature Neuroscience* 16(7): 966–973.

Storm BC (2011) The benefit of forgetting in thinking and remembering. *Current Directions in Psychological Science* 20(5): 291–295.

Straube T, Korz V, Balschun D, and Frey JU (2003) Requirement of beta-adrenergic receptor activation and protein synthesis for LTP-reinforcement by novelty in rat dentate gyrus. *The Journal of Physiology* 552(Pt 3): 953–960.

Sulzer J, Sitaram R, Blefari ML, Kollias S, Birbaumer N, Stephan KE, Luft A, and Gassert R (2013) Neurofeedback-mediated self-regulation of the dopaminergic midbrain. *NeuroImage* 83: 817–825.

Sutton RS and Barto AG (1998) Reinforcement learning: An introduction. *IEEE Transactions on Neural Networks* 9(5): 1054.

Swanson LW (1982) The projections of the ventral tegmental area and adjacent regions: A combined fluorescent retrograde tracer and immunofluorescence study in the rat. *Brain Research Bulletin* 9(1-6): 321–353.

Swanson-Park JL, Coussens CM, Mason-Parker SE, Raymond CR, Hargreaves EL, Dragunow M, Cohen AS, and Abraham WC (1999) A double dissociation within the hippocampus of dopamine D1/D5 receptor and beta-adrenergic receptor contributions to the persistence of long-term potentiation. *Neuroscience* 92(2): 485–497.

Swant J and Wagner JJ (2006) Dopamine transporter blockade increases LTP in the CA1 region of the rat hippocampus via activation of the D3 dopamine receptor. *Learning & Memory* 13(2): 161–167.

Takahashi YK, Batchelor HM, Liu B, Khanna A, Morales M, and Schoenbaum G (2017) Dopamine neurons respond to errors in the prediction of sensory features of expected rewards. *Neuron* 95(6): 1395–1405.e3.

Takeuchi T, Duszkiewicz AJ, Sonneborn A, Spooner PA, Yamasaki M, Watanabe M, Smith CC, Fernández G, Deisseroth K, Greene RW, and Morris RGM (2016) Locus coeruleus and dopaminergic consolidation of everyday memory. *Nature* 537(7620): 357–362.

Talarico JM, Berntsen D, and Rubin DC (2009) Positive emotions enhance recall of peripheral details. *Cognition & Emotion* 23(2): 380–398.

Tambini A and Davachi L (2013) Persistence of hippocampal multivoxel patterns into postencoding rest is related to memory. *Proceedings. National Academy of Sciences. United States of America*. https://doi.org/10.1073/pnas.1308499110/-/DCSupplemental.

Tambini A, Ketz N, and Davachi L (2010) Enhanced brain correlations during rest are related to memory for recent experiences. *Neuron* 65(2): 280–290.

Tang W, Kochubey O, Kintscher M, and Schneggenburger R (2020) A VTA to basal amygdala dopamine projection contributes to signal salient somatosensory events during fear learning. *The Journal of Neuroscience* 40(20): 3969–3980.

Taschereau-Dumouchel V, Cushing CA, and Lau H (2022) Real-time functional MRI in the treatment of mental health disorders. *Annual Review of Clinical Psychology* 18: 125–154.

Taylor JR, Olausson P, Quinn JJ, and Torregrossa MM (2009) Targeting extinction and reconsolidation mechanisms to combat the impact of drug cues on addiction. *Neuropharmacology* 56(Suppl. 1): 186–195.

Thibault RT, MacPherson A, Lifshitz M, Roth RR, and Raz A (2018) Neurofeedback with fMRI: A critical systematic review. *NeuroImage* 172: 786–807.

Thurm F, Schuck NW, Fauser M, Doeller CF, Stankevich Y, Evens R, Riedel O, Storch A, Lueken U, and Li S-C (2016) Dopamine modulation of spatial navigation memory in Parkinson's disease. *Neurobiology of Aging* 38: 93–103.

Torregrossa MM and Taylor JR (2013) Learning to forget: Manipulating extinction and reconsolidation processes to treat addiction. *Psychopharmacology* 226(4): 659–672.

Totah NKB, Kim Y, and Moghaddam B (2013) Distinct prestimulus and poststimulus activation of VTA neurons correlates with stimulus detection. *Journal of Neurophysiology* 110(1): 75–85.

Trantham-Davidson H, Neely LC, Lavin A, and Seamans JK (2004) Mechanisms underlying differential D1 versus D2 dopamine receptor regulation of inhibition in prefrontal cortex. *The Journal of Neuroscience* 24(47): 10652–10659.

Treadway MT and Zald DH (2013) Parsing anhedonia: Translational models of reward-processing deficits in psychopathology. *Current Directions in Psychological Science* 22(3): 244–249.

Tsai H-C, Zhang F, Adamantidis A, Stuber GD, Bonci A, de Lecea L, and Deisseroth K (2009) Phasic firing in dopaminergic neurons is sufficient for behavioral conditioning. *Science* 324(5930): 1080–1084.

Tsetsenis T, Badyna JK, Wilson JA, Zhang X, Krizman EN, Subramaniyan M, Yang K, Thomas SA, and Dani JA (2021) Midbrain dopaminergic innervation of the hippocampus is sufficient to modulate formation of aversive memories. *Proceedings of the National Academy of Sciences of the United States of America* 118(40). https://doi.org/10.1073/pnas.2111069118.

Tursic A, Eck J, Lührs M, Linden DEJ, and Goebel R (2020) A systematic review of fMRI neurofeedback reporting and effects in clinical populations. *NeuroImage Clinical* 28: 102496.

Undieh AS (2010) Pharmacology of signaling induced by dopamine D(1)-like receptor activation. *Pharmacology & Therapeutics* 128(1): 37–60.

van Kesteren MTR, Ruiter DJ, Fernández G, and Henson RN (2012) How schema and novelty augment memory formation. *Trends in Neurosciences* 35(4): 211–219.

Walton ME and Bouret S (2019) What is the relationship between dopamine and effort? *Trends in Neurosciences* 42(2): 79–91.

Wang S-H and Morris RGM (2010) Hippocampal-neocortical interactions in memory formation, consolidation, and reconsolidation. *Annual Review of Psychology* 61(49–79): C1–C4.

Watanabe T, Sasaki Y, Shibata K, and Kawato M (2017) Advances in fMRI Real-time neurofeedback. *Trends in Cognitive Sciences* 21(12): 997–1010.

Wehe HS, Rhodes MG, and Seger CA (2015) Evidence for the negative impact of reward on self-regulated learning. *Quarterly Journal of Experimental Psychology* 68(11): 2125–2130.

Wei X, Ma T, Cheng Y, Huang CCY, Wang X, Lu J, and Wang J (2018) Dopamine D1 or D2 receptor-expressing neurons in the central nervous system. *Addiction Biology* 23(2): 569–584.

Weiskopf N (2012) Real-time fMRI and its application to neurofeedback. *NeuroImage* 62(2): 682–692.

Wessel JR, Danielmeier C, Morton JB, and Ullsperger M (2012) Surprise and error: Common neuronal architecture for the processing of errors and novelty. *The Journal of Neuroscience* 32(22): 7528–7537.

Westbrook A and Braver TS (2016) Dopamine does double duty in motivating cognitive effort. *Neuron* 89(4): 695–710.

Westbrook A, van den Bosch R, Määttä JI, Hofmans L, Papadopetraki D, Cools R, and Frank MJ (2020) Dopamine promotes cognitive effort by biasing the benefits versus costs of cognitive work. *Science* 367(6484): 1362–1366.

Williams GV and Goldman-Rakic PS (1995) Modulation of memory fields by dopamine D1 receptors in prefrontal cortex. *Nature* 376(6541): 572–575.

Wimmer GE and Shohamy D (2012) Preference by association: How memory mechanisms in the hippocampus bias decisions. *Science* 338(6104): 270–273.

Wimmer GE, Braun EK, Daw ND, and Shohamy D (2014) Episodic memory encoding interferes with reward learning and decreases striatal prediction errors. *The Journal of Neuroscience* 34(45): 14901–14912.

Wise RA (2004) Dopamine, learning and motivation. *Nature Reviews. Neuroscience* 5(6): 483–494.

Wittkuhn L and Schuck NW (2021) Dynamics of fMRI patterns reflect sub-second activation sequences and reveal replay in human visual cortex. *Nature Communications* 12(1): 1795.

Wittmann BC, Schott BH, Guderian S, Frey JU, Heinze H-J, and Düzel E (2005) Reward-related FMRI activation of dopaminergic midbrain is associated with enhanced hippocampus-dependent long-term memory formation. *Neuron* 45(3): 459–467.

Wittmann BC, Bunzeck N, Dolan RJ, and Düzel E (2007) Anticipation of novelty recruits reward system and hippocampus while promoting recollection. *NeuroImage* 38(1): 194–202.

Wolosin SM, Zeithamova D, and Preston AR (2012) Reward modulation of hippocampal subfield activation during successful associative encoding and retrieval. *Journal of Cognitive Neuroscience* 24(7): 1532–1547.

Wolosin SM, Zeithamova D, and Preston AR (2013) Distributed hippocampal patterns that discriminate reward context are associated with enhanced associative binding. *Journal of Experimental Psychology. General* 142(4): 1264–1276.

Yebra M, Galarza-Vallejo A, Soto-Leon V, Gonzalez-Rosa JJ, de Berker AO, Bestmann S, Oliviero A, Kroes MCW, and Strange BA (2019) Action boosts episodic memory encoding in humans via engagement of a noradrenergic system. *Nature Communications* 10(1): 3534.

Yonelinas AP and Ritchey M (2015) The slow forgetting of emotional episodic memories: An emotional binding account. *Trends in Cognitive Sciences* 19(5): 259–267.

Young KD, Siegle GJ, Zotev V, Phillips R, Misaki M, Yuan H, Drevets WC, and Bodurka J (2017) Randomized clinical trial of real-time fMRI amygdala neurofeedback for major depressive disorder: Effects on symptoms and autobiographical memory recall. *The American Journal of Psychiatry* 174(8): 748–755.

Yu Q, Liu Y-Z, Zhu Y-B, Wang Y-Y, Li Q, and Yin D-M (2019) Genetic labeling reveals temporal and spatial expression pattern of D2 dopamine receptor in rat forebrain. *Brain Structure & Function* 224(3): 1035–1049.

Zacks JM, Speer NK, Swallow KM, Braver TS, and Reynolds JR (2007) Event perception: A mind-brain perspective. *Psychological Bulletin* 133(2): 273–293.

Zacks JM, Kurby CA, Eisenberg ML, and Haroutunian N (2011) Prediction error associated with the perceptual segmentation of naturalistic events. *Journal of Cognitive Neuroscience* 23(12): 4057–4066.

Zeithamova D, Gelman BD, Frank L, and Preston AR (2018) Abstract representation of prospective reward in the hippocampus. *The Journal of Neuroscience*: 718–719.

Zweifel LS, Parker JG, Lobb CJ, Rainwater A, Wall VZ, Fadok JP, Darvas M, Kim MJ, Mizumori SJY, Paladini CA, Phillips PEM, and Palmiter RD (2009) Disruption of NMDAR-dependent burst firing by dopamine neurons provides selective assessment of phasic dopamine-dependent behavior. *Proceedings of the National Academy of Sciences of the United States of America* 106(18): 7281–7288.