CHARACTERIZING THREAT'S INFLUENCE IN POST-ENCODING REACTIVATION AND ITS DOWNSTREAM CONSEQUENCES ON MEMORY REPRESENTATIONS

A Dissertation
Submitted to
the Temple University Graduate Board

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

---

by
Busra Tanriverdi
December 2024

Examining Committee Members:

Jason Chein, Advisory Chair, Cognition and Neuroscience
Ingrid R. Olson, Cognition and Neuroscience
Vishnu P. Murty, Cognition and Neuroscience
Chelsea Helion, Social Psychology
Emily T. Cowan, Adelphi University
Maureen Ritchey, External Reader, Boston College

ABSTRACT

Threatening events influence memory systems in complex ways. While it was once believed that emotion enhanced all aspects of memory, recent evidence suggests that it improves recall of emotional central features, but not neutral peripheral details (Payne & Kensinger, 2011). Other studies show that emotion can enhance context, retroactively benefiting related neutral events over time (Dunsmoor et al., 2015). Notably, both effects emerge after sleep, indicating a role for memory consolidation. Recently, Cowan et al. (2021) proposed that consolidation not only strengthens salient information but also adaptively transforms memories via semanticization and integration. In this dissertation, we adopt this adaptive memory framework to investigate behavioral and neural markers of threat memory transformation. First, using free recall changes over a week as a behavioral measure of memory transformation, we show that higher subjective arousal predicts greater semanticization, with fewer episodic details retained over time. Next, functional connectivity analyses reveal a division between anterior and posterior hippocampus: the posterior hippocampus, in conjunction with the basolateral amygdala and sensory cortex during encoding, is linked to less memory semanticization, while the anterior hippocampus, coupled with the lateral occipital cortex and precuneus during post-encoding, predicts greater semanticization. Moreover, representational similarity analyses reveal that long-term memory reinstatement is strongest in the precuneus, resembling early encoding patterns, with both hippocampal regions shifting over time towards gist representations, albeit with varying granularity. Finally, we report a negative relationship between neural reinstatement in the lateral occipital cortex and memory semanticization, suggesting that detailed cortical representations help preserve

event details over time. These findings support the adaptive memory model (Cowan et al., 2021), emphasizing the dynamic roles of the hippocampus, amygdala and cortex in threat memory transformation.

To my younger self who continuously

proved many doubters (mostly men) wrong.

And to my future self, may you continue to

challenge society's expectations of you.

ACKNOWLEDGMENTS

I have an extremely long list of people to thank as mine has been an unusual journey with ups and downs, and many moves across institutions. They say it takes a village, and I truly never would have seen this date if it were not for mine. First and foremost, my unwavering gratitude to my advisors Dr. Ingrid Olson and Dr. Jason Chein. Thank you for sharing your wisdom and expertise with me, but more important to me is your unlimited kindness, patience, understanding and unconditional support in my pursuits, even when it meant that I have taken my research outside of your domain of expertise or interest. On that note, I cannot thank my unofficially third advisor Dr. Vishnu "Deepu" Murty enough on this page, or ever, for giving me a chance when no one else would, opening this wonderful path for me at Temple, and for believing in me, supporting me as one of his own graduate trainees for five long years, and making this dissertation possible. A good academic mentor is hard to find, I should know, but finding three of the most brilliant mentors with true kindness is extremely rare and I am one grateful trainee.

As if I was not already the luckiest mentee at Temple, my unbelievable luck has brought me two additional wonderful mentors in Dr. Emily Cowan and Dr. Lena Skalaban. I am forever indebted to you both for the countless hours of discussions of memory theories and methods and for all the wisdom you shared along with your friendship over the years. My endless gratitude to Dr Wei Ji Ma, who stepped in as a mentor and savior when I was going through the hardest time in my career, whose guidance ultimately led my path to Temple to start over. To my long-term mentors Dr. Irvin Cemil Shick, Dr. Reyyan Bilge, Dr. Ceren Acartürk, and Dr. Ilke Büyükduman,

thank you for showing me the way with so much grace and kindness over the last decade.

Next, I could not imagine my graduate years without my fellow graduate students and friends. I had found a brilliantly funny team of best friends in Ginny Ulichney and Nick Ruiz, who have listened to me vent about grad school and life way too many times over tahini shakes, have given me confidence when I needed it the most, and have constantly encouraged me to go on. You have made this experience all the more worthwhile and I will forever cherish our memories and cannot thank you both enough for the love, laughter, kindness and support we have shared this past four years. Thank you to my friends, theoretical soulmates and co-founders of the Trauma Discussion Group, Camille Johnston and Dr. Holly Sullivan-Toole, for the countless hours of discussions around all-things trauma, theoretical and personal, for the joyous hours of dreaming and working together and for your love, support and kindness. Thank you to my lab mate and friend Dr Kim Nguyen for helping me live my best social life as a Ph.D. student and encouraging me be unhinged as we discuss theories of memory and Taylor Swift alike. My friends Dr. Maria Brucato, Dr. Xinxu "Karen" Shen, Dr. Elizabeth Horwath, and Dr. Merve Tansan deserve much love and gratitude for the countless times you have lifted me up every time I came to you with confusion about my work, grad school, and concerns over my life in the US. I have been gifted with three big labs with so many friends with big hearts from each, and while it is hard to list every single one, I am thankful for my current and former lab mates Ga In Shin, Dr. Liz Beard, Dr. Michelle Chiu, Steven Martinez, Dr. Susan Benear, Dr. Haroon Popal, Dr. Katie Jobson, Naoya Tani, Linda Hoffman, and Julia Foley for the time we shared together in the Chein, Olson and Murty labs.

I could not have collected this data without the help of my friend and collaborator Dr David Gregory, and the help of our undergraduate research interns Harry Green, Yuliana Fartachuk, Katie Floyd, Sheila Jimenez, and Anouska Jha, and our master's student Julia Foley who I have been blessed to work with on two projects now. This dissertation would not have been possible without the countless hours our participants have dedicated. Thank you to our former lab manager Isabel Leiva for her help with the IRB.

Finally, and most importantly, I must acknowledge my family and close friends. To my parents, you are the first ones who have inspired me to go far for the pursuit of knowledge, even though it meant for you to send me oceans away, I am forever grateful for your wisdom, love and support. Thank you to my sisters Merve and Zikra for always having my back, showering me with your unconditional love and support for everything I do, and particularly through the most difficult period of my life. To my friend and Elif Nur Poyraz, with whom I shared this long academic journey with all its ups and downs since before I came to Temple: thank you for your dedication to our friendship, for your kindness and support through one of the worst times in my career and life, and your openness and willingness to always hold a space for me. To my friends Ayşenur, Bilge, Burçin, Esma, Hande, Kübra, Melike, Meryem, Seda, Şeyma, and Zeynep, who never allowed the long-distance and hours between us to make me feel alone all these years. To my therapist, who has helped me find my healthy adult voice, and sort of become another mentor and friend to me over the years, whose own research and expertise very much influenced my thinking about memory in the context of trauma and helped me grow not only as a person but also as a scientist. Last but certainly not least, all my love and

heartfelt gratitude to my best friend and husband, my chosen family, Emirhan, who has loved, cherished, and supported me for 13 long years. Thank you for growing with me, supporting me through thick and thin, believing in me when no one else would, including myself, and for helping me find joy and laughter every day. Your love is the reason I am still here.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1

INTRODUCTION

"In this world, nothing is as it seems nor as it is lived.
Everything is as it is remembered!" (Barış Bıçakçı, 2003)

Our lives are filled with various emotional experiences. Not all emotional experiences are made equal, however. Some enrich our behavior, well-being and relationships positively, while others have detrimental effects on many aspects of our lives. It is those in the latter category that sometimes have the biggest impact on us, particularly in how we perceive their effect on our current and future behavior, and thus, how we remember those experiences carry much weight. Consider the example of a car accident where a person riding their motorcycle gets struck and injured by a red car. Remembering the details of the accident, such as the time and place, the accident's impact on their physical and mental wellbeing, as well as any additional contextual details will all prove helpful to prevent getting in future accidents. For example, the person *specifically* remembering that they were sleep-deprived, and that it was a rainy day, both important contextual details that probably contributed to the accident, may help them decide not to ride their motorcycle under similar circumstances again. Alternatively, the person may recall that it was a red car that caused their injuries and consequently make the *generalization* that all red cars are generally more dangerous, and that they should therefore avoid cars of this color the next time they are on the road. Notably, in such life-threatening experiences, we humans keep an account of both specific details that we believe are important and unique to the experience, and also the commonalities that hold across similar events we experience (or learn about through others' experience). In the cases where individuals feel a heightened sense of threat associated with such

experiences, these different recollections may lead to component symptoms of psychiatric conditions, such as the fear over-generalization and intrusions that are characteristic of PTSD. The question that therefore arises is how seemingly disparate recollections of the same experience, one with highly specific details and another with only a general sense of what happened, are formed and kept in memory.

While people have extensively speculated on this question in the clinical literature (Holmes & Bourne, 2008; Brewin, 2014; Rigoli et al., 2016), it has become increasingly clear that discrepant claims within this literature regarding fear generalization versus vivid intrusions are hard to resolve without a clear understanding of the neural circuitry supporting threat memories (Parsons & Ressler, 2013; Lopresto, Schipper, & Homberg, 2016; Iyadurai et al., 2019). Thus, it is no surprise this question has also been at the center of brain research spanning multiple stages of memory from encoding to consolidation to retrieval (McGaugh, 2000; Guskjolen & Cembrowski, 2023; Sridhar, Kharmaj, & Asthana, 2023), as well as in work exploring emotion's modulatory role on these processes (LaLumiere et al., 2017; Crowley, Bendor, & Javadi, 2018).

To tackle this conundrum in the lab, we first need to consider how emotional experiences, particularly those with high subjective and physiological arousal, are encoded into long-term memory representations (LaBar & Cabeza, 2006; Murty et al., 2010; Yonelinas & Ritchey, 2015; Clewett & Murty, 2019). Second, as Bıçakçı's quote above brilliantly captures, our memories are not recalled as they are experienced and initially encoded. They are rather dynamic representations that live in different parts of our brain, and that are susceptible to changes, updates and forgetting. Thus, we need to understand how memories are consolidated and transformed over time, and relatedly,

how psychophysiological arousal as one experiences memory forming events modulate these consolidation process (Kumaran et al., 2016; Robin & Moscovitch, 2017; Favila, Lee, & Kuhl, 2020; Cowan et al., 2021; Moscovitch & Gilboa, 2021). Research in these domains has implicated particular neural regions and in broader memory processes (e.g., hippocampus and neocortex) and in emotional memories (e.g., amygdala). Crucially, however, these neural systems do not act in isolation, but rather, are intertwined in supporting the various stages of memories for highly arousing, emotional experiences. Thus, it is essential that we consider their interaction at different stages of memory transformation.

Roadmap to this Dissertation

The overarching goal of this dissertation is to understand the neural underpinnings of threat's downstream effects in long-term memory reorganization. To that end, our first goal is to identify behavioral indices of long-term memory transformation that are affected by arousal. Second, we aim at characterizing threat-induced alterations and biases that arise during both memory encoding and consolidation. Third, we aim at characterizing the neural indices of long-term memory transformation in the hippocampus and cortex. Our final goal is to explore how threat-related post-encoding consolidation processes relate to behavioral and neural indices of threat memory transformation.

In this opening chapter (Chapter 1), we first provide a theoretical background that is necessary for understanding the concepts we hope to integrate in this work. This includes an overview of the memory consolidation and transformation processes, threat's influence on memory, particularly through arousal, and the interaction of these processes

in supporting long-term memories of emotional experiences, as well as a discussion of open questions. In Chapter 2, we present the methods utilized in the current study to address some of the open questions introduced in Chapter 1. In Chapter 3, we provide evidence revealing how threat-related arousal influences the encoding and post-encoding processes, including indices of both the behavioral and neural transformation of memories. Finally, in Chapter 4, we end with a discussion of these results as interpreted into the context of the broader theoretical framework introduced in Chapter 1, along with a consideration of limitations of our study, and future directions, including implications of our results for psychiatric conditions.

Theoretical Background

Memory Consolidation

It is crucial to understand the fundamentals of systems consolidation in order to understand threat's downstream influence on these processes, and how threat thereby shapes the nature of memories. Memories do not stay unchanged after their initial encoding. Rather, a stabilization process, called *consolidation*, follows encoding, that this process determines which experiences are ultimately retained in long-term memory. During consolidation memories are selectively prioritized, strengthened and transformed over time, at both the cellular and systems levels. Below, we first briefly explain memory consolidation mechanisms, and then discuss how threat-related information might be selectively prioritized during consolidation.

Cellular memory consolidation refers to the process by which transient, short-term memories are transformed into long-term, stable, memories at the cellular level. This process involves structural and functional changes in neurons, primarily within the

hippocampus (Cahill & McGaugh, 1998; Dudai, Karni, & Born, 2015), taking place via various forms of synaptic plasticity, including long-term potentiation (LTP) and long-term depression (LTD). LTP and LTD balance each other in strengthening and weakening of synapses formed between neurons that were active during an experience, allowing the prioritization and reorganization of synaptic networks for efficient storage of relevant information while filtering out unnecessary details. Further protein synthesis plays a crucial role in stabilizing these synaptic changes, allowing the memory trace to persist in the long-term (Abraham & Williams, 2003; Dudai et al., 2015). While these cellular changes help explain the selective stabilization of memories, it is not obvious how they may translate into memory transformation at the scale we are interested in, for several reasons: One, there is consensus that cellular consolidation takes place within the hours after learning while the memory transformation in question requires days, if not weeks, months or years (Genzel & Wixted, 2017). Further, and relatedly, the cellular consolidation framework does not account for processes like gist-extraction that contribute to memory transformation, and are at the center of this dissertation, which emerge in later stages of memory organization through interactions across a broad network of regions (Wang & Morris, 2010).

An alternative framework to cellular consolidation provides more direct insights regarding long-term memory organization: systems consolidation. According to the standard model of systems consolidation, memories that are initially dependent on the hippocampus are reorganized and distributed across cortex over a period of time that spans from days to years (Squire & Alvarez 1995; McClelland, McNaughton, & O'Reilly, 1995), which might explain the retrograde amnesia wherein remote memories

remain intact while recent memories prior to hippocampal and broader medial temporal lobe lesions are forgotten (Scoville & Milner, 1957; Squire et al., 1984). Critically, these early models posit that the hippocampus rapidly forms neural patterns representing episodic events, and then trains the neocortex to slowly form a stable representation, that is aggregated over many repeated reactivations of these patterns, such that remote memory recall no longer depends on hippocampus (McClelland et al., 1995; O'Reilly et al., 2014).

Other systems consolidation models, such as multiple trace and trace transformation theories, propose an alternative explanation to the amnesic reports: multiple neural traces of the same memory might coexist in the hippocampus and cortex, instead of a gradual shift from hippocampal to cortical representations (Nadel & Moscovitch, 1997; Winocur & Moscovitch, 2011). Under these alternative models, the hippocampus forms a new neural trace each time a memory is reactivated. Accordingly, as each trace is communicated to the cortex, a hippocampal – cortical ensemble is created, which gradually extracts the overlapping information contained across traces and consequently forms a gist-level, semantic representation. Both theories suggest that there is a connection between neural and psychological representations, asserting that the hippocampus is essential for any memory requiring detailed representation, regardless of its age or type (episodic, spatial, or semantic) (Tompary & Murty, 2024). Trace transformation theory, in particular, highlights a dynamic interaction between hippocampus-based episodic memories and cortex-based gist memories, suggesting that their relative strength or the demands of the task will determine which will be retrieved.

Methodological Approaches to Systems Consolidation. Now that we have presented the fundamental principles of systems consolidation, particularly emphasizing the dynamic interaction between episodic versus gist-level representations, we next discuss the neural mechanisms contributing to this representational granularity. Considerable evidence from both animal and human studies suggests that *replay* is an important mechanism for systems consolidation. Replay refers to a neural process wherein hippocampal cells *re*-activate neuronal firing patterns that are initially formed at encoding, later in sleep (Buzsáki, 1989; Wilson & McNaughton, 1993; Skaggs & McNaughton, 1996; Girardeau & Zugaro, 2011) or awake rest (Foster & Wilson, 2006; Diba & Buzsáki, 2007; Karlsson & Frank, 2009; Jadhav et al., 2012). Accordingly, neural replay selectively strengthens encoding patterns represented in the hippocampus (Rasch & Born, 2007; Carr, Karlsson, & Frank, 2012), and cortex (Ji & Wilson, 2007; Lansink et al., 2009; Tambini & Davachi, 2019; Tanriverdi et al., 2023).

In the last few decades, human brain imaging studies have utilized various approaches to characterize the neural processes that take place during post-encoding phases as part of memory consolidation. Many studies have adopted multivariate approaches, such as multi-voxel pattern analysis (MVPA) and representational similarity analysis (RSA), to identify the similarity between encoding and post-encoding neural patterns occurring in the hippocampus and cortex, and treat this as a proxy for the neural replay observed in single- and multi-cell recording studies conducted in rodents (e.g., Buzsáki, 1989; Wilson & McNaughton, 1993; Foster & Wilson, 2006; Diba & Buzsáki, 2007; Jadhav et al., 2012). With such multivariate approaches, a higher correlation between neural patterns observed at encoding with those observed at post-encoding

phases is considered as evidence for neural reactivation. Generally, studies have found that greater pattern re-activation during post-encoding periods is associated with better subsequent memory (Deuker et al., 2013; Schlichting & Preston, 2014; Schapiro et al., 2018; Alm, Ngo & Olson, 2019; also see Tambini & Davachi, 2019 for a review).

As briefly discussed earlier, systems consolidation requires a coordinated communication between the hippocampus and neocortex in order for the cortex to extract the gist-level information across episodes. This hippocampal – cortical communication is also characterized during post-encoding consolidation phases and linked with subsequent memory using functional connectivity (Tambini, Ketz, & Davachi, 2010; Tompary, Duncan & Davachi, 2015; Tompary & Davachi, 2017; Murty et al., 2017; Liu, Grady & Moscovitch, 2018). While functional connectivity analysis provides insight into the concurrent neural dynamics between regions over an entire learning or rest period, it provides only a "state" level (i.e., *global*) signal regarding the cross-regional communication, limiting our understanding of communication across regions at the event-level. Recently, we have characterized the concurrent-reactivations (co-reactivations) occurring across the hippocampus and cortex, similar to the co-replay studies in rodents, to further investigate the hippocampus – cortex coordinated communication at particular timeframes within the consolidation window (Tanriverdi et al., 2023). This RSA-based approach allowed us to model neural similarity across two regions at specific time points, providing insight into event-specific communication across the hippocampus and cortex.

Both functional connectivity and representational similarity analyses provide unique windows into the dynamic nature of memory transformation, and these

approaches are utilized separately in this dissertation to 1) uncover the encoding and post-encoding processes (functional connectivity) supporting memory transformation, and 2) expose the neural transformation that memories undergo over the course of a week (representational similarity).

Open Questions in Systems Consolidation Research. While this dissertation builds on previous systems consolidation models in evaluating memory transformation, there are several open questions in the systems consolidation literature that we would like to highlight here. Systems consolidation models we have discussed so far have consider the hippocampus and cortex with little specification of the potentially separate functional roles of specific subregions, which is important to acknowledge for several reasons.

First, the hippocampus is not a functionally unified region, with recent work highlighting a functional differentiation along its long axis. Specifically, the anterior third of the hippocampus supports more gist-level representations through pattern completion, while the posterior third supports more detailed representations through pattern separation (Yassa & Stark, 2011; Poppenk et al., 2013; Brunec et al., 2020). This functional division is also evident in how these two subregions communicate across a network of other memory regions: while the anterior hippocampus shows more functional connectivity with the anterior temporal lobe and other regions on the anterior gradient of the brain, the posterior hippocampus shows more functional coupling with a network of more posterior brain areas (Ranganath & Ritchey, 2012; Ritchey et al., 2015). Therefore, we might expect to see differences in how the anterior versus posterior hippocampus engage as memories undergo consolidation and subsequent transformation.

Second, while previous theories highlighted neocortical areas, particularly the

medial prefrontal cortex (mPFC), for keeping more gist-level representations, they are rather implicated in forming generalizations through integration over related experiences, with overlapping information (Cowan et al., 2021). Thus, other cortical areas, rather, might play a more critical role in the transformation that unique episodic memories undergo –as investigated in this dissertation. To that end, more recent work in both rodents and humans has offered evidence of memory reactivation in sensory and parietal cortices (e.g., Bang et al., 2018; Wittkuhn & Shuck, 2021; Skalaban, 2022), as well as a coordinated reactivation between the hippocampus and visual cortices (e.g., Ji & Wilson, 2007; Tanriverdi et al., 2023; Yu et al., 2024). For instance, the precuneus has been consistently highlighted for its role in long-term neural reinstatement, particularly during autobiographical recall (e.g., Favila et al., 2018; Gilmore et al., 2021). Additional studies report that greater post-encoding functional coupling between the hippocampus and visual cortex in association with better subsequent memory retrieval (e.g., Tambini, Ketz, & Davachi, 2010; Murty et al., 2017). However, we have previously found that co-reactivations of hippocampus – category-selective cortex during post-encoding rest were higher for items that are either incorrectly recognized or forgotten over a week-long delay (Tanriverdi et al., 2023), raising questions about the granularity of representations that co-exist in the hippocampus and cortex. Together, these findings warrant a broader search for consolidation markers in parietal and sensory cortices, as well as in their interaction with the hippocampus.

Threat's Influence on Memory

Having reviewed the memory consolidation framework, we can now turn to threat's influence on memory encoding, consolidation and retrieval processes.

Behaviorally, threat's influence on memory has been investigated using a variety of fear-conditioning and episodic memory paradigms, with an emphasis on the psychophysiological responses associated with threatening experiences, such as arousal and negative emotional reactions (Murty et al., 2010; Murty & Adcock, 2017; Clewett & Murty, 2019). Memories for events that elicited emotional responses were initially thought to be distinctive, characterized by vividness, accuracy, and high levels of confidence in recall. In an array of early behavioral studies, participants reported highly vivid episodic recollections regarding their experiences of learning about natural disasters (e.g., Bahrick et al., 1998), assassinations (e.g., Brown & Kulik, 1977; Christianson, 1989) and terrorist attacks (e.g., Pezdek, 2003; Smith et al., 2003; Paradis et al., 2004; Budson et al., 2004; Budson et al., 2007).

However, additional work has shown that while participants may report greater confidence for emotional than neutral experiences, their recollections of episodic details may not necessarily reflect higher accuracy for emotional events (e.g., Neisser & Harsch, 1992; Talarico & Rubin, 2003; Sharot et al., 2007). To complicate things further, even when studies find emotion-related memory enhancement, this effect appears to be selective and does not uniformly improve the accuracy of all event details. Indeed, two separate lines of behavioral evidence highlight that threat-induced arousal biases memory retrieval towards remembering the emotional gist of an experience, at times at the expense of event details. Crucially, both of these effects are unique to emotional stimuli and not shown for neutral information, and both appear to depend on memory consolidation. First, as evident across many item–background trade-off studies, emotionally salient central details are remembered better compared to neutral

peripheral/contextual details following a sleep-filled delay (e.g., Christianson, 1984; Burke, Heuer & Reisberg, 1992, Kensinger et al., 2007a, 2007b; Payne et al., 2008; Payne & Kensinger, 2011). Second, category-level emotional saliency retroactively boosts memory for items that are initially encoded under neutral conditions, but only after a 24-h delay (e.g., Dunsmoor et al., 2015; Patil et al., 2017), suggesting that the emotional salience associated with the overall category is generalized to items within that category, even when those items were not initially paired with aversive outcomes. Arguably, the findings from item–background trade-off studies hint at selective prioritization and stabilization through consolidation, while the retroactive memory effects highlight memory reorganization and transformation.

With regard to neural circuitry supporting threat memories, both the amygdala and hippocampus are shown to play important, but separable roles (e.g., Bechara et al., 1995; LaBar & Cabeza, 2006; Mather, 2007; Yonelinas & Ritchey, 2015). Early models have primarily focused on the amygdala's role in fear conditioning, particularly basolateral amygdala (BLA), supporting acquisition of fear associations (Campeau & Davis, 1995; Rabinak & Maren, 2008; Roesler et al., 2021). Studies of patients with amygdala damage showed that amygdala damage prevents the memory advantage for central details in emotional stimuli, which further emphasized amygdala's functional role in emotional learning, particularly of central details, or gist (Adolphs, Denburg, & Tranel, 2001; Adolphs, Tranel, & Buchanan, 2005). The hippocampus's role in threat encoding, however, is more complicated. While it is generally presumed that hippocampal engagement during emotional memory encoding will enhance memory details (Bechara et al., 1995), there is also considerable evidence (and theoretical consideration) that

excessive threat impairs hippocampal function (e.g., Kim & Diamond, 2002; McEwen, 2007, Schwabe & Wolf, 2012; Clewett & Murty, 2019). Given the hippocampus's role in item – context association learning, such impairment in hippocampal function would be disruptive for emotional binding, potentially giving rise to generalized representations for emotional experiences (Maren et al., 2013).

It is crucial to emphasize that encoding processes, whether in the amygdala or hippocampus, are not the sole determinants of how arousing events are remembered. Equally, if not more, important are consolidation processes, which play a key role in shaping how emotional experiences are stored in long-term memory. The previously discussed behavioral findings showing that highly arousing stimuli are better remembered compared to their neutral counterparts, particularly after a delay filled with sleep, strongly suggest an adaptive consolidation effect (Cowan et al., 2021), wherein emotionally salient information is selectively prioritized (item–background trade-off effects) and adaptively integrated (retroactive memory effects). Functional MRI studies have started to uncover how these consolidation effects might unfold during post-encoding rest. For instance, de Voogd and colleagues reported higher post-encoding reactivation for stimuli associated with aversive but not neutral outcomes in cortical areas (de Voogd et al., 2016). Critically, cortical reactivations for these stimuli were driven by higher hippocampal – cortical functional connectivity, and were associated with subsequent memory benefits.

More recently, Clewett and colleagues (2022) have highlighted neural mechanisms supporting the previously reported retroactive memory effects in aversive conditioning tasks (e.g., Dunsmoor et al., 2015). They have shown that category-selective

cortical reinstatement during fear conditioning was associated with retroactive memory effects for aversive stimuli. Further, increased post-encoding hippocampal–category selective cortex connectivity was associated with greater retroactive memory effects for the aversive category. Crucially, emotion related memory enhancement for neutral information could happen prospectively, as Tambini and colleagues have recently demonstrated (Tambini et al., 2017). These authors found that when emotional learning is followed by neutral learning, amygdala–anterior hippocampus connectivity patterns observed during initial emotion learning persisted over time, well into the period of neutral learning ("emotional carry over"), suggesting a proactive encoding benefit for unrelated neutral items that are learned after emotional stimuli (Tambini et al., 2017). Further, hippocampal multivoxel patterns that characterized recollection-based emotional memory formation were reinstated and similarly supported the later recollection of neutral stimuli that followed emotional stimuli. Collectively, these studies underscore the adaptive influence of arousal on encoding (Tambini et al., 2017) and post-encoding (de Voogd et al., 2016; Clewett et al., 2022) processes. Accordingly, during complex naturalistic experiences, such as watching threatening events unfold in a short video clip (as we implement in this dissertation), information will be adaptively processed throughout both encoding and consolidation and retained in memory with varying degrees of granularity.

The final piece of the puzzle that has been missing in our discussion thus far is the influence of threat-induced arousal on memory transformation and reorganization post-consolidation. To address that, we must consider alterations in emotional memories *after* they are stabilized through consolidation. In a pioneering study, Misanin and colleagues

have shown that administering electroconvulsive shocks after retrieval leads to retrograde amnesia for previously consolidated fear memories (Misanin et al., 1968). Nader and colleagues later showed similar effects with infusion of a protein-synthesis inhibitor (i.e., anisomycin) in basolateral amygdala post-retrieval (Nader et al., 2000). Crucially, the same treatment did not alter memories in the absence of reactivation, suggesting that memories become labile again upon reactivation, and interventions targeting protein synthesis post-reactivation may disrupt the retrieval advantage for emotional material (Nader et al., 2000; Kindt et al., 2009). More recent evidence suggest that similar disruptions may be achieved by behavioral interventions immediately after reactivation (e.g., Agren et al., 2014). These studies further highlight the adaptive nature of memory reorganization and open the field for new questions about the downstream effects of emotional memory reactivation in long-term memory representations.

Open Questions in Threat Memory Research. While we have highlighted recent evidence for threat's adaptive influence on memory processes, we are far from a complete picture considering the inconsistent findings discussed above. We argue that there is more to uncover, particularly regarding the dynamic representational changes across the different stages of memory reorganization.

First, we would like to revisit the functional division between anterior and posterior hippocampus in the context of threat memory consolidation (Bannerman et al., 2004; Strange et al., 2014; Pronier, Morici & Girerdeau, 2023). Given their division in pattern separation and completion, it has been recently hypothesized that anterior hippocampus engagement would contribute to gist via increased representational similarity for fear-related information (e.g., Leal et al., 2014). On the other hand, the

posterior hippocampus contributes to memory differentiation for the emotional materials through pattern separation and the retrieval of contextual details (e.g., Lissek et al., 2014). Crucially, basolateral amygdala projections to anterior versus posterior hippocampus might further and separately modulate this functional division in threat memory consolidation (Huff et al., 2016; Yang & Wang, 2017). Therefore, probing the amygdala – hippocampus connectivity at the level of subnuclei (e.g., testing basolateral – anterior hippocampus coupling separately), might yield additional insights regarding their role in various stages of memory processing and transformation.

Additionally, the threat-related memory effects we have discussed throughout the encoding, post-encoding consolidation, and retrieval (or post-consolidation) phases have mostly been studied in isolation, which hinders our understanding of the dynamic nature of threat memories. Thus, we suggest that a comprehensive study design wherein markers of both behavioral and neural transformation are probed across all stages of memory has the potential to substantially improve our understanding of threat memory.

Theoretical Overview and the Current Study

Clearly, there are several areas of disagreement that remain in the literature. First, it is still not understood how threat-related information would be retained over time: with specific details or as gist. Relatedly, the hippocampus's role, particularly along the long axis, in dynamic reorganization of threat memory remains unresolved: do these processes rely more or less on anterior versus posterior hippocampus? Similarly, does the cortex support detailed or gist-level representations? Finally, does systems consolidation introduce selective bias for arousal-inducing stimuli through replay, at the expense of contextual details, thereby hindering episodic recollections?

This dissertation addresses key open questions by testing the following hypotheses: 1) Memory recall will undergo a transformation over time, with specific event details gradually fading while a more generalized, emotionally focused representation is retained in the long term. This transformation is expected to be influenced by subjective arousal. 2) Although the hippocampus will be crucial for encoding, consolidating, and retrieving threat-related memories, we anticipate functional differences along its long axis. Specifically, the posterior hippocampus will be more active during early stages to ensure accurate encoding of episodic details, while the anterior hippocampus will play a larger role in post-encoding consolidation and long-term retrieval, supporting the shift toward a gist-like memory representation. 3) We predict distinct functional connectivity patterns for the anterior versus posterior hippocampus with the amygdala and various cortical regions, including the precuneus and visual cortices, aiding in memory reorganization. 4) Lastly, the anterior, but not posterior, hippocampus and associated cortical regions will show long-term memory reinstatement, which will correlate with behavioral memory transformation.

CHAPTER 2

METHODS

Our goal for the described methodology in Chapter 2 is to understand how threat-related arousal influences memory transformation, both behaviorally and neurally. Previous research highlights that threat and non-threat memories might be remembered with different levels of granularity, i.e., on a spectrum from highly detailed episodic to highly general emotional gist. In following the evidence provided by the extant literature, we hypothesize that the number of details remembered from threatening events will change over time, as memories go through consolidation. Thus, we aim to uncover the neural underpinnings of such transformation. In order to test our assumptions, we have conducted a three-session experiment which took place over the course of a week (Figure 1). Here, we describe our study design and analytic approach in detail.

Participants

Forty-eight young adults from the Temple University community were recruited and compensated for their time ($60 for Day-1 and Day-2, $50 for Day-8, and an additional $50 for study completion). Participants were native English speakers, had normal or corrected-to-normal vision, and reported no psychiatric conditions. One participant did not complete the study, and therefore is removed from all analysis, leaving us with an N = 47 (28F, M_{age} = 20.24, SD_{age} = 2.02). One additional participant was removed from all the analyses because of behavioral data loss due to computer issues during the Day-2 memory test. Two additional participants were excluded from fMRI data analyses, and from the tests of brain behavioral correlates, because their Day-1 fMRI data could not be preprocessed due to technical problems at the scanner, which left only 44 participants for

the Day-1 neural analysis. Finally, an additional five participants were removed from all of the Day1-Day8 neural similarity analyses, and related brain-behavior correlates, because their Day-8 fMRI data could not be preprocessed due to technical problems with the data obtained from the scanner (four) or because of excessive noise during the functional runs (one), leaving a sample of 39 participants for these analyses.

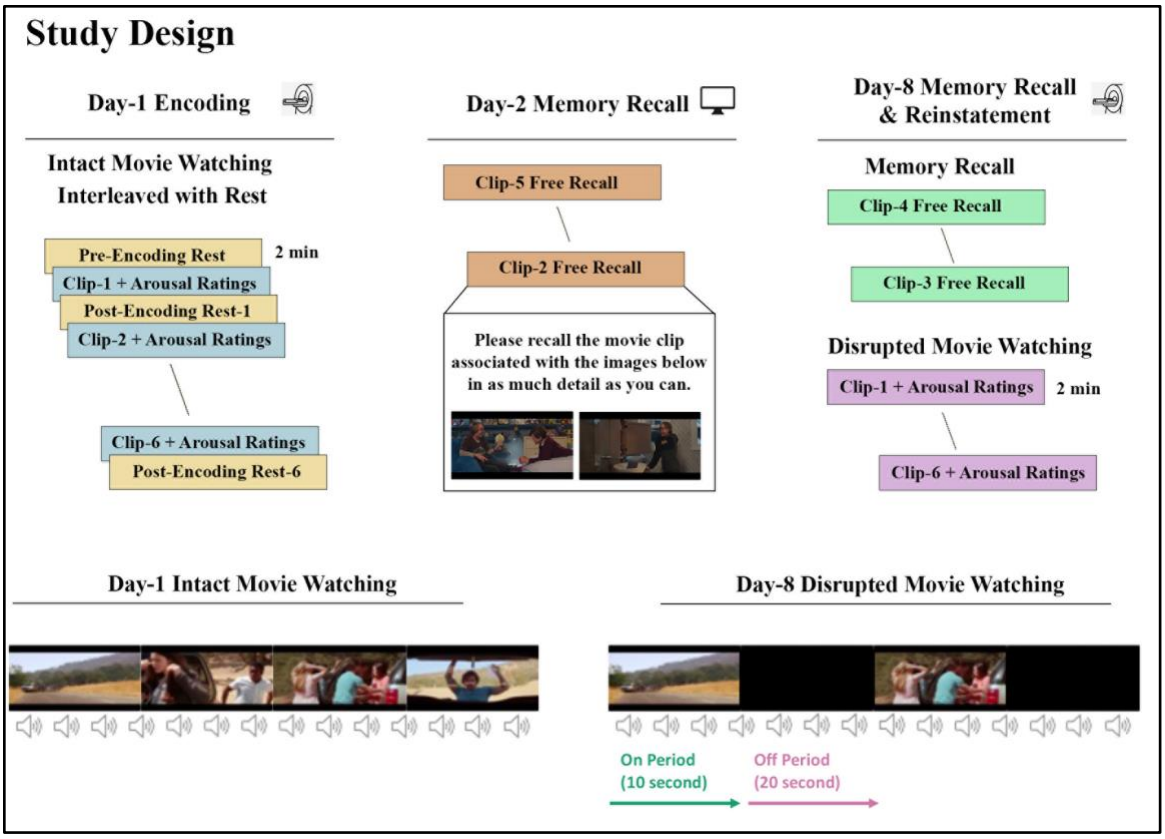

Figure 1. Experimental procedure. Encoding (Day-1) consisted of a baseline rest scan, 6 encoding scans wherein participants watched a short clip (3 aversive, 3 neutral, all intact versions), and 6 post-encoding rest scans. The first cued-recall task was completed behaviorally, 24-h after encoding (Day-2). The second cued-recall task was completed in the scanner, 1-week after encoding (Day-8). On Day-8, participants also rewatched all 6 clips (disrupted versions) in the scanner.

Study Materials

For encoding, we selected six horror movies from a pool of over 100 available films reviewed on Shudder VOD. These movies were selected to evoke varying levels of negative emotion and arousal in viewers. One particular goal in selecting these movies was to ensure that we would capture individual differences in self-reported ratings of arousal (which we probed after each clip (see Experimental Procedure)) as we did not want to rely on an assumed valence dimension (negative versus neutral) when probing threat memory transformation. To that end, movies were carefully selected to highlight suspenseful and psychological horror over more overt, bloody/body horror as we wanted to capture arousal-related to threat anticipation instead of disgust, which might be evoked through overt horror imagery. Further, by showing participants a variety of clips in which threat is depicted in different ways (e.g., domestic violence versus acts of self-harm), we reasoned, would capture idiosyncratic differences in self-reported ratings of arousal across participants.

All movies selected were small budget or independent to ensure low familiarity of the movie to participants. For each movie, we selected two 2-minute clips depicting an aversive scene and a neutral scene, which were validated to yield individual differences in subjective feelings of arousal and valence through an online behavioral study (Gregory, 2024). When extracting these short clips, we prioritized finding clips that contained a full scene including a beginning, middle and end, while also balancing basic features described: The aversive and neutral clips taken from the same movie were matched on simple aesthetics such as setting, filming, characters, and dialogue/music to

control for these potential confounds. Notably, each participant only viewed the aversive or neutral clip from each movie during the study.

For intermittent reactivation (see *Experimental Procedure* and Figure 2C), borrowing from Skalaban (2022), we created disrupted versions of each clip. Accordingly, each disrupted clip had a 10- second video-on and 20- second video-off sequence, resulting in a total of 4 *on* and 4 *off* segments. During the off periods, a dark blank screen was presented while the audio continued (i.e., the audio persisted, undisturbed, across the is on and off periods). Due to experimenter error, the disrupted version of one of the clips was improperly prepared to have a 10 second on and 10 second off periods and was thereby excluded from all analyses.

Finally, for each clip, the still images of the first and the last frame were extracted to be used as cues for free recall on Day-2 and Day-8.

Experimental Procedure

In order to test the neural underpinnings of threat memory transformation, we have conducted a three-session experiment, with in-person lab visits spanning over the course of one week. The experimental sequence was as follows: 1) Day-1 (in the MRI scanner) consisted of instruction and encoding phases, where participants first watched clips as they underwent functional imaging, and then rated each clip for their emotional reactions. Critically, each clip encoding was interleaved with a functional rest scan to probe post-encoding memory consolidation, 2) Day-2 consisted of a temporal memory test, cued-free recall, and a questionnaire phase (24-hours after Day-1), and 3) Day-8 consisted of cued-free recall and intermittent reactivation tasks in the scanner as well as a brief questionnaire after the scan, and took place one week after encoding (Figure 1).

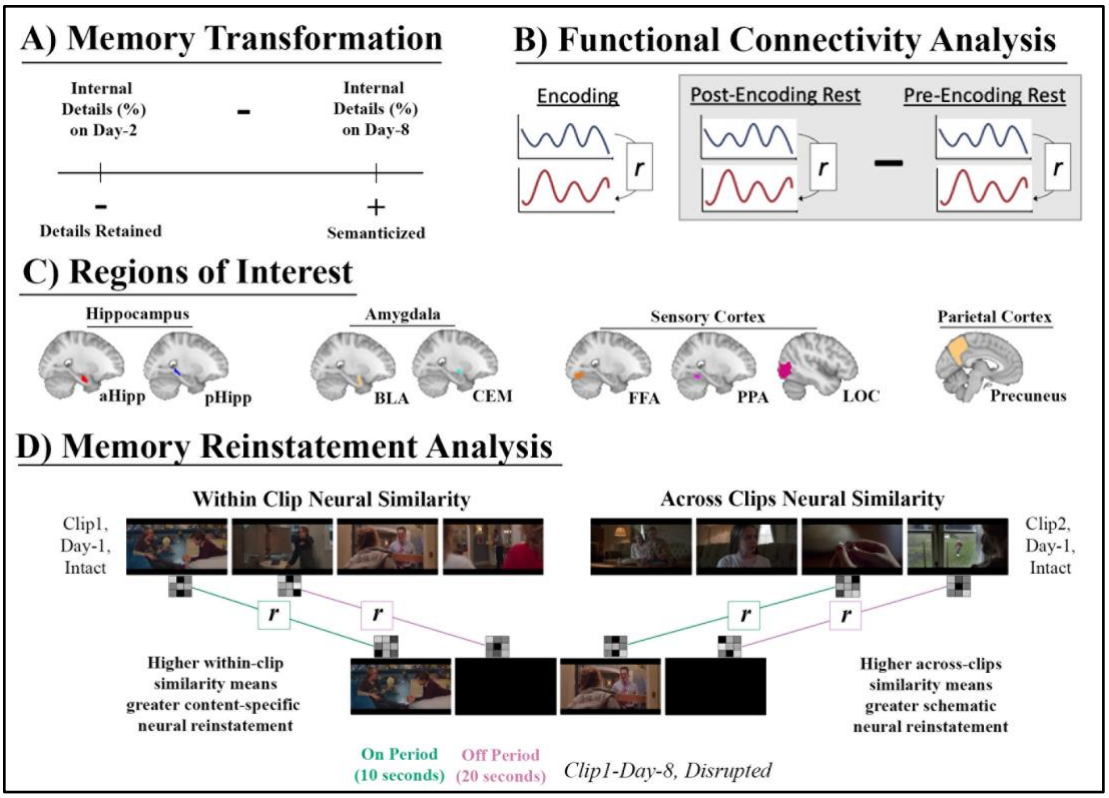

Figure 2. Data analytical approach and brain regions of interest (ROIs). A. Behavioral memory transformation score is calculated as the difference between internal details (%) recalled on Day-2 and Day-8. B. Functional connectivity analyses were conducted for all of the encoding and rest scans on Day-1. Anterior and posterior hippocampus were considered the seed regions, whereas all amygdala and cortical regions were target regions. In order to capture clip-specific post-encoding patterns, for any given ROI pair, we have subtracted the pre-encoding (i.e., baseline) connectivity from post-encoding connectivity. C. Regions of Interest. aHipp: anterior hippocampus, pHipp: posterior hippocampus, BLA: basolateral amygdala, CEM: centromedial amygdala. FFA: fusiform face area, PPA: parahippocampal place area, LOC: lateral occipital cortex. D. For the long-term memory reinstatement analysis, a within-clip and an average across-clips similarity score is calculated. For *within*-clip similarity, we calculated the correlations (Pearson's *r*) between neural patterns observed during the day-8 disrupted version of a clip (e.g., clip1-day8-disrupted) and its day-1 intact version (e.g., clip1-day1-intact). The pattern similarity was separately calculated for each on- and off-period and was then averaged for the on- and off-periods. For the *across*-clips similarity, using the same approach, we calculated the correlations between neural patterns observed during the day-8 disrupted version of a clip (e.g., clip1-day8-disrupted) and the day-1 intact version of another clip (e.g., clip2-day1-intact). We then took the average of all the across-clips similarities to get a mean "across-clips similarity score" per clip. Thus, a greater within-clip similarity score corresponds to content-specific reinstatement of events for a given clip, whereas greater across-clips similarity score would correspond to greater schematic reinstatement (e.g., a general schema of events one would expect from the horror-clips genre).

On Day-1, participants first practiced watching a movie clip and performing ratings prior to entering the fMRI. This allowed participants to understand the ratings that needed to be performed after each clip for arousal, valence, coherence, and familiarity. A soundcheck was also administered to familiarize participants with varying levels of audio across clips, and to ensure that an average and comfortable hearing quality was achieved across participants. The encoding phase in the scanner started with T1-weighted anatomic imaging, followed by a baseline rest scan for 120 seconds. Then, participants viewed each movie clip in a pseudorandomized and counterbalanced order, interleaved with rest scans. For any given clip, they were first presented with a cue for 5 seconds indicating whether the upcoming clip was expected to be aversive or neutral, with the goal of priming the condition for the clip to prevent any anticipation-related arousal for the neutral clips, and to lessen the emotional carry-over effects from the previous clip. Participants then viewed a movie clip for 120 seconds, which they then rated at the end for evoked levels of arousal, valence, coherence, and familiarity, using a continuous visual analog scale ranging with labeled endpoints. A resting scan (post-clip/encoding) followed each movie clip. During each rest scan, participants were instructed to keep their eyes open, stay still, and look at the fixation cross on the screen. These rest scans were also 120 seconds in length to match the movie clips. In total, participants completed 7 separate runs of rest scans and 6 separate runs of single movie clip presentation trials with 3 neutral and 3 aversive clips presented in a pseudo-randomized order. Pseudo-randomization was achieved by generating individual stimulus orders in which no two clips were drawn from the same movie. No more than two movie clips drawn from the

same condition appeared in a row, and the encoding phase did not start or end with two movie clips drawn from the same condition.

Following the movie-clip encoding completed on Day-1, participants returned to the lab after 24-hours (Day-2) to complete a temporal memory task, a cued-free recall task and individual difference questionnaires. The temporal memory task was designed to probe both recency discriminations and temporal duration estimations, which are out of the scope of the current study and are discussed elsewhere (Gregory, 2024). The cued-free recall task completed on Day-2 was administered behaviorally in the lab, using a randomized order for clips to prevent primacy- or recency-induced biases. Participants were shown two images corresponding to the first and the last frames in each movie clip they watched the day before, and were given the instructions "Please try to remember the events that took place in the clip associated with these images". They were then instructed to type their recollections for as long as they took, without worrying about the typological errors.

Following the memory phase, participants completed two questionnaires. They first completed a genre questionnaire, where they indicated their enjoyment on a scale from 1 ("do not enjoy at all") to 5 ("enjoy very much") of three genres of films: Horror, Action, and Thriller. This questionnaire was intended as a control to capture individual preferences for different types of emotional clips, and is not discussed any further. Participants then completed the self-report, PTSD Checklist for DSM-5 (PCL-5). The PCL-5 gauges the presence and severity of PTSD-related symptoms and provides subscale scores which are matched to DSM-5 categories. This questionnaire was included to capture individual differences related to possible PTSD symptoms, and the PCL-5 is

often used as a screening and provisional measure in similar research. This questionnaire is not used for the main analyses of this project, but was obtained to be utilized as a potential covariate in future exploratory analyses.

One-week after encoding (Day-8), participants came back to the imaging center and completed a cued-recall task as well as an intermittent reactivation task in the scanner. The Day-8 cued-recall task and instructions were identical to that of Day-2, with the exception that participants completed the recall task in the scanner, wherein each clip recall was completed in a separate functional run. To accommodate individual differences in recall time and detail, participants were given up to five minutes per clip in the scanner, and the scans were stopped as soon as the participants indicated that they were done recalling a given clip. Day-8 recall data is collected by having participants speak into an MRI-compatible microphone while being audio-recorded. While the behavioral cued-free recall data is included in the current manuscript, the neural data associated with the recall on Day-8 will be analyzed in future studies, and is therefore left out from the current manuscript.

After the cued-recall period, participants proceeded to complete the intermittent reactivation task, where they watched the disrupted (with the blank screen) versions of each of the six movie clips, which were followed by the same arousal, valence, coherence and familiarity ratings. The disrupted versions were watched in separate functional runs, in the same order that they were watched during encoding (Figure 1).

Brain Imaging Data Acquisition and Preprocessing

MRI data was collected at the Temple University Brain Research & Imaging Center using a 3T Siemens Prisma scanner with a 20-channel parallel array transmit-

receive head coil. On both Day-1 and Day-8, participants first completed the T1-weighted anatomic imaging, and then the fMRI study task. T1-weighted images were used for coregistration. During encoding (Day-1) and intermittent reactivation (Day-8), 77 brain volumes were collected in separate runs of each of the 19 blocks (6 movie clips and 7 rests on Day-1, and 6 movie clips on Day-8), each lasting for 120 seconds. We did not collect functional data during the arousal, valence, coherence and familiarity ratings that followed each movie clip. During the cued-free recall on Day-8, participants were given up to 5 minutes to complete their recall. Individual differences in recall stopping time resulted in a variable number of brain volumes collected from each participant.

Before preprocessing, DICOM images were converted to NIFTI format with Brain Imaging Data Structure (BIDS) nomenclature using dcm2niix (Li et al., 2016) and were visually inspected for conversion errors. BIDS-formatted imaging data was then preprocessed using the standard fMRIPrep pipeline (Esteban et al., 2019), which included skull stripping, segmentation of gray matter, white matter, and CSF. Additional steps included spatial normalization with nonlinear registration to MNI152NLin6Asym space, head motion estimation, slice time correction, susceptibility distortion correction, registration from EPI to T1w, resampling to standard space, and confound estimation.

Data Analysis

All statistical analyses reported below were performed using R Statistical Software (version 2023.0.3.386, Posit Team 2023). The pairwise Pearson's correlations were calculated using the *cor* function from the *corrr* package (https://cran.r-project.org/package=corrr). The linear mixed modeling analyses were conducted using the *lmer* function from the *lme4* (https://cran.r-project.org/package=lme4) and *lmertest*

function from the *lmerTest* packages (https://cran.r-project.org/web/packages/lmerTest) in R.

Behavioral Data Analysis

The behavioral data analyzed in the current study consist of the subjective arousal ratings from the Day-1 encoding session as well as the cued-free recall data from both Day-2 and Day-8. Day-1 Arousal ratings were normalized within participant by calculating the z-score of all arousal ratings provided for each clip by the participant. The z-scored Day-1 arousal ratings were then used as an independent variable to predict Day-2 and Day-8 cued-recall as well as the free recall transformation over the course of the week (see below). Arousal ratings were additionally entered as a covariate in reported *lmer* models testing the relationship between different neural variables and the free recall transformation. Importantly, we collapsed the arousal variable across conditions (aversive and neutral) for all behavioral and neural data analyses to better investigate the downstream effects of subjective arousal beyond a primed, behavioral context effect.

For the cued-free recall analyses, the automated autobiographical interview scoring pipeline from van Genugten and Schacter (2024) was utilized. As explained before (see *Experimental Procedure*), participants typed their answers to the recall prompts on Day-2. The textual data recorded from this computerized task was manually inspected by a research assistant and the current author to correct any typographical errors, and then preprocessed as required by the automated scoring pipeline (van Genugten and Schachter, 2024). Day-8 cued-free recall task was first transcribed from audio using a natural language processing tool, Whisper AI (Radford et al., 2022). The transcriptions for each recall session, obtained from Whisper AI, were then manually

checked by two research assistants and the current author for any mistakes or typographical errors. A total of 10 participant's audio recordings proved difficult to concisely transcribe through Whisper AI because of low signal-to-noise in the audio recording. For those cases, the two research assistants independently transcribed the audio recordings from scratch. We then calculated the cosine similarity for a subset of transcripts (from 29 participants, including the 10 participants with problematic audio), using the *textstat_simil* function from the *quenteda.textstats* package in R, which revealed a mean similarity of .89 (Sd = 0.16), suggesting high inter-RA agreement. All Day-8 recall transcriptions were further preprocessed according to the guidelines for the automated autobiographical interview scoring pipeline (van Genugten and Schachter, 2024). The automated autobiographical interview scoring analysis was then run, providing us with predicted proportion of internal details, of external details, and the total word counts per clip per participant, per day. For each day, we then calculated the percentage of internal details by dividing the predicted proportion of internal details by the total word count.

Finally, for the analysis of recall changes over the course of the week, we subtracted the Day-8 percent internal details from Day-2 percent internal details to obtain a *recall transformation* score, wherein positive scores reflect larger transformation towards a semanticized, gist-like, memory representation whereas negative scores reflect a preservation or increase of remembered details at the end of the week (Figure 2A).

Brain Imaging Data Analysis

Regions of Interest. The following regions were used based on a priori hypotheses regarding threat-related activity, as well as memory reactivation, and

consolidation: basolateral (BLA) and centromedial (CEM) amygdala, hippocampus (Hipp), fusiform face area (FFA) and parahippocampal place area (PPA), lateral occipital cortex (LOC), and precuneus (Figure 2C). Hippocampus masks, obtained separately for left and right hemispheres, were taken from the Harvard-Oxford subcortical atlas and thresholded at 50%. The hippocampus mask was further segmented into thirds along the long-axis, and the anterior (aHipp) and posterior (pHipp) thirds were separately used for all reported analyses. LOC and precuneus masks were obtained from the Harvard-Oxford cortical atlas, separately masked for left and right hemispheres, and thresholded at 50%. FFA and PPA masks were similarly obtained from the Harvard-Oxford cortical atlas, masked separately for left and right hemispheres, and thresholded at 50%. Finally, amygdala masks as well as two control regions (Heschl's gyrus, A1, from the primary auditory cortex and V1 from the visual cortex) were extracted from the Juelich Histological Atlas, and separately masked for left and right hemispheres, and then thresholded at 50%.

fMRI Univariate Analysis. Following preprocessing, a general linear model (GLM) was run where each movie clip condition (neutral, aversive) was modeled with a separate regressor and convolved with a double-gamma hemodynamic response function (HRF) as an event-related response, capturing a single extended trial for each run. Six head-motion parameters and their first derivatives, as well as the time series extracted from both cerebrospinal fluid (CSF) and white matter (WM), were added as covariates to the model to reduce noise.

The GLMs were run using fMRI Expert Analysis Tool (FEAT) as implemented in FMRIB Software Library (FSL). Correction for multiple comparisons was carried out

within a priori ROIs at a cluster significance level of $p < .05$. The subsequent z-statistical images were warped from native space to the MNI152 2mm template brain using flirt. Beta-parameters for the first level contrast of clip versus baseline were then extracted for basolateral and centromedial amygdala (BLA and CEM, respectively) as well as anterior and posterior hippocampus (aHipp and pHipp, respectively) separately for each hemisphere, from each clip at the subject-level.

fMRI Functional Connectivity Analyses. For the functional connectivity analyses, we took a background connectivity approach (Murty et al., 2017). First, using FSL-FEAT, a separate general linear model (GLM) was run for each movie clip wherein the noise parameters obtained from fMRIPrep (i.e., the six head-motion parameters, and their first derivatives, time series extracted from cerebrospinal fluid (CSF) and white matter (WM), and framewise displacement (FD) rates) were regressed out of the neural signal. Low frequency trends from the residual masks were then removed using a high-pass filter with a cut-off of 0.009 Hz, similar to previous studies utilizing similar approaches to functional coupling (e.g., Tambini et al., 2010, 2013; Murty et al., 2017).

Next, the nodal time series were extracted from the bandpass filtered residual masks as the mean aggregate time course across voxels in each region of interest. Functional connectivity was then defined as the Pearson's correlation between the time series of a seed and a target region, generating *r* values to test our hypotheses for functional coupling between ROI seeds and ROI targets ("ROI pairs" henceforth).

For post-encoding rest connectivity analyses, each rest scan was modeled in an identical way to the encoding models described above for encoding connectivity. All post-encoding rest functional connectivity analyses were performed at the clip level (i.e.,

a unique correlation was computed per clip). We then subtracted the pre-encoding rest correlations from the post-encoding rest correlations for each ROI pair. This approach was chosen as a means to highlight the functional coupling across consolidation periods, similar to previous studies (e.g., Murty et al., 2017; Gruber et al., 2016). This post–pre-encoding rest difference score was then used for all reported post-encoding rest connectivity analyses (Figure 2B).

For the purposes of the current study, aHipp and pHipp were considered seed ROIs, while the two amygdala subnuclei (BLA and CEM) and the cortical ROIs (LOC, Precuneus, FFA and PPA) were considered target ROIs for all functional connectivity analyses. The two control regions, A1 and V1, were not targeted in these analyses as we rather expected greater hippocampal engagement with the higher-order cortical areas given the complex nature of our stimuli.

fMRI Multivariate Analysis: Intermittent Reactivations. The first level GLMs for the intermittent reactivation analysis were also performed in FSL (Jenkinson et al., 2012), modeling each movie clip's functional run with eight main regressors for the on- and off- periods ("epochs" hereafter), convolved with a double-gamma HRF. An additional regressor was included to model the initial 5-second-long condition cue period (aversive or neutral). Six head-motion parameters and their first derivatives, along with the time series extracted from both CSF and WM, were also added to the model to reduce noise. No temporal or spatial filter was applied. The same model was used for each intact and disrupted movie clip run from Day-1 and Day-8. The GLMs were run using FEAT as implemented in FSL, with on > baseline and off > baseline contrasts. Correction for multiple comparisons was carried out within a priori ROIs at a cluster significance level

of $p < .05$. The subsequent t-statistical images were warped from native space to the MNI152 2mm template brain using flirt. Voxel-wise activity was then extracted from the t-stat maps for each contrast for each ROI (see below), to address the noise from highly variable voxels (Dimsdale-Zucker & Ranganath, 2018).

A representational similarity analysis was conducted to address whether the visual disruption manipulation meaningfully interfered with the brain activity, as would be expected. To that end, a Pearson's correlation score was calculated and Fisher z-transformed as the neural similarity between the corresponding epochs across the two watching experiences (Day-1, Day-8) of each clip (see Figure 2D). To compare the averaged neural similarity during the on- and off-periods in the visual and auditory control regions (V1 and A1, respectively), we ran a multilevel regression model for each region, where the neural similarity score was predicted by the contrast (on vs off) with laterality as a control variable, while participant ID and the unique movie identifier name were included as random slopes. This analysis provided evidence that the disruption manipulation successfully altered the neural representations in an expected manner (see Chapter 3), thereby justifying the planned intermittent reactivation analysis, which aimed at investigating content-specific reinstatement in memory regions (aHipp, pHipp, Precuneus, LOC, FFA and PPA), based on prior work (e.g., Tambini et al., 2010; Skalaban, 2022; Tanriverdi et al., 2023).

For clip-specific content reinstatement, we hypothesized that the Day-8 neural activity associated with a given clip would resemble the Day-1 neural activity for that same clip (within-clip similarity) more than the Day-1 neural activity of another clip (across-clip similarity) (Figure 2D). Accordingly, the within clip similarity was

calculated as the similarity of the Day-1 (e.g., clip1-Day1-on1) and Day-8 movie-watching experience (e.g., clip1-Day8-on1) for the same clip during the same epoch. The across clip similarity was calculated as the similarity of a given clip's Day-8 watching experience (e.g., clip1-Day8-on1) to each other clip's Day-1 watching experience during the corresponding epoch (e.g., clip2-Day1-on1). All within clip similarity scores were calculated as a Pearson's correlation, Fisher z-transformed, and then averaged across the specific epoch (e.g., across all on- periods) (Figure 2D). From this, an average score was calculated based on each clip's similarity to other clips, producing an "across clip similarity" score for each clip in an identical way. Finally, we completed two types of test: first comparing within versus across clip similarity (on average for on- and off-periods) per ROI to investigate which regions showed significant content-specific reinstatement; and second testing how within minus across similarity difference score was related to cued free-recall transformation over the course of the week.

CHAPTER 3

RESULTS

Behavioral Findings

More Internal than External Details are Recalled on Day-2 and Day-8

Prior research has defined internal details as the specific "what, when, and where" information related to the main event within an experience (Levine et al., 2002; van Genugten & Schacter, 2024). On the other hand, external details are recollections that are not directly related to, or informative of, the event itself, such as factual or repetitive information (Levine et al., 2002; van Genugten & Schacter, 2024). Here, we hypothesized that successful memory recall would include higher rates of internal than external details. Therefore, we first tested whether participants recalled more internal than external details for clips. Given that participants recalled a total of six video clips, we have conducted multilevel regression model where percentage of details recalled was entered as the dependent variable and detail type was entered as a categorical predictor (internal versus external), with movie name and participant ID as random slopes to control for within participant and within movie effects: (Percent Details ~ Detail Type + (1|movieName) + (1|PID)). This analysis was conducted separately for Day-2 and Day-8 recall. The results revealed that participants recalled more internal than external details on both Day-2 (β = .843, SE = .015, $p < .001$) and Day-8 (β = .796, SE = .012, $p < .001$).

Cued-Free Recall Transformation as a Function of Subjective Arousal

Having established that participants recalled internal details at both delays, we next asked whether the subjective arousal at the time of encoding significantly predicted memory transformation, which was calculated as a difference score between Day-2 and

Day-8 percentage internal details (see *Methods*). To that end, we tested another multilevel regression model where memory transformation score was predicted by Day-1 arousal: (Internal Details Difference Across Days ~ Day1Arousal + (1|movieName) + (1|PID)). This analysis showed that higher subjective arousal during encoding was associated with greater memory transformation towards a semanticized, gist-like, representation (i.e., the loss of internal detail; $\beta = .026$, $SE = .011$, $p = .020$) (Figure 3A).

To ensure that this finding was evidential of memory transformation due to arousal, rather than a failure to retrieve episodic details for highly arousing experiences, we next tested whether subjective arousal at the time of encoding predicted the percentage of internal details recalled on both Day-2 and Day-8. To that end, we conducted two multilevel regression models based on Day-2 and Day-8 recall, wherein percentage of internal details was entered as a dependent variable, with Arousal as a predictor and movie name and participant ID as random slopes: (Percent Internal ~ Day1Arousal + (1|movieName) + (1|PID)). We found that higher subjective arousal at encoding was significantly associated with a higher percentage of internal details recalled on Day-2 ($\beta = .031$, $SE = .011$, $p = .005$) but not on Day-8 ($\beta = .006$, $SE = .008$, $p = .52$) (Figure 3B), suggesting that episodic details for emotional memories are initially retained in memory, but are then forgotten in longer retention periods as memories undergo further transformation.

Having found behavioral evidence for threat's (negative arousal) influence on memory transformation, we next investigate the neural predictors of this memory transformation. Accordingly, all following analyses focus on the memory transformation score between Day-2 and Day-8.

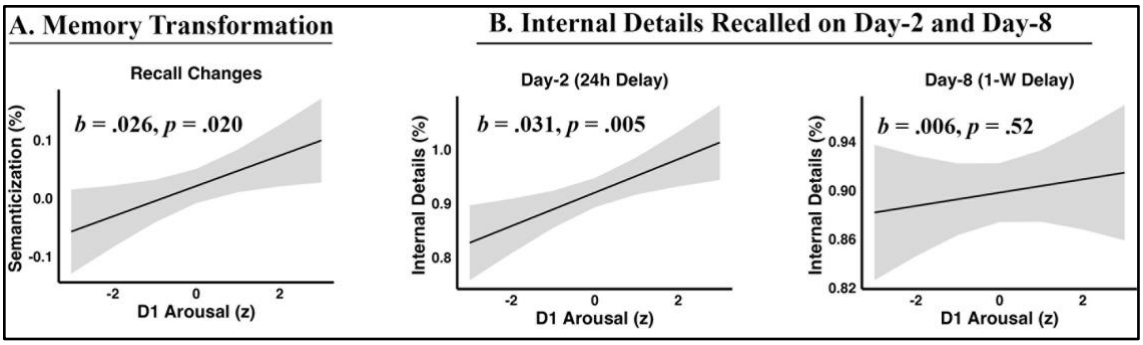

Figure 3. Cued recall as a function of subjective arousal at encoding. A. Memory transformation over the course of the week as a function of arousal. B. Percentage of internal details recalled as a function of arousal on Day-2 (left) and on Day-8 (right).

Encoding Findings

Memory Transformation is not Predicted by Univariate Encoding Activity

Given our observation that there is considerable memory transformation over the course of a week, we considered whether this transformation could be explained by activity in key memory nodes (amgygdala and hippocampus) at the time of encoding. We conducted separate multilevel models for each ROI, wherein the univariate activity of a given ROI was the independent predictor, with memory transformation (i.e., the change in percentage of internal details) being the dependent variable. Additionally, we added laterality as a categorical predictor, instead of running separate models for left and right-hemisphere, to reveal any hemispheric differences that might be present in the data, while minimizing the multiple comparisons problem. Finally, similar to the previous multilevel regression models discussed above, movie name and participant ID were included as random slopes, and Day-1 Arousal was added in all models as a covariate due to its significant association with memory transformation. The results of these statistical models revealed that none of the ROIs showed significant relationship between their encoding activity level and the magnitude of memory transformation (see Table 1).

Although both the amygdala and hippocampus were previously implicated in threat encoding, these nonsignificant results suggest that their univariate encoding activity does not impact subsequent memory transformation.

Table 1. Multilevel linear regression models with univariate activity and control variables predicting memory transformation

ROI	*Predictors*	*β*	*SE*	*p-value*
Basolateral Amygdala (BLA)	BOLD activity	0.001	0.013	0.911
	Hemisphere: Right > Left	0.000	0.014	0.999
	Day1 Arousal (z)	**0.024**	**0.008**	**0.001**
Centromedial Amygdala (CEM)	BOLD activity	-0.014	0.009	0.118
	Hemisphere: Right > Left	0.001	0.014	0.953
	Day1 Arousal (z)	**0.026**	**0.001**	**0.001**
Anterior Hippocampus (aHipp)	BOLD activity	0.004	0.011	0.698
	Hemisphere: Right > Left	-0.001	0.014	0.971
	Day1 Arousal (z)	**0.025**	**0.008**	**0.001**
Posterior Hippocampus (pHipp)	BOLD activity	0.015	0.011	0.167
	Hemisphere: Right > Left	-0.0002	0.014	0.986
	Day1 Arousal (z)	**0.025**	**0.008**	**0.001**

Note. All continuous variables are standardized. Significant effects were highlighted with bold.

Encoding-related Posterior Hippocampus Functional Connectivity with Basolateral Amygdala and Sensory Cortex Preserves Episodic Details

Considering that univariate encoding activity in the hippocampus and amygdala did not account for the amount of long-term memory transformation observed behaviorally, we next asked whether encoding period functional connectivity between the hippocampus and amygdala, or the hippocampus and cortex, predicted long-term memory transformation. To that end, we conducted separate multilevel models for each ROI pair, wherein functional connectivity of a hippocampal seed region and an amygdalar or

cortical target region was the independent predictor, with memory transformation being the dependent variable. Similar to the univariate analyses, we added laterality and Day-1 arousal as covariates, and movie name and participant ID as random slopes. The complete model results are reported in Table 2. Below, we highlight the significant findings.

The findings from these analyses revealed that posterior, but not anterior, hippocampus plays an important role, via its functional coupling with the amygdala and cortical ROIs during encoding, in preserving episodic details as memories undergo transformation. In particular, the posterior hippocampus's encoding period functional connectivity with the basolateral amygdala (BLA; β = -.089, *SE* = .045, p = .049) was significantly associated with less memory transformation over the course of the week (see Figure 4). These findings provide evidence supporting our initial hypothesis that the posterior hippocampus would be important in preserving event details, and that the basolateral amygdala would selectively enhance hippocampal encoding to support preservation of episodic details. Critically, greater posterior hippocampus encoding connectivity with both the lateral occipital cortex (LOC; β = -.11, *SE* = .045, p = .014) and parahippocampal place area (PPA; β = -.096, *SE* = .046, p = .037) was also significantly associated with lower memory transformation scores, highlighting that hippocampal–cortical communication in support of detailed episodic recollections is evident as early as initial encoding. Notably, memory transformation was not significantly predicted by anterior hippocampus encoding connectivity with either the amygdala or with cortical regions, emphasizing the functional division along hippocampal long axis.

Table 2. Multilevel linear regression models with encoding functional connectivity and control variables predicting memory transformation

Seed ROI	*Target ROI*	*Predictors*	*β*	*SE*	*p-value*
aHipp	BLA	Functional Connectivity	-0.046	0.050	0.354
		Hemisphere: Right > Left	-0.003	0.014	0.860
		Day1 Arousal (z)	**0.023**	**0.008**	**0.003**
	CEM	Functional Connectivity	0.084	0.046	0.067
		Hemisphere: Right > Left	-0.003	0.014	0.844
		Day1 Arousal (z)	**0.024**	**0.008**	**0.003**
	Precuneus	Functional Connectivity	0.032	0.043	0.452
		Hemisphere: Right > Left	-0.001	0.014	0.957
		Day1 Arousal (z)	**0.023**	**0.008**	**0.003**
	LOC	Functional Connectivity	-0.037	0.046	0.424
		Hemisphere: Right > Left	0.001	0.014	0.957
		Day1 Arousal (z)	**0.023**	**0.008**	**0.004**
	FFA	Functional Connectivity	0.053	0.046	0.246
		Hemisphere: Right > Left	-0.002	0.014	0.888
		Day1 Arousal (z)	**0.024**	**0.008**	**0.002**
	PPA	Functional Connectivity	0.025	0.045	0.580
		Hemisphere: Right > Left	-0.001	0.014	0.929
		Day1 Arousal (z)	**0.024**	**0.008**	**0.003**
pHipp	BLA	**Functional Connectivity**	**-0.089**	**0.045**	**0.049**
		Hemisphere: Right > Left	-0.001	0.014	0.948
		Day1 Arousal (z)	**0.024**	**0.008**	**0.002**
	CEM	Functional Connectivity	-0.023	0.048	0.636
		Hemisphere: Right > Left	0.001	0.014	0.972
		Day1 Arousal (z)	**0.023**	**0.008**	**0.003**
	Precuneus	Functional Connectivity	-0.018	0.042	0.673
		Hemisphere: Right > Left	-0.0004	0.014	0.980
		Day1 Arousal (z)	**0.023**	**0.008**	**0.003**
	LOC	**Functional Connectivity**	**-0.110**	**0.045**	**0.014**
		Hemisphere: Right > Left	0.003	0.014	0.840
		Day1 Arousal (z)	**0.022**	**0.008**	**0.005**
	FFA	Functional Connectivity	-0.080	0.046	0.080
		Hemisphere: Right > Left	0.003	0.014	0.818
		Day1 Arousal (z)	**0.023**	**0.008**	**0.005**
	PPA	**Functional Connectivity**	**-0.096**	**0.046**	**0.038**
		Hemisphere: Right > Left	0.003	0.014	0.839
		Day1 Arousal (z)	**0.023**	**0.008**	**0.003**

Note. All continuous variables are standardized. Significant effects are highlighted with bold.

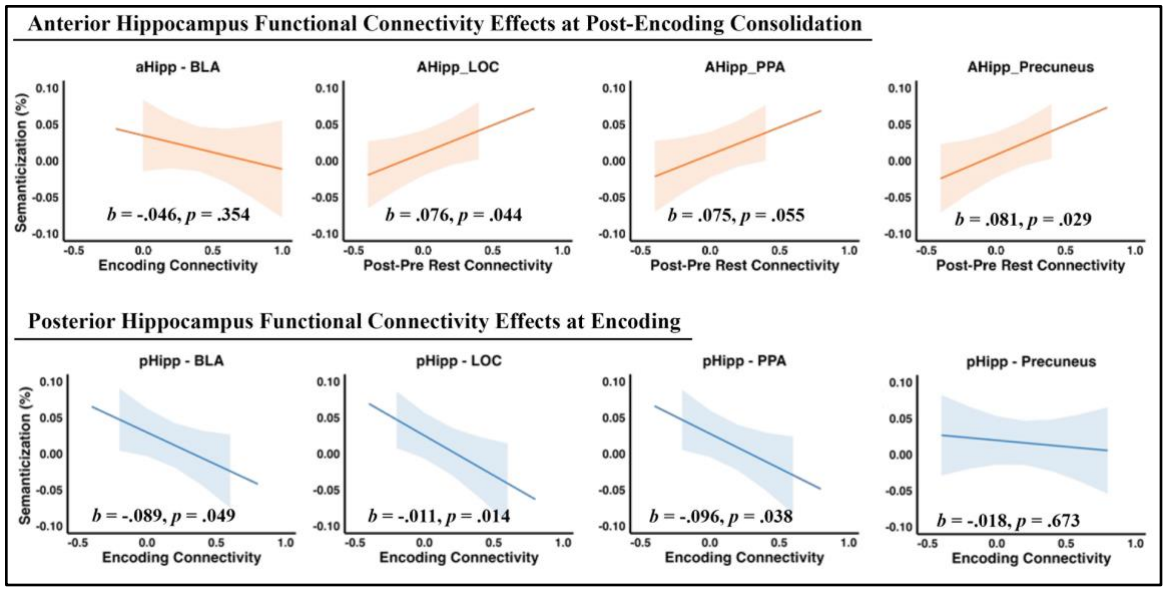

Figure 4. Anterior and posterior hippocampus differentially engage with amygdala and cortex at encoding and post-encoding consolidation phases to support memory transformation. aHipp: anterior hippocampus, pHipp: posterior hippocampus, BLA: basolateral amygdala, LOC: lateral occipital cortex, PPA: parahippocampal place area.

Post-Encoding Findings

Post-Encoding Anterior Hippocampus Functional Connectivity with Sensory and Parietal Cortex Predicts Memory Transformation towards Gist

Having shown a functional division between anterior and posterior hippocampus encoding functional connectivity profiles, we next explored how their connectivity at *post-encoding rest* related to memory transformation.

Here, we found further evidence supporting the functional division along the long axis such that anterior, but not posterior, hippocampus, via its post-encoding functional connectivity with sensory and parietal cortices biased memory transformation towards gist (Table 3). More specifically, we found that anterior hippocampus post-encoding connectivity with the lateral occipital cortex (LOC; β = .076, *SE* = .038, p = .044) and the precuneus (β = .081, *SE* = .037, p = .029) significantly predicted greater memory

transformation over the course of the week. Anterior hippocampus–parahippocampal cortex post-encoding connectivity showed a similar, albeit trending, relationship with memory transformation (PPA; $\beta = .079$, $SE = .039$, $p = .055$). Intriguingly, anterior hippocampus–amygdala post-encoding connectivity was not significantly associated with memory transformation scores. Finally, post-encoding posterior hippocampus connectivity with neither the amygdala nor cortical regions showed significant associations with memory transformation. These findings are in line with our initial hypothesis that the anterior hippocampus selectively plays an important role in memory consolidation and transformation, biasing memories towards a more generalized gist-like representation.

Table 3. Multilevel linear regression models with post-encoding functional connectivity and control variables predicting memory transformation

Seed ROIs	*Target ROIs*	*Predictors*	*β*	*SE*	*p-value*
aHipp	BLA	Functional Connectivity	-0.008	0.041	0.860
		Hemisphere: Right > Left	0.0001	0.014	0.993
		Day1 Arousal (z)	**0.023**	**0.008**	**0.003**
	CEM	Functional Connectivity	-0.011	0.037	0.768
		Hemisphere: Right > Left	0.00003	0.014	0.998
		Day1 Arousal (z)	**0.023**	**0.008**	**0.003**
	Precuneus	**Functional Connectivity**	**0.081**	**0.037**	**0.029**
		Hemisphere: Right > Left	0.0004	0.014	0.976
		Day1 Arousal (z)	**0.022**	**0.008**	**0.005**
	LOC	**Functional Connectivity**	**0.076**	**0.038**	**0.044**
		Hemisphere: Right > Left	0.002	0.014	0.874
		Day1 Arousal (z)	**0.022**	**0.008**	**0.006**
	FFA	Functional Connectivity	0.057	0.036	0.109
		Hemisphere: Right > Left	0.001	0.014	0.962
		Day1 Arousal (z)	**0.021**	**0.008**	**0.007**
	PPA	Functional Connectivity	0.075	0.039	0.055
		Hemisphere: Right > Left	0.002	0.014	0.870
		Day1 Arousal (z)	**0.021**	**0.008**	**0.006**
pHipp	BLA	Functional Connectivity	0.018	0.042	0.668
		Hemisphere: Right > Left	-0.001	0.014	0.971
		Day1 Arousal (z)	**0.023**	**0.008**	**0.004**
	CEM	Functional Connectivity	-0.004	0.039	0.915
		Hemisphere: Right > Left	0.000	0.014	1.000
		Day1 Arousal (z)	**0.023**	**0.008**	**0.003**
	Precuneus	Functional Connectivity	-0.011	0.039	0.782
		Hemisphere: Right > Left	0.0001	0.014	0.995
		Day1 Arousal (z)	**0.023**	**0.008**	**0.003**
	LOC	Functional Connectivity	0.008	0.038	0.834
		Hemisphere: Right > Left	0.0003	0.014	0.983
		Day1 Arousal (z)	**0.023**	**0.008**	**0.004**
	FFA	Functional Connectivity	0.026	0.036	0.483
		Hemisphere: Right > Left	-0.00003	0.014	0.998
		Day1 Arousal (z)	**0.023**	**0.008**	**0.004**
	PPA	Functional Connectivity	0.027	0.040	0.499
		Hemisphere: Right > Left	0.00023	0.014	0.983
		Day1 Arousal (z)	**0.0235**	**0.008**	**0.004**

Note. All continuous variables are standardized. Significant effects were highlighted with bold.

Post-Consolidation Findings

Intermittent Reactivation Task Alters Neural Similarity in Visual but not Auditory Cortex

The disrupted movie watching experience was administered on Day-8 to probe neural reinstatement from memory, particularly during the video-off periods of the clips. Here, we hypothesized that neural similarity in the primary visual cortex (V1) between the two movie watching experiences (intact on Day-1 and disrupted on Day-8) should be high during the video-on periods compared to video-off periods. Importantly, given that the audio was kept intact across all on and off epochs during the disrupted versions, we expected that neural similarity in the primary auditory cortex (A1) would not differ across the on- and off-periods. To test these hypotheses, we conducted separate multilevel regression models for each control region, wherein average neural similarity was predicted by video period (On versus Off), with laterality as a co-variate, while movie name and participant ID were added as random slopes: (Average Neural Similarity ~ Period (On/Off) + Laterality (Left/Right) + (1|movieName) + (1|PID)). These models revealed that our intermittent reactivation task, as predicted, altered neural similarity in V1 but not A1 during video-off periods: V1 showed lower neural similarity during the off- than on-periods (β = .064, SE = .006, p < .001), A1 did not show any such difference (β = -.019, SE = .012, p = .105) (Figure 5). Having confirmed that the task manipulation worked as expected, we next proceeded with the neural similarity analyses for intermittent reactivation during on- vs off- periods.

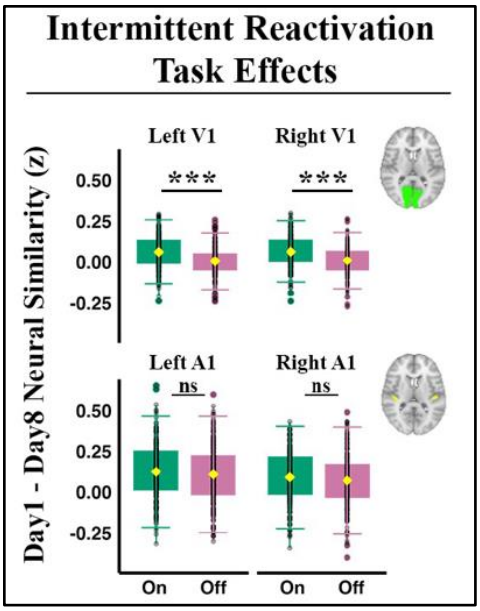

Figure 5. Intermittent reactivation task alters neural similarity in primary visual cortex (V1) but not primary auditory cortex (A1). *** $p < .001$; *ns*: none-significant, $p > .05$.

Precuneus Shows Higher Within versus Across Clip Neural Similarity.

From a theoretical standpoint, the neural similarity between the first watching experience (intact, on Day-1) and the second watching experience (disrupted, on Day-8) observed in canonical memory regions, particularly during the off-periods, should reflect memory reinstatement. An additional point could be made that memory reinstatement should be specific to the content of each clip ("within clip similarity") rather than a similarity shared across clips, which would instead be reflective of general schematic representations associated with watching a movie clip ("across clips similarity"). The multilevel regression models, conducted separately for the on- and off-periods in each of the memory regions of interest revealed that only the precuneus showed higher within > across clip similarity, and this was true for both on- and off-periods (On: $\beta = .020$, $SE = .007$, $p = .004$; Off: $\beta = .016$, $SE = .007$, $p = .034$) (Figure 6). While the anterior hippocampus did not show any difference between within and across clips similarity, for

either of the on- or off-periods (Table 4), the right posterior hippocampus showed significantly lower within versus across clips neural similarity during movie-on periods (β = -.011, SE = .006, p = .041). Like V1, higher-level visual cortices, FFA, PPA, LOC, all showed significantly higher within versus across clips similarity during on- but not off- periods (Table 4). Additionally, there were not any laterality main effects in any of the models, and accordingly, we collapsed the neural similarity data across hemispheres for subsequent analyses pertaining to the within > across clips similarity.

Table 4. Multilevel linear regression models of within versus across clips neural similarity

ROI	*Period*	*Predictors*	*β*	*SE*	*p-value*
Anterior Hippocampus (aHipp)	On	Within > Across	0.004	0.005	0.461
		Hemisphere: Right > Left	0.002	0.005	0.637
	Off	Within > Across	0.003	0.005	0.616
		Hemisphere: Right > Left	-0.002	0.005	0.776
Posterior Hippocampus (pHipp)	On	**Within > Across**	**-0.011**	**0.006**	**0.041**
		Hemisphere: Right > Left	0.005	0.006	0.396
	Off	Within > Across	-0.009	0.006	0.139
		Hemisphere: Right > Left	0.003	0.006	0.628
Precuneus	On	**Within > Across**	**0.020**	**0.005**	**0.0001**
		Hemisphere: Right > Left	0.002	0.005	0.684
	Off	**Within > Across**	**0.016**	**0.005**	**0.004**
		Hemisphere: Right > Left	-0.005	0.005	0.352
Lateral Occipital Cortex (LOC)	On	**Within > Across**	**0.021**	**0.007**	**0.001**
		Hemisphere: Right > Left	0.002	0.007	0.728
	Off	Within > Across	0.002	0.006	0.760
		Hemisphere: Right > Left	-0.002	0.006	0.757
Fusiform Face Area (FFA)	On	**Within > Across**	**0.016**	**0.007**	**0.020**
		Hemisphere: Right > Left	0.010	0.007	0.154
	Off	Within > Across	0.011	0.006	0.088
		Hemisphere: Right > Left	0.008	0.006	0.238
Parahippocampal Place Area (PPA)	On	**Within > Across**	**0.016**	**0.007**	**0.018**
		Hemisphere: Right > Left	0.009	0.007	0.201
	Off	Within > Across	0.004	0.007	0.562
		Hemisphere: Right > Left	-0.005	0.007	0.434

Note. All continuous variables are standardized. Significant effects were highlighted with bold.

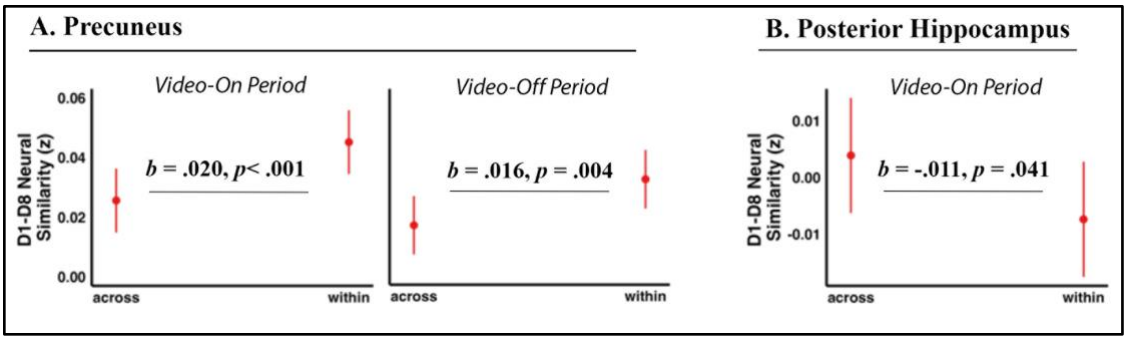

Figure 6. Within versus across clips neural similarity in precuneus and posterior hippocampus.

Post-Encoding Anterior Hippocampus – Precuneus Connectivity Predicts Long-Term Reinstatement in Anterior Hippocampus.

We next tested whether the long-term memory reinstatement on Day-8 is predicted by post-encoding connectivity between hippocampal subregions and each of the target ROIs. Here we operationalized long-term memory reinstatement as the difference between the within-clip and across-clips neural similarity scores (obtained separately for on- and off-periods from the above-reported analyses). Using the within-minus-across ("within>across" henceforth) similarity difference as our dependent variable in multilevel regression models, we tested whether post-encoding functional connectivity between the hippocampus and cortical ROIs predicted higher within>across clip similarity in either the hippocampus or cortex. Importantly for this analysis, we collapsed both the within>across clip similarity (DVs) and functional connectivity (IVs) variables across the two hemispheres given we had not found any laterality effects in our previous analyses. Additionally, we included the reinstatement period (O*n* or O*ff*) as an interaction term, and participant ID as random slope in all models. The following model, therefore, was run for all ROIs with all functional connectivity ROI pairs: (Within > Across Clip Similarity ~ Post-Encoding Connectivity * Period (On/Off) + (1|PID)). Importantly, when predicting

long-term reinstatement in hippocampal ROIs, we tested the influence of post-encoding connectivity between both hippocampal and all cortical ROIs. However, when predicting long-term reinstatement in cortical ROIs, we only tested the influence of post-encoding connectivity between either of the hippocampal and with the given cortical ROI of the interest. The results of all the models are reported in Table 5, while the significant effects obtained in the anterior hippocampus are highlighted below.

The results of these models revealed that stronger post-encoding connectivity between the anterior hippocampus and precuneus significantly predicted higher within>across clip similarity in the anterior hippocampus between Day-1 and Day-8 (β = .048, SE = .023, p = .034). Notably, there was no main effect of period, and no connectivity by period interaction (Table 5). Moreover, we did not find a comparable effect of post-encoding connectivity between the posterior hippocampus and precuneus for within>across clip similarity (β = .048, SE = .023, p = .034) (Figure 7).

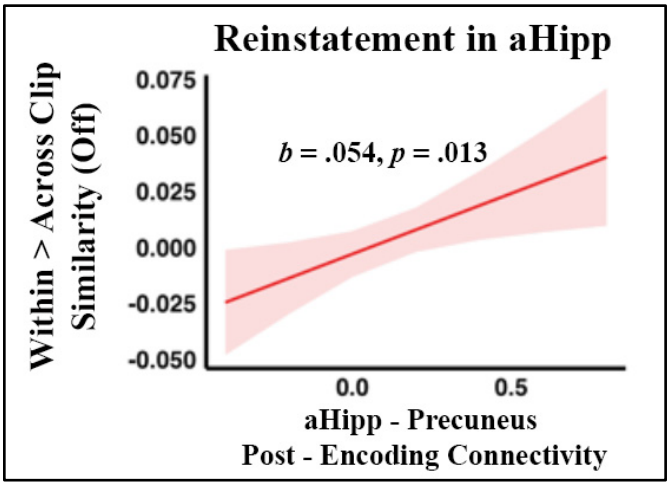

Figure 7. Post-encoding anterior hippocampus – precuneus connectivity predicts long-term reinstatement in anterior hippocampus (aHipp).

Table 5. Multilevel linear regression models with post-encoding (PE) functional connectivity and control variables predicting within > across clips neural similarity within hippocampal and cortical ROIs

ROI	*Predictors*	*β*	*SE*	*p-value*
aHipp	**aHipp - Precuneus PE Connectivity**	**0.048**	**0.023**	**0.034**
	Period: On > Off	0.0003	0.007	0.958
	aHipp - Precuneus PE Connectivity: On (interaction)	0.002	0.030	0.952
	aHipp - LOC PE Connectivity	0.007	0.024	0.757
	Period: On > Off	0.001	0.007	0.903
	aHipp - LOC PE Connectivity: On (interaction)	-0.008	0.031	0.798
	aHipp - FFA PE Connectivity	0.012	0.022	0.601
	Period: On > Off	0.001	0.007	0.907
	aHipp - FFA PE Connectivity: On (interaction)	-0.009	0.029	0.767
	aHipp - PPA PE Connectivity	0.006	0.026	0.814
	Period: On > Off	0.001	0.007	0.935
	aHipp - PPA PE Connectivity: On (interaction)	-0.003	0.034	0.929
pHipp	pHipp - Precuneus PE Connectivity	-0.019	0.035	0.582
	Period: On > Off	-0.002	0.008	0.773
	pHipp - Precuneus PE Connectivity: On (interaction)	0.009	0.045	0.835
	pHipp - LOC PE Connectivity	-0.010	0.032	0.752
	Period: On > Off	-0.002	0.008	0.816
	pHipp - LOC PE Connectivity: On (interaction)	-0.018	0.040	0.647
	pHipp - FFA PE Connectivity	-0.027	0.032	0.395
	Period: On > Off	-0.001	0.0083	0.893
	pHipp - FFA PE Connectivity: On (interaction)	-0.019	0.040	0.633
	pHipp - PPA PE Connectivity	0.004	0.034	0.909
	Period: On > Off	-0.001	0.008	0.894
	pHipp - PPA PE Connectivity: On (interaction)	-0.021	0.043	0.621
Precuneus	aHipp - Precuneus PE Connectivity	0.041	0.034	0.225
	Period: On > Off	0.005	0.011	0.676
	aHipp - Precuneus PE Connectivity: On (interaction)	-0.011	0.044	0.812
	pHipp - Precuneus PEConnectivity	0.007	0.040	0.868
	Period: On > Off	0.004	0.010	0.692
	pHipp - Precuneus PE Connectivity: On (interaction)	-0.021	0.053	0.692

Table 5. continued

ROI	*Predictors*	*β*	*SE*	*p-value*
LOC	aHipp - LOC PE Connectivity	0.030	0.035	0.401
	Period: On > Off	**0.022**	**0.011**	**0.044**
	aHipp - LOC PE Connectivity: On (interaction)	-0.032	0.050	0.524
	pHipp - LOC PE Connectivity	-0.003	0.037	0.933
	Period: On > Off	**0.021**	**0.010**	**0.047**
	pHipp - LOC PE Connectivity: On (interaction)	-0.046	0.052	0.376
FFA	aHipp - FFA PE Connectivity	0.015	0.037	0.689
	Period: On > Off	0.004	0.01	0.715
	aHipp - FFA PE Connectivity: On (interaction)	0.017	0.050	0.730
	pHipp - FFA PE Connectivity	0.016	0.041	0.689
	Period: On > Off	0.004	0.011	0.719
	pHipp - FFA PE Connectivity: On (interaction)	0.015	0.055	0.781
PPA	aHipp - PPA PE Connectivity	0.043	0.043	0.321
	Period: On > Off	0.015	0.011	0.165
	aHipp - PPA PE Connectivity: On (interaction)	-0.030	0.054	0.584
	pHipp - PPA PE Connectivity	0.029	0.045	0.518
	Period: On > Off	0.014	0.011	0.182
	pHipp - PPA PE Connectivity: On (interaction)	-0.022	0.054	0.690

Note. All continuous variables are standardized. Significant effects were highlighted with bold.

Long-Term Cortical Reinstatement is Associated with the Preservation of Internal Details

Our final analyses tested whether long-term neural reinstatement was associated with memory transformation over the course of the week. To test this relationship, the following model was separately run for all ROIs: (Memory Transformation ~ Neural Similarity (Within > Across Clips) * Period (on/off) + Day1 Arousal + (1|PID)). Analyses revealed that higher within > across clips neural similarity in LOC (β = -.252, SE = .075, p < .001) was negatively associated with the memory transformation score

(Figure 8), suggesting that long-term neural reinstatement in this cortical region is linked with more detailed recollections of the movie clips over the long-term (see Table 6 for full model results).

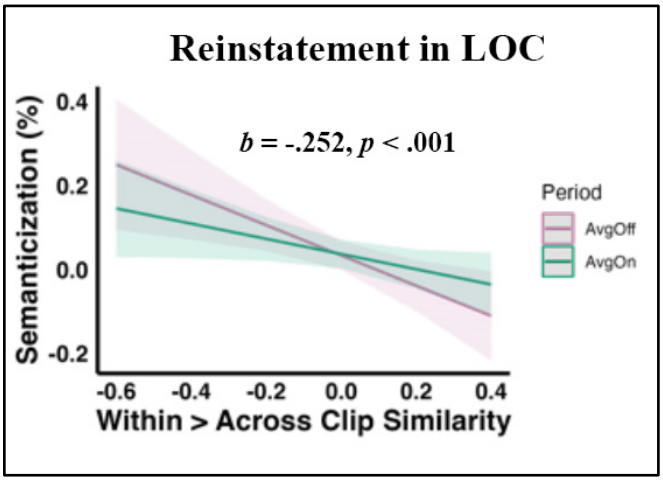

Figure 8. Long-term reinstatement in lateral occipital cortex (LOC) is associated with preservation of internal details.

Table 6. Multilevel linear regression models with within > across clips neural similarity and control variables predicting memory transformation

ROI	*Predictors*	*β*	*SE*	*p-value*
aHipp	Within > Across Clips Neural Similarity	0.175	0.167	0.295
	Period: On > Off	0.000	0.016	0.993
	Day-1 Arousal (z)	**0.024**	**0.009**	**0.008**
	Within>Across Similarity: On (interaction)	-0.051	0.231	0.826
pHipp	Within > Across Clips Neural Similarity	-0.027	0.129	0.832
	Period: On > Off	0.000	0.016	0.985
	Day-1 Arousal (z)	**0.023**	**0.009**	**0.009**
	Within>Across Similarity: On (interaction)	-0.021	0.180	0.908
Precuneus	Within > Across Clips Neural Similarity	-0.115	0.113	0.310
	Period: On > Off	0.000	0.016	0.998
	Day-1 Arousal (z)	**0.025**	**0.009**	**0.006**
	Within>Across Similarity: On (interaction)	0.022	0.157	0.891
LOC	**Within > Across Clips Neural Similarity**	**-0.361**	**0.128**	**0.005**
	Period: On > Off	0.003	0.015	0.830
	Day-1 Arousal (z)	**0.026**	**0.009**	**0.003**
	Within>Across Similarity: On (interaction)	0.179	0.155	0.249
FFA	Within > Across Clips Neural Similarity	-0.181	0.107	0.091
	Period: On > Off	-0.001	0.016	0.944
	Day-1 Arousal (z)	**0.025**	**0.009**	**0.005**
	Within>Across Similarity: On (interaction)	0.131	0.139	0.344
PPA	Within > Across Clips Neural Similarity	-0.204	0.105	0.052
	Period: On > Off	0.003	0.015	0.860
	Day-1 Arousal (z)	**0.024**	**0.009**	**0.006**
	Within>Across Similarity: On (interaction)	-0.009	0.138	0.947

Note. All continuous variables are standardized. Significant effects were highlighted with bold.

CHAPTER 4

DISCUSSION

Our ability to remember threatening experiences, such as a car accident, is essential in guiding our future behavior. Our memories, however, are not written in stone as we experience them, but rather, are continuously and adaptively transformed over time, allowing us to flexibly alternate between recalling episodic details versus an emotional gist memory. Several systems consolidation theories, such as Multiple Trace Theory (Nadel & Moscovitch, 1997) and Trace Transformation Theory (Winocur & Moscovitch, 2011) have described how the hippocampus and cortex are likely to support this transformation. Accordingly, in contrast to earlier systems consolidation models (e.g., Squire & Alvarez, 1995), these alternative theories suggest that episodic memory recall might continue to recruit the hippocampus long after representations are stabilized into long-term memory. On the other hand, the representational cortex, particularly the mPFC, is thought to represent a generalized, gist-level memory derived from abstraction and integration across multiple related episodes (e.g., Tompary & Davachi, 2017; Schultz et al., 2022). Crucially, both theories posit that both hippocampal (detailed, episodic) and cortical (gist-level, generalized) representations co-exist, and might dynamically be retrieved based on task demands. Given the considerable evidence on functional division along the hippocampal long axis (Poppenk et al., 2013), a recently updated Trace Transformation Theory (Sekeres et al., 2018) proposed further specification for these dynamic representations: the posterior hippocampus, along with its interactions with posterior cortical regions, represents detailed episodic event memories, while the anterior hippocampus, together with mPFC, represents a generalized, gist memory. Notably, there

is considerable agreement across these models that hippocampal–cortical interactions, particularly during the post-encoding consolidation window, is essential for enabling the cortex to extract gist-level representations.

While this model accounts for memory transformation for neutral experiences, there are several open questions regarding how psychophysiological arousal modulates these processes in the hippocampus or cortex. From an adaptive memory transformation perspective (Cowan et al., 2021), we would expect the hippocampus to prioritize and stabilize episodic representations under heightened arousal. This expectation would be in line with behavioral evidence that arousal enhances emotional gist memories, at the expense of contextual details (e.g., Payne & Kensinger, 2011). However, heightened arousal may also impair hippocampal function (Kim & Diamond, 2002; McEwen, 2007) or shift resources away from the hippocampus during threat-encoding, thereby resulting in impaired episodic memory (Murty & Adcock, 2017; Clewett & Murty, 2019), perhaps because arousal leads to a bias in emotional gist memory supported by other regions like amygdala. Finally, while the medial prefrontal cortex has been implicated in generalized fear memories (Spalding, 2018), evidence is lacking regarding how arousal might modulate memory reorganization in the posterior cortical regions, which are otherwise implicated in long-term episodic recollection.

Having identified these open questions, this project set out to test the hypotheses that: 1) Memory recall goes through a transformation such that over time event details will slowly be forgotten, and a more generalized representation, with particular emphasis around emotional aspects of an event, will be retained in the long term. Thus, we hypothesized that this representational transformation is driven by subjective experiences

of arousal. 2) While the hippocampus plays an important role in threat-encoding, consolidation and long-term retrieval, given the functional division between anterior and posterior hippocampus, we expected to see the differences along the hippocampal long-axis. Specifically, while (a) the posterior hippocampus was predicted to be more engaged at early stages to ensure successful encoding of episodic details, (b) the anterior hippocampus was predicted to be more important during post-encoding consolidation and long-term retrieval in support of memory transformation towards a gist-like representation. 3) We predicted that both the anterior and posterior hippocampus would show differential functional connectivity with various cortical regions, from precuneus to visual cortices, in support of memory reorganization. 4) Finally, we predicted that the anterior and posterior hippocampus, along with cortical regions, would show long-term memory reinstatement, which in return would be related to behavioral memory transformation.

To test these hypotheses, we conducted a multi-session functional neuroimaging study that spanned the course of a week (Figure 1): Participants completed three in-person visits, wherein they watched short aversive and neutral clips in the scanner (encoding), interleaved with rest scans (post-encoding consolidation) on Day-1. Additionally, they rated their subjective arousal at the end of each clip, allowing us to probe the influence of arousal in memory processes. Twenty-four hours after the first session, they returned to the lab and completed a behavioral, computerized cued-free recall task (Day-2 recall). Finally, one week after the initial encoding, they returned to the scanner, completed a cued free recall task in the scanner (Day-8 recall), and then proceeded to rewatch the clips (Day-8 neural reinstatement). Crucially, on Day-8, they

watched only the visually disrupted versions of each clip, allowing us to probe neural reinstatement from memory (Figure 2).

Subjective Arousal Drives Memory Transformation towards Gist (Hypothesis 1)

Behaviorally, our analyses focused on subjective arousal ratings from the initial encoding session and how they relate to memory transformation over time, as operationalized as the change in percentage of internal details recalled on Day-2 versus Day-8. We found that higher subjective arousal at encoding was significantly associated with greater memory transformation over the course of the week, such that participants retained less internal details in their recollections. To ensure that this change in internal details could be considered evidential of memory transformation over time, instead of a failure to encode episodic details for highly arousing experiences, we also tested how many internal versus external details participants recalled, and explored how subjective arousal related with overall internal details recalled on Day-2 and Day-8, separately. We found that participants recalled more internal than external details on both Day-2 and Day-8, suggesting that they successfully encoded event details. Moreover, higher subjective arousal was positively correlated with higher percentage of internal details recalled on Day-2, but not on Day-8 (Figure 3). Therefore, we argue that while initial consolidation might strengthen detailed representations, our findings indicate a loss or forgetting of said details in the long-term, as memories continue to undergo reorganization.

Previous behavioral studies have argued that there is a retrieval bias for emotional versus neutral stimuli, wherein emotional items are remembered better particularly after periods of consolidation (e.g., Payne et al., 2008; Payne & Kensinger, 2011; Dunsmoor et

al., 2015; Patil et al., 2017). Here, we show evidence that partially supports this claim: our finding that higher subjective arousal is significantly associated with more internal details recalled on Day-2 is in line with these previous behavioral reports on the subsequent memory benefits of emotional stimuli. Importantly, similar to those studies, our arousal-enhanced subsequent memory effects are observed after a 24-h delay. However, this enhancement did not persist over the course of the week. Instead, we observed that memories underwent a transformation throughout the week towards a more gist-level representation, increasingly losing internal (perceptual and episodic) details, and this loss of internal details was significantly associated with greater subjective arousal at the time of encoding. Therefore, we highlight that while arousal may initially bias memory stabilization through consolidation, this biasing does not necessarily engender emotional memories that preserve their initially enhanced episodic components in the long-term.

Hippocampal Subregions Differentially Relate to the Preservation of Memory Details through Functional Coupling with the Amygdala and Visual Cortex at Encoding (Hypotheses 2a and 3)

Having found support for our first hypothesis that memory transformation is evident in behavioral free recall, particularly for experiences associated with higher subjective arousal, we proceeded to test our hypotheses about the neural mechanisms supporting this memory transformation for highly emotional experiences. Here, we turn to both our analyses of hippocampal and amygdala univariate activity as well as their functional connectivity at encoding. Additionally, we report the role that encoding hippocampal–cortical functional coupling plays in memory transformation.

First, we found no evidence that would suggest that univariate encoding activity in either the amygdala or hippocampus supports memory transformation. The lack of an amygdala activity effect is interesting given that at least one study has previously linked univariate encoding activity in the amygdala to persistence of emotional but not neutral recollections (Ritchey, Dolcos, & Cabeza, 2008). We speculate that the apparent discrepancy between the findings of our study and that of Ritchey et al might stem from 1) the different operationalization of memory persistence, and 2) the role that subjective arousal plays in our models. Ritchey et al operationalized memory persistence at the gist level, wherein a ratio of memory success on Day-1 versus on Day-8 was calculated and contrasted across emotional and neutral information. Crucially, memory on Day-1 and Day-8 were tested for separate items within emotional and neutral categories, further emphasizing that the reported memory persistence effects are at the emotional gist-level. In contrast, our memory transformation score reflects changes (or lack thereof) in details recalled from the same events across the two sessions. Therefore, while univariate activity may support gist-level emotional persistence effects (Ritchey et al., 2008), it may not support the unique transformations that each event's representation undergoes over time (our findings).

An additional difference is that we attempted to predict the memory transformation score (collapsed across aversive and neutral clips) from univariate activity while controlling for subjective arousal, based on our initial finding that arousal is significantly associated with the memory transformation score. In all of the models from this univariate analysis (Table 1), we found that subjective arousal remained a significant predictor of memory transformation score, while univariate activity in the basolateral and

centromedial amygdala did not predict memory transformation. Therefore, we argue that subjective arousal, but not univariate amygdala activity, might better explain memory transformation over time.

From an adaptive memory transformation perspective, we hypothesized that amygdalar involvement might bias the hippocampus towards more gist-level representational transformation for aversive experiences. Similarly, our model posits that memory transformation would rely on hippocampal–cortical interactions, rather than univariate hippocampal activity on its own. Therefore, we proceeded to test our hypotheses that hippocampus – cortex and hippocampus – amygdala functional connectivity would support memory transformation. Here, we found that posterior, but not anterior, hippocampus encoding period functional connectivity with both the amygdala and cortex was associated negatively with memory transformation, preserving episodic details over time (Figure 4). Namely, we first showed that stronger encoding period functional connectivity between the posterior hippocampus and basolateral amygdala was significantly associated with lower memory transformation score. This finding suggests that the basolateral amygdala positively biases the posterior hippocampus towards preserving previously encoded episodic details for aversive experiences. Notably, however, encoding period functional connectivity between the anterior hippocampus and the basolateral amygdala did not significantly relate to memory transformation score. This pattern of findings is interesting given our initial hypothesis that the basolateral amygdala would bias the anterior hippocampus towards an emotional gist memory. That said, our hypothesis was based on previous studies highlighting the involvement of the anterior hippocampus and basolateral amygdala in emotional memory

at other stages of memory, including retrieval (Adolphs, Tranel, & Buchanan, 2005; McGaugh, 2004; Richardson, Strange, & Dolan, 2004), their intrinsic connectivity during rest (Gregory et al., 2020) and their post-acquisition co-reactivation for fear memory (Girardeau, Inema & Buzsáki, 2017). However, the current study specifically tests their interaction in predicting memory transformation in complex naturalistic experiences during encoding, which might explain why we did not find supporting evidence for this hypothesis. Nonetheless, the unique effect observed for posterior hippocampus–basolateral amygdala connectivity is in line with the broader threat learning literature, which has asserted that the basolateral amygdala uniquely interacts with hippocampal subregions in support of episodic memories for emotional experiences (Huff et al., 2016; Yang & Wang, 2017). Additionally, this finding dovetails well with the emotional binding model (Yonelinas & Ritchey, 2015), which suggests that amygdala-mediated item-emotion bindings are forgotten more slowly.

Crucially, we found similar effects when we tested hippocampal–cortical functional connectivity in association with memory transformation. As expected, we found that heightened encoding period functional coupling between the posterior hippocampus and visual cortices, particularly with the lateral occipital cortex and parahippocampal place area, was associated negatively with memory transformation. Similar effects, albeit only at the trend level, were observed for encoding period posterior hippocampus with fusiform face area connectivity. These findings suggest that posterior hippocampus–visual cortex functional coupling during encoding plays an important role in learning and preserving episodic and perceptual details for emotionally salient experiences. Notably, we did not find any significant associations between posterior

hippocampus–precuneus encoding period functional connectivity and memory transformation. Given the precuneus's well-defined role in long term memory (e.g., Bird et al., 2015; Oedekoven et al., 2017), this finding is interesting as it hints at the likelihood that the precuneus's role in memory emerges later as memories undergo a transformation through consolidation (discussed in more detail later).

Finally, we did not find any significant relationship between anterior hippocampus–cortex encoding period functional connectivity and memory transformation, further highlighting the functional division between the anterior and posterior hippocampus in their time-dependent role in supporting memory reorganization.

Overall, we found strong evidence supporting our initial hypothesis that posterior hippocampus plays an important role in successful encoding of episodic details, which subsequently helps protect perceptual and episodic details against forgetting during memory transformation.

Anterior Hippocampus Supports Emotional Gist Memory through Functional Coupling with Cortex at Consolidation (Hypotheses 2b and 3)

Having found that encoding functional connectivity between the posterior hippocampus and basolateral amygdala, as well as several visual cortical regions, are implicated in the preservation of episodic details, we next turn to post-encoding connectivity between these hippocampal seed regions and the amygdala and cortical target regions. Here, we reasoned that post-encoding communication between the anterior hippocampus and cortex would be related to memory transformation, given the previously discussed role of the anterior hippocampus in gist extraction and the representation of generalized memories (Sekeres et al., 2018). In accord with this

expectation, we found that greater post-encoding functional connectivity between the anterior hippocampus and lateral occipital cortex was significantly associated with higher memory transformation scores. Post-encoding functional connectivity between the anterior hippocampus and parahippocampal cortex also exhibited a similar trend towards predicting more memory transformation over the course of the week, though this association did not reach significance (Figure 4).

The fact that the anterior hippocampus's functional coupling with visual cortices at post-encoding is associated with the loss of internal details further supports the idea that the anterior hippocampus drives gist-extraction during consolidation, especially in light of the observation that these same cortical regions showed connectivity with the *posterior* hippocampus during encoding to support preservation of episodic details. Notably, post-encoding connectivity between the posterior hippocampus and cortical regions was not significantly related with memory transformation, which further strengthens our argument regarding the functional division along the long axis in supporting memory transformation.

Crucially, we also found that post-encoding functional connectivity between precuneus and anterior hippocampus, but not posterior hippocampus, was significantly associated with higher memory transformation scores. Taken together with the prior observation that posterior hippocampus–precuneus connectivity at encoding was not significantly linked with memory transformation score, the pattern of evidence suggests that the precuneus starts to represent a more generalized event memory, which it appears to acquire slowly through interactions with the anterior hippocampus some time after the initial encoding. Interestingly, however, this process does not seem to lead to an overall

fear generalization in the precuneus, as the precuneus still preserves differentiable memory representations for distinct experiences, as we evaluate next.

Together, these findings add to previously reported consolidation effects on hippocampus–cortex functional coupling, and the impact of these effects in stabilizing emotionally salient information (e.g., de Voogd et al., 2016; Murty et al., 2017). First, we expand on these early findings that post-encoding hippocampus–cortex communication plays a role that extends beyond just memory stabilization, and that it actually drives memory transformation, particularly for threat memories. Moreover, we show evidence that this transformation is selectively supported by the anterior hippocampus, in line with theoretical predictions (Sekeres et al., 2018).

Long-Term Reinstatement in Hippocampus and Cortex (Hypothesis 4)

Following our finding that post-encoding coupling between anterior hippocampus and precuneus was associated with more memory transformation towards a gist-level representation, we assessed how the precuneus might be representing event memories in the long-term. Importantly, the precuneus has previously been associated with long-term memory reinstatement (e.g., Kuhl & Chun, 2014; Oedekoven et al., 2017), and we thus hypothesized that it would show greater neural reinstatement at the one-week follow-up session. Borrowing from Skalaban (2022), we designed an intermittent reactivation task, wherein participants rewatched a disrupted version of each previously encoded clip during the one-week follow-up session in the scanner (Day-8), allowing us to test long-term reinstatement from memory. Here, the disruption was implemented visually such that the video was turned off periodically, while the video-on periods and undisrupted audio acted as cues for scene reconstruction from memory during the video-off periods.

We operationalized memory reinstatement as higher within-minus-across (within > across) clips neural similarity between Day-1 intact and Day-8 disrupted movie watching experiences (Figure 2). This particular analytical approach allowed us to characterize content-specific memory reinstatement, wherein higher within > across neural similarity meant higher clip-specific reinstatement from memory, while controlling for a clip's similarity to other clips' events. In this way, greater within > across similarity would signal greater episodic memory reinstatement. In contrast, a lower within > across neural similarity would signal lower differentiation across clips, suggesting that a more general neural reinstatement that is representative of common event structures across many clips.

We found that while all visual cortical regions showed higher within > across clips neural similarity during video-on periods, only the precuneus produced higher within > across clips neural similarity during video-off periods (Figure 6). For all visual cortical regions, one should expect to see higher within > across clips neural similarity during video-on periods, since these periods are filled with identical ongoing visual information processing. On the other hand, a greater within > across clips neural similarity during video-off periods in the precuneus, we argue, is strong evidence that the precuneus is an essential cortical site for representing highly specific episodic memories, instead of broad schematizations of similar event structures that may be extracted across multiple movie clips. Importantly, this finding replicates the findings from the original design from Skalaban (2022), as it also dovetails well with previous reports of content reinstatement in precuneus and broader posterior medial network (e.g., Ranganath & Ritchey, 2012; Kuhl & Chun, 2014; Bird et al., 2015; Ritchey et al., 2015; Wing, Ritchey, & Cabeza, 2015; Oedekoven et al., 2017; Jonker et al., 2018).

While we found evidence for content-specific long-term reinstatement in the precuneus, it is not yet clear what drives these effects, as we did not find any significant relationship for this region's functional coupling with the anterior hippocampus during post-encoding rest phases. Crucially, long-term memory reinstatement in the precuneus was also not significantly associated with our behavioral measure of memory transformation. Therefore, while precuneus–anterior hippocampus functional coupling at post-encoding rest might emphasize memory transformation towards gist, it appears that the precuneus itself is more involved in keeping a detailed neural representation over the long-term than it is in keeping a gist-level memory for these experiences.

Having found evidence for long-term memory reinstatement in cortex, we next asked whether long-term neural reinstatement is evident in the hippocampus as well. One of the open questions we raised in our introduction regarded how involved the hippocampus would be after memories are stabilized through post-encoding consolidation. As we highlighted previously, while early models of systems consolidation argued that memories become independent of the hippocampus for long-term retrieval and reactivation, several accounts such as the multiple traces and trace transformation models have suggested that the hippocampus continues to keep a detailed episodic representation even long after consolidation, which could be flexibly recalled depending on task demands (Winocur & Moscovitch, 2011; Sekeres et al., 2018). Given our emphasis on the functional division along the hippocampal long axis, we first tested whether either of the anterior or posterior hippocampus showed neural reinstatement for specific movie clips. We found an interesting dynamic with the posterior hippocampus, which showed negative within versus across clip neural similarity during video-on

periods on Day-8. This was unexpected given that the posterior hippocampus was hypothesized to continue to represent episodic detail (Sekeres et al., 2018) and given our initial finding that its connectivity with the basolateral amygdala and sensory cortex during encoding retained episodic details. This group of findings may suggest that in the long-term, representations in the posterior hippocampus may undergo further neural transformation towards gist memory. In line with this interpretation, others have previously reported greater similarity for items with shared context, suggesting generalization (Tompary & Davachi, 2017), particularly at longer delays (Dandolo & Schwabe, 2018).

While we see partial evidence for gist extraction in the posterior hippocampus over the course of the week, the within versus across clips neural similarity was not significant in the anterior hippocampus, which suggests that there may be moderate levels of gist-representation in the anterior hippocampus in the long-term, wherein within clip events are not too distinct, yet differentiated enough from the events of other clips. Importantly, however, greater post-encoding functional connectivity between the anterior hippocampus and precuneus significantly predicted greater within > across clips neural similarity difference in anterior hippocampus (Figure 7). Together, these two findings suggest that anterior hippocampus–precuneus coupling during consolidation supports a moderately generalized representation of each unique experience in the long term. Given this phenomenon occurs through the connectivity with precuneus, we argue, this constitutes a novel finding suggesting that although the post-encoding interaction between these two regions predicts a gist-level representation in the anterior hippocampus, the precuneus itself continues to retain highly specific episodic details.

Our long-term reinstatement findings in both hippocampal regions and the precuneus thus far present a challenge to our field's previous assumptions that the hippocampus holds the episodic details while the cortex reflects gist-level representation. It seems that the picture is more complex when we consider the functional divisions within hippocampus together with how various cortical regions engage with different aspects of episodic memory across different timepoints (encoding, consolidation, retrieval). Our finding that stronger clip-specific neural reinstatement in the lateral occipital cortex is negatively associated with the behavioral indices of memory transformation further adds to this complexity (Figure 8). This later finding strongly suggests that the visual cortex continues to represent a detailed episodic memory, which in turn prevents loss of details over the long-term. As we discuss next, these findings have important implications for long-term threat memory transformation and psychiatric symptoms alike.

Implications for Systems Consolidation in the Context of Threat Memory and PTSD

So far, we have briefly discussed our findings from the assumptions of systems consolidation models, particularly multi-trace models like the trace transformation framework. Several of our findings however are in direct contrast with the assumptions of such models, and warrant further discussion regarding how they might inform theoretical considerations for threat memory transformations.

First, while the anterior hippocampus drives gist extraction through its post-encoding connectivity with cortex, as evident in its associations with greater memory transformation scores (i.e., less internal details retained over time), it also continues to represent content-specific episodic memory in the long-term, as evidenced by its post-

encoding connectivity with cortex. Second, the posterior hippocampus drives preservation of episodic details through its encoding connectivity with both the amygdala and cortex, while over time it comes to represent a gist-level memory in threatening contexts. Third, several cortical areas (not just the hippocampus) represent highly detailed episodic recollections in the long-term. Notably, at least one of these cortical regions, the lateral occipital cortex, showed evidence that long-term content-specific neural reinstatement was related with smaller behavioral changes in free recall, thus marking the importance of these representations in sustaining the preservation of internal details over the course of a week.

Given that these findings regarding both hippocampal and cortical processes are in stark contrast with the assumptions of previous consolidation models, we argue that threat memory consolidation may be more dynamic than previously thought. Recently, Cowan et al (2021) proposed an adaptive memory system that necessitates not only selective stabilization of emotionally salient, or goal-relevant, information, but also memory transformation that dynamically supports both episodic recollections and schematic representations that are extracted and integrated across episodes. We suggest that our findings further emphasize the need for an adaptive memory system whose characteristics go well beyond those characterized in traditional consolidation frameworks, particularly for a dynamic representation of threat-related experiences.

If we revisit our example of getting into a car accident, it is not only adaptive to recall the specific details of where, when and how the accident happened, but also the emotional experience surrounding the accident more broadly (i.e., emotional gist memory). Consider talking to your therapist in the aftermath of the car accident, chances

are, in doing so, you will try to recall as many episodic and perceptual details as possible while also keeping your focus on the emotional gist, for several reasons: For instance, one of the goals in the therapy room is to identify the factors that led to the accident so you can prevent it from happening again, which requires recall of unique contextual details. Moreover, your therapist might ask you to specifically recall some details upon learning that you have been experiencing intrusions like nightmares with flashbacks of the accident, and wants to understand the extent to which these details live in vivid imagery in your memory. Evidently, several studies have highlighted that vivid perceptual recollections in visual cortex might drive intrusive symptomology in PTSD (e.g., Meyer et al., 2016; Clancy et al., 2024). Here, we argue that our findings that posterior cortical regions showed greater clip-specific reinstatement for aversive experiences, and that these detailed reinstatement in visual cortex was associated with behavioral indices of reduced memory transformation and the preservation of more internal details offer further insights for visual imagery driven intrusions.

On the other hand, your therapist might be probing your overall emotional reactivity to the experience, at the gist level, to figure out how likely you are to draw fearful generalizations that could become a maladaptive symptom on its own. Both the hippocampus and medial prefrontal cortex are previously implicated in overgeneralization of fear responses in PTSD (Morey et al., 2015; Kaczkurkin et al., 2017; Spalding, 2018; Lecei & Winkel, 2020). While we have not tested whether memory transformation is linked with representations in medial prefrontal cortex (see *Limitations* for more discussion), our findings regarding the anterior and posterior hippocampus representing gist level information over the long-term fits well with this

broader idea. Crucially, our findings, particularly from the posterior hippocampus, point to the dynamic hippocampal engagement in threat memory transformation that might be linked with PTSD symptoms. Notably, our previous work in trauma-exposed participants also showed similar dynamic changes within posterior hippocampus during fear encoding: while greater transient fear-related posterior hippocampal activity was linked with reduced PTSD symptomology, greater sustained fear-related posterior hippocampal activity was linked with greater PTSD symptomology (Tanriverdi et al., 2022). Together, the results from both studies further support the dynamic nature of hippocampal engagement throughout threat memory transformation, with clear implications for psychiatric symptoms.

Limitations and Future Directions

This endeavor has laid the groundwork for understanding the neural basis of memory transformation for aversive, arousal-inducing experiences, while integrating across models of memory consolidation and transformation. However, there are a few limitations that we would like to highlight for future directions. First, while we discuss threat memory transformation over consolidation and long-term reinstatement, we have not fully uncovered all of the rich information that can be mined from our free recall data, textually as well as neurally. For one, we evaluated threat memory transformation in terms of the overall percentage of internal details lost over the course of the week, using automated autobiographical interview scoring (van Genugten & Schachter, 2024). While helpful for the purposes of our study, one limitation of this automated scoring toolbox is that it does not differentiate between the different sub-classifications of internal (such as perceptual, emotional, or contextual) details (Levine et al., 2002). Given the rich textual

data that is available, a closer look at the internal details that are actually forgotten or retained with language models might further inform our understanding of long-term memory transformation. Thus, while we speculate on memory transformation based on the overall internal details retained, further work is needed to further parse out the types of internal details affected, in order to test how much of the perceptual versus emotional (or contextual) details are retained versus lost, as well as the neural underpinnings of those specific changes in memory. A similar consideration for external details might also provide additional insights, for instance, do people recall more external details over time as they lose internal details, and could that be part of the memory transformation? Additionally, we have functional MRI data available for the Day-8 recall sessions, which when analyzed will most likely provide further insights about the neural processes engaged during long-term recall on Day-8. Moreover, a neural reinstatement analysis similar to our intermittent reactivation approach could be applied to assess the neural similarity between encoding and cued-free recall, which might provide further insights regarding neural transformation for threat memories.

Importantly, our analyses have mainly focused on the hippocampus and posterior cortical regions. Yet, as we have discussed, memory systems are extremely dynamic, and regions other than those investigated might further improve our understanding of threat memory transformation. For instance, consolidation and adaptive memory systems models consider the medial prefrontal cortex (mPFC) as a hub for memory integration across related episodes, thereby supporting schemas and gist memory (Robin & Moscovitch, 2017; Sekeres et al., 2018; Cowan et al., 2021). However, within the context of fear learning and PTSD, this same region is implicated in inhibiting fear responses,

which arguably prevents fear overgeneralization and supports discrimination between danger and safety cues (Spalding, 2018; Lecei & Winkel, 2020). One limitation of our study is that it was particularly designed to investigate the neural and behavioral transformation threat memories undergo on their own, which precluded analysis of either assumption regarding the role the mPFC might play in threat memory reorganization. One interesting way to update the current study design, in order to test the consolidation assumption that the mPFC supports gist through integration across related event representations, would be to have participants watch both the aversive and neutral clips from the same movies, which would allow an analysis of memory integration over related but distinct episodes. Critically, such changes in the implementation of the study design would also allow testing the mPFC's role in supporting the differentiation of the aversive and neutral events in memory.

Further, regions in medial temporal lobe cortex, such as the perirhinal cortex, may show a bias towards gist-level threat memories, particularly through interactions with subjective arousal (Clewett & Murty, 2019). Future analysis of these regions' engagement with threat memory may therefore meaningfully advance our understanding of memory consolidation and transformation for aversive experiences.

Finally, while we have briefly touched upon our study's implications for PTSD research, we have yet to analyze data we collected from participants using the PTSD Checklist for DSM-5 (PCL-5), particularly in relation to the neural signatures of gist versus detail representations for aversive memories. Importantly, our sample excluded participants who reported psychiatric conditions, and thus, their self-reports may not be as informative or reflect as much individual variability as they might in an unrestricted

sample. Regardless, it could be interesting to leverage this data to explore how scores from different subscales of the PCL-5 (e.g., intrusive subscale) correlate with the neural markers of memory transformation we obtained in this study.

Concluding Remarks

Overall, our findings provide compelling evidence that arousal-inducing aversive experiences are selectively encoded and adaptively consolidated and represented in memory. We have demonstrated that subjective arousal at the time of encoding predicts not only the level of episodic details recalled after a 24-h delay, but also how memories are reorganized into emotional gist, with the loss of some details over the course of a week. Further, we have demonstrated that brain regions previously implicated in episodic and fear memories differentially support memory representation with different granularity. Specifically, our results highlight the role of the posterior hippocampus and its connectivity with the amygdala and visual cortices in sustaining episodic details over the long-term, while the anterior hippocampus through its post-encoding connectivity with posterior parietal and visual cortices supports gist-extraction. Moreover, we have shown that both the anterior and posterior hippocampus represent gist-level emotional memories at different early timepoints in memory transformation, while the visual cortex and precuneus represent episodic events after a period of consolidation. Together, this work underscores the role threat, specifically through subjective experiences of arousal, plays in modulating memory consolidation dynamics and long-term memory transformation.

BIBLIOGRAPHY

Abraham, W. C., & Williams, J. M. (2003). Properties and mechanisms of LTP maintenance. *The Neuroscientist: a review journal bringing neurobiology, neurology and psychiatry, 9(6),* 463–474. https://doi.org/10.1177/1073858403259119

Adolphs, R., Denburg, N. L., & Tranel, D. (2001). The amygdala's role in long-term declarative memory for gist and detail. *Behavioral Neuroscience*, *115*(5), 983–992. https://doi.org/10.1037/0735-7044.115.5.983

Adolphs, R., Tranel, D., & Buchanan, T. W. (2005). Amygdala damage impairs emotional memory for gist but not details of complex stimuli. *Nature Neuroscience*, *8*(4), 512–518. https://doi.org/10.1038/nn1413

Adolphs, R., Tranel, D., & Denburg, N. (2000). Impaired Emotional Declarative Memory Following Unilateral Amygdala Damage. *Learning & Memory*, *7*(3), 180–186. https://doi.org/10.1101/lm.7.3.180

Ågren, T. (2014). Human reconsolidation: A reactivation and update. *Brain Research Bulletin, 105(105)*, 70–82. https://doi.org/10.1016/j.brainresbull.2013.12.010

Alm, K. H., Ngo, C. T., & Olson, I. R. (2019). Hippocampal signatures of awake targeted memory reactivation. *Brain Structure and Function, 224*, 713–726. https://doi.org/10 .1007/s00429-018-1790-2

Bahrick, L. E., Parker, J.F., Fivush, R., & Levitt, M. (1998). The effects of stress on young children's memory for a natural disaster. *Journal of Experimental Psychology: Applied, 4*, 308–331.

Bang, J. W., Sasaki, Y., Watanabe, T., & Rahnev, D. (2018). Feature-Specific Awake Reactivation in Human V1 after Visual Training. *The Journal of Neuroscience, 38(45),* 9648–9657. https://doi.org/10.1523/JNEUROSCI.0884-18.2018

Bannerman, D. M., Rawlins, J. N. P., McHugh, S. B., Deacon, R. M. J., Yee, B. K., Bast, T., Zhang, W.-N., Pothuizen, H. H. J., & Feldon, J. (2004). Regional dissociations within the hippocampus—Memory and anxiety. *Neuroscience & Biobehavioral Reviews*, *28*(3), 273–283. https://doi.org/10.1016/j.neubiorev.2004.03.004

Bechara, A., Tranel, D., Damasio, H., Adolphs, R., Rockland, C., & Damasio, Antonio R. (1995, August 25). *Double dissociation of conditioning and declarative knowledge relative to the amygdala and hippocampus in humans*. Science. https://pubmed.ncbi.nlm.nih.gov/7652558/

Bird, C. M., Keidel, J. L., Ing, L. P., Horner, A. J., & Burgess, N. (2015). Consolidation of Complex Events via Reinstatement in Posterior Cingulate Cortex. *The Journal of Neuroscience*, *35*(43), 14426–14434. https://doi.org/10.1523/JNEUROSCI.1774-15.2015

Brewin, C. R. (2014). Episodic memory, perceptual memory, and their interaction: Foundations for a theory of posttraumatic stress disorder. Psychological Bulletin, 140,69-97. doi: 10.1037/a0033722.

Brown, R., & Kulik, J. (1997). Flashbulb memories. *Cognition, 5,* 73–99.

Brunec, I. K., Bellana, B., Ozubko, J. D., Man, V., Robin, J., Liu, Z.-X., Grady, C., Rosenbaum, R. S., Winocur, G., Barense, M. D., & Moscovitch, M. (2018). Multiple Scales of Representation along the Hippocampal Anteroposterior Axis in Humans. *Current Biology, 28(13),* 2129-2135.e6. https://doi.org/10.1016/j.cub.2018.05.016

Buchanan, T. W., & Adolphs, R. (2002). 2. The role of the human amygdala in emotional modulation of long-term declarative memory. In S. C. Moore & M. Oaksford (Eds.), *Advances in Consciousness Research* (Vol. 44, pp. 9–34). John Benjamins Publishing Company. https://doi.org/10.1075/aicr.44.02buc

Buchanan, T. W., Karafin, M. S., & Adolphs, R. (2003). Selective effects of triazolam on memory for emotional, relative to neutral, stimuli: Differential effects on gist versus detail. *Behavioral Neuroscience*, *117*(3), 517–525. https://doi.org/10.1037/0735-7044.117.3.517

Buchanan, T. W., Tranel, D., & Adolphs, R. (2005). Emotional Autobiographical Memories in Amnesic Patients with Medial Temporal Lobe Damage. *The Journal of Neuroscience*, *25*(12), 3151–3160. https://doi.org/10.1523/JNEUROSCI.4735-04.2005

Buchanan, T. W., Tranel, D., & Adolphs, R. (2006). Memories for emotional autobiographical events following unilateral damage to medial temporal lobe. *Brain*, *129*(1), 115–127. https://doi.org/10.1093/brain/awh672

Budson, A., E., Simons, J., S., Sullivan, A., L., Beier, J., S., Soloman, P., R., Scinto, L., F., et al. (2004). Memory and emotions for the September 11, 2001, terrorist attacks in patients with Alzheimer's disease, patients with mild cognitive impairment, and healthy older adults. *Neuropsychology, 18*, 315–327.

Budson, A., E., Simons, J., S., Waring, J., D., Sullivan, A., L., Hussoin, T., & Schacter, D., L. (2007). Memory for the September 11, 2001, terrorist attacks one year later in patients with Alzheimer's disease, patients with mild cognitive impairment, and healthy older adults. *Cortex*, *43*, 875–888.

Burke, A., Heuer, F., & Reisberg, D. (1992). Remembering emotional events. *Memory & Cognition, 20(3),* 277–290. https://doi.org/10.3758/BF03199665

Buzsáki, G. (1989). Two-Stage model of memory trace formation: A role for "noisy" brain states. *Neuroscience, 31*, 551-570. https://doi.org/10.1016/0306-4522(89)90423-5

Cahill, L., and McGaugh, J.L. (1998). Mechanisms of emotional arousal and lasting declarative memory. *Trends in Neurosciences 21*, 294-299.

Campeau, S., & Davis, M. (1995). Involvement of the central nucleus and basolateral complex of the amygdala in fear conditioning measured with fear-potentiated startle in rats trained concurrently with auditory and visual conditioned stimuli. *The Journal of neuroscience, 15(3, Pt 2),* 2301–2311. https://doi.org/10.1523/JNEUROSCI.15-03-02301.1995

Christianson, S., Å. (1984). The relationship between induced emotional arousal and amnesia. *Scandinavian Journal of Psychology, 25(2),* 147–160. https://doi.org/10.1111/j.1467-9450.1984.tb01007.x

Christianson, S., A. (1989). Flashbulb memories: Special, but not so special. *Memory and Cognition, 17*, 435-443.

Clancy, K. J., Devignes, Q., Ren, B., Pollmann, Y., Nielsen, S. R., Howell, K., Kumar, P., Belleau, E. L., & Rosso, I. M. (2024). Spatiotemporal dynamics of hippocampal-cortical networks underlying the unique phenomenological properties of trauma-related intrusive memories. *Molecular Psychiatry*. https://doi.org/10.1038/s41380-024-02486-9

Clewett, D., Dunsmoor, J., Bachman, S. L., Phelps, E. A., & Davachi, L. (2022). Survival of the salient: Aversive learning rescues otherwise forgettable memories via neural reactivation and post-encoding hippocampal connectivity. *Neurobiology of Learning and Memory*, *187*, 107572. https://doi.org/10.1016/j.nlm.2021.107572

Clewett, D., & Murty, V. P. (2019). Echoes of Emotions Past: How Neuromodulators Determine What We Recollect. Eneuro, 6(2), ENEURO.0108-18.2019. https://doi.org/10.1523/ENEURO.0108-18.2019

Cowan, E. T., Schapiro, A. C., Dunsmoor, J. E., & Murty, V. P. (2021). Memory consolidation as an adaptive process. Psychonomic Bulletin & Review. https://doi.org/10.3758/s13423-021-01978-x

Crowley, R., Bendor, D., & Javadi, A., H. (2019). A review of neurobiological factors underlying the selective enhancement of memory at encoding, consolidation, and retrieval. *Progress in Neurobiology*, *179*, 101615. https://doi.org/10.1016/j.pneurobio.2019.04.004

Dandolo, L. C., & Schwabe, L. (2018). Time-dependent memory transformation along the hippocampal anterior–posterior axis. *Nature Communications*, *9*(1), 1205. https://doi.org/10.1038/s41467-018-03661-7

Deuker, L., Olligs, J., Fell, J., Kranz, T. A., Mormann, F., Montag, C., et al. (2013). Memory consolidation by replay of stimulus-specific neural activity. *Journal of Neuroscience, 33*, 19373–19383. https://doi.org/10.1523/JNEUROSCI.0414-13 .2013

de Voogd, L. D., Fernández, G., & Hermans, E. J. (2016). Awake reactivation of emotional memory traces through hippocampal–neocortical interactions. *Neuroimage, 134,* 563–572. https://doi.org/10.1016/j.neuroimage.2016.04.026

Diba, K., & Buzsáki, G. (2007). Forward and reverse hippocampal place-cell sequences during ripples. *Nature Neuroscience, 10*, 1241–1242. https://doi.org/10.1038 /nn1961

Dimsdale-Zucker, H. R., & Ranganath, C. (2018). Representational similarity analyses. In Handbook of behavioral neuroscience (Vol. 28, pp. 509–525). Elsevier. https://doi.org/10.1016/ B978-0-12-812028-6.00027-6

Dudai, Y., Karni, A., and Born, J. (2015). The Consolidation and Transformation of Memory. *Neuron 88*, 20–32.

Dunsmoor, J.E., Murty, V.P., Davachi, L., and Phelps, E.A. (2015). Emotional learning selectively and retroactively strengthens memories for related events. *Nature 520*, 345–348.

Esteban, O., Birman, D., Schaer, M., Koyejo, O. O., Poldrack, R. A., & Gorgolewski, K. J. (2017). MRIQC: Advancing the automatic prediction of image quality in MRI from unseen sites. *PLoS One, 12*, e0184661. https://doi.org/10.1371/journal .pone.0184661

Favila, S. E., Lee, H., & Kuhl, B. A. (2020). Transforming the Concept of Memory Reactivation. *Trends in Neurosciences*, S0166223620302137. https://doi.org/10.1016/j.tins.2020.09.006

Favila, S. E., Samide, R., Sweigart, S. C., & Kuhl, B. A. (2018). Parietal Representations of Stimulus Features Are Amplified during Memory Retrieval and Flexibly Aligned with Top-Down Goals. *The Journal of Neuroscience*, *38*(36), 7809–7821. https://doi.org/10.1523/JNEUROSCI.0564-18.2018

Foster, D. J., & Wilson, M. A. (2006). Reverse replay of behavioural sequences in hippocampal place cells during the awake state. Nature, 440, 680–683. https://doi.org/10.1038 /nature04587

Genzel, L., & Wixted, J. T. (2017). Cellular and Systems Consolidation of Declarative Memory. In N. Axmacher & B. Rasch (Eds.), Cognitive Neuroscience of Memory Consolidation (pp. 3–16). Springer International Publishing. https://doi.org/10.1007/978-3-319-45066-7_1

Gilmore, A. W., Quach, A., Kalinowski, S. E., González-Araya, E. I., Gotts, S. J., Schacter, D. L., & Martin, A. (2021). Evidence supporting a time-limited hippocampal role in retrieving autobiographical memories. *Proceedings of the National Academy of Sciences*, *118*(12), e2023069118. https://doi.org/10.1073/pnas.2023069118

Girardeau, G., Inema, I., & Buzsáki, G. (2017). Reactivations of emotional memory in the hippocampus–amygdala system during sleep. *Nature Neuroscience*, *20*(11), 1634–1642. https://doi.org/10.1038/nn.4637

Gregory, D. F. (2024). Horror-evoked arousal and amygdala bias of the medial temporal lobe. [Doctoral dissertation, Temple University]. ProQuest Dissertations & Theses Global

Gregory, D. F., Ritchey, M., & Murty, V. P. (2020). Amygdala and ventral tegmental area differentially interact with hippocampus and cortical medial temporal lobe during rest in humans. *Hippocampus*, *30*(10), 1073–1080. https://doi.org/10.1002/hipo.23216

Gruber, M. J., Ritchey, M., Wang, S.-F., Doss, M. K., & Ranganath, C. (2016). Post-learning Hippocampal Dynamics Promote Preferential Retention of Rewarding Events. *Neuron, 89(5),* 1110–1120. https://doi.org/10.1016/j.neuron.2016.01.017

Guskjolen, A., & Cembrowski, M. S. (2023). Engram neurons: Encoding, consolidation, retrieval, and forgetting of memory. *Molecular Psychiatry*, *28*(8), 3207–3219. https://doi.org/10.1038/s41380-023-02137-5

Holmes, E. A., & Bourne, C. (2008). Inducing and modulating intrusive emotional memories: A review of the trauma film paradigm. *Acta Psychologica*, *127*(3), 553–566. https://doi.org/10.1016/j.actpsy.2007.11.002

Huff, M. L., Emmons, E. B., Narayanan, N. S., & LaLumiere, R. T. (2016). Basolateral amygdala projections to ventral hippocampus modulate the consolidation of footshock, but not contextual, learning in rats. *Learning & Memory*, *23*(2), 51–60. https://doi.org/10.1101/lm.039909.115

Iyadurai, L., Visser, R. M., Lau-Zhu, A., Porcheret, K., Horsch, A., Holmes, E. A., & James, E. L. (2019). Intrusive memories of trauma: A target for research bridging cognitive science and its clinical application. *Clinical Psychology Review*, *69*, 67–82. https://doi.org/10.1016/j.cpr.2018.08.005

Jadhav, S. P., Kemere, C., German, P. W., & Frank, L. M. (2012). Awake hippocampal sharp-wave ripples support spatial memory. *Science, 336*, 1454–1458. https://doi.org/10.1126 /science.1217230

Jenkinson, M., Beckmann, C., F., Behrens, T., E., Woolrich, M., W., & Smith, S. M. (2012). FSL. *Neuroimage 62*, 782–790.

Ji, D., & Wilson, M. A. (2007). Coordinated memory replay in the visual cortex and hippocampus during sleep. *Nature Neuroscience, 10*, 100–107. https://doi.org/10.1038/nn1825

Jonker, T. R., Dimsdale-Zucker, H., Ritchey, M., Clarke, A., & Ranganath, C. (2018). Neural reactivation in parietal cortex enhances memory for episodically linked information. *Proceedings of the National Academy of Sciences, 115(43),* 11084–11089. https://doi.org/10.1073/pnas.1800006115

Kaczkurkin, A. N., Burton, P. C., Chazin, S. M., Manbeck, A. B., Espensen-Sturges, T., Cooper, S. E., Sponheim, S. R., & Lissek, S. (2017). Neural Substrates of Overgeneralized Conditioned Fear in PTSD. *American Journal of Psychiatry*, *174*(2), 125–134. https://doi.org/10.1176/appi.ajp.2016.15121549

Kensinger, E. A. (2009). Remembering the Details: Effects of Emotion. *Emotion Review*, *1*(2), 99–113. https://doi.org/10.1177/1754073908100432

Kensinger, E. A., Garoff-Eaton, R. J., & Schacter, D. L. (2007a). Effects of emotion on memory specificity: Memory trade-offs elicited by negative visually arousing stimuli. *Journal of Memory and Language*, *56*(4), 575–591. https://doi.org/10.1016/j.jml.2006.05.004

Kensinger, E. A., Garoff-Eaton, R. J., & Schacter, D. L. (2007b). How Negative Emotion Enhances the Visual Specificity of a Memory. *Journal of Cognitive Neuroscience*, *19*(11), 1872–1887. https://doi.org/10.1162/jocn.2007.19.11.1872

Kim, J. J., & Diamond, D. M. (2002). The stressed hippocampus, synaptic plasticity and lost memories. *Nature Reviews Neuroscience, 3(6),* 453–462. https://doi.org/10.1038/nrn849

Kindt, M., & Soeter, M. (2013). Reconsolidation in a human fear conditioning study: A test of extinction as updating mechanism. *Biological Psychology, 92(1),* 43–50. https://doi.org/10.1016/j.biopsycho.2011.09.016

Kuhl, B. A., & Chun, M. M. (2014). Successful Remembering Elicits Event-Specific Activity Patterns in Lateral Parietal Cortex. *The Journal of Neuroscience, 34(23),* 8051–8060. https://doi.org/10.1523/JNEUROSCI.4328-13.2014

Kumaran, D., Hassabis, D., & McClelland, J. L. (2016). What learning systems do intelligent agents need? Complementary learning systems theory updated. Trends in Cognitive Sciences, 20, 512–534. https://doi.org/10.1016/j.tics.2016.05 .004

LaBar, K. S., & Cabeza, R. (2006). Cognitive neuroscience of emotional memory. *Nature Reviews Neuroscience*, *7*(1), 54–64. https://doi.org/10.1038/nrn1825

LaLumiere, R. T., McGaugh, J. L., & McIntyre, C. K. (2017). Emotional Modulation of Learning and Memory: Pharmacological Implications. *Pharmacological Reviews*, *69*(3), 236–255. https://doi.org/10.1124/pr.116.013474

Leal, S. L., Tighe, S. K., Jones, C. K., & Yassa, M. A. (2014). Pattern separation of emotional information in hippocampal dentate and CA3. *Hippocampus, 24(9),* 1146–1155. https://doi.org/10.1002/hipo.22298

Lecei, A., & van Winkel, R. (2020). Hippocampal pattern separation of emotional information determining risk or resilience in individuals exposed to childhood trauma: Linking exposure to neurodevelopmental alterations and threat anticipation. *Neuroscience & Biobehavioral Reviews, 108*, 160–170. https://doi.org/10.1016/j.neubiorev.2019.11.010

Levine, B., Svoboda, E., Hay, J. F., Winocur, G., & Moscovitch, M. (2002). Aging and autobiographical memory: Dissociating episodic from semantic retrieval. *Psychology and Aging*, *17*(4), 677–689. https://doi.org/10.1037/0882-7974.17.4.677

Li, X., Morgan, P. S., Ashburner, J., Smith, J., & Rorden, C. (2016). The first step for neuroimaging data analysis: DICOM to NIfTI conversion. *J Neurosci Methods 264,* 47–56.

Lissek, S., Kaczkurkin, A. N., Rabin, S., Geraci, M., Pine, D. S., & Grillon, C. (2014). Generalized Anxiety Disorder Is Associated With Overgeneralization of Classically *Conditioned Fear. Biological Psychiatry, 75(11),* 909–915. https://doi.org/10.1016/j.biopsych.2013.07.025

Liu, Z., X., Grady, C., & Moscovitch, M. (2018). The effect of prior knowledge on post-encoding brain connectivity and its relation to subsequent memory. *Neuroimage, 167*, 211–223. https://doi.org/10.1016/j.neuroimage.2017.11.032

Lopresto, D., Schipper, P., & Homberg, J. R. (2016). Neural circuits and mechanisms involved in fear generalization: Implications for the pathophysiology and treatment of posttraumatic stress disorder. *Neuroscience & Biobehavioral Reviews*, *60*, 31–42. https://doi.org/10.1016/j.neubiorev.2015.10.009

Maren, S., Phan, K. L., & Liberzon, I. (2013). The contextual brain: Implications for fear conditioning, extinction and psychopathology. *Nature Reviews Neuroscience, 14(6),* 417–428. https://doi.org/10.1038/nrn3492

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

McClelland, J. L., McNaughton, B. L., & O'Reilly, R. C. (1995). Why there are complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory. *Psychological Review, 102(3),* 419–457. https://doi.org/10.1037/0033-295X.102.3.419

McEwen B. S. (2007). Physiology and neurobiology of stress and adaptation: central role of the brain. *Physiological reviews, 87(3),* 873–904. https://doi.org/10.1152/physrev.00041.2006

McGaugh, J. L. (2000). Memory—A century of consolidation. Science, 287(5451), 248–251. https://doi.org/10.1126/science.287.5451.248

McGaugh, J. L. (2004). The amygdala modulates the consolidation of memories of emotionally arousing experiences. *Annual Review of Neuroscience*, *27*(1), 1–28. https://doi.org/10.1146/annurev.neuro.27.070203.144157

Meyer, T., Krans, J., Van Ast, V., & Smeets, T. (2017). Visuospatial context learning and configuration learning is associated with analogue traumatic intrusions. *Journal of Behavior Therapy and Experimental Psychiatry*, *54*, 120–127. https://doi.org/10.1016/j.jbtep.2016.07.010

Misanin, J. R., Miller, R. R., & Lewis, D. J. (1968). Retrograde amnesia produced by electroconvulsive shock after reactivation of a consolidated memory trace. Science (New York, N.Y.), 160(3827), 554–555. https://doi.org/10.1126/science.160.3827.554

Morey, R. A., Dunsmoor, J. E., Haswell, C. C., Brown, V. M., Vora, A., Weiner, J., Stjepanovic, D., Wagner, H. R., VA Mid-Atlantic MIRECC Workgroup, Brancu, M., Marx, C. E., Naylor, J. C., Van Voorhees, E., Taber, K. H., Beckham, J. C., Calhoun, P. S., Fairbank, J. A., Szabo, S. T., & LaBar, K. S. (2015). Fear learning circuitry is biased toward generalization of fear associations in posttraumatic stress disorder. *Translational Psychiatry*, *5*(12), e700–e700. https://doi.org/10.1038/tp.2015.196

Moscovitch, M., & Gilboa, A. (2021). Systems consolidation, transformation and reorganization: Multiple trace theory, trace transformation theory and their competitors. PsyArXiv. https://doi.org/10.31234/osf.io/yxbrs

Murty, V. P., LaBar, K. S., Hamilton, D. A., & Adcock, R. A. (2011). Is all motivation good for learning? Dissociable influences of approach and avoidance motivation in declarative memory. *Learning & Memory*, *18*(11), 712–717. https://doi.org/10.1101/lm.023549.111

Murty, V. P., Ritchey, M., Adcock, R. A., & LaBar, K. S. (2010). fMRI studies of successful emotional memory encoding: A quantitative meta-analysis. *Neuropsychologia*, *48*(12), 3459–3469. https://doi.org/10.1016/j.neuropsychologia.2010.07.030

Murty, V. P., & Tompary, A. (2024). "3.17. Systems Consolidation." In Learning and Memory: A Comprehensive Reference, 3rd Edition, to be published by Elsevier.

Murty, V. P., Tompary, A., Adcock, R. A., & Davachi, L. (2017). Selectivity in postencoding connectivity with high-level visual cortex is associated with reward-motivated memory. *Journal of Neuroscience, 37,* 537–545. https://doi.org/10.1523/JNEUROSCI.4032-15.2016

Nadel, L., & Moscovitch, M. (1997). Memory consolidation, retrograde amnesia and the hippocampal complex. Current opinion in neurobiology, 7(2), 217–227. https://doi.org/10.1016/s0959-4388(97)80010-4

Nader, K., Schafe, G. E., & LeDoux, J. E. (2000). The labile nature of consolidation theory. *Nature Reviews Neuroscience, 1(3),* 216–219. https://doi.org/10.1038/35044580

Neisser, U. & Harsch, N. (1992). Phantom flashbulbs: false recollections of hearing the news about Challenger. In: Winograd, E.; Neisser, U., editors. Affect and accuracy in recall: Studies of 'flashbulb' memories. New York: Cambridge University Press, 9-31.

Oedekoven, C. S. H., Keidel, J. L., Berens, S. C., & Bird, C. M. (2017). Reinstatement of memory representations for lifelike events over the course of a week. *Scientific Reports*, *7*(1), 14305. https://doi.org/10.1038/s41598-017-13938-4

O'Reilly, R. C., Bhattacharyya, R., Howard, M. D., & Ketz, N. (2014). Complementary learning systems. Cognitive science, 38(6), 1229–1248. https://doi.org/10.1111/j.1551-6709.2011.01214.x

Paradis, C., M., Solomon, L., Z., Florer, F., & Thompson, T. (2004). Flashbulb memories of personal events of 9/11 and the day after for a sample of New York City residents. *Psychological Reports, 95,* 304–310.

Parsons, R. G., & Ressler, K. J. (2013). Implications of memory modulation for post-traumatic stress and fear disorders. *Nature Neuroscience*, *16*(2), 146–153. https://doi.org/10.1038/nn.3296

Patil, A., Murty, V.P., Dunsmoor, J.E., Phelps, E.A., and Davachi, L. (2017). Reward retroactively enhances memory consolidation for related items. *Learning & Memory 24,* 65–69.

Payne, J. D., & Kensinger, E. A. (2011). Sleep Leads to Changes in the Emotional Memory Trace: Evidence from fMRI. *Journal of Cognitive Neuroscience*, *23*(6), 1285–1297. https://doi.org/10.1162/jocn.2010.21526

Payne, J. D., Stickgold, R., Swanberg, K., & Kensinger, E. A. (2008). Sleep Preferentially Enhances Memory for Emotional Components of Scenes. *Psychological Science*, *19*(8), 781–788. https://doi.org/10.1111/j.1467-9280.2008.02157.x

Pezdek, K. (2003). Event memory and autobiographical memory for the events of September 11, 2001. *Applied Cognitive Psychology, 17*, 1033–1045.

Poppenk, J., Evensmoen, H. R., Moscovitch, M., & Nadel, L. (2013). Long-axis specialization of the human hippocampus. *Trends in Cognitive Sciences*, *17*(5), 230–240. https://doi.org/10.1016/j.tics.2013.03.005

Posit team (2023). RStudio: Integrated Development Environment for R. Posit Software, PBC, Boston, MA. URL: http://www.posit.co/.

Pronier, É., Morici, J. F., & Girardeau, G. (2023). The role of the hippocampus in the consolidation of emotional memories during sleep. *Trends in Neurosciences*, *46*(11), 912–925. https://doi.org/10.1016/j.tins.2023.08.003

Rabinak, C. A., & Maren, S. (2008). Associative structure of fear memory after basolateral amygdala lesions in rats. *Behavioral Neuroscience, 122(6),* 1284–1294. https://doi.org/10.1037/a0012903

Radford, A., Kim, J. W., Xu, T., Brockman, G., McLeavey, C., & Sutskever, I. (2022). *Robust Speech Recognition via Large-Scale Weak Supervision*. https://doi.org/10.48550/arXiv.2212.04356

Ranganath, C., & Ritchey, M. (2012). Two cortical systems for memory-guided behaviour. *Nature Reviews Neuroscience, 13(10),* 713–726. https://doi.org/10.1038/nrn3338

Richardson, M. P., Strange, B. A., & Dolan, R. J. (2004). Encoding of emotional memories depends on amygdala and hippocampus and their interactions. *Nature Neuroscience*, *7*(3), 278–285. https://doi.org/10.1038/nn1190

Rigoli, M. M., Silva, G. R., Oliveira, F. R. D., Pergher, G. K., & Kristensen, C. H. (2016). The role of memory in posttraumatic stress disorder: Implications for clinical practice. *Trends in Psychiatry and Psychotherapy*, *38*(3), 119–127. https://doi.org/10.1590/2237-6089-2014-0063

Ritchey, M., Dolcos, F., & Cabeza, R. (2008). Role of Amygdala Connectivity in the Persistence of Emotional Memories Over Time: An Event-Related fMRI Investigation. *Cerebral Cortex*, *18*(11), 2494–2504. https://doi.org/10.1093/cercor/bhm262

Ritchey, M., Libby, L. A., & Ranganath, C. (2015). Cortico-hippocampal systems involved in memory and cognition. In Progress in Brain Research (Vol. 219, pp. 45–64). Elsevier. https://doi.org/10.1016/bs.pbr.2015.04.001

Robin, J., & Moscovitch, M. (2017). Details, gist and schema: Hippocampal–neocortical interactions underlying recent and remote episodic and spatial memory. *Current Opinion in Behavioral Sciences*, *17*, 114–123. https://doi.org/10.1016/j.cobeha.2017.07.016

Roesler, R., Parent, M. B., LaLumiere, R. T., & McIntyre, C. K. (2021). Amygdala-hippocampal interactions in synaptic plasticity and memory formation. *Neurobiology of Learning and Memory*, *184*, 107490. https://doi.org/10.1016/j.nlm.2021.107490

Schapiro, A. C., McDevitt, E. A., Rogers, T. T., Mednick, S. C., & Norman, K. A. (2018). Human hippocampal replay during rest prioritizes weakly learned information and predicts memory performance. *Nature Communications, 9*, 3920. https://doi.org/10.1038/s41467-018-06213-1

Schlichting, M. L., & Preston, A. R. (2014). Memory reactivation during rest supports upcoming learning of related content. *Proceedings of the National Academy of Sciences, U.S.A., 111*, 15845–15850. https://doi.org/10.1073/pnas.1404396111

Schultz, H., Sommer, T., & Peters, J. (2022). Category-sensitive incidental reinstatement in medial temporal lobe subregions during word recognition. *Learning & Memory, 29(5)*, 126–135. https://doi.org/10.1101/lm.053553.121

Schwabe, L., & Wolf, O. T. (2012). Stress Modulates the Engagement of Multiple Memory Systems in Classification Learning. *Journal of Neuroscience, 32(32),* 11042–11049. https://doi.org/10.1523/JNEUROSCI.1484-12.2012

Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery, and Psychiatry, 20(1)*, 11–21.

Sekeres, M. J., Winocur, G., & Moscovitch, M. (2018). The hippocampus and related neocortical structures in memory transformation. *Neuroscience Letters, 680,* 39–53. https://doi.org/10.1016/j.neulet.2018.05.006

Sharot, T., Martorella, E., A., Delgado, M., R., & Phelps, E., A. (2007). How personal experience modulates the neural circuitry of memories of September 11. *Proceedings of the National Academy of Sciences, 104*, 389–394.

Sharot, T., & Phelps, E. A. (2004). How arousal modulates memory: Disentangling the effects of attention and retention. *Cognitive, Affective, & Behavioral Neuroscience*, *4*(3), 294–306. https://doi.org/10.3758/CABN.4.3.294

Sharot, T., & Yonelinas, A. P. (2008). Differential time-dependent effects of emotion on recollective experience and memory for contextual information. *Cognition*, *106*(1), 538–547. https://doi.org/10.1016/j.cognition.2007.03.002

Skalaban, L. J. (2022). *How do cognitive demands during encoding influence subsequent memory across development*. [Doctoral dissertation, Yale University]. ProQuest Dissertations & Theses Global

Smith, M., C., Bibi, U., & Sheard, D., E. (2003). Evidence for the differential impact of time and emotion on personal and event memories for September 11, 2001. *Applied Cognitive Psychology, 17*, 1047–1055.

Spalding K. N. (2018). The role of the medial prefrontal cortex in the generalization of conditioned fear. Neuropsychology, 32(1), 1–17. https://doi.org/10.1037/neu0000384

Squire, L. R., & Alvarez, P. (1995). Retrograde amnesia and memory consolidation: A neurobiological perspective. Current Opinion in Neurobiology, 5(2), 169–177. https://doi.org/10.1016/0959-4388(95)80023-9

Squire, L. R., Cohen, N. J., & Nadel, L. (1984). The Medial Temporal Region and

Memory Consolidation: A New Hypothesis. In Memory Consolidation. Psychology Press

Sridhar, S., Khamaj, A., & Asthana, M. K. (2023). Cognitive neuroscience perspective on memory: Overview and summary. *Frontiers in Human Neuroscience*, *17*, 1217093. https://doi.org/10.3389/fnhum.2023.1217093

Strange, B. A., Witter, M. P., Lein, E. S., & Moser, E. I. (2014). Functional organization of the hippocampal longitudinal axis. *Nature Reviews Neuroscience, 15(10),* 655–669. https://doi.org/10.1038/nrn3785

Talarico, J., M., & Rubin, D., C. (2003). Confidence, not consistency, characterizes flashbulb memories. *Psychological Science, 14,* 455–461.

Tambini, A., & Davachi, L. (2019). Awake reactivation of prior experiences consolidates memories and biases cognition. *Trends in Cognitive Sciences, 23*, 876–890. https://doi.org/10 .1016/j.tics.2019.07.008

Tambini, A., Ketz, N., & Davachi, L. (2010). Enhanced brain correlations during rest are related to memory for recent experiences. *Neuron, 65*, 280–290. https://doi.org/10.1016/j .neuron.2010.01.001

Tambini, A., Rimmele, U., Phelps, E. A., & Davachi, L. (2017). Emotional brain states carry over and enhance future memory formation. *Nature Neuroscience*, *20*(2), 271–278. https://doi.org/10.1038/nn.4468

Tanriverdi, B., Cowan, E. T., Metoki, A., Jobson, K. R., Murty, V. P., Chein, J., & Olson, I. R. (2023). Awake Hippocampal–Cortical Co-reactivation Is Associated with Forgetting. *Journal of Cognitive Neuroscience*, *35*(9), 1446–1462. https://doi.org/10.1162/jocn_a_02021

Tanriverdi, B., Gregory, D. F., Olino, T. M., Ely, T. D., Harnett, N. G., Van Rooij, S. J. H., Lebois, L. A. M., Seligowski, A. V., Jovanovic, T., Ressler, K. J., House, S. L., Beaudoin, F. L., An, X., Neylan, T. C., Clifford, G. D., Linnstaedt, S. D., Germine, L. T., Bollen, K. A., Rauch, S. L., … Murty, V. P. (2022). Hippocampal Threat Reactivity Interacts with Physiological Arousal to Predict PTSD Symptoms. *The Journal of Neuroscience*, *42*(34), 6593–6604. https://doi.org/10.1523/JNEUROSCI.0911-21.2022

Tompary, A., & Davachi, L. (2017). Consolidation promotes the emergence of representational overlap in the hippocampus and medial prefrontal cortex. *Neuron, 96*, 228–241. https://doi.org/10.1016/j.neuron.2017.09.005

Tompary, A., Duncan, K., & Davachi, L. (2015). Consolidation of associative and item memory is related to post-encoding functional connectivity between the ventral tegmental area and different medial temporal lobe subregions during an unrelated task. *Journal of Neuroscience, 35*, 7326–7331. https://doi.org/10.1523/JNEUROSCI.4816-14.2015

Van Genugten, R. D. I., & Schacter, D. L. (2024). Automated scoring of the autobiographical interview with natural language processing. *Behavior Research Methods*, *56*(3), 2243–2259. https://doi.org/10.3758/s13428-023-02145-x

Wang, S. H., & Morris, R. G. M. (2010). Hippocampal-Neocortical Interactions in Memory Formation, Consolidation, and Reconsolidation. *Annual Review of Psychology*, *61*(1), 49–79. https://doi.org/10.1146/annurev.psych.093008.100523

Wilson, M. A., & McNaughton, B. L. (1993). Dynamics of the hippocampal ensemble code for space. *Science, 261*, 1055–1058. https://doi.org/10.1126/science.8351520

Wing, E. A., Ritchey, M., & Cabeza, R. (2015). Reinstatement of Individual Past Events Revealed by the Similarity of Distributed Activation Patterns during Encoding and Retrieval. *Journal of Cognitive Neuroscience*, *27*(4), 679–691. https://doi.org/10.1162/jocn_a_00740

Winocur, G., & Moscovitch, M. (2011). Memory transformation and systems consolidation. *Journal of the International Neuropsychological Society: JINS, 17(5),* 766–780. https://doi.org/10.1017/S1355617711000683

Wittkuhn, L., & Schuck, N. W. (2021). Dynamics of fMRI patterns reflect sub-second activation sequences and reveal replay in human visual cortex. *Nature Communication 12*, 1795. https://doi.org/10.1038/s41467-021-21970-2

Yang, Y., & Wang, J.-Z. (2017). From Structure to Behavior in Basolateral Amygdala-Hippocampus Circuits. *Frontiers in Neural Circuits*, *11*, 86. https://doi.org/10.3389/fncir.2017.00086

Yassa, M. A., & Stark, C. E. L. (2011). Pattern separation in the hippocampus. *Trends in Neurosciences, 34*, 515–525. https:// doi.org/10.1016/j.tins.2011.06.006

Yonelinas, A. P., & Ritchey, M. (2015). The slow forgetting of emotional episodic memories: An emotional binding account. Trends in Cognitive Sciences, 19(5), 259–267. https://doi.org/10.1016/j.tics.2015.02.009

Yu, W., Zadbood, A., Chanales, A. J. H., & Davachi, L. (2024). Repetition dynamically and rapidly increases cortical, but not hippocampal, offline reactivation. *Proceedings of the National Academy of Sciences*, *121*(40), e2405929121. https://doi.org/10.1073/pnas.2405929121