

**NEURAL CORRELATES OF DECISION UNCERTAINTY
AND MEMORY ENHANCEMENT DURING
HYPOTHESIS TESTING**

A Dissertation
Submitted to
the Temple University Graduate Board

In Partial Fulfillment
of the Requirements for the Degree
DOCTOR OF PHILOSOPHY

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August 2024

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ABSTRACT

Humans are motivated to actively seek information to reduce uncertainty, which have been shown to alter episodic memory (Shen et al., 2022). Specifically, we found that uncertainty during hypothesis testing was both linearly and quadratically related to episodic memory. Yet, little is known about the neural mechanisms underlying how hypothesis testing relates to subsequent memory. In the current fMRI study, 40 participants were presented with three multi-dimension keys. They were instructed to figure out the target feature of a key to open a treasure chest. Reinforcement learning model was used to capture decision uncertainty around different features of the keys. We replicated our prior findings and showed that a reinforcement learning model captured hypothesis-testing behavior and there was a quadratic relationship between decision uncertainty and memory, such that memory was enhanced at the intermediate level of decision uncertainty. In terms of neural results, we found that the quadratic term of decision uncertainty was coded in the ventral striatum. We also found that decreasing decision uncertainty was related to greater activation in the ventral striatum, anterior and posterior hippocampus, and ventromedial prefrontal cortex, while increasing decision uncertainty was related to greater activation in the ventral tegmental area. More importantly, we found that activation in the ventral striatum in response to the quadratic term of decision uncertainty correlated with the quadratic relationship between decision uncertainty and memory, such that participants with greater activation in the ventral striatum showed a more pronounced quadratic relationship between decision uncertainty and memory. Together, this work extends existing research on how uncertainty influences memory via changes in motivation in the framework of hypothesis testing.

ACKNOWLEDGMENTS

I would like to extend my deepest gratitude to my advisors, Dr. Deepu Murty and Dr. David Smith, for their unwavering support and guidance throughout this research journey. Their mentorship has been invaluable to me, both professionally and personally. I am so grateful, and I will always cherish my time working with them.

I am also grateful to my colleagues in the Adaptive Memory Lab - Nick Ruiz, Elizabeth Horwath, Ga In Shin, David Gregory, Steven Martinez, Isabel Leiva, Büşra Tanrıverdi, Blake Elliott and Lena Skalaban, and the Neuroeconomics Lab - Daniel Sazhin, Jen Yang, Jimmy Wyngaarden, Melanie Kos, Tia Tropea, Avi Dachs and Cooper Sharp for their advice in this project and my previous work. Their insights have spurred my thinking in many ways. Special thanks to Isabel Leiva, Ga In Shin, David Gregory, Avi Dachs, Cooper Sharp, Sheila Jimenez, Ashley Hawk, and Enes Yanilmaz for their assistance in recruitment and data collection. I must also acknowledge the support from Dr. Ian Ballard and his insights on reinforcement learning models and analyses for this project.

On a personal note, I thank my parents Lifang Wang and Qiang Shen, my sibling Xinyi Shen, my partner Weiyi Gong, and all my friends for their endless love and encouragement.

This dissertation would not have been possible without the contributions and support of each one of you.

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CHAPTER 1

1. OVERVIEW OF HYPOTHESIS TESTING AND MEMORY

Hypothesis testing is a fundamental cognitive process wherein individuals generate, evaluate, and refine predictions within uncertain environments. This iterative process entails a continuous adjustment of prior beliefs in response to new evidence, aiming to enhance decision accuracy and reduce uncertainty (Oaksford & Chater, 2007). Hypothesis testing is crucial in daily scenarios requiring individuals to make decisions by accumulating information from incomplete or ambiguous data. For example, a shopper in an unfamiliar grocery store might hypothesize that milk is typically located in the back corners, based on previous experiences. If the milk is not found in the expected location, it prompts further hypothesis testing – the shopper will search for another hypothesized location until the milk is found. Different strategies can be used during hypothesis testing. For example, either methodically searching aisle by aisle or organizing the search around grocery concepts like dairy or beverages.

Further, hypothesis testing is suggested to enhance memory. Previous research indicates that exploration enhances memory by stimulating cognitive engagement, motivation, and attentional processes, which in turn facilitate deeper encoding and improved retrieval of information (Schomaker et al., 2022; Schomaker & Wittmann, 2021). Recently, we conducted a study to explicitly test the role of hypothesis testing on episodic memory formation, which confirmed that hypothesis testing enhances memory (Shen et al., 2022). These memory enhancements are beneficial, even for incidental information, as they may enhance future decision-making by enabling refined hypothesis

generation based on newly encoded memories. For instance, remembering the actual location of milk can lead to more efficient navigation during subsequent visits.

What, then, underlies the enhancement of memory through hypothesis testing? Our previous research suggests that changes in decision uncertainty and motivational states during hypothesis testing provide a plausible explanation (Shen et al., 2022). A growing body of literature has explored intrinsic motivational states during information seeking, revealing an inverted U-shaped relationship with task difficulty during problem-solving (Metcalf & Kornell, 2003, 2005). Specifically, individuals exhibit peak motivation when facing problems of intermediate task difficulty, which correspondingly leads to the most significant reduction in uncertainty (Metcalf & Kornell, 2003). Within the framework of hypothesis testing, we propose that resolving moderate levels of uncertainty should likewise induce a heightened motivational state.

Motivation has been shown to enhance memory by activating neural pathways that prioritize and reinforce the encoding of goal-relevant information (Murty & Dickerson, 2016). The dopaminergic pathway, in particular, is implicated in motivation, facilitating deeper information processing and enhancing memory encoding and consolidation (Lisman & Grace, 2005; Murty & Dickerson, 2016). Research has demonstrated that when participants are given the agency to select the information, a very simple manipulation of motivated information seeking, there is a notable improvement in memory performance (Murty et al., 2015). This enhancement is attributed to the interaction between the mesolimbic and declarative memory systems, which manifested as interactions across the striatum and hippocampus, respectively.

Despite significant advances in understanding the behavioral and neurobiological aspects of information-seeking and memory, research that directly connects these domains within the context of hypothesis testing is still limited. Addressing this gap could profoundly enrich our understanding of how cognitive processes like hypothesis testing interact with motivational states to influence memory.

1.1 Roadmap to this Dissertation

The goal of this dissertation is to understand the neural representation of decision uncertainty during hypothesis testing and its downstream influence on memory. In Chapter 1, we first provide a theoretical background that is necessary to understand the individual concepts we hope to integrate in this work. This includes an overview of information-seeking/hypothesis-testing behavior via the lens of motivation, the influence of motivation on memory, and the interaction between the two systems. Each section includes a discussion of behavioral work as well as the neural bases supporting each process. In Chapter 2, we provide a consolidated introduction to the dissertation work, followed by the specific research methods and analyses. Chapter 3 includes the results of the study and a brief summary of the findings. Chapter 4 includes a more in-depth discussion of the results interpreted in the context of the broader theoretical frameworks reviewed in Chapter 1, limitations of the current study, and some future directions.

1.2 Theoretical Background

1.2.1 Motivation as a Lens for Understanding Information-seeking Behaviors.

We propose that a heightened motivational state underpins the memory enhancement observed during hypothesis testing. To elucidate the neural mechanisms

behind hypothesis testing and its effect on memory, it is crucial to first understand information-seeking and hypothesis-testing behaviors through the lens of motivation.

A growing body of research has explored intrinsic motivational states during information-seeking activities, revealing an inverted U-shaped relationship with task difficulty in problem-solving contexts (Metcalf & Kornell, 2003, 2005). According to the region of proximal learning theory, individuals, when offered a choice, preferentially allocate their study time to items of intermediate difficulty rather than to those that are easiest or most difficult (Metcalf & Kornell, 2005). For instance, Atkinson's (1972) study on optimal learning strategies found that the most effective approach involved focusing on partially learned items rather than on those easily remembered or not yet learned (Atkinson, 1972). This suggests that engaging with items that are neither too challenging nor too simplistic is most conducive to achieving study objectives, thereby maximizing motivation for items of intermediate difficulty.

This research underscores the connection between motivation and information acquisition, indicating that information within the region of proximal learning is most valuable for guiding decisions, with individuals showing the greatest motivation to pursue this information. Relatedly, results of two behavioral experiments found that people tended to seek more information about face-name associations in a subsequent restudy phase for names with feelings of knowing experience (Brooks et al., 2021). Participants have also been found to be more curious in a tip-of-tongue state, where a person is temporarily unable to retrieve a word from memory though they have a strong feeling that they know it and may recall partial information about it. Research showed that participants were roughly twice as likely to want to see the answer when they were in

a tip-of-tongue state as when they were not (Metcalf et al., 2020), implicating a high motivational state induced by an intermediate level of uncertainty during information-seeking.

In the context of hypothesis testing, individuals test various hypotheses with the aim of reducing decision uncertainty and achieving specific goals. We suggest that decision uncertainty during hypothesis testing mirrors trial difficulty in the problem-solving context and affects individuals' judgment of learning, with trials of moderate decision uncertainty posing intermediate difficulty. Given the inverted U-shaped relationship between task difficulty and motivation to resolve the problem prior research has shown (Metcalf & Kornell, 2003, 2005), we suggest that trials of intermediate decision uncertainty are most likely to spur motivation to resolve uncertainty in the context of hypothesis testing.

What, then, is the neural basis of information-seeking? Prior studies and review have established the crucial role of dopamine in driving motivated behavior for information seeking (Dayan, 2009; Eschmann et al., 2023; Shen et al., 2023; Vellani et al., 2020). Direct evidence from animal studies, such as those involving mice with elevated dopamine levels, demonstrates the involvement of the dopaminergic system in enhanced motivation (Cagniard et al., 2006). Key subcortical regions like the ventral tegmental area (VTA) and the substantia nigra (SN) are believed to facilitate information-seeking behaviors. For example, human research indicates that information-seeking behavior correlates with increased activity and functional connectivity in the mesolimbic dopaminergic system, particularly between the VTA and nucleus accumbens (NAcc), emphasizing the importance of the dopaminergic system in information-seeking

behaviors (Brydevall et al., 2018; Charpentier et al., 2018; Lau et al., 2020). Additionally, increased activation in the SN/VTA and ventral striatum has been observed in response to information about potential gains (Charpentier et al., 2018). Finally, information prediction error signals have been identified in dopamine-rich brain regions (E. Bromberg-Martin & Monosov, 2020; E. S. Bromberg-Martin & Hikosaka, 2009)

The interaction between the ventral striatum and the ventromedial prefrontal cortex (vmPFC) is also critical for information-seeking behavior. The ventral striatum, which receives dopaminergic inputs from the VTA, plays a pivotal role in processing reward signals and motivational salience, essential for valuing information and influencing subsequent decision-making processes (Schultz, 2006; Tricomi & Fiez, 2012). Concurrently, the BOLD signal in vmPFC has often been shown to correlate with the current subjective value of various different types of choices during decision-making (Hunt et al., 2012; McNamee et al., 2013; Walton et al., 2015). vmPFC has also been suggested to be involved in comparing decision inputs (values) between the chosen and unchosen options (Hunt et al., 2012). These evidence point towards an important role for vmPFC in assessing the values of different behavioral options to optimize goal-directed decision-making during information-seeking (Hunt et al., 2012). The ventral striatum and vmPFC might also communicate with the vmPFC to process decisions related to subjective value of options (Euston et al., 2012).

Together, we suggest that VTA, the ventral striatum, and the ventromedial prefrontal cortex constitute a vital network that dynamically regulates information-seeking behaviors, driven by underlying motivational states and the anticipated rewards of the information obtained. These interactions highlight the significance of the VTA,

ventral striatum, and vmPFC in supporting motivation-related brain circuits that adaptively guide information-seeking, ensuring behaviors align with the current goals. We further suggest that these regions might be crucial for hypothesis testing and the heightened motivational state observed during decisions of moderate uncertainty as well.

1.2.2 Memory Systems: Interaction Between Motivational States and Episodic Memory

Behavioral studies have consistently shown that motivational states such as agency and curiosity significantly enhance memory encoding (M. Gruber & Ranganath, 2019, 2019; Murphy et al., 2020; Murty et al., 2015). For example, individuals show enhanced memory when they engage in tasks where they can exercise choice (Murty et al., 2015; Ruiz et al., 2023). Moreover, substantial evidence suggests that curiosity motivates and energizes an individual to seek information to relieve that state (Eschmann et al., 2023; FitzGibbon et al., 2020; Murphy et al., 2020), which enhances memory. For example, in one prior study, participants were presented with a list of trivia questions associated with high curiosity and low curiosity. Results showed that participants' memory was better for both the trivia questions and for the faces (incidental information during the trial) associated with high curiosity than low curiosity (Gruber et al., 2014). Together, these findings suggest that a high motivational state enhances memory encoding behaviorally.

The medial temporal lobe (MTL) is central to the neurobiological processes underpinning memory, as evidenced by extensive research involving both animal models and human subjects (Eichenbaum et al., 2007). The MTL, comprising structures like the hippocampus and the surrounding cortexes, is vital for episodic memory encoding. Evidence comes from prior research showing that hippocampal-damaged patients showed

impaired recognition (Eichenbaum et al., 2007). Furthermore, functional MRI studies have validated the role of the MTL in both encoding and retrieving episodic memories, highlighting its importance across memory processes (H. Kim, 2011; Spaniol et al., 2009).

Motivational influences on memory are mediated through the integration of the MTL with motivation-associated brain regions. The MTL is intricately connected to the motivational circuitry, including the ventral tegmental area (VTA), ventral striatum, and ventromedial prefrontal cortex (vmPFC), part of the mesolimbic and mesocortical pathways. This connectivity is crucial for the motivational modulation of memory. The VTA-hippocampal loop, as proposed by Lisman and Grace (2005), illustrates how dopamine released in response to novelty signals from the hippocampus to the VTA facilitates long-term potentiation, crucial for embedding new information into long-term memory (Lisman & Grace, 2005).

Neuroimaging studies on agency and curiosity further illustrated the influence of motivational states on memory enhancements, mediated by dopaminergic activity. Prior research suggested that high curiosity levels triggered by a trivia question activate the ventral striatum and hippocampus, predicting memory enhancements for the answers (Gruber et al., 2014). Moreover, variations in curiosity-induced activity in the SN/VTA and hippocampus, along with their functional connectivity, predict the degree of memory enhancements for incidental images viewed during curiosity states (M. J. Gruber et al., 2014a; M. Gruber & Ranganath, 2019).

Additionally, research suggests that anticipation of making choices is associated with increased activity in the ventral striatum (Wang and Delgado, 2019). Another

research on perceived agency revealed that anticipatory activation of the striatum associated with decision-making is important for choice-induced memory enhancements in behavior. Specifically, anticipatory signals in the striatum during the decision phase were associated with subsequent memory effects in the hippocampus, suggesting a modulatory relationship of the striatum over the hippocampus (Murty et al., 2015). Together, these results illustrate how the interaction between the dopaminergic system and the hippocampus is fundamental for memory enhancement driven by motivation.

1.2.3 The Impact of Decision Uncertainty on Memory Encoding During Hypothesis Testing

We have discussed the behavioral and neural evidence related to information-seeking behavior and motivated memory. Despite these insights, the effects of information-seeking in uncertain environments on memory, particularly within the context of hypothesis testing, remain poorly understood. We propose that a high motivational state induced at an intermediate level of decision uncertainty is the critical underlying mechanism. Therefore, the objective of this dissertation is to integrate research on information-seeking and motivated memory within a hypothesis-testing framework to further elucidate the complex relationships among these factors.

In the framework of hypothesis testing, behaviorally, we suggest that hypothesis testing requires an assessment of the relative uncertainty in the environment. These assessments likely influence episodic memory by modulating the internal motivational state during encoding, given that prior research showed an inverted U-shaped relationship between motivation and task difficulty (Metcalf & Kornell, 2003, 2005). Notably, in the hypothesis testing paradigm, we suggest that an intermediate level of decision uncertainty may foster a state of heightened motivational state, enhancing memory retention not only

for the direct targets of the goal but also for various incidental information in the environment (Murty & Adcock, 2014a).

To test whether a high motivational state induced by decision uncertainty facilitates memory encoding during hypothesis testing, we designed a hypothesis-testing task in which participants need to figure out rules to unlock treasure chests using different strategies (Shen et al., 2022). We adapted the task from another paradigm that characterized resolving uncertainty in a multi-featured decision-making task (Niv et al., 2015). On each trial, participants were given three different keys that differed on three different dimensions and only one correct feature could unlock the closed treasure chest. Participants completed a surprise recognition task after about 24 hours of delay. We found that a feature reinforcement learning model was able to capture the decision-making process in the hypothesis testing task. Using the feature reinforcement learning model, we observed that participants formulated and tested hypotheses about target features and extended this learning to new stimuli, suggesting that individuals learned high-order concepts during hypothesis testing (Shen et al., 2022). Furthermore, we found that hypothesis testing enhanced incidental memory (trial-unique object in the treasure chest) compared to a visuo-motor-matched control condition (Shen et al., 2022). Importantly, memory enhancements were only apparent when participants experienced moderate levels of decision uncertainty, derived from the feature reinforcement learning model, which theoretically represents the peak motivational state for information seeking. These findings support our prediction that decision uncertainty during hypothesis testing bolsters memory encoding for incidental information encountered during exploration.

However, since we did not directly measure motivational states in this behavioral study, our interpretations might be considered speculative. To address this, in this dissertation we conducted a follow-up neuroimaging study using the same hypothesis-testing paradigm to explore the neural representations of decision uncertainty, motivated memory, and how these different systems interact to support enhanced memory during hypothesis testing.

Considering the literature we discussed above that implicates the dopaminergic system in information-seeking behaviors and motivated memory, we propose that the representation of decision uncertainty during hypothesis testing likely involves the mesolimbic dopaminergic system as well, particularly the ventral tegmental area (VTA) and ventral striatum. The ventral striatum plays a crucial role in assessing and signaling optimal levels of uncertainty (Buzzell et al., 2016), which in turn leads to a high motivational state during hypothesis testing. Other studies have also demonstrated the intricate relationship between dopaminergic activity in the striatum and the encoding of uncertainty related to anticipated rewards during decision-making tasks. Additionally, the prefrontal cortex is pivotal in managing decision uncertainty, with increased activation observed as uncertainty levels rise (Huettel et al., 2005). Given the role of hypothesis testing in reducing decision uncertainty through information accumulation, we anticipate the involvement of the striatum, VTA, and ventromedial prefrontal cortex in representing decision uncertainty during the hypothesis-testing process. We further suggest that these regions might not only be sensitive to the linear term of decision uncertainty but also sensitive to the quadratic term of decision uncertainty, given that behaviorally we found an inverted U-shaped relationship between decision uncertainty and memory (Shen et al.,

2022). It is possible that the ventral striatum, VTA, and vmPFC showed higher activation corresponding to the intermediation level of decision uncertainty than high and low levels of decision uncertainty.

We also suggest that the dopaminergic system's role in motivation may significantly impact memory encoding during hypothesis testing. Enhanced motivation, driven by dopamine release during hypothesis testing, can facilitate the encoding of information into memory by increasing the salience of stimuli, illustrating the relationship between dopamine activity and enhanced hippocampal-dependent memory (Murty & Adcock, 2014a). The hippocampus is pivotal in this process, and subsequent memory effects will be encoded there. The vmPFC, important for integrating value-based information and emotional responses, plays a critical role in decision-making and memory (Lisman & Grace, 2005). It likely interacts with the hippocampus to prioritize which memories are stored based on their perceived value and relevance to future decisions. This interaction assists in encoding memories that are not only based on immediate outcomes but also on how these outcomes align with the goals of the current task.

In all, while research has begun integrating information-seeking and memory through the lens of motivation, significant gaps remain in understanding their interplay within the hypothesis-testing framework. Therefore, this study aims to build on previous behavioral research to replicate the enhanced memory effect during hypothesis testing, to elucidate the neural mechanisms supporting decision uncertainty and subsequent memory effects during hypothesis testing, and to investigate how different brain regions interact to support memory enhancement during hypothesis testing through the lens of motivation.

CHAPTER 2

2. INTRODUCTION TO THE CURRENT STUDY

Humans are motivated to actively seek information to reduce uncertainty, which we have previously shown to alter episodic memory. Hypothesis testing – individuals constantly test and validate beliefs about the surrounding world to reduce uncertainty, is essential during information-seeking. Hypothesis testing has been shown to enhance memory for incidental information, given that prior research showed that individuals are most motivated to resolve problems with intermediate level of difficulty and we suggest that the high motivational state drive enhanced memory effect (Metcalfe & Kornell, 2003; Shen et al., 2022). However, little is known about the neural mechanism underlying this process and how hypothesis testing enhances memory. Therefore, the goal of the current study is to understand the neural mechanisms involved in hypothesis testing and the related enhanced memory effect.

In our recent review of information-seeking, we suggest that information-seeking is determined by motivation for information, invigorated either by instrumental utility or hedonic utility, wherein one's personal or environmental context moderates this relationship (Shen et al., 2023). We further speculate that the final common denominator in guiding information-seeking is the engagement of different neuromodulatory circuits such as the dopaminergic pathway. In the hypothesis testing framework, we suggest that the intrinsic value of acquired information during hypothesis testing and the affirmation of hypotheses are thought to trigger intrinsic rewards, which motivate and reinforce information-seeking behaviors (E. S. Bromberg-Martin & Sharot, 2020; Sharot & Sunstein, 2020), implicating the mesolimbic dopaminergic system—specifically, the

ventral tegmental area (VTA) and striatum (Ballard et al., 2018; E. S. Bromberg-Martin & Hikosaka, 2009; E. S. Bromberg-Martin & Sharot, 2020; Charpentier et al., 2018).

Prior research found heightened activation within the SN/VTA and ventral striatum for information on forthcoming gains (Charpentier et al., 2018). Here, we propose that the ventral striatum and VTA will be important in supporting hypothesis-testing behaviors.

The goal of hypothesis testing is to reduce uncertainty. Therefore, the decision uncertainty level decreased during the process of hypothesis testing with accumulated information (Shen et al., 2022). The representation of decision uncertainty has been suggested to involve the mesolimbic dopaminergic system as well, particularly the ventral tegmental area (VTA) and striatum (Kobayashi & Hsu, 2017). Studies, such as Behrens et al. (2007), illustrated the intricate relationship between dopaminergic activity in the striatum and the encoding of uncertainty tied to anticipated rewards during decision-making tasks (Behrens et al., 2007). Therefore, we hypothesize that the mesolimbic system would play an important role in resolving uncertainty during hypothesis testing. However, few studies have directly tested the involvement of the dopaminergic system, specifically the ventral striatum and the VTA, during hypothesis testing.

Another pivotal area might be involved in the hypothesis testing process is the ventromedial prefrontal cortex (vmPFC), which is essential for goal-directed behaviors and decision-making. vmPFC integrates emotional and cognitive information to guide actions, especially in uncertain situations, playing a crucial role in resolving decision uncertainty by leveraging accumulated information (Huettel et al., 2005). Given that the hypothesis testing process decreases decision uncertainty by accumulating information,

we predict that the striatum, ventral tegmental area, and ventromedial prefrontal cortex will all be involved during hypothesis testing.

In our behavioral paradigm on hypothesis testing and memory, participants were presented with three multi-dimension keys, and they were instructed to figure out the target feature of a key to open a treasure chest. We found a quadratic relationship between decision uncertainty during hypothesis testing and memory accuracy, which is consistent with prior research showing an inverted U-shaped relationship with task difficulty during problem-solving (Metcalf & Kornell, 2003, 2005). We suggest that changes in motivational states during information-seeking could explain this quadratic relationship. Specifically, resolving intermediate levels of uncertainty should lead to the most information uptake and reduction in uncertainty, which leads to the highest motivation to seek information at moderate levels of decision uncertainty. Prior research suggested that individuals' motivational state is important for memory, and dopamine plays a critical role in modulating motivation-related memory encoding and consolidation (Murty et al., 2018; Murty & Adcock, 2014a). We propose that the dopaminergic system's involvement in motivation may impact memory encoding during hypothesis testing, such that enhanced motivation for information driven by dopamine release during hypothesis testing can facilitate the encoding of information into memory by increasing the salience of stimuli, illustrating the relationship between dopamine activity and enhanced hippocampal-dependent memory (Adcock et al., 2006; Murty & Adcock, 2014a).

Overall, the goal of the current study is to directly investigate the neural mechanisms underlying hypothesis testing and the downstream effect on memory. We hypothesize that the ventral striatum, ventral tegmental area, and ventromedial prefrontal

cortex are involved in the hypothesis-testing process. These regions, along with the hippocampus, will also be involved in hypothesis-testing-related memory enhancement. To test these hypotheses, we conducted a neuroimaging study using our previous hypothesis testing study paradigm, combined with reinforcement learning models, to illustrate the neural mechanisms underlying hypothesis testing and the related memory effect.

2.1 Methods

2.1.1 Participants

Forty participants were recruited for this study from the Temple University community. Eligibility criteria include being ages 18-35, no history of neurological disorders, learning disorders, or cognitive impairment, and normal or corrected-to-normal vision. Temple University's Institutional Review Board approved study materials and procedures. All participants provided informed consent and were paid \$60 in total for their time. All forty participants met our performance criteria, and the forty data were used for the behavioral analysis. We set a performance threshold of 14 minutes 30 seconds based on pilot and previous behavior study, given that the hypothesis testing task was self-paced (see description of the task below). Participants who did not complete the hypothesis testing task within the time limit were excluded and did not return for the memory task on the second day (N=40 was after performance exclusion). For neuroimaging analysis, five participants were excluded due to poor image quality. Image quality was defined using the fd_mean and tSNR values from MRIQC (Esteban et al., 2017). Participants were excluded for fd_mean values greater than 1.5 times the interquartile range, or for tSNR values below the lower bound of 1.5 times the

interquartile range, per the distribution from neuroimaging data of otherwise eligible participants. Participants with more than two unusable runs were excluded. This resulted in a final sample of 35 participants for neuroimaging analysis.

2.1.2 Hypothesis Testing Task

The hypothesis testing task took place in the fMRI scanner. We adapted the task from a previous paradigm looking at uncertainty resolution in a multi-featural decision space (Niv et al., 2015). Each run of the hypothesis-testing task started with a 45-second fixation cross, followed by 10 seconds of instructions telling participants to try their best to open as many treasure chests as possible for the task. Then, in the task, participants were presented with a closed treasure chest and three different keys on each trial (Figure 1). Keys differed in three dimensions – key color, key tip shape, and key handle shape. For each dimension, there were three different features (key color: red, yellow, blue; key tip shape: one bar, two bars, three bars; key handle shape: circle, triangle, rectangle), resulting in a total of twenty-seven different keys. For each trial, three of the twenty-seven keys were randomly selected and presented, each representing distinct features. Participants were instructed to choose a key within three seconds, with the goal of opening the treasure chest. They were also instructed that only one target feature could open the treasure chest for a given trial. If participants did not make a choice within three seconds, “too slow” would be presented on the screen for three seconds and the task would be moved to the next trial automatically. After a key was chosen, the chosen key would be highlighted for 0.5 seconds, followed by an inter-stimulus jittered fixation (ISI was from 1s to 3s, with mean = 2s). The time difference between the three-second time limit and reaction time was added to the jittered fixation duration. Then the outcome of

the choice (either closed or open treasure chest) was presented on the screen for three seconds. The treasure chest would open if the participant selected a key that included the target feature and participants would view a trial-unique object inside the treasure chest. The outcomes of the task were deterministic. Treasure chests would open as long as a key with the correct feature was chosen. A jittered inter-trial fixation cross (ITI was from 3s to 5s, with mean = 4s) was presented after trial outcomes. Participants needed to use the outcome of each trial to guide their decision for the next trial. After participants opened 20 treasure chests (encoded 20 images), the current run ended with a 30-second fixation cross. Based on the behavioral study of the hypothesis testing task, to ensure participants were doing the hypothesis testing throughout the run, target features changed after participants responded correctly for four consecutive trials. A new target feature was randomly selected from a total of nine different features. Participants were not told that the target feature would change after certain trials, and they needed to figure out the feature change by themselves.

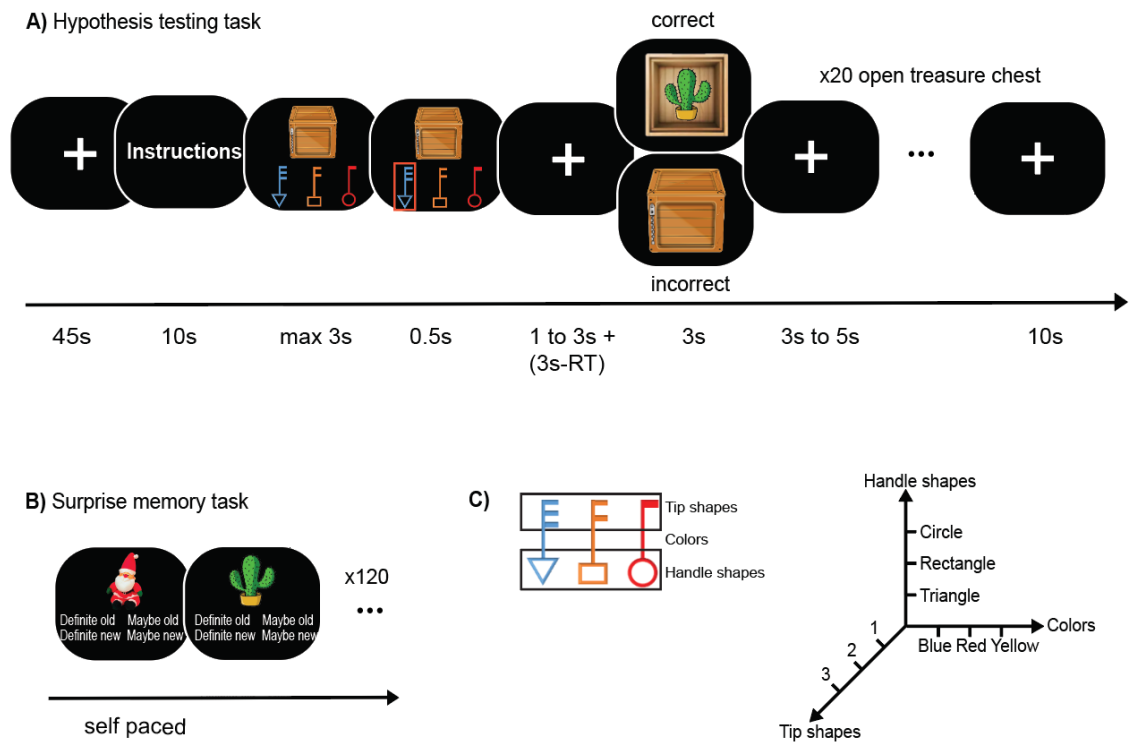


Figure 1. Task Design. (A) Hypothesis testing task. Participants were instructed to choose a key from three keys given, with the goal to open treasure chests. Choosing a key with target feature would open the treasure chest and a trial-unique object would be shown inside the treasure chest. Otherwise, treasure chest stayed closed. (B) Surprise memory task. Participants were presented with 60 images from the hypothesis testing task 60 new images. Participants need to indicate whether they saw the image during encoding. (C) Three different dimensions for a key and three different features for each dimension.

2.1.3 Surprise Memory Task

At a ~24-hour delay, participants were instructed to perform a surprise, self-paced recognition task testing their memory for the objects revealed by the treasure chests, allowing us to relate memory performance to signals, such as decision uncertainty, from the hypothesis testing task on the first day. For each trial, participants were presented with an object image and had to indicate whether they previously saw the object image and their confidence (“definitely old,” “maybe old,” “maybe new,” and “definitely new”).

Participants completed 120 recognition trials including 60 objects from three runs of the hypothesis testing task and 60 novel objects.

2.1.4 Procedures

On the first day, upon participants' arrival, in a behavioral testing room, they first received on-screen instructions showing them the three different dimensions (color, key handle shape, and key tip shape) of a key and were instructed that in the hypothesis testing task, for each trial, only one target feature could open the treasure chest. Participants practiced six trials in which the target features were instructed, then they completed an instruction quiz to ensure they understood the instructions. Then, participants completed a practice run of the hypothesis testing task in which target features were not instructed. The practice run was identical to a task run but used different stimuli (keys with the same three dimensions but different features).

Next, participants completed the actual task in an MRI scanner. Inside the scanner, participants started with a localizer and an anatomical T1 scan. Then they completed three runs of the hypothesis testing task and three runs of the resting scan (each hypothesis testing task was followed by one resting scan), where participants were instructed to look at a fixation cross for five minutes during the resting scan. After participants completed the tasks, they completed a post-encoding survey outside the scanner, asking them about strategies they used to complete the task and their expectations/predictions of the task they would be doing on the second day.

After around 24 hours of delay, participants completed the surprise memory task in a behavioral testing room, and they received their compensation after they completed the surprise memory task.

2.1.5 Reinforcement Learning Model and Decision Uncertainty

To capture trial-by-trial decision-making processes during the hypothesis testing task, we fit a feature-updating reinforcement learning model (RL; validated in our previous behavioral paper). Feature updating RL implies a higher-order concept learning strategy in which participants generalize across keys to isolate the reward-predictive feature. Participants learn and update feature weights based on the received outcome from each trial: $W_f^{new} = W_f^{old} + \alpha(R - W_f^{old})$. More reward-predictive features were enhanced during the hypothesis testing. The value of each key, $V(K)$ is the sum of values of its three features: $V(K) = \sum_{f \in K} W_f$. The values of unchosen features are decayed, with the decay rate controlled by γ . The inclusion of the decay parameter improved the performance of the feature RL model, consistent with previous reports (Niv et al., 2015; Shen et al., 2022). Values of the nine different features are initialized at 0 at the beginning of each run. We then modeled choices using a softmax decision function over the values of keys, $p(K_i) = \frac{e^{mV(K_i)}}{\sum_{j=1}^3 e^{mV(K_j)}}$, to calculate the chosen probability of each key for a given trial. m is the inverse temperature parameter that controls the level of noise in the decision process. We fit the model by maximizing the log likelihood of observed choices for all other subjects using SciPy’s minimize function with the BFGS method.

Decision uncertainty estimates how uncertain participants were about the three given options on each trial. In our behavioral paper (Shen et al., 2022), decision uncertainty was defined as: $1 - (P_k^{highest} - P_k^{second\ highest})$. P is the probability of action for each key under the softmax function. We then used the difference between the highest chosen probability and the second highest chosen probability of keys to calculate decision uncertainty for each trial. A higher value of difference indicates higher decision

uncertainty. Here we used an alternative approach to model decision uncertainty, we calculated the difference of chosen probabilities for the top two features, instead of keys: $1 - (P_w^{highest} - P_w^{second\ highest})$. We argue that during hypothesis testing, participants were keeping track of the values of different features, rather than keys to make their decisions. Therefore, features of keys were a more direct measure of decision uncertainty than keys. We confirmed this measure by showing that the quadratic relationship between decision uncertainty and memory still holds with decision uncertainty derived from features instead of keys using data from our previous behavioral paper.

2.1.6 Behavioral Analyses

All statistical analyses for behavioral data were conducted in R version 3.6.1. Mixed-effects models were run using the “lme4” package glmer function (Bates et al. 2015). Each model included a random slope for each participant to control for individual differences in memory performance and a random intercept for each object image to control for different memorability of object images. Hits and misses were used for memory accuracy measures. Both linear and quadratic terms of decision uncertainty were submitted as fixed effects. Orthogonal polynomials of the first and second levels were generated using the poly() function in R and used as the linear and quadratic terms of decision uncertainty, given that orthogonal polynomials reduce the collinearity among the polynomial functions and isolate the contribution of each term to explaining variance in the outcome.

We tested a model with both high and low confidence memory, such that we grouped “definitely old” and “maybe old” items as hit and grouped “definitely new” and “maybe new” items as miss. (Model 1) memory (high and low confidence hit and miss) ~

$\text{poly}(\text{decision uncertainty}, 2, \text{raw} = \text{FALSE}) + (1 | \text{Image}) + (\text{poly}(\text{decision uncertainty}, 2, \text{raw} = \text{FALSE}) | \text{PID})$. We tested another model separating high confidence hit and low confidence hit. (Model 2) memory (high confidence hit and high and low confidence miss) $\sim \text{poly}(\text{decision uncertainty}, 2, \text{raw} = \text{FALSE}) + (1 | \text{Image}) + (\text{poly}(\text{decision uncertainty}, 2, \text{raw} = \text{FALSE}) | \text{PID})$. (Model 3) memory (low confidence hit and high and low confidence miss) $\sim \text{poly}(\text{decision uncertainty}, 2, \text{raw} = \text{FALSE}) + (1 | \text{Image}) + (\text{poly}(\text{decision uncertainty}, 2, \text{raw} = \text{FALSE}) | \text{PID})$.

2.1.7 MRI Data Acquisition and Pre-processing

MRI data was collected at the Temple University Brain Research & Imaging Center using a 3T Siemens Prisma scanner with a 20-channel parallel transmit-receive head coil. Functional whole brain blood-oxygen-level dependent (BOLD) images were collected in a sagittal acquisition (TR = 1730 ms, TE = 25 ms, flip angle = 76 deg, FOV = 200 mm, matrix size 84 x 84, voxel size 2.4 x 2.4 x 2.4 mm). Slices were positioned parallel to the AC-PC and included coverage of our regions of interests.

Neuroimaging data were converted to the Brain Imaging Data Structure (BIDS). Results included in this manuscript come from preprocessing performed using fMRIPrep 23.1.3 (Esteban et al. (2019); Esteban et al. (2018); RRID:SCR_016216), which is based on Nipype 1.8.6 (K. Gorgolewski et al. (2011); K. J. Gorgolewski et al. (2018); RRID:SCR_002502).

Anatomical data preprocessing: The T1-weighted (T1w) image was corrected for intensity non-uniformity (INU) with N4BiasFieldCorrection (Tustison et al. 2010), distributed with ANTs (version unknown) (Avants et al. 2008, RRID:SCR_004757), and used as T1w-reference throughout the workflow. The T1w-reference was then skull-

stripped with a Nipype implementation of the antsBrainExtraction.sh workflow (from ANTs), using OASIS30ANTs as target template. Brain tissue segmentation of cerebrospinal fluid (CSF), white-matter (WM) and gray-matter (GM) was performed on the brain-extracted T1w using fast (FSL (version unknown), RRID:SCR_002823, Zhang, Brady, and Smith 2001). Volume-based spatial normalization to one standard space (MNI152NLin2009cAsym) was performed through nonlinear registration with antsRegistration (ANTs (version unknown)), using brain-extracted versions of both T1w reference and the T1w template. The following template was selected for spatial normalization and accessed with TemplateFlow (23.0.0, Ciric et al. 2022): ICBM 152 Nonlinear Asymmetrical template version 2009c [Fonov et al. (2009), RRID:SCR_008796; TemplateFlow ID: MNI152NLin2009cAsym].

Functional data preprocessing: For each of the 5 BOLD runs found per subject (across all tasks and sessions), the following preprocessing was performed. First, a reference volume and its skull-stripped version were generated using a custom methodology of fMRIPrep. Head-motion parameters with respect to the BOLD reference (transformation matrices, and six corresponding rotation and translation parameters) are estimated before any spatiotemporal filtering using mcflirt (FSL, Jenkinson et al. 2002). BOLD runs were slice-time corrected to 0.824s (0.5 of slice acquisition range 0s-1.65s) using 3dTshift from AFNI (Cox and Hyde 1997, RRID:SCR_005927). The BOLD time-series (including slice-timing correction when applied) were resampled onto their original, native space by applying the transforms to correct for head-motion. These resampled BOLD time-series will be referred to as preprocessed BOLD in original space, or just preprocessed BOLD. The BOLD reference was then co-registered to the T1w

reference using `mri_coreg` (FreeSurfer) followed by `flirt` (FSL, Jenkinson and Smith 2001) with the boundary-based registration (Greve and Fischl 2009) cost-function. Co-registration was configured with six degrees of freedom. Several confounding time-series were calculated based on the preprocessed BOLD: framewise displacement (FD), DVARS and three region-wise global signals. FD was computed using two formulations following Power (absolute sum of relative motions, Power et al. (2014)) and Jenkinson (relative root mean square displacement between affines, Jenkinson et al. (2002)). FD and DVARS are calculated for each functional run, both using their implementations in Nipype (following the definitions by Power et al. 2014). The three global signals are extracted within the CSF, the WM, and the whole-brain masks. Additionally, a set of physiological regressors were extracted to allow for component-based noise correction (CompCor, Behzadi et al. 2007). For aCompCor, three probabilistic masks (CSF, WM and combined CSF+WM) are generated in anatomical space. The implementation differs from that of Behzadi et al. in that instead of eroding the masks by 2 pixels on BOLD space, a mask of pixels that likely contain a volume fraction of GM is subtracted from the aCompCor masks. This mask is obtained by thresholding the corresponding partial volume map at 0.05, and it ensures components are not extracted from voxels containing a minimal fraction of GM. Finally, these masks are resampled into BOLD space and binarized by thresholding at 0.99 (as in the original implementation). Components are also calculated separately within the WM and CSF masks. For each CompCor decomposition, the k components with the largest singular values are retained, such that the retained components' time series are sufficient to explain 50 percent of variance across the nuisance mask (CSF, WM, combined, or temporal). The remaining

components are dropped from consideration. The head-motion estimates calculated in the correction step were also placed within the corresponding confounds file. The confound time series derived from head motion estimates and global signals were expanded with the inclusion of temporal derivatives and quadratic terms for each (Satterthwaite et al. 2013). Frames that exceeded a threshold of 0.5 mm FD or 1.5 standardized DVARS were annotated as motion outliers. The BOLD time-series were resampled into standard space, generating a preprocessed BOLD run in MNI152NLin2009cAsym space. First, a reference volume and its skull-stripped version were generated using a custom methodology of fMRIPrep. All resamplings can be performed with a single interpolation step by composing all the pertinent transformations (i.e. head-motion transform matrices, susceptibility distortion correction when available, and co-registrations to anatomical and output spaces). Gridded (volumetric) resamplings were performed using `antsApplyTransforms` (ANTs), configured with Lanczos interpolation to minimize the smoothing effects of other kernels (Lanczos 1964). Non-gridded (surface) resamplings were performed using `mri_vol2surf` (FreeSurfer).

2.1.8 Brain Regions of Interest

In exploring the neural correlates of decision uncertainty and its influence on memory, we emphasized five critical regions of interest (ROIs) that are suggested to be involved in the hypothesis testing process based on prior research: the anterior hippocampus, posterior hippocampus, ventral striatum, ventral tegmental area (VTA), and ventromedial frontal cortex (vmPFC) (figure 2). Firstly, the hippocampus is a crucial component for memory encoding, and given its differentiation across the long axis, we were interested in the difference in the anterior and posterior hippocampus in decision-

uncertainty related memory effect. The ventral striatum is known to play a central role in reward processing and decision-making, particularly under conditions of uncertainty (Delgado, 2007), which therefore, would be critical in resolving uncertainty during the hypothesis testing task. Given that the ventral tegmental area is essential for dopaminergic signaling that modulates both reward anticipation and associative learning (Lisman & Grace, 2005) and we propose that the dopaminergic system would be involved in hypothesis testing, we are interested in VTA. Finally, the ventromedial frontal cortex is involved in goal-oriented behaviors and decision-making, integrating emotional and cognitive inputs to guide behavior under uncertainty (Bechara et al., 2000). Collectively, these regions are hypothesized to interact dynamically to shape how decision uncertainty impacts memory processes, providing a comprehensive neural basis for understanding these mechanisms.

The hippocampus was defined using the Harvard-Oxford subcortical atlas integrated within FSL. We divided the hippocampus lengthwise into equal segments delineating the anterior and posterior hippocampus. The target area of the limbic (ventral) striatum was defined using a connectivity-based segmentation atlas with subdivisions for sensorimotor, executive, and limbic regions (Tziortzi et al., 2014). The vmPFC mask was defined from Bhanji et al. (2019). This mask is an inclusive vmPFC/OFC mask that includes the whole area of prefrontal cortex that is both ventral ($z < 0$ in standardized coordinate space) and medial (i.e., superior and inferior medial gyri, anterior cingulate gyrus, gyrus rectus, medial orbital gyrus, and the adjacent sulci). The seed ROI for the SN/VTA was defined using a probabilistic atlas of human SN/VTA (Murty et al., 2014). We used a 50% probability threshold.

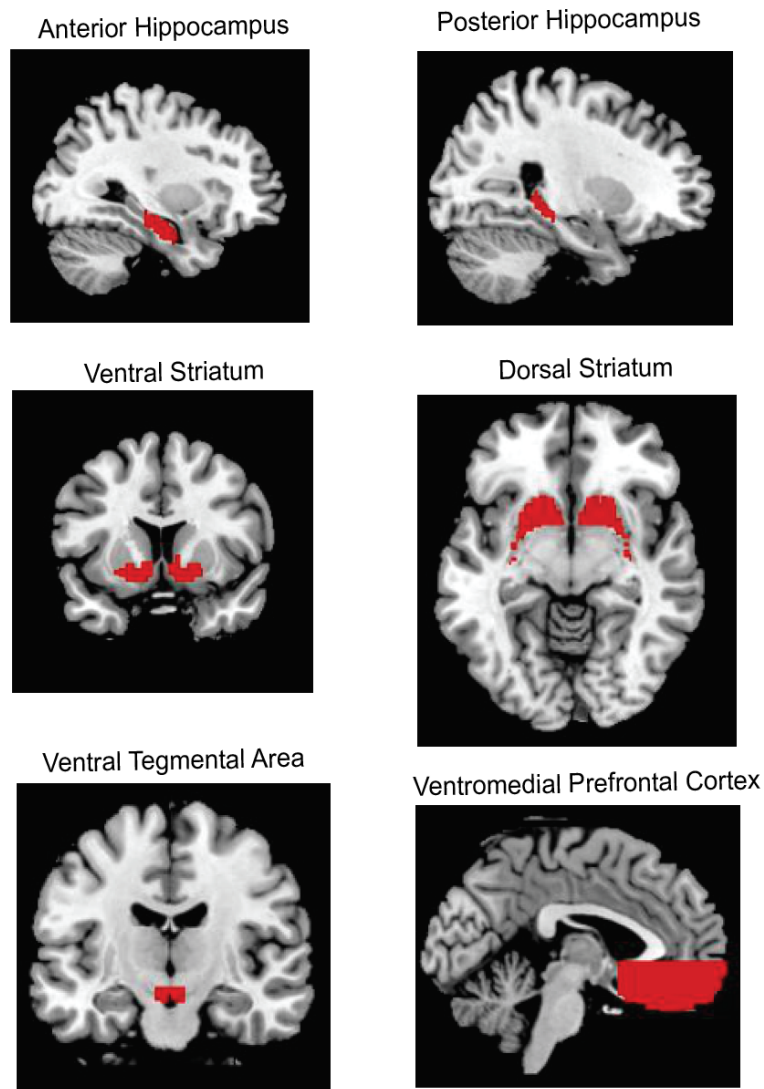


Figure 2. Regions of Interests.

2.1.9 Neuroimaging Analysis

General linear model: decision uncertainty-related activations. To investigate activation as a function of linear and quadratic terms of decision uncertainty, we constructed first-level (within-run) general linear models (GLMs) that included four regressors that modeled decision phase, linear term of decision uncertainty (first-level

orthogonal polynomial of decision uncertainty), quadratic term of decision uncertainty (second-level orthogonal polynomial of decision uncertainty), and the missing trials. All regressors were modeled with event durations collapsing over the decision and outcome phase (from the onset of the treasure chest stimulus to the onset of ITI). Six motion parameters (three rotation, three translation), first six aCompCor values, framewise_displacement, non-steady state, and cosine-basis regressors were included as regressors of no interest. All regressors were convolved with a double-gamma hemodynamic response function. Using this GLM, individual maps of parameter estimates were generated for two contrasts of interest: (1) linear term of decision uncertainty, (2) quadratic term of (inverted U-shaped) decision uncertainty. Second-level analyses for each of these contrasts (i.e., across runs, within participants) were modeled using a fixed-effect analysis. Parameter estimates (zstats maps) from linear and quadratic terms of decision uncertainty contrasts were extracted from all five ROIs using fslmeans.

General linear model: memory success activations. To investigate task-related activations as a function of memory success, we constructed first-level GLMs that included four regressors that modeled subsequently remembered choice with high confidence encoding trials, subsequently remembered choice with low confidence encoding trials, subsequently forgotten choice encoding trials, missing and incorrect trials. Again, six motion parameters (three rotation, three translation), the first six aCompCor values, framewise_displacement, non-steady state, and cosine-basis regressors were included as regressors of no interest. Trials in which the encoded object was endorsed confidently as old during recognition (“definitely old”) were considered subsequently remembered with high confidence. Trials in which the encoded object was

endorsed without confidence as old during recognition (“maybe old”) were considered subsequently remembered with low confidence, and trials in which the encoded object was endorsed as new for both high and low confidence were considered subsequently forgotten (“maybe new” and “definitely new”). All regressors were convolved with a double-gamma hemodynamic response function. Using this GLM, individual maps of parameter estimates were generated for two contrasts of interest: (1) choice remembered with high confidence > forgotten events and (2) choice remembered with low confidence > forgotten events. Second-level analyses for each of these contrasts (i.e., across runs but within participants) were modeled using fixed-effect analyses. Parameter estimates (zstats maps) from both contrasts of interest were extracted from all five ROIs using `fsleastsq`.

Group-level analysis. We modeled group-level analyses using the mixed-effects analyses in FSL [FLAME 1 + 2]. We note that Z statistic images were thresholded parametrically (Gaussian Random Field Theory) using clusters determined by $Z > 3.1$ and a (corrected) cluster significance threshold of $P = .05$. These whole brain analyses are corrected for multiple comparisons. ROI analyses were performed to probe activation in the Ventral Striatum, Anterior Hippocampus, Posterior Hippocampus, Ventromedial frontal cortex (vmPFC), and the Ventral Tegmental area (VTA).

2.1.10 Correlates Neuroimaging Analysis to Behaviors

To understand how neural responses predict behaviors, we constructed robust regression models where parameter estimate for each participant from the behavioral model (model 2 above given that model comparison suggested that high confidence hit drives the observed memory effect) was submitted as the dependent variable, and parameter estimates (β maps) from the GLM memory success model (see description

above) for anterior hippocampus, posterior hippocampus, and vmppfc, and parameter estimates (β maps) from the GLM decision uncertainty model (see description above) for ventral striatum were submitted as the fixed effects.

To reduce the collinearity effect of average memory performance, we also ran Least Absolute Shrinkage and Selection Operator regression (LASSO regression) using the `glmnet()` function in R. We performed 10-fold cross-validation to find the optimal λ value that minimized the mean squared error to get the best-fit LASSO regression model.

CHAPTER 3

3. RESULTS

3.1 Does Reinforcement Learning Model Capture Hypothesis-testing Behaviors?

Prior research has suggested that participants navigate in a multi-dimensional environment using a feature-updating strategy (Niv et al., 2015). During feature updating, individuals attempt to learn the value of individual features of the key (e.g., handle color) and pick the key with the most predictive features. This strategy integrates across multiple experiences to identify the most reward-predictive features of the environment. In the instructions, participants were instructed to figure out the correct keys by testing out different features, therefore, we hypothesize that the feature updating strategy would predict and capture participants' hypothesis-testing behaviors. Cross-validated model prediction showed that the feature updating strategy significantly predicted behavior across three runs (mean learning rate: 0.45; run1: mean probability: 0.52, chance: 0.33; $t = 27.29$, $p < 0.001$; run2: mean probability: 0.52, chance: 0.33; $t = 27.36$, $p < 0.001$; run3: mean probability: 0.54, chance: 0.33; $t = 28.66$, $p < 0.001$).

We next examined trial-level performance to confirm that within a run, feature learning captured an individual's hypothesis-testing behavior. The four trials before a feature switch are important for testing our models because these are trials in which we assume participants have identified a strategy that can successfully figure out the correct key. Therefore, we are expected to see increasing predictive accuracy from the four consecutive trials before a feature switch. Indeed, we found increasing predictive accuracy from four trials before a feature change to the feature changing trial for the feature updating RL model ($\hat{y}_{-4} = 0.45$, $\hat{y}_{-3} = 0.63$, $\hat{y}_{-2} = 0.71$, $\hat{y}_{-1} = 0.77$, $\hat{y}_0 = 0.77$;

figure 3a). Together, results from our feature RL model showed that the model can capture people's hypothesis-testing behaviors and we will use signals derived from the feature RL model, such as decision uncertainty for further analysis.

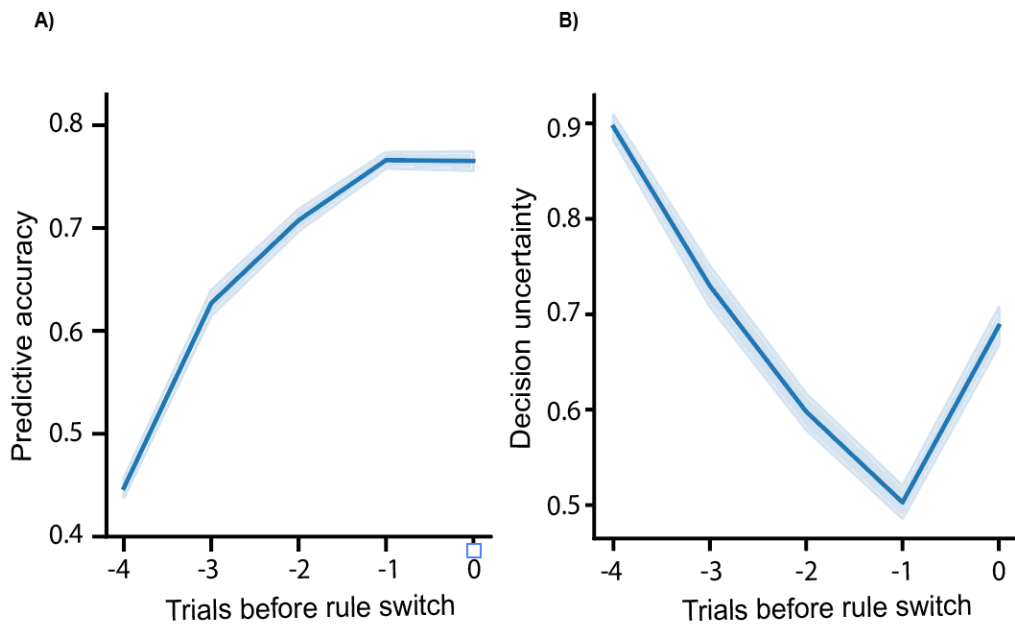


Figure 3. Predictive Accuracy for the Feature RL Model and Decision Uncertainty Changes. (A) On the trial level, there is increasing predictive accuracy for the last four trials before a feature switch and the switching trial for the feature RL model. Participants did not know the switching trial until they saw the feedback. (B) On the trial level, decision uncertainty decreased across the last four trials before a feature switch as participants were doing hypothesis testing and decision uncertainty increased at the feature switching trial.

3.2 Does Decision Uncertainty Derived from Reinforcement Learning Model Predict Memory?

Decision uncertainty varied throughout the hypothesis testing task. We theorized that initially uncertainty will be high as participants were mostly guessing without any knowledge of the correct feature. As they engaged in hypothesis testing and eliminated incorrect features, uncertainty will then decrease. Then, the lowest decision uncertainty

would occur in the trials preceding a feature switch when participants had identified the correct feature, and uncertainty would increase again following a feature switch.

To assess changes in decision uncertainty throughout the task, we modeled decision uncertainty by comparing the value difference between the highest and second highest features among the nine different features, based on the feature updating reinforcement learning model for each trial. A small value difference indicates high decision uncertainty, making it difficult to choose between features, while a large difference indicates low decision uncertainty, as participants are more likely to select the highest-value feature. We found that decision uncertainty decreased across the four trials before a feature change and increased for the feature switching trial (decision uncertainty₍₋₄₎ = 0.90, decision uncertainty₍₋₃₎ = 0.73, decision uncertainty₍₋₂₎ = 0.60, decision uncertainty₍₋₁₎ = 0.50, decision uncertainty_(switch) = 0.69) (figure 3b).

Next, we examined how decision uncertainty influences memory. We found a significant quadratic relationship (inverted-U) between decision uncertainty and memory ($\beta = -5.86$, $SE = 2.51$, $p = 0.02$), such that memory was enhanced at an intermediate level of decision uncertainty, compared to high and low levels of decision uncertainty, demonstrating that intermediate level of decision uncertainty results in enhanced declarative memory. We did not find a significant linear relationship between decision uncertainty and memory ($\beta = -1.78$, $SE = 2.54$, $p = 0.48$). Because participants could view an object only when they chose the correct feature and opened the treasure chest, therefore trials at feature change mostly constituted low decision uncertainty, the fourth trial before a feature change mostly constituted high decision uncertainty, and the second and the third trials before a feature change mostly constituted the intermediate decision

uncertainty. Additionally, we found that the quadratic relationship between decision uncertainty and memory remained significant when limiting the analysis to high confidence hit (“definitely old” response; $\beta = -5.86$, $SE = 2.50$, $p = 0.02$) (figure 4a), but not for low confidence memory (“maybe old” response; $\beta = -2.23$, $SE = 2.24$, $p = 0.32$) (figure 4b). Together, our results suggested that decision uncertainty derived from the feature reinforcement learning model can predict memory, particularly high-confidence memory, such that memory was enhanced at an intermediate level of decision uncertainty.

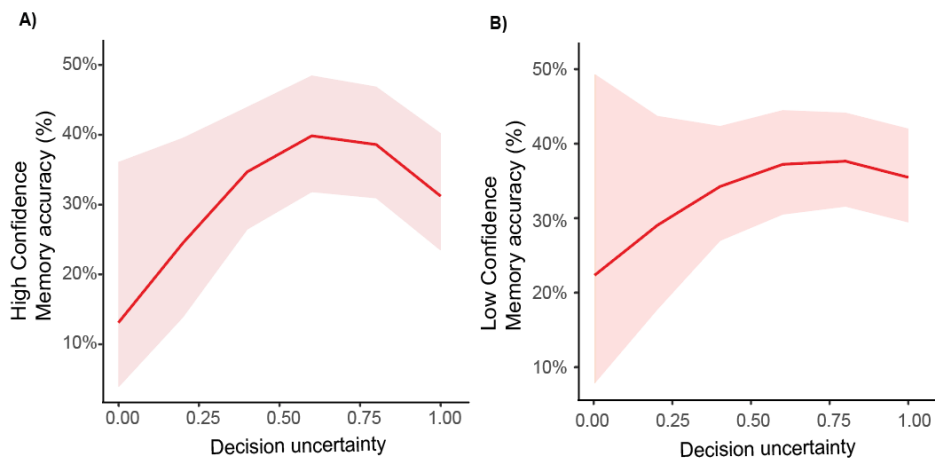


Figure 4. Memory Accuracy and Decision Uncertainty. (A) There was a significant quadratic relationship between decision uncertainty and memory accuracy, such that memory was the best at the intermediate level of decision uncertainty for only high-confidence items. (B) There was no significant linear or quadratic relationship between decision uncertainty and memory accuracy or low high-confidence items.

3.3 Where is Decision Uncertainty Coded as a Linear Function in the Brain?

3.3.1 Regions of Interest (ROI) Results

Having examined the behavioral interactions between decision uncertainty and memory performance in the hypothesis testing task, we now turn our attention to the neural correlates underlying these phenomena. First, we aim to understand how decision

uncertainty is represented in the brain. To identify brain regions that were modulated by decision uncertainty, we created a parametric regressor for trial-wise linear term decision uncertainty and extracted the average activation across three runs (z-stat) within each ROI for each participant. This ROI analysis focused on effects from the onset of cues to the end of the outcome presentation because we suggest there is a carry-over effect of decision uncertainty from the decision phase to the outcome phase. Therefore, we modeled the entire decision and outcome phase together. We found significant modulation of activity in all five ROIs by the parametric regressor representing linear changes in decision uncertainty. Specifically, we observed increased activation in the ventral striatum ($t_{(34)} = -4.90, p < 0.001$), anterior hippocampus ($t_{(34)} = -7.81, p < 0.001$), posterior hippocampus ($t_{(34)} = -5.08, p < 0.001$) and vmPFC ($t_{(34)} = -8.78, p < 0.001$) with decreased decision uncertainty, suggesting that higher uncertainty may dampen engagement in areas related to reward processing, memory, and evaluation of outcomes. In contrast to these regions, we found increased activation in the ventral tegmental area ($t_{(34)} = 2.81, p = 0.008$) with increased decision uncertainty (figure 5a), suggesting that higher uncertainty may enhance VTA engagement. Together, these findings highlight neural mechanisms associated with linear representations of uncertainty in hypothesis-testing processes.

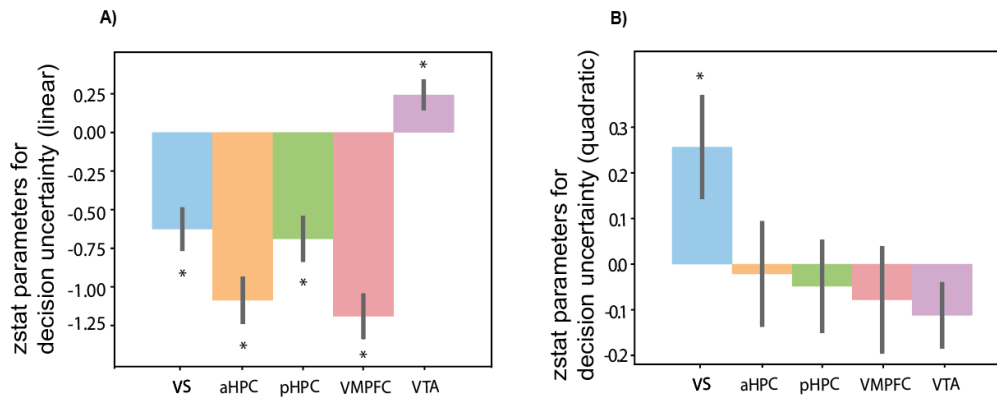


Figure 5. ROI Analysis for Linear Term and Quadratic Term of Decision Uncertainty. (A) Increased decision uncertainty (linear term) was significantly associated with decreased activation in the ventral striatum, anterior hippocampus, posterior hippocampus, and vmPFC. Increased decision uncertainty (linear term) was also significantly associated with increased activation in the VTA. (B) The quadratic term of decision uncertainty was significantly associated with increased activation in the ventral striatum. There was no significant activation in the other four ROIs for the quadratic term of decision uncertainty.

3.3.2 Whole-brain Results

After completing the ROI analysis to pinpoint brain regions involved in decision uncertainty (linear term), we extended our investigation through a whole-brain contrast. This analysis aimed to identify areas showing differential BOLD activity associated with the linear term decision uncertainty during hypothesis testing, from the onset of cues to the end of the outcome presentation. We found that linear term decision uncertainty was associated with greater activation in a broad network of regions, including the dorsolateral prefrontal cortex, inferior temporal gyrus, insula, and cerebellum, etc ($p < 0.05$, whole-brain corrected; Table 1).

Table 1. *Regions Associated with the Linear Term of Decision Uncertainty*

Region	x	y	z	Z
Inferior parietal gyru	-44.1	-58.7	51.3	8.49
frontal gyrus	34.5	29.4	33.8	7.42
frontal gyrus	-44.1	24.6	33.8	7.73
cerebellum	-10.8	-73	-26.1	5.91
Supplementary motor area	-1.26	12.7	51.3	6.52
cerebellum	36.8	-63.5	-51	6.04
frontal gyrus	-15.5	3.22	13.9	5.34
frontal gyrus	-29.8	53.2	6.36	7.34
Pulvinar medial	15.4	-25.4	11.4	5.07
Inferior temporal gyrus	60.6	-42	-16.1	5.55
insula	-27.5	24.6	1.37	5.13
Inferior temporal gyrus	-51.3	-53.9	-13.6	5.88
insula	32.1	22.3	-1.12	4.98
frontal_pareital	-1.26	-34.9	26.3	3.91

x,y, and z are MNI coordinates, Z is peak z-score

3.4 Where is Decision Uncertainty Coded as a Quadratic Function in the Brain?

3.4.1 Regions of Interest (ROI) Results

Given the observed quadratic relationship between decision uncertainty and memory performance at the behavioral level, we wanted to characterize any brain regions that reflect quadratic representations of decision uncertainty, instead of just the linear representations. Specifically, we are interested in the inverted-U shape. Therefore, for the next analysis, we are particularly interested in exploring brain regions where activity is modulated by the quadratic term of decision uncertainty, which show more complex patterns of enhancement or suppression depending on the level of decision uncertainty. We created a parametric regressor for trial-wise quadratic term decision uncertainty using orthogonal polynomials and extracted the average activation (z-stat) within each ROI for each participant. Similar to the ROI analysis for linear term decision uncertainty, we modeled the entire decision and outcome phase together. We observed significant modulation of activity in the ventral striatum ($t(35) = 2.35$, $p = 0.02$) corresponding to the quadratic term of decision uncertainty, such that activation in the ventral striatum peaks at

an intermediate level of decision uncertainty. (figure 5b). We did not find significant modulation of activity in the other four ROIs (anterior hippocampus: $t_{(35)} = -0.19, p = 0.85$; posterior hippocampus: $t_{(35)} = -0.49, p = 0.62$; vmPFC: $t_{(35)} = -0.49, p = 0.69$; VTA: $t_{(35)} = -1.64, p = 0.11$) associated with the quadratic term of decision uncertainty.

Together, these findings suggest that the ventral striatum exhibits significant activation in response to the non-linearity of decision uncertainty, such that the ventral striatum showed the highest activation for the intermediate level of decision uncertainty.

3.4.2 Whole-brain Results

Next, we also computed a whole-brain contrast to identify regions exhibiting differential BOLD activity with quadratic term decision uncertainty during hypothesis testing. Again, this finding focused on effects from the onset of cues to the end of the outcome presentation. We found that the quadratic term of decision uncertainty (both U-shaped and inverted-U shaped) was associated with greater activation in the lingual gyrus, middle occipital gyrus, and the putamen ($p < 0.05$, whole-brain corrected; Table 2).

Table 2. *Regions Associated with the Quadratic Term of Decision Uncertainty*

Region	x	y	z	Z	
Lingual gyrus		15.4	-84.9	-8.61	4.83
Middle occipital gyrus		-10.8	-96.8	-1.12	4.9
Putamen		20.2	10.4	-6.12	4.1

x,y, and z are MNI coordinates, Z is peak z-score

3.5 Where is Subsequent Memory for High Confidence Coded in the Brain?

3.5.1 Regions of Interest (ROI) Results

The above findings focused on brain activation related to the representation of decision uncertainty (both linear and quadratic). We next shifted our focus to brain activation associated with subsequent memory. Behaviorally, we found a significant quadratic

relationship between decision uncertainty and memory for only high-confidence memory, but not for low-confidence memory, aligning with previous studies that have identified a subsequent memory effect predominantly in cases of high-confidence recall. Therefore, in this analysis, we identified brain regions that display significant memory effects for high-confidence memory (high confidence hit > forgotten) and low-confidence memory (high confidence hit > forgotten). Our ROI analyses demonstrated significant subsequent memory effects for high-confidence memory in the anterior hippocampus ($t_{(34)} = 3.53, p = 0.001$), posterior hippocampus ($t_{(34)} = 2.04, p = 0.048$), and vmPFC ($t_{(34)} = 3.55, p = 0.001$), but not in ventral striatum ($t_{(34)} = -0.15, p = 0.88$) and VTA ($t_{(34)} = -1.77, p = 0.09$) (figure 6a), which is consistent with prior research highlighting the importance of the hippocampus in memory encoding. However, we did not find a subsequent memory effect for low confidence memory during encoding in any of the ROI (ventral striatum: $t_{(35)} = -0.04, p = 0.96$; anterior hippocampus: $t_{(35)} = 1.42, p = 0.17$; posterior hippocampus: $t_{(35)} = 1.37, p = 0.18$; vmPFC: $t_{(35)} = 0.60, p = 0.55$; VTA: $t_{(35)} = -0.66, p = 0.51$) (figure 6b). Together, these findings underscore that the anterior hippocampus, posterior hippocampus, and vmPFC play a critical role in encoding memories that are later recalled with high confidence during hypothesis testing.

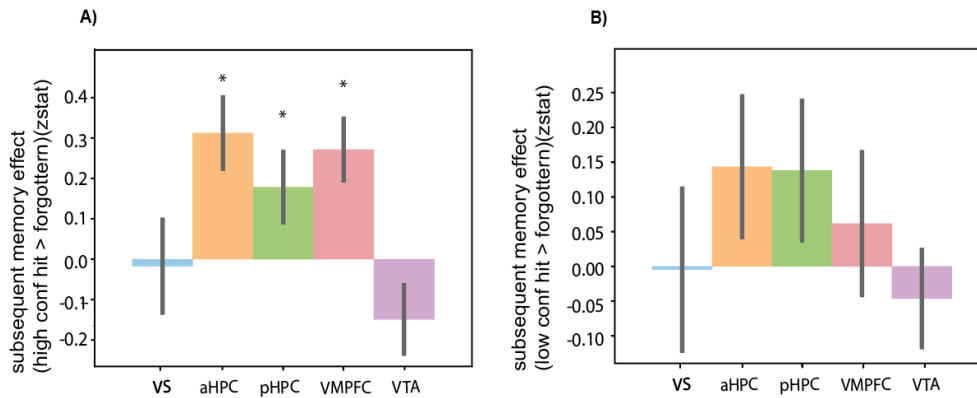


Figure 6. ROI Analysis of Subsequent Memory Effects. (A) Significant activations associated with high-confidence memory encoding were observed in the anterior hippocampus, posterior hippocampus, and ventromedial prefrontal cortex (vmPFC), indicating their roles in successful memory retention. (B) No significant memory effects were detected for low-confidence items across all five regions of interest, including the ventral striatum, anterior and posterior hippocampus, vmPFC, and ventral tegmental area (VTA).

3.5.2 Whole-brain Results

Finally, we computed whole-brain contrasts to identify brain regions associated with subsequent memory effects for high-confidence memory and low-confidence memory. Our findings revealed a network of regions, including the fusiform gyrus, inferior occipital gyrus, and superior frontal gyrus displayed significant subsequent memory effects (high confidence hit > forgotten) for high-confidence memories (Table 3). We also found the fusiform gyrus activation was associated with subsequent memory effects for low-confidence memory (low confidence hit > forgotten).

Table 3. *Regions Showing a Subsequent Memory Effect for High-confidence Items*

Region	x	y	z	Z	
Fusiform gyrus		-44.1	-61.1	-16.1	5
Inferior occipital gyrus		32.1	-92	-6.12	4.66
Superior frontal gyrus, medial orbital		-3.64	36.6	-13.6	4.42

x,y, and z are MNI coordinates, Z is peak z-score

Table 4. *Regions Showing a Subsequent Memory Effect for Low-confidence Items*

Region	x	y	z	Z	
Fusiform gyrus		-20.3	-82.5	-11.1	4.05
Fusiform gyrus		20.2	-82.5	-11.1	3.99

x,y, and z are MNI coordinates, Z is peak z-score

3.6 Integrating Neural and Behavioral Dynamics

Our previous analyses demonstrated that ventral striatal activation during encoding correlates significantly with the quadratic term (inverted U) of decision uncertainty, while activations in the hippocampus and vmPFC are significantly correlated with memory encoding for items subsequently remembered with high confidence. However, how activations in these regions support the observed quadratic (inverted-U) relationship between decision uncertainty and memory in the behavioral finding remain poorly understood. To further explore these dynamics, we investigated whether any of our neural effects (i.e., quadratic representations in the striatum and subsequent memory effects in hippocampus and vmPFC) are associated with the quadratic (inverted-U) behavioral effects of decision uncertainty on memory. Specifically, we extracted parameter estimates (β estimates) for responses in the ventral striatum related to the quadratic term of decision uncertainty and responses in the anterior hippocampus, posterior hippocampus, and vmPFC related to subsequent memory effects with high confidence for each participant and each run. We then averaged the parameter estimates across three runs and examined whether brain activation at the run level predicted the

parameter estimates of the quadratic relationship between decision uncertainty and memory behaviorally.

We regressed parameter estimates from the anterior hippocampus, posterior hippocampus, vmPFC (defined from the contrast of high confidence hit > forgotten), and the ventral striatum (defined from the contrast of the quadratic term of decision uncertainty) against the parameter estimate for the quadratic fit between decision uncertainty and memory behaviorally across participants using robust regression analysis. The results demonstrated significant contributions from the ventral striatum ($\beta = -0.35$, $SE = 0.15$, $t(35) = -2.35$, $p = 0.03$) (figure 7). Specifically, greater activation in the ventral striatum in response to the quadratic (inverted-U) term of decision uncertainty was linked to a more pronounced quadratic (inverted-U) relationship between decision uncertainty and memory performance. This implies that participants exhibited optimal memory performance at an intermediate level of decision uncertainty, demonstrating that these brain regions contribute significantly to the modulation of memory under different levels of decision uncertainty. We did not find significant contributions from the anterior hippocampus ($\beta = -0.13$, $SE = 0.20$, $t(35) = -0.66$, $p = 0.52$), the posterior hippocampus ($\beta = -0.33$, $SE = 0.19$, $t(35) = -2.69$, $p = 0.10$), and the vmPFC ($\beta = -0.27$, $SE = 0.16$, $t(35) = -1.72$, $p = 0.09$).

To further validate our findings, we employed a Least Absolute Shrinkage and Selection Operator regression (LASSO regression) analysis as a complementary method. LASSO regression, by applying a penalty to the coefficients of the regression variables, effectively reduces issues of collinearity, ensuring that only the most predictive variables are retained. Our LASSO analysis led to the exclusion of the anterior hippocampus from

the full model, indicating that its activation did not significantly predict the behavioral quadratic fit between decision uncertainty and memory. Conversely, the posterior hippocampus, ventromedial prefrontal cortex (vmPFC), and ventral striatum were retained as predictors. To refine our understanding of the influence of these regions, we then implemented a robust regression model with the three retained factors. Our findings demonstrated that the ventral striatum was the only region that significantly predicted behaviors ($\beta = -0.32$, $SE = 0.13$, $t(35) = -2.44$, $p = 0.02$). Neither the vmPFC ($\beta = -0.18$, $SE = 0.17$, $t(35) = -1.06$, $p = 0.30$) nor the posterior hippocampus ($\beta = -0.17$, $SE = 0.22$, $t(35) = -0.77$, $p = 0.45$) showed significant predictive power. This analysis highlights the ventral striatum's crucial role in relating activation related to the quadratic term of decision uncertainty to behavioral outcomes. Further research is needed to explore the roles of the hippocampus and vmPFC in this context. In summary, our findings indicate that the ventral striatum may have a pivotal role in the integration of cognitive processes related to decision uncertainty and memory formation. This finding enhances our understanding of how these regions interact to support memory in complex decision-making scenarios, such as hypothesis testing, where decision uncertainty is a central element.

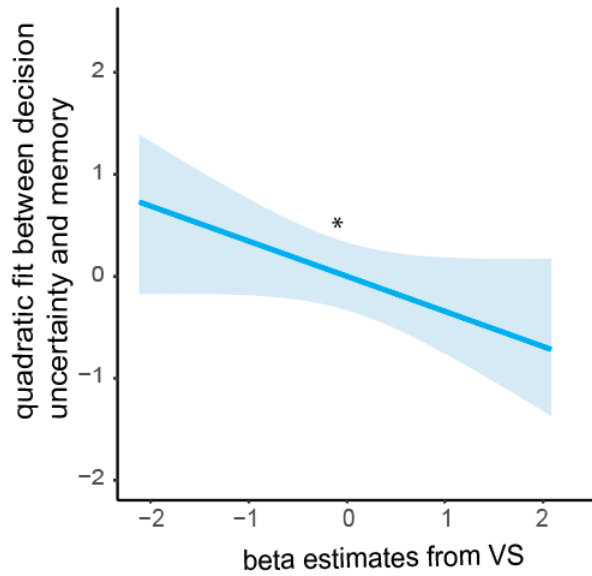


Figure 7. Relationship Between the Behavioral Quadratic Fit for Decision Uncertainty and Memory and Parameter Estimates for the Ventral Striatum. The scatter plot displays individual data points, with the fit line and confidence intervals indicating trends in the data. The negative slope indicated greater activation in the ventral striatum in response to the quadratic term of decision uncertainty was linked to a more pronounced quadratic relationship (inverted-U shape) between decision uncertainty and memory performance.

CHAPTER 4

4. GENERAL DISCUSSION

Hypothesis testing is the process where decision-makers test the relationship between their beliefs and decisions to reduce uncertainty, which might have a downstream effect on memory due to increased motivation. Prior efforts have been made to investigate the neural mechanism of information-seeking and how information-seeking influences memory, but little research investigates the question in the framework of hypothesis testing. Still little is known about the hypothesis testing process and the involved neural underlying mechanism, as well as its downstream effects on memory. Thus, the objective of this dissertation was to delve deeper into the relationship between information-seeking and motivated memory by examining hypothesis testing behavior and its underlying neural mechanism.

We employed a reinforcement learning model and neuroimaging techniques to investigate the representation of decision uncertainty and subsequent memory effect during hypothesis testing. Overall, our study uncovers learning and memory mechanisms underlying hypothesis testing, suggesting that individuals learn information about higher-order features to update their beliefs about an uncertain environment and an intermediate level of decision uncertainty enhances memory during hypothesis testing. We also found that the ventral striatum is important for the representing of quadratic (U-shaped) term of decision uncertainty while the anterior hippocampus, posterior hippocampus, and VMPFC are important for the subsequent memory effect. Additionally, we found that activation in the ventral striatum in response to the quadratic term of decision uncertainty predicts the quadratic fit between decision uncertainty and memory during hypothesis

testing, such that greater activation in the ventral striatum is associated with more pronounced memory enhanced at an intermediate level of decision uncertainty.

4.1 Behavioral Effect of Decision Uncertainty on Memory

Our current neuroimaging study replicates previous behavioral findings (Shen et al., 2022). Consistent with the behavioral study, we first validated that the reinforcement learning model was able to capture decision-making behavior in hypothesis testing. Then, using decision uncertainty derived from the reinforcement learning model, we replicated the quadratic relationship between decision uncertainty and memory, such that memory enhancements only emerged when individuals had moderate amounts of decision uncertainty, which theoretically represents when individuals should be most motivated to seek information.

In our current study, we used a slightly different approach to calculate decision uncertainty compared to the method used in the behavioral study (Shen et al., 2022). In the paradigm, on each trial, participants were shown three keys with three different features. The value of a given key is the sum of the values of the constituted three features. Therefore, we assume participants strategically keep track of the value of each feature and test hypotheses about the correct feature throughout the task. They were making decisions about different features, rather than keys. Therefore, calculating decision uncertainty using the feature space will be a more direct measure, so rather than using the difference between the highest and second highest chosen probability of keys, we calculated decision uncertainty using the difference between the values of the top two features for a given trial. To validate the effectiveness of this revised measure of decision uncertainty, we reanalyzed the behavioral study data using the new decision uncertainty

measure. The results confirmed that the inverted U-shaped relationship between decision uncertainty and memory persists using this new measure.

Our study replicated the inverted U-shaped relationship between decision uncertainty and memory enhancement, with memory performance enhanced at moderate levels of decision uncertainty. This finding aligns with prior research by suggesting that optimal learning occurs with tasks that are neither too simple nor overly challenging (Metcalf & Kornell, 2003). In the context of hypothesis testing, decision uncertainty reflects trial difficulty, influencing individuals' judgments of learning. Therefore, trials characterized by moderate decision uncertainty—which correspond to tasks of intermediate difficulty—are believed to optimally engage individuals' motivation to reduce uncertainty (Friston & Kiebel, 2009). Such motivational states during encoding are known to enhance hippocampus-dependent memory, particularly for incidental information within a reward context (Murty & Adcock, 2014) and our findings extend these mechanisms to the domain of hypothesis testing. Our results are also consistent with the literature on curiosity and memory, which shows that individuals are most curious when there is intermediate decision uncertainty (Gottlieb et al., 2016), which may then enhance the incidental encoding of the environment (M. J. Gruber et al., 2014; M. Gruber & Ranganath, 2019; Murphy et al., 2020).

4.2 Representation of Decision Uncertainty in the Brain

Our study revealed a negative relationship between the activation in the ventral striatum (VS), ventromedial prefrontal cortex (vmPFC), the anterior and posterior hippocampus with decision uncertainty, and a positive relationship between the activation in the VTA with decision uncertainty. These findings are consistent with prior research on

neurobiological underpinnings of information-seeking behaviors, motivation, and decision-making under uncertainty. The ventral striatum (VS), a critical component of the mesolimbic dopaminergic system, has been suggested to play a pivotal role in motivation and reward processing (Cardinal et al., 2002; Filimon et al., 2020; Liljeholm & O’Doherty, 2012; Pool et al., 2022). Prior neuroimaging studies have shown that the evaluation of reward decisions typically involves bilateral activation of the ventral striatum (Delgado, 2007). The negative relationship observed in our study implies that as decision uncertainty increases, the expected value of potential rewards diminishes, leading to decreased activation in this region. This finding is consistent with findings from prior studies that linked the ventral striatum to reward prediction and valuation processes (Knutson et al., 2001).

One of our recent works on dissociating the effect of affective and informative components of rewards also showed that the ventral striatum showed differential sensitivity to affective and informative reward magnitudes, such that the ventral striatum showed greater activation to more predictive informative feedback, suggesting that ventral striatum is sensitive to predictiveness of information (Shen et al., 2024 in prep). The VTA, which supplies dopaminergic inputs to the ventral striatum, on the opposite, showed increased activation with increased uncertainty, suggesting increased motivation to reduce uncertainty in a high uncertain environment.

We also found activation in the ventromedial prefrontal cortex (VMPFC) decreased as a function of increasing decision uncertainty. The vmPFC is extensively documented for its role in processing and integrating emotionally and motivationally relevant information to guide behavior and decision-making (Euston et al., 2012;

Rushworth et al., 2011). Therefore, we speculate that as decision uncertainty decreased, participants were able to successfully identify the correct feature in the hypothesis testing task, thus the activation within the vmPFC increased, which corresponds to successful goal achievement. This finding aligns with the vmPFC's established role in evaluating the value of chosen actions based on expected outcomes (Rushworth et al., 2011), suggesting that as uncertainty is resolved and goals are successfully met, vmPFC activation reflects the enhanced valuation of outcomes.

Our findings that anterior and posterior hippocampus activation decreases as decision uncertainty increases align with existing research on the hippocampus's role in responding to prediction errors and uncertainty. The hippocampus has been suggested to be involved in identifying discrepancies from the cognitive map and encoding new information (Bein et al., 2020; Chen et al., 2015; Duncan et al., 2012; Kumaran & Maguire, 2006). When prediction errors occur—when outcomes differ from expectations—the hippocampus activates to update these cognitive maps. Prior functional MRI studies have shown that hippocampal activation increases after predictions are violated, which suggests that the hippocampus mnemonic prediction errors. In the hypothesis testing framework, we suggest that under conditions of high decision uncertainty, participants were unable to form specific predictions about the correct feature and are mostly guessing. However, as decision uncertainty decreases, they begin to formulate and evaluate predictions about the correct feature, which activates the hippocampus. Our results that responses in the hippocampus increased when events became more predictable (reduction in uncertainty) support the notion that the hippocampal system may be sensitive to uncertainty (Harrison et al., 2006).

Together, the observed relationship between these brain regions and decision uncertainty provides critical insights into the neurobiological mechanisms of motivation in uncertain scenarios. This is reflected in the reduced neural activation in areas such as the ventral striatum, which is associated with reward processing and decision-making. Our findings extend the understanding of the interplay between uncertainty and motivation in the context of hypothesis testing.

4.3 Representation of Quadratic Term of Decision Uncertainty in the Ventral Striatum

We found that the quadratic term of decision uncertainty is coded in the ventral striatum, which is significant and novel. This relationship implies that the ventral striatum activation is the highest at an intermediate level of decision uncertainty, decreasing when uncertainty is either too low or too high. This pattern aligns with and extends existing theoretical models and empirical research on how uncertainty influences motivational states and behaviors (Buzzell et al., 2016). Behaviorally, prior research suggests that individuals are most engaged and motivated by an optimal level of difficulty or uncertainty (Metcalf & Kornell, 2003, 2005). The quadratic representation in the ventral striatum reflects a neurobiological mechanism where the ventral striatum mediates the motivational components of reward-based learning and adjusts the individual's engagement level. The enhanced activation at moderate uncertainty might also represent an optimal state for updating beliefs based on new sensory information

In sum, the identification of a quadratic representation of uncertainty in the ventral striatum extends the information-seeking literature by demonstrating how neural responses in the ventral striatum are modulated not merely by the presence of uncertainty but by its structure, with peak activations signaling optimal levels of uncertainty during

information-seeking and learning. While previous studies have established that the ventral striatum responds to rewards and the anticipation of rewards (Delgado, 2007; Delgado et al., 2000; Tricomi & Fiez, 2012), our findings suggest that this region is also finely attuned to the complexity of decision-making scenarios, specifically to the levels of uncertainty in an uncertain environment.

4.4 Subsequent Memory Effect During Hypothesis Testing

During information seeking, individuals encounter different information and only a fraction of information is converted into memories that can be later recalled. A critical question is identifying the specific neural activities that predict which events will be remembered and which will be forgotten. Substantial neuroimaging research has focused on the role of the prefrontal cortex (PFC) and the medial temporal lobe (MTL) in subsequent memory effects, which describe how neural activity during encoding relates to later memory performance (Buckner et al., 2001; Fernandez and Tendolkar, 2001; Simons and Spiers, 2003). For example, studies have demonstrated that anticipatory activation within the midbrain, and its functional connectivity with the medial temporal lobe regions including the hippocampus (HPC), are predictive of successful memory formation (Gruber et al., 2014; Wittmann et al., 2007). Intriguingly, in one such study where participants were motivated by intrinsic curiosity, memory was enhanced not only for the information of interest but also for irrelevant incidental information, suggesting a sustained state of enhanced encoding (M. J. Gruber et al., 2014).

Consistent with prior research, our research identified significant subsequent memory effects in the anterior and posterior hippocampus, and the ventromedial prefrontal cortex (vmPFC) during hypothesis testing. In other words, increased activation

in these areas was associated with a greater likelihood of items being accurately recalled after a 24-hour delay. More importantly, this enhancement was for incidental, rather than goal-relevant information, during encoding.

Moreover, our ROI analysis results suggested that this subsequent memory effect was specific to high-confidence memory recall. This observation is in line with the dual-process theory of recognition memory, which suggests that memory retrieval operates via two distinct processes: recollection and familiarity (see review: Eichenbaum et al., 2007; Rugg & Yonelinas, 2003; Yonelinas, 2002). The hippocampus is thought to be essential for recollection, which involves retrieving the contextual details of an experience, whereas structures like the perirhinal cortex is implicated in familiarity-based recognition.

Several fMRI studies have shown that greater hippocampal activation during the encoding correlates with higher subsequent memory performance, particularly for those memories later recalled with high confidence. For instance, one prior study illustrated that the degree of hippocampal engagement during encoding can predict the likelihood of memory being confidently retrieved. This effect is often not observed for low-confidence memories, suggesting that the hippocampus may specifically support the encoding of information that is later remembered with high confidence (Kim & Cabeza, 2007). Another study supports the hippocampus's vital role in high-confidence recollections by suggesting that enhanced hippocampal activity facilitates detailed and context-rich memories (Eldridge et al., 2005).

In summary, our findings extend the existing literature by delineating the specific neural correlates associated with high-confidence memory encoding during hypothesis

testing. We emphasize the crucial roles of the hippocampus and vmPFC in facilitating effective memory encoding during hypothesis testing.

4.5 Neural Dynamics of Uncertainty and Memory Enhancement

Our final analysis that connects neural to behavioral results revealed that the ventral striatum activation in response to decision uncertainty predicts the inverted-U shaped relationship between decision uncertainty and memory. Specifically, greater activation from the ventral striatum, linked to the quadratic term of decision uncertainty, predicted a more pronounced quadratic relationship between decision uncertainty and memory performance. This indicates that participants with greater neural activations in the ventral striatum exhibited the most memory enhancements at an intermediate level of decision uncertainty.

The striatal activation is widely recognized for its involvement in processes such as perceived agency, reward processing, and valuation (Buzzell et al., 2016; Delgado, 2007; Murty et al., 2015; Tricomi & Fiez, 2012). Building on these insights, our study demonstrates how the ventral striatum activation supports memory enhancement specifically at an intermediate level of decision uncertainty. This neural finding could be linked to our behavioral insights, suggesting that motivation is pivotal. We argue behaviorally that an optimal level of uncertainty can significantly enhance memory encoding due to the high motivational state it induces. In terms of neural results, we illustrate that this quadratic relationship is contingent upon the ventral striatum which evaluates decision uncertainty. These findings enrich the existing literature on the neural substrates of uncertainty and memory by highlighting the crucial role played by the

ventral striatum in optimizing memory encoding through the modulation of decision uncertainty during hypothesis testing.

Our research supports the notion that motivation significantly influences information-seeking behaviors. According to our recent review (Shen et al., 2023), information-seeking is shaped by both an individual's intrinsic motivation for information and the surrounding context. We identify two primary motivators that drive this behavior: the instrumental and hedonic utilities of information. Factors such as judgment of learning and curiosity can affect these utilities, thereby influencing motivation for information. We argue that hypothesis testing modifies an individual's judgment of learning by integrating newly acquired information, which leads to further information-seeking and enhanced memory. This suggests a possible role of the dopaminergic system in motivation. Furthermore, curiosity appears to peak at moderate levels of decision uncertainty, potentially increasing hedonic utility and thereby driving information-seeking behaviors and improving memory through enhanced motivation.

In summary, our findings present a novel context to illuminate the role of the ventral striatum, specifically during hypothesis testing. We emphasize the critical role of motivation in driving the enhanced memory effect at intermediate levels of decision uncertainty and the ventral striatum activation predicts the inverted-U shaped relationship between decision uncertainty and memory during hypothesis testing.

4.6 Limitations

While our study yields valuable insights into the representation of decision uncertainty and its impact on the subsequent memory effect, it is important to recognize several limitations that suggest directions for future research. Firstly, the design of our

experiment constrained the memory data to trials where participants successfully unlocked the treasure chest by identifying the correct feature. This limitation means that we lack memory measures for trials characterized by very high decision uncertainty, typically observed in the initial trials of each rule set. For future studies, incorporating encoding items in these high-uncertainty trials would provide a more comprehensive understanding of how uncertainty across the entire spectrum influences memory retention.

Secondly, the complexity of hypothesis testing in real-world scenarios often exceeds the conditions simulated in our experimental design. Real-world outcomes depend not only on an individual's actions but also on environmental uncertainties that were not fully captured by our deterministic paradigm (Choung et al., 2017; Wilson & Niv, 2012). In our study, if a participant chose a key that failed to open the treasure chest, they could definitively conclude that the chosen key was incorrect and consequently eliminate associated features from consideration. However, real-world hypothesis testing frequently involves situations where outcomes cannot be attributed to single causes, nor can options be conclusively ruled out. Future studies might benefit from adopting a probabilistic design, where an unopened treasure chest could result from selecting an incorrect key or could be due to the probabilistic nature of the task environment, better mimicking the complexity of real-life decision-making under uncertainty.

Thirdly, our study, while providing insights into the neural correlates of decision uncertainty and memory, did not directly measure motivational states, which are crucial for a holistic understanding of the observed effects. Future research could benefit from integrating assessments of motivational dynamics, possibly through physiological

markers such as heart rate variability. This would allow for a deeper exploration of how motivation interacts with decision uncertainty to influence memory formation and retrieval.

4.7 Future Directions

For future analysis, we will investigate whether memory performance is associated with elevated connectivity between the hippocampus and regions implicated in hypothesis testing processing (e.g., ventral striatum) in responses to the quadratic term of decision uncertainty.

To support enhanced memory during hypothesis testing, the regions discussed above – the ventral striatum, VTA, vmPFC, and the hippocampus, do not function independently but interact. Specifically, we hypothesize that the ventral striatum initially evaluates the uncertainty level and communicates this information to both the hippocampus and the vmPFC. The hippocampus processes and stores detailed context, outcomes of decisions, and incidental information, while the vmPFC evaluates the relevance and emotional significance of the information towards goal achievement. This interaction is hypothesized to create a feedback loop that enhances memory encoding specifically at intermediate levels of uncertainty, where cognitive engagement and learning potential are maximized.

For analysis, we will conduct a psychophysiological interaction (PPI) analysis with the ventral striatum as a seed and areas related to subsequent memory effects as target regions. A GLM will be constructed that includes four standard task-related regressors from the same model described in chapter 2, one physiological regressor (VS), and four PPI regressors. Task-related regressors modeled subsequently remembered high

confidence trials, subsequently remembered low confidence trials, subsequently forgotten trials, and a nuisance regressor (i.e., missing trials). The physiological regressor will be a time course extracted from ventral striatum identified in the quadratic term of decision uncertainty contrast. The PPI regressors multiplied the striatal physiological regressor against subsequently remembered and forgotten trials. The contrast of PPI regressors will be compared for subsequently remembered versus forgotten trials for high and low confidence, respectively. The PPI model will also include a common set of confound regressors - the six motion parameters (rotations and translations), the first six aCompCor components explaining the most variance, non-steady state volumes, and the framewise displacement (FD) across time. Then the connectivity models will be run through a second-level analysis that combines the three runs. Specifically, we hypothesized that we would observe a decision uncertainty x memory interaction, such that enhanced striatal-hippocampal connectivity will predict memory at different levels of decision uncertainty.

Numerous questions remain open in the study of hypothesis testing and its influence on memory. Specifically, it is critical to explore how different hypothesis-testing strategies may affect memory outcomes. In our research, we employed a reinforcement learning model to approximate decision uncertainty, operating under the assumption that participants engaged in the hypothesis testing task in a manner consistent with reinforcement learning principles. However, it is possible that alternative strategies could influence memory differently. Moreover, little is known about how to quantify performance in the hypothesis testing, and how does individual differences in performance during hypothesis testing influence memory? It could be the case that participants who performed better showed more of a quadratic relationship between

decision uncertainty and memory. Therefore, future work is needed to further understand hypothesis testing behavior and its subsequent effect on memory.

4.8 Final Remark

In conclusion, this study significantly advances our understanding of how decision uncertainty influences memory, particularly through its effects on motivational states and underlying neural mechanisms. We highlight the crucial roles of the ventral striatum (VS), ventral tegmental area (VTA), ventromedial prefrontal cortex (vmPFC), and the anterior and posterior hippocampus in encoding decision uncertainty. Particularly, the ventral striatum is noteworthy for its peak activation at an intermediate level of uncertainty, suggesting its modulation is not just triggered by the presence of uncertainty but also by its optimal level, which facilitates information-seeking and learning. Consistent with existing literature, our findings also demonstrate a subsequent memory effect within the hippocampal regions and vmPFC during hypothesis testing. Moreover, the ventral striatum activation in response to the quadratic term of decision uncertainty supports the inverted-U shaped relationship between decision uncertainty and memory, which underscores the importance of motivation, with intermediate levels of uncertainty enhancing memory through heightened motivational states. Further exploration is needed to look into these complex interactions to better understand the cognitive and neural mechanisms during hypothesis testing.

REFERENCES

- Adcock, R. A., Thangavel, A., Whitfield-Gabrieli, S., Knutson, B., & Gabrieli, J. D. E. (2006). Reward-Motivated Learning: Mesolimbic Activation Precedes Memory Formation. *Neuron*, *50*(3), 507–517. <https://doi.org/10.1016/j.neuron.2006.03.036>
- Atkinson, R. C. (1972). Optimizing the learning of a second-language vocabulary. *Journal of Experimental Psychology*, *96*(1), 124–129. <https://doi.org/10.1037/h0033475>
- Ballard, I., Miller, E. M., Piantadosi, S. T., Goodman, N. D., & McClure, S. M. (2018). Beyond Reward Prediction Errors: Human Striatum Updates Rule Values During Learning. *Cerebral Cortex*, *28*(11), 3965–3975. <https://doi.org/10.1093/cercor/bhx259>
- Behrens, T. E. J., Woolrich, M. W., Walton, M. E., & Rushworth, M. F. S. (2007). Learning the value of information in an uncertain world. *Nature Neuroscience*, *10*(9), 1214–1221. <https://doi.org/10.1038/nn1954>
- Bein, O., Duncan, K., & Davachi, L. (2020). Mnemonic prediction errors bias hippocampal states. *Nature Communications*, *11*(1), 3451. <https://doi.org/10.1038/s41467-020-17287-1>
- Bromberg-Martin, E., & Monosov, I. E. (2020). *Neural Circuitry of Information Seeking* [Preprint]. PsyArXiv. <https://doi.org/10.31234/osf.io/3qjpf>
- Bromberg-Martin, E. S., & Hikosaka, O. (2009). Midbrain Dopamine Neurons Signal Preference for Advance Information about Upcoming Rewards. *Neuron*, *63*(1), 119–126. <https://doi.org/10.1016/j.neuron.2009.06.009>
- Bromberg-Martin, E. S., & Sharot, T. (2020). The Value of Beliefs. *Neuron*, *106*(4), 561–565. <https://doi.org/10.1016/j.neuron.2020.05.001>
- Brooks, G., Yang, H., & Köhler, S. (2021). Feeling-of-knowing experiences breed curiosity. *Memory*, *29*(2), 153–167. <https://doi.org/10.1080/09658211.2020.1867746>
- Brydevall, M., Bennett, D., Murawski, C., & Bode, S. (2018). The neural encoding of information prediction errors during non-instrumental information seeking. *Scientific Reports*, *8*(1). <https://doi.org/10.1038/s41598-018-24566-x>
- Buzzell, G. A., Roberts, D. M., Fedota, J. R., Thompson, J. C., Parasuraman, R., & McDonald, C. G. (2016). Uncertainty-dependent activity within the ventral striatum predicts task-related changes in response strategy. *Cognitive, Affective, & Behavioral Neuroscience*, *16*(2), 219–233. <https://doi.org/10.3758/s13415-015-0383-2>

- Cagniard, B., Balsam, P. D., Brunner, D., & Zhuang, X. (2006). Mice with Chronically Elevated Dopamine Exhibit Enhanced Motivation, but not Learning, for a Food Reward. *Neuropsychopharmacology*, *31*(7), 1362–1370. <https://doi.org/10.1038/sj.npp.1300966>
- Cardinal, R. N., Parkinson, J. A., Hall, J., & Everitt, B. J. (2002). Emotion and motivation: The role of the amygdala, ventral striatum, and prefrontal cortex. *Neuroscience & Biobehavioral Reviews*, *26*(3), 321–352. [https://doi.org/10.1016/S0149-7634\(02\)00007-6](https://doi.org/10.1016/S0149-7634(02)00007-6)
- Charpentier, C. J., Bromberg-Martin, E. S., & Sharot, T. (2018). Valuation of knowledge and ignorance in mesolimbic reward circuitry. *Proceedings of the National Academy of Sciences*, *115*(31), E7255–E7264. <https://doi.org/10.1073/pnas.1800547115>
- Chen, J., Cook, P. A., & Wagner, A. D. (2015). Prediction strength modulates responses in human area CA1 to sequence violations. *Journal of Neurophysiology*, *114*(2), 1227–1238. <https://doi.org/10.1152/jn.00149.2015>
- Choung, O., Lee, S. W., & Jeong, Y. (2017). Exploring Feature Dimensions to Learn a New Policy in an Uninformed Reinforcement Learning Task. *Scientific Reports*, *7*(1), 17676. <https://doi.org/10.1038/s41598-017-17687-2>
- Dayan, P. (2009). Dopamine, Reinforcement Learning, and Addiction. *Pharmacopsychiatry*, *42*(S 01), S56–S65. <https://doi.org/10.1055/s-0028-1124107>
- Delgado, M. R. (2007). Reward-Related Responses in the Human Striatum. *Annals of the New York Academy of Sciences*, *1104*(1), 70–88. <https://doi.org/10.1196/annals.1390.002>
- Delgado, M. R., Nystrom, L. E., Fissell, C., Noll, D. C., & Fiez, J. A. (2000). Tracking the Hemodynamic Responses to Reward and Punishment in the Striatum. *Journal of Neurophysiology*, *84*(6), 3072–3077. <https://doi.org/10.1152/jn.2000.84.6.3072>
- Duncan, K., Ketz, N., Inati, S. J., & Davachi, L. (2012). Evidence for area CA1 as a match/mismatch detector: A high-resolution fMRI study of the human hippocampus. *Hippocampus*, *22*(3), 389–398. <https://doi.org/10.1002/hipo.20933>
- Eichenbaum, H., Yonelinas, A. P., & Ranganath, C. (2007). The Medial Temporal Lobe and Recognition Memory. *Annual Review of Neuroscience*, *30*(1), 123–152. <https://doi.org/10.1146/annurev.neuro.30.051606.094328>
- Eldridge, L. L., Engel, S. A., Zeineh, M. M., Bookheimer, S. Y., & Knowlton, B. J. (2005). A Dissociation of Encoding and Retrieval Processes in the Human Hippocampus. *The Journal of Neuroscience*, *25*(13), 3280–3286. <https://doi.org/10.1523/JNEUROSCI.3420-04.2005>

- Eschmann, K. C. J., Pereira, D. F. M. M., Valji, A., Dehmelt, V., & Gruber, M. J. (2023). Curiosity and mesolimbic functional connectivity drive information seeking in real life. *Social Cognitive and Affective Neuroscience*, *18*(1), nsac050. <https://doi.org/10.1093/scan/nsac050>
- Euston, D. R., Gruber, A. J., & McNaughton, B. L. (2012). The Role of Medial Prefrontal Cortex in Memory and Decision Making. *Neuron*, *76*(6), 1057–1070. <https://doi.org/10.1016/j.neuron.2012.12.002>
- Filimon, F., Nelson, J. D., Sejnowski, T. J., Sereno, M. I., & Cottrell, G. W. (2020). The ventral striatum dissociates information expectation, reward anticipation, and reward receipt. *Proceedings of the National Academy of Sciences*, 201911778. <https://doi.org/10.1073/pnas.1911778117>
- FitzGibbon, L., Lau, J. K. L., & Murayama, K. (2020). The seductive lure of curiosity: Information as a motivationally salient reward. *Current Opinion in Behavioral Sciences*, *35*, 21–27. <https://doi.org/10.1016/j.cobeha.2020.05.014>
- Friston, K., & Kiebel, S. (2009). Predictive coding under the free-energy principle. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *364*(1521), 1211–1221. <https://doi.org/10.1098/rstb.2008.0300>
- Gottlieb, J., Lopes, M., & Oudeyer, P.-Y. (2016). Motivated Cognition: Neural and Computational Mechanisms of Curiosity, Attention, and Intrinsic Motivation. In S. Kim, J. Reeve, & M. Bong (Eds.), *Advances in Motivation and Achievement* (Vol. 19, pp. 149–172). Emerald Group Publishing Limited. <https://doi.org/10.1108/S0749-742320160000019017>
- Gruber, M. J., Gelman, B. D., & Ranganath, C. (2014a). States of Curiosity Modulate Hippocampus-Dependent Learning via the Dopaminergic Circuit. *Neuron*, *84*(2), 486–496. <https://doi.org/10.1016/j.neuron.2014.08.060>
- Gruber, M. J., Gelman, B. D., & Ranganath, C. (2014b). States of Curiosity Modulate Hippocampus-Dependent Learning via the Dopaminergic Circuit. *Neuron*, *84*(2), 486–496. <https://doi.org/10.1016/j.neuron.2014.08.060>
- Gruber, M., & Ranganath, C. (2019). *How curiosity enhances hippocampus-dependent memory: The Prediction-Appraisal-Curiosity-Exploration (PACE) Framework* [Preprint]. Open Science Framework. <https://doi.org/10.31219/osf.io/5v6nm>
- Harrison, L. M., Duggins, A., & Friston, K. J. (2006). Encoding uncertainty in the hippocampus. *Neural Networks*, *19*(5), 535–546. <https://doi.org/10.1016/j.neunet.2005.11.002>
- Hunt, L. T., Kolling, N., Soltani, A., Woolrich, M. W., Rushworth, M. F. S., & Behrens, T. E. J. (2012). Mechanisms underlying cortical activity during value-guided choice. *Nature Neuroscience*, *15*(3), 470–476. <https://doi.org/10.1038/nn.3017>

- Kim, H. (2011). Neural activity that predicts subsequent memory and forgetting: A meta-analysis of 74 fMRI studies. *NeuroImage*, *54*(3), 2446–2461. <https://doi.org/10.1016/j.neuroimage.2010.09.045>
- Kim, H., & Cabeza, R. (2007). Trusting Our Memories: Dissociating the Neural Correlates of Confidence in Veridical versus Illusory Memories. *The Journal of Neuroscience*, *27*(45), 12190–12197. <https://doi.org/10.1523/JNEUROSCI.3408-07.2007>
- Knutson, B., Fong, G. W., Adams, C. M., Varner, J. L., & Hommer, D. (2001). Dissociation of reward anticipation and outcome with event-related fMRI: *Neuroreport*, *12*(17), 3683–3687. <https://doi.org/10.1097/00001756-200112040-00016>
- Kobayashi, K., & Hsu, M. (2017). Neural Mechanisms of Updating under Reducible and Irreducible Uncertainty. *The Journal of Neuroscience*, *37*(29), 6972–6982. <https://doi.org/10.1523/JNEUROSCI.0535-17.2017>
- Kumaran, D., & Maguire, E. A. (2006). An Unexpected Sequence of Events: Mismatch Detection in the Human Hippocampus. *PLoS Biology*, *4*(12), e424. <https://doi.org/10.1371/journal.pbio.0040424>
- Lau, J. K. L., Ozono, H., Kuratomi, K., Komiya, A., & Murayama, K. (2020). Shared striatal activity in decisions to satisfy curiosity and hunger at the risk of electric shocks. *Nature Human Behaviour*. <https://doi.org/10.1038/s41562-020-0848-3>
- Liljeholm, M., & O’Doherty, J. P. (2012). Contributions of the striatum to learning, motivation, and performance: An associative account. *Trends in Cognitive Sciences*, *16*(9), 467–475. <https://doi.org/10.1016/j.tics.2012.07.007>
- Lisman, J. E., & Grace, A. A. (2005). The Hippocampal-VTA Loop: Controlling the Entry of Information into Long-Term Memory. *Neuron*, *46*(5), 703–713. <https://doi.org/10.1016/j.neuron.2005.05.002>
- McNamee, D., Rangel, A., & O’Doherty, J. P. (2013). Category-dependent and category-independent goal-value codes in human ventromedial prefrontal cortex. *Nature Neuroscience*, *16*(4), 479–485. <https://doi.org/10.1038/nn.3337>
- Metcalf, J., & Kornell, N. (2003). The Dynamics of Learning and Allocation of Study Time to a Region of Proximal Learning. *Journal of Experimental Psychology: General*, *132*(4), 530–542. <https://doi.org/10.1037/0096-3445.132.4.530>
- Metcalf, J., & Kornell, N. (2005). A Region of Proximal Learning model of study time allocation. *Journal of Memory and Language*, *52*(4), 463–477. <https://doi.org/10.1016/j.jml.2004.12.001>

- Metcalfe, J., Schwartz, B. L., & Eich, T. S. (2020). Epistemic curiosity and the region of proximal learning. *Current Opinion in Behavioral Sciences*, 35, 40–47. <https://doi.org/10.1016/j.cobeha.2020.06.007>
- Murphy, C., Dehmelt, V., Yonelinas, A. P., Ranganath, C., & Gruber, M. (2020). *Sparkling curiosity—But not satisfying—Enhances memory for incidental information* [Preprint]. PsyArXiv. <https://doi.org/10.31234/osf.io/d5pz4>
- Murty, V. P., & Adcock, R. A. (2014a). Enriched Encoding: Reward Motivation Organizes Cortical Networks for Hippocampal Detection of Unexpected Events. *Cerebral Cortex*, 24(8), 2160–2168. <https://doi.org/10.1093/cercor/bht063>
- Murty, V. P., & Adcock, R. A. (2014b). Enriched Encoding: Reward Motivation Organizes Cortical Networks for Hippocampal Detection of Unexpected Events. *Cerebral Cortex*, 24(8), 2160–2168. <https://doi.org/10.1093/cercor/bht063>
- Murty, V. P., & Dickerson, K. C. (2016). Motivational Influences on Memory. In S. Kim, J. Reeve, & M. Bong (Eds.), *Advances in Motivation and Achievement* (Vol. 19, pp. 203–227). Emerald Group Publishing Limited. <https://doi.org/10.1108/S0749-742320160000019019>
- Murty, V. P., DuBrow, S., & Davachi, L. (2015). The Simple Act of Choosing Influences Declarative Memory. *Journal of Neuroscience*, 35(16), 6255–6264. <https://doi.org/10.1523/JNEUROSCI.4181-14.2015>
- Murty, V. P., DuBrow, S., & Davachi, L. (2018). *Decision-making increases episodic memory via post-encoding consolidation* [Preprint]. Neuroscience. <https://doi.org/10.1101/311571>
- Niv, Y., Daniel, R., Geana, A., Gershman, S. J., Leong, Y. C., Radulescu, A., & Wilson, R. C. (2015). Reinforcement Learning in Multidimensional Environments Relies on Attention Mechanisms. *Journal of Neuroscience*, 35(21), 8145–8157. <https://doi.org/10.1523/JNEUROSCI.2978-14.2015>
- Oaksford, M., & Chater, N. (2007). *Bayesian Rationality*. Oxford University Press. <https://doi.org/10.1093/acprof:oso/9780198524496.001.0001>
- Pool, E. R., Munoz Tord, D., Delplanque, S., Stussi, Y., Cereghetti, D., Vuilleumier, P., & Sander, D. (2022). Differential Contributions of Ventral Striatum Subregions to the Motivational and Hedonic Components of the Affective Processing of Reward. *The Journal of Neuroscience*, 42(13), 2716–2728. <https://doi.org/10.1523/JNEUROSCI.1124-21.2022>
- Ruiz, N. A., DuBrow, S., & Murty, V. P. (2023). Agency as a bridge to form associative memories. *Journal of Experimental Psychology: General*, 152(6), 1797–1813. <https://doi.org/10.1037/xge0001356>

- Schomaker, J., Baumann, V., & Ruitenberg, M. F. L. (2022). Effects of exploring a novel environment on memory across the lifespan. *Scientific Reports*, *12*(1), 16631. <https://doi.org/10.1038/s41598-022-20562-4>
- Schomaker, J., & Wittmann, B. C. (2021). Effects of active exploration on novelty-related declarative memory enhancement. *Neurobiology of Learning and Memory*, *179*, 107403. <https://doi.org/10.1016/j.nlm.2021.107403>
- Schultz, W. (2006). Behavioral Theories and the Neurophysiology of Reward. *Annual Review of Psychology*, *57*(1), 87–115. <https://doi.org/10.1146/annurev.psych.56.091103.070229>
- Sharot, T., & Sunstein, C. R. (2020). How people decide what they want to know. *Nature Human Behaviour*, *4*(1), 14–19. <https://doi.org/10.1038/s41562-019-0793-1>
- Shen, X., Ballard, I. C., Smith, D. V., & Murty, V. P. (2022). Decision uncertainty during hypothesis testing enhances memory accuracy for incidental information. *Learning & Memory*, *29*(4), 93–99. <https://doi.org/10.1101/lm.053458.121>
- Shen, X., Helion, C., Smith, D. V., & Murty, V. P. (2023). Motivation as a Lens for Understanding Information-seeking Behaviors. *Journal of Cognitive Neuroscience*, 1–14. https://doi.org/10.1162/jocn_a_02083
- Spaniol, J., Davidson, P. S. R., Kim, A. S. N., Han, H., Moscovitch, M., & Grady, C. L. (2009). Event-related fMRI studies of episodic encoding and retrieval: Meta-analyses using activation likelihood estimation. *Neuropsychologia*, *47*(8–9), 1765–1779. <https://doi.org/10.1016/j.neuropsychologia.2009.02.028>
- Tricomi, E., & Fiez, J. A. (2012). Information content and reward processing in the human striatum during performance of a declarative memory task. *Cognitive, Affective, & Behavioral Neuroscience*, *12*(2), 361–372. <https://doi.org/10.3758/s13415-011-0077-3>
- Vellani, V., de Vries, L. P., Gaule, A., & Sharot, T. (2020). A selective effect of dopamine on information-seeking. *eLife*, *9*, e59152. <https://doi.org/10.7554/eLife.59152>
- Walton, M. E., Chau, B. K., & Kennerley, S. W. (2015). Prioritising the relevant information for learning and decision making within orbital and ventromedial prefrontal cortex. *Current Opinion in Behavioral Sciences*, *1*, 78–85. <https://doi.org/10.1016/j.cobeha.2014.10.005>
- Wilson, R. C., & Niv, Y. (2012). Inferring Relevance in a Changing World. *Frontiers in Human Neuroscience*, *5*. <https://doi.org/10.3389/fnhum.2011.00189>
- Wittmann, B. C., Bunzeck, N., Dolan, R. J., & Düzel, E. (2007). Anticipation of novelty recruits reward system and hippocampus while promoting recollection. *NeuroImage*, *38*(1), 194–202. <https://doi.org/10.1016/j.neuroimage.2007.06.038>

