UHH
Universität Hamburg
DER FORSCHUNG | DER LEHRE | DER BILDUNG

An Insightful Trio: Stress, Imagination and the Angular Gyrus Shape Mnemonic Integration

---

Dissertation

zur Erlangung des Doktorgrades der Naturwissenschaften

an der Universität Hamburg,

Fakultät für Psychologie und Bewegungswissenschaften,

Institut für Psychologie

vorgelegt von

Anna-Maria Grob

Hamburg, 2023

Tag der mündlichen Prüfung: 26.01.2024

Promotionsprüfungsausschuss

Vorsitzender: Prof. Dr. Martin Spieß

1. Dissertationsgutachter: Prof. Dr. Lars Schwabe
2. Dissertationsgutachter: Prof. Dr. Christian Doeller

1. Disputationsgutacherin: Prof. Dr. Kirsten Hötting
2. Disputationsgutachter: Prof. Dr. Ulf Liszkowski

Acknowledgements

As I sit at my desk, writing this final section, I find myself reflecting on the journey of the past four years. The knowledge I`ve gained and the work I`ve accomplished during this time would not have been possible without the support of so many people. First, I express my sincere gratitude to Prof. Dr. Lars Schwabe for his continuous support and encouraging responsiveness to my many questions during these past years. Additionally, I extend my appreciation to Prof. Dr. Christian Doeller for welcoming me into his research group at the MPI in Leipzig, and to Dr. Branka Milivojevic for her supportive co-mentorship. I would like to thank Franzi, Gundi, Anna, Felix, Stefan, and Nadine for paving the way into my doctorate and also Carlo, Kai, Antonia, Valentina, Sterre, Elena, Fabian, Blazej, Jacqueline, and Jessica for creating an inspiring work environment. I am sincerely grateful to Kaja and Hendrik for making great sparring partners while writing this thesis. Thank you, Hendrik, for being the best office colleague I could have hoped for. This journey has been sweetened by my wonderful friends here in Hamburg who were always ready to share laughter, good food and a glass of wine with me and above all, direct my gaze to the beauty of the present moment. Thank you Katharina, Elena, Mats, Manuel, Matteo, Lucina, Christoph, Patrizia, Francesco, Roberto, Elena, Paolo, Jenny, Elisabeth, Nicoletta, Sara, Tommaso, Maria T., Maria P., Stefano, and Marco. Thank you, Mike, for lightening any moment with a perfectly fitting meme. Thank you, Laetitia, for sharing all kinds of tears – of frustration or joy. To my parents, brothers and sisters, I am deeply grateful for supporting me in pursuing an academic path as the first in our family while always reminding me of the value of life's many nuances and concepts. Last, but certainly not least, I want to thank you, Ben, for standing by my side through every twist and turn in these past four years.

Abstract

Updating memory is essential for maintaining an accurate model of the world. Yet, our understanding of how we integrate new information into existing memory has remained limited. Therefore, this work aims to delineate the factors that shape mnemonic integration. Building upon prior research emphasizing the anterior hippocampus's role in mnemonic integration and the impact of stress on hippocampal function, *Study* 1 leveraged fMRI to explore how acute stress affects mnemonic integration. Although stress boosted recognition, it disrupted a representational change in the anterior hippocampus, likely by decreasing hippocampal activity during insight. Inspired by the anterior hippocampus’s role in mnemonic integration and imagination, *Study* 2 utilized fMRI to investigate the behavioral and neural consequences of imagination-based insight. While improving overall memory, imagination resulted in lower immediate insight and abolished a representational change in the anterior hippocampus, possibly due to heightened hippocampal activity during imagination. To explore the role of the angular gyrus in mnemonic integration, given its implications in memory and imagination, we combined inhibitory continuous theta burst stimulation (cTBS) at the angular gyrus with electroencephalography (EEG) in *Study* 3. Angular gyrus inhibition reduced the memory boost for integrated narratives and eliminated representational changes for linked events in the theta band. These findings converge in a comprehensive model, positing the angular gyrus as a buffer and proposing an inverted U-shaped relationship between hippocampal activity and mnemonic reconfiguration when integrating previously separate events. Altogether, these insights enhance our comprehension of mnemonic integration and may aid in developing a better understanding of the etiology of conditions such as posttraumatic stress disorder (PTSD).

Contents

List of Figures

List of Abbreviations

cTBS	Continuous theta burst stimulation
BOLD	Blood oxygenation level dependent
dlPFC	Dorsolateral prefrontal cortex
DMN	Default mode network
EEG	Electroencephalography
fMRI	Functional magnetic resonance imaging
MAT	Multi-arrangements task
MVPA	Multi-voxel pattern analysis
NIT	Narrative-insight task
PTSD	Posttraumatic stress disorder
RSA	Representational similarity analysis
TSST	Trier social stress test

1. General Introduction

Memory is a remarkably dynamic phenomenon. New experiences may trigger reactivation of existing memory representations, thus rendering them susceptible to change (McKenzie & Eichenbaum, 2011; Nadel et al., 2012). Moreover, the reactivation of memory representations heightens the probability of integrating new information into existing memory (Hupbach et al., 2007). This process of memory updating in response to new information is highly adaptive and fundamental for maintaining an accurate model of the world around us. Over time, the integration of new information into memory may organize memories into hierarchical networks, thus aiding future use (Collin et al., 2017). Information can be integrated by seamlessly weaving the new experience into a unified narrative alongside the existing memory representations (Collin et al., 2015, 2017; Milivojevic et al., 2015), aligning with the classical assumption that the brain stores episodic memories as coherent narratives (Tulving, 1983). The efficiency of this process may, however, depend on a shared spatial (Deuker et al., 2016; Nielson et al., 2015) or temporal context (Hsieh et al., 2014; Zou et al., 2023).

Memory integration is an everyday phenomenon. Imagine yourself following your usual route to work, which passes by the local bank, you suddenly snap to attention as a van parked in front of the bank roars to life, its tires screeching as it speeds away. The faded lettering on the side of the white van reveals its affiliation with a nearby scaffolding company. The lettering is orange, and a small, cheerful logo of an orange figure on a ladder accompanies it. Resuming your journey to work, you ponder the peculiar event. A few minutes later, the blaring sirens of several police cars rush past you. You arrive at your workplace and later in the day, as you scan the news, a headline catches your attention: “Unidentified Suspects Flee Morning Bank Robbery – Public Assistance Requested”, featuring an image of the local bank along your daily route. In that moment, it becomes clear – the van´s hasty departure from the bank and the subsequent cacophony of police sirens were pieces of the same puzzle. Armed with this newfound insight, you pick up the phone and call the police to share a vital piece of information – the logo of the scaffolding company you saw on the van.

In that moment of gaining insight into the relationship between the seemingly separate events – the white van taking off and the police cars approaching – these previously distinct events converge into an integrated episode of the witnessed bank robbery (Fig. 1). These emerging overlapping memory representations are formed when new learning experiences share a common element with existing memories, such as the local bank, thereby catalyzing the integration of novel information into the pre-existing memory network (Schlichting & Preston, 2017). Such mnemonic integration underlies a whole range of behaviors, facilitating novel inferences (Spalding et al., 2018; Zeithamova et al., 2012) that aid efficient navigation (Coutanche et al., 2013; Fernandez et al., 2023; He et al., 2022) and decision-making (Boorman et al., 2021; Kumaran et al., 2009; Shohamy & Daw, 2015). Overall, mnemonic integration is a complex process underlying a wide range of human behaviors and probably depends on various brain regions and their interactions. Despite its importance for behavior, facilitative or inhibitory modulators of this fundamental memory process in conjunction with their neural underpinnings have remained elusive. This far, previous work on mnemonic integration has focused on the role of the hippocampus, given its long-standing implications in memory (Scoville & Milner, 1957).

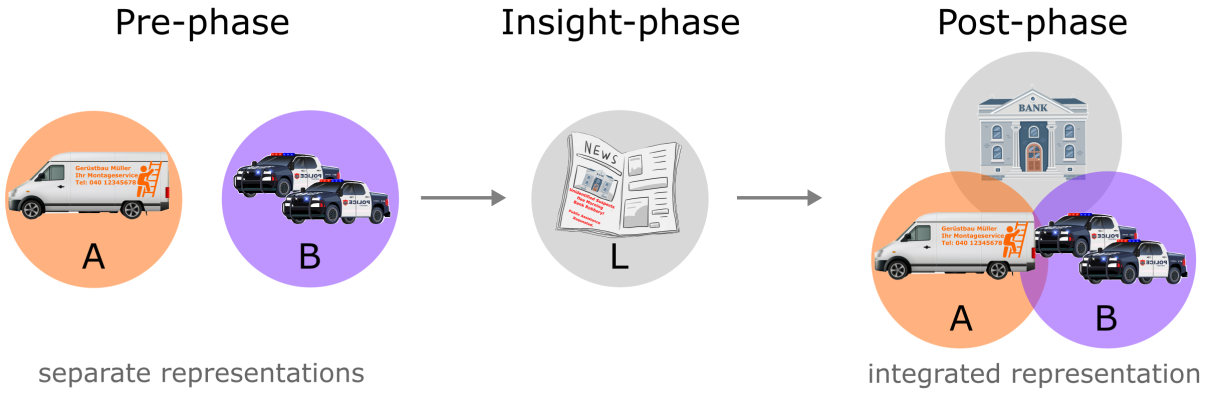


Figure 1. Conceptual illustration of mnemonic integration. In the initial pre-phase, the representations of the white van departing (A) and the approaching police cars (B) are represented separately, as there seems to be no link between these events. In the subsequent insight-phase, insight is gained through reading a newspaper headline (L) revealing that there was a bank robbery at the local bank this morning. This newfound insight acts as a catalyst, propelling the previously separate memory representations into an integrated representation of the witnessed bank robbery in the post-phase. Images were designed by Freepik.

1.1. The role of the hippocampus in mnemonic integration

While the hippocampus is generally central to memory processes (Eichenbaum & Cohen, 2014; Squire & Zola-Morgan, 1991), studies involving patients with hippocampal damage have specifically shown that such damage disrupts the ability to form associations between events (Borders et al., 2017; Horner et al., 2012; Mayes et al., 2004). This aligns with influential theories that not only posited the hippocampus as ideally suited for rapid event encoding (Marr, 1971) but also for organizing and associating events (O'Keefe & Nadel, 1979). Indeed, there is evidence that the hippocampus acts as a convergence zone by actively binding information (Backus et al., 2016). Therefore, the hippocampus emerges as a prime candidate for integrating rapidly acquired novel information into memory.

Distinguishing which events to integrate into a coherent episode and which to maintain separate represents a fundamental memory mechanism, demanding a nuanced interplay between pattern completion and separation processes (Horner & Burgess, 2014; Nakazawa et al., 2002; Rolls & Kesner, 2006; Yassa & Stark, 2011). Pattern completion enables the comprehensive recall of an entire event from partial input (Horner & Burgess, 2014), allowing for the initiation from any element of that memory (Rolls, 2016). On a neural level, this recollective process necessitates the reinstatement of encoding-related cortical activity, which is closely linked to hippocampal activity (Bosch et al., 2014; Horner et al., 2015; Staresina et al., 2012). Conversely, pattern separation involves disentangling overlapping input patterns, thereby effectively reducing interference (Horner & Doeller, 2017). This mechanism may allow for the precise recall of past events, as similar experiences are mapped onto distinct neural codes, ensuring a high degree of specificity (Ngo et al., 2021). In line with this, recent research has shown that depending on the extent of neural overlap, pattern separation may be enhanced, thereby resolving interference between memory representations (Chanales et al., 2017; Wanjia et al., 2021). These processes of pattern completion and separation have been shown to both critically hinge upon the hippocampus (Marr, 1971; McClelland & Goddard, 1996; McNaughton & Nadel, 1990). Given its crucial role in these processes, it is not surprising that the hippocampus has been identified as a key region for mnemonic integration (Collin et al., 2015; Horner et al., 2015; Schlichting et al., 2015).

One central mechanism that may underpin this integrative function of the hippocampus is the theta rhythm (Clouter et al., 2017). Notably, increased hippocampal theta activity has been observed preceding successful memory encoding (Fell et al., 2011), and it has been suggested that the integration of new information with existing memory may be facilitated through the synchronization of cortical regions with hippocampal theta (Schonhaut et al., 2020). Consistently, hippocampal theta oscillations have been found to support mnemonic integration (Backus et al., 2016; Nicolás et al., 2021). However, the hippocampus is not a functionally homogenous region. Earlier research has revealed a hierarchical distribution along its longitudinal axis: anterior portions were more closely tied to memory integration, whereas posterior areas were more associated with memory separation, resulting in memory representations of differing levels of granularity (Brunec et al., 2020; Eichenbaum, 2004; Schlichting et al., 2015; Fig. 2). The anterior hippocampus, in particular, has emerged as a central hub for mnemonic integration by representing overlapping memory representations (Collin et al., 2015; Schlichting et al., 2015). While the extensively connected hippocampus (Ranganath et al., 2005; Zeidman et al., 2015) plays a crucial role in mnemonic integration, contributing to the construction of a representation of the current experience, the precise mechanisms and their dependence on external factors, such as a stressful experience, have remained unknown.

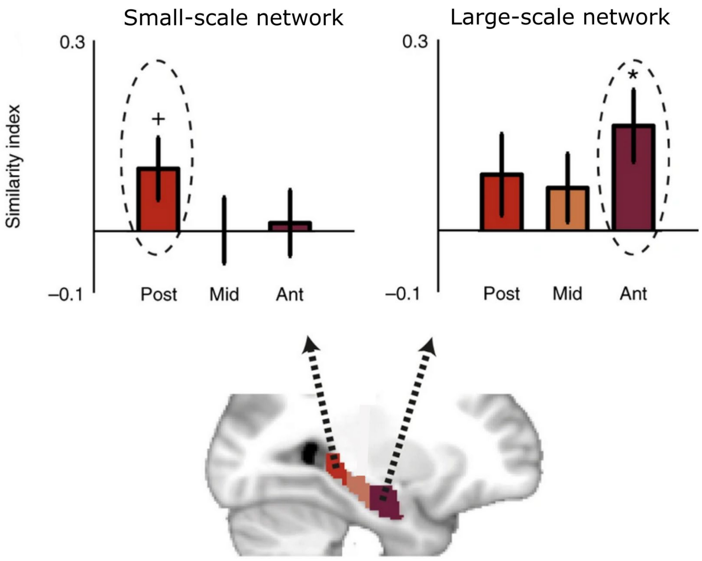


Figure 2. Episodic integration across the hippocampal long axis. Posterior portions primarily represent episodic memories with finer granularity (small-scale network), while anterior subregions integrate information across episodic memories (large-scale network). Adapted from Collin et al. (2015).

1.2. Stress effects on memory

Acute stress is a potent modulator of learning and memory (Sandi & Pinelo-Nava, 2007; Schwabe et al., 2012; Shields et al., 2017). This influence of stress on memory functions constitutes an integral component of the adaptive fight-or-flight response, aiding in effective coping with the challenges at hand (Schwabe et al., 2022). Picture again the introductory scenario: while walking along your usual morning route, heading towards the local bank, suddenly a masked figure runs past you armed with a gun and swiftly boards the white van that screeches away. In this moment, your body's stress response is triggered in reaction to this life-threatening situation. When faced with acute stress, several critical changes occur aimed towards memorizing the key features of the stressful event: heightened attention of emotionally salient events, increased dependence on established habits, and reduced processing of stressor-irrelevant information (Schwabe et al., 2022). These stress effects are substrated through a coordinated action of stress hormones on prefrontal and medial temporal areas (McEwen et al., 1986; Reul & De Kloet, 1985). Following the rapid release of catecholamines, specifically adrenaline and noradrenaline, in response to a stressful event, the hypothalamus initiates a hormonal cascade that culminates in the secretion of glucocorticoids, primarily cortisol in humans, from the adrenal cortex (de Kloet et al., 2005; Joëls & Baram, 2009). Cortisol, being a steroid hormone, passes through the blood-brain barrier (Banks, 2012), particularly affecting regions densely populated with glucocorticoid receptors, such as the hippocampus and prefrontal regions (McEwen et al., 1986; Patel et al., 2000), which renders them particularly susceptible to stress-induced changes (Arnsten, 2009; Kim et al., 2001; Pruessner et al., 2008). Depending on factors such as the timing of the stressor, it is widely accepted that stress unrelated to learning tends to decrease hippocampal activity and disrupt hippocampus-dependent processes (Joëls et al., 2011; Kim & Diamond, 2002; Pruessner et al., 2008).

However, the impact of stress transcends these well-established effects on hippocampal activity by biasing the utilization of multiple memory systems (Schwabe & Wolf, 2012). Specifically, stress shifts the balance away from hippocampus-dependent 'relational' memory to more habit-like forms of memory, reliant on structures, such as the dorsal striatum

(Goldfarb et al., 2017; Schwabe, 2017; Vogel et al., 2016). Consequently, stress often results in an enhancement of dorsal striatum dependent memory, heightening the dependence on well-established routines for adaptive behavior (Kim et al., 2001; Schwabe et al., 2007). This rapid shift, however, comes at the cost of the more flexible hippocampus-dependent memory system, impairing its ability to flexibly transfer or integrate memories. Indeed, acute stress has been shown to impair the ability to integrate new information into pre-existing memory, primarily due to the influence of cortisol (Kluen et al., 2017). This effect may be attributed to the alteration of hippocampal activity under acute stress while processing new information, which was shown to result in impaired subsequent memory (Vogel et al., 2018b). Furthermore, recent research has shown a direct link between stress-induced reductions in the ability to transfer memories to novel contexts and elevated cortisol levels (Dandolo & Schwabe, 2016).

When faced with acute stress, such as encountering an armed person outside the local bank, a notable consequence is the simultaneous decrease in hippocampal activity and a shift towards reliance on other memory systems. These neural changes may disrupt the capacity to integrate the previously separate events (white van and police cars) into a coherent episode via a common narrative (bank robbery). However, whether and how stress may affect this process of dynamic memory integration has remained unknown. While being generally adaptive, overly strong or aberrant stress effects on cognitive processing, particularly on memory formation, can become maladaptive and contribute to stress-related mental disorders (de Quervain et al., 2017; Pitman et al., 2012). Stress-related disorders such as posttraumatic stress disorder (PTSD) are characterized by fragmented memories (Amir et al., 1998; Berntsen et al., 2003; Guez et al., 2011). These fragmented memories may result from reduced cognitive flexibility due to stress, leading to rigid memory fragments that lack contextual detail (Simon-Kutscher et al., 2019; van Ast et al., 2013; Wirz et al., 2018). Understanding how stress affects mnemonic integration could shed light on the etiology of memory fragmentation in stress-related disorders and potentially contribute to the development of interventions to treat or alleviate symptoms. Beyond acute stress potentially disrupting mnemonic integration, it is essential to explore how events are linked into a narrative. Forming a coherent narrative may differ strikingly when the linking information is mentally constructed instead of directly observed.

1.3. Imagining the link

Have you ever wondered what role our imagination plays in reshaping our memories and weaving them into cohesive narratives? In the introductory example, we gained insight into the story of the bank robbery. However, this insight emerged while sitting at our desk at work, reading a newspaper headline. When reading this headline, it triggered the reactivation of two memory representations: a white van speeding away and police cars rushing past us. We linked these memory representations to form a coherent episode by imagining the missing pieces: the earlier bank robbery, the suspect escaping in the white van, and the bank accountant urgently calling the police, who arrived swiftly at the scene. In daily life, we often gain insight not only by directly experiencing the missing connections, but also by using our imagination to fill in gaps. This imagination-based insight may also involve weaving the previously separate memory representations into a coherent episode through a narrative, possibly reflecting a fundamental organizational principle within the brain (Bower & Clark, 1969; Collin et al., 2017; Tulving, 1983). In addition, imaginative mnemonic techniques, like the loci method, have consistently demonstrated memory-enhancing effects in early research (Bower, 1970; Hockley & Christi, 1996; Yesavage & Rose, 1984) and have proven valuable in various contexts, ranging from educational settings to memory championships (Maguire et al., 2003; Richmond et al., 2008).

Regarding the mechanics of imagination, the consensus view suggests that, much like recollection, imagination is a constructive process that draws upon elements

(e. g. people, locations, and objects) stored in memory to construct novel or future scenarios (Addis et al., 2007; Bartlett, 1932; Hassabis 2007a; Pearson, 2019). This conception is corroborated by research indicating that imagined and recalled events share similar content (D'Argembeau & van der Linden, 2004; Szpunar & McDermott, 2008; Thakral et al., 2019). This notion also aligns with findings from studies on patients with medial temporal lobe damage, particularly in the hippocampus, showing that these individuals not only experienced a loss of episodic memory but also of their ability to imagine events (Hassabis et al., 2007b; Race et al., 2011; Squire et al., 2010). Neuroimaging studies have further substantiated this idea by revealing similar brain activity during both recollection and imagination, encompassing brain regions such as the hippocampus (Addis et al., 2009; Benoit & Schacter, 2015; Buckner & Carroll, 2007). These findings led to the *prospective brain* hypothesis, which postulates that the brain leverages stored information to imagine, plan, and predict future events (Schacter et al., 2007). This capacity to construct a scene, whether remembered or imagined, relies on the hippocampus, which continuously constructs spatial event representations beyond current sensory input (Barry et al., 2019; Gaesser et al., 2013; Maguire & Mullally, 2013).

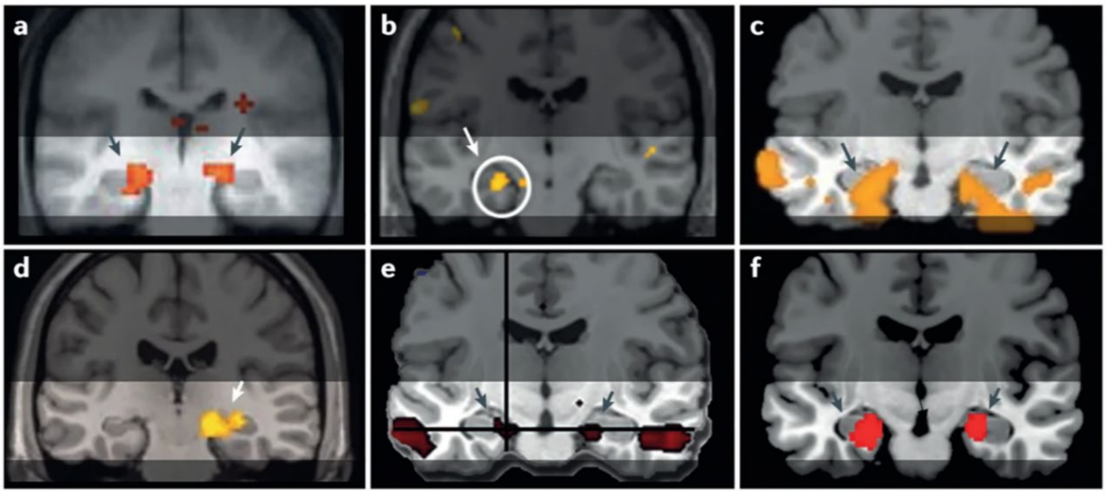


Figure 3. Anterior hippocampus activation during recall and imagination. Panels (a-f) display functional MRI (fMRI) findings of consistent activation of the anterior hippocampus (indicated by arrows) during both recall and imagination tasks. Adapted from Zeidman & Maguire (2016).

Within the hippocampus a specific role has emerged for its anterior subregion, known for its involvement in memory integration (Collin et al., 2015; Schlichting et al., 2015). Notably, this region has been suggested to function as a central hub for scene construction (Zeidman & Maguire, 2016; Fig. 3), implying that it becomes particularly engaged when assembling a coherent and novel scene. Therefore, imagination-based insight, where previously separate events are linked by our imagination into a coherent episode, relies on retrieving memory representations and converging them into a novel narrative, possibly with a key role for the anterior hippocampus. Until now, the mechanisms of imagination-based insight, particularly how we connect initially unrelated events, and the neural processes involved therein, have remained largely unexplored. Investigating insight via imagination may not only advance our grasp of the process of mnemonic integration itself but also provide guidance for contexts where knowledge units are frequently linked via imagination, such as educational settings. While the hippocampus plays a crucial role in integrating memories (Collin et al., 2015; Milivojevic et al., 2015; Schlichting et al., 2015), it does not act in isolation but collaborates with cortical areas (Backus et al., 2016; Pehrs et al., 2018; Schlichting & Preston, 2015; Spalding et al., 2018). Nonetheless, our understanding of the specific brain regions involved in mnemonic integration beyond the hippocampus has remained limited. Additionally, current data on the neural basis of mnemonic integration are mainly correlational, leaving a critical gap in our understanding of regions that causally contribute to integrating initially separate memories into cohesive representations.

1.4. A role for the angular gyrus in mnemonic integration?

One promising candidate that may contribute to mnemonic integration is the angular gyrus. Situated at the junction of the occipital, temporal and parietal lobes, the angular gyrus serves as a crucial interface, facilitating the integration of information across the brain (Seghier, 2013). This function is underscored by extensive large-scale connectivity analyses, which have consistently identified the angular gyrus as a major connector hub, linking different neural subsystems (Hagmann et al., 2008; Petit et al., 2023; Tomasi & Volkow, 2011). Among its numerous connections, the angular gyrus has demonstrated strong connectivity with the hippocampus (Thakral et al., 2020; Uddin et al., 2010; Wang et al., 2014). While being strongly connected to the hippocampus, the angular gyrus further constitutes an integral component of the default mode network (DMN; Shulman et al., 1997), which primarily constructs coherent internal narratives (Menon, 2023). This creation of internal narratives may facilitate the integration of new information with pre-existing memory (Collin et al., 2017). Indeed, the angular gyrus has been implicated in processing new information that could be integrated with pre-existing memory (Vogel et al., 2018b).

To gain deeper insights into the functions of the angular gyrus, a reverse inference analysis utilizing the NeuroSynth database (Yarkoni et al., 2011) at a previously identified angular gyrus coordinate (MNI: −48, −67, 30; Thakral et al., 2017) revealed various associated cognitive functions, including autobiographical memory, semantics, and mentalizing. In line with these functions, it has been observed that lesions in the parietal cortex, including the angular gyrus, result in fragmented memories lacking contextual detail (Ahmed et al., 2018; Berryhill et al., 2010; Irish et al., 2015). Accordingly, the angular gyrus may not be considered essential for the core memory elements – the white van (*what*) taking off at the local bank (*where*) in the morning (*when*). However, it has been posited as necessary for the integration of multi-modal details into a rich spatiotemporal representation (Bonnici et al., 2016; Ramanan et al., 2018b).

Think of the orange lettering and the cheerful orange figure on a ladder adorning the white van and the blaring sirens of the approaching police cars, which transform the episode into a rich, contextualized spatiotemporal representation. In line with this idea, recent research showed that recalling associated images with greater vividness corresponded to increased angular gyrus activity (Tibon et al., 2019). This integrative function is further supported by other work, demonstrating robust angular gyrus activity in healthy individuals when integrating multiple elements into imagined scenes (Summerfield et al., 2010). Similarly, a recent study showed that inhibition of the angular gyrus reduced performance in both the imagination and the recall of events (Thakral et al., 2017).

These observations support the notion that the angular gyrus is not only crucial for long-term memory (Bonnici et al., 2018; Kwon et al., 2022; Ritchey & Cooper, 2020; Wang et al., 2014) but also plays a pivotal role in imagination (Ramanan et al., 2018a; Thakral et al., 2017, 2020). However, how these putative functions of the angular gyrus relate to one another has remained elusive. A recent theory posits that the angular gyrus may function as an integrative dynamic buffer, combining multiple modalities into rich spatiotemporal representations (Humphreys et al., 2021). This buffering capacity may allow the angular gyrus to transiently maintain the detailed representations of the initially separate events in order to integrate them into coherent narratives, especially during imagination. Thus, the angular gyrus likely plays a role in integrating (imagination-based) insights into memory and facilitating the reconfiguration of memory representations in light of new information. Understanding which brain regions are involved in mnemonic integration may enhance our grasp of mnemonic integration and offer a better understanding of memory fragmentation in mental disorders.

1.5. Research overview

While highly important and fundamental for human behavior (Fernandez et al., 2023; Shohamy & Wagner, 2008; Zeithamova et al., 2012), our understanding of mnemonic integration and the factors influencing this process is lacking. Mnemonic integration involves the integration of new information into pre-existing memories requiring a common element, which propels previously separate events into an overlapping memory representation (Schlichting et al., 2015). This integration may be achieved by weaving new information and existing memories together through a common narrative (Milivojevic et al., 2015; Tulving, 1983). While the hippocampus, particularly its anterior subregion, is recognized as crucial for mnemonic integration (Collin et al., 2015; Schlichting et al., 2015), the precise mechanisms and neural processes have remained elusive. This present work aims to explore mnemonic integration and the factors that may interfere with this cognitive process.

One prominent factor is evident in clinical accounts, where stress-related disorders, such as PTSD, are found to be characterized by disrupted memory integration (Amir et al., 1998). Given the stress-induced decreases in hippocampal activity and the shift at the cost of hippocampal processing (Kim & Diamond, 2002; Schwabe & Wolf, 2012), it is likely that stress interferes with mnemonic integration. In *Study* 1, we set out to investigate whether acute stress disrupts mnemonic integration. To this end, we combined a psychosocial stress induction procedure (TSST; Kirschbaum et al., 1993) with a narrative-insight task (NIT; Milivojevic et al., 2015), univariate and multivariate fMRI analyses, and a comprehensive behavioral analysis. We hypothesized that stress specifically impairs mnemonic reconfiguration in the (anterior) hippocampus. To better understand the factors affecting mnemonic integration, *Study* 2 explores the process of gaining insight when the linking event is not directly observed, but imagined. This is inspired by the anterior hippocampus's dual role in both mnemonic integration and imagination (Collin et al., 2015; Zeidman & Maguire, 2016).

To address this question, we employed a modified narrative-insight task, where one group gained insight through imagination and the other through observation, and combined this task with univariate and multivariate fMRI analyses and an extensive behavioral analysis. We hypothesized heightened hippocampal activity while gaining insight through imagination, which may potentially interfere with memory reconfiguration. While the first two studies focused on the hippocampus during mnemonic integration, we sought to identify other brain regions involved in this complex memory process. Therefore, in *Study* 3, we investigated the potential causal role of the angular gyrus in mnemonic integration, given its robust connectivity with different brain regions, including the hippocampus (Uddin et al., 2010), and its relevance to memory and imagination (Thakral et al., 2017; Wang et al., 2014). To establish causality, we applied inhibitory continuous theta burst stimulation (cTBS) at the angular gyrus before insight acquisition through an adapted narrative-insight task, involving both insight via imagination and observation. This task was combined with multivariate electroencephalography (EEG) analysis in the theta range (Backus et al., 2016) and comprehensive behavioral analysis. Our hypothesis posited that inhibiting the angular gyrus before gaining insight into the relationship between initially separate events would diminish the impact of insight on memory and disrupt insight-driven memory reconfiguration.

2. Experimental Studies

2.1. Study 1: Mnemonic integration under stress

Grob, A.-M., Milivojevic, B., Alink, A., Doeller, C. F., & Schwabe, L. (2023). Stress disrupts insight-driven mnemonic reconfiguration in the medial temporal lobe. *NeuroImage*, *265*, 119804. https://doi.org/10.1016/j.neuroimage.2022.119804 – Appendix A

2.1.1. Background

Stress is a powerful modulator of learning and memory (Joëls et al., 2011; Schwabe et al., 2022; Shields et al., 2017). This impact is evident in stress-related disorders like PTSD, characterized by fragmented memories (Amir et al., 1998; Bisby et al., 2020). Generally, stress effects are substrated by the action of stress mediators, such as cortisol, on brain regions, like the hippocampus (McEwen et al., 1986), with the anterior hippocampus specifically implicated in episodic memory integration (Milivojevic et al., 2015; Schlichting et al., 2015). However, stress unrelated to learning reduces hippocampal activity (Kim & Diamond, 2002; Schwabe & Wolf, 2012), potentially diminishing the ability to integrate separate events into a coherent episode. Until now, the precise influence of stress on episodic memory integration remained unknown. Here, we aimed to investigate if acute stress disrupts mnemonic integration, particularly impairing insight-driven mnemonic reconfiguration in the (anterior) hippocampus.

2.1.2. Methods

We tested fifty-nine healthy individuals on two days, a week apart. On the first day, participants underwent stress induction (TSST; Kirschbaum et al., 1993) or a control manipulation. They then completed a narrative-insight task (NIT; Milivojevic et al., 2015) during MRI scanning. In this task, participants first repeatedly watched three videos (A, B, and

X) showing specific episodes (pre-phase). Thereafter, a new linking event (L) was presented that linked two of the previously seen events (A and B) but left the third event non-linked (X; insight-phase). Finally, the now linked or non-linked events were presented again to examine insight-driven representational changes (post-phase). A week later, participants completed a memory test encompassing free recall, a multi-arrangements task (MAT; Kriegeskorte & Mur, 2012), and a forced-choice recognition task. To unravel stress effects on episodic memory integration, we combined behavioral analysis with univariate fMRI analysis and representational similarity analysis (RSA).

2.1.3. Results

The stress induction proved to be effective. In the NIT, all participants gained insight into the relationship between initially separate events. One week later, in the MAT, they correctly positioned linked events closer and non-linked events farther apart, without stress effects. Across both groups, memory for linked events was enhanced in free recall, suggesting a memory advantage for integrated narratives. Notably, in the forced-choice recognition test, stress boosted performance. At the neural level, stress reduced insight-related activity in the parahippocampus, orbitofrontal cortex, and putamen. Most strikingly, stress abolished an increase in neural dissimilarity between linked events in the anterior hippocampus. Additionally, while gaining insight into the relationship between events, stress reduced medial temporal lobe activity.

2.1.4. Conclusion

In sum, these findings emphasize that acute stress has a significant impact on the neural integration of previously separate events into coherent episodes. While learning about the relationship between events, stress downregulated medial temporal lobe activity, reflecting a stress-induced shift away from a ‘cognitive’, medial temporal lobe-based system (Schwabe &

Wolf, 2012), and hindered an insight-induced increase in this region. Strikingly, stress abolished an insight-driven representational change in the anterior hippocampus, integral to mnemonic integration (Collin et al., 2015; Schlichting et al., 2015). In contrast to these stress-induced neural impairments, stress boosted recognition memory, likely due to delayed cortisol effects (Schwabe et al., 2022; van Ast et al., 2013). Therefore, these results suggest that acute stress disrupts the neural foundations of memory integration while simultaneously enhancing long-term recognition memory.

2.2. Study 2: Gaining insight via imagination

Grob, A.-M., Milivojevic, B., Alink, A., Doeller, C. F., & Schwabe, L. (2023). Imagining is not seeing: lower insight-driven memory reconfiguration when imagining the link between separate events. *Cerebral Cortex*, 33(12), 7409–7427, https://doi.org/10.1093/cercor/bhad048 – Appendix B

2.2.1. Background

In daily life, insight often emerges through imagination. Despite its importance for educational settings and mnemonic strategies (Bower, 1970; Hockley & Christi, 1996), prior research on mnemonic integration has primarily focused on insight gained via direct experience. The capacity to imagine is consistently associated with anterior hippocampal activity (Benoit & Schacter, 2015; Gaesser et al., 2013; Zeidman & Maguire, 2016) – a region equally important for mnemonic integration (Milivojevic et al., 2015; Schlichting et al., 2015). This raises a fundamental question: Can memory integration be effectively accomplished when the hippocampus is partly engaged by imaginative processes? Thus far, the precise mechanisms of mnemonic integration through imagination and its underlying neural processes have remained elusive. Therefore, the present study seeks to uncover these neural processes and probe the behavioral consequences of gaining insight through imagination.

2.2.2. Methods

We tested fifty-six healthy individuals on two days, one week apart. On the first day they completed a modified narrative-insight task (NIT; Milivojevic et al., 2015) in an MRI scanner. In this task, participants first watched three videos (A, B, and X; pre-phase). The subsequent insight-phase, which differed from *Study* 1, involved two groups: the observation group gained insight into the link between events (A and B) from a video (L), as in *Study* 1, while the imagination group gained this insight though an imagination instruction (I). The third event (X) remained non-linked. Finally, the now linked (A and B) or non-linked (X) events were presented again to examine insight-driven representational changes (post-phase). One week later, participants completed a delayed memory test, including free recall, a multi-arrangements task (MAT), and forced-choice recognition. To explore the impact of gaining insight through imagination vs. observation of the linking event, we combined comprehensive behavioral analysis with univariate fMRI and representational similarity analysis (RSA).

2.2.3. Results

While insight via imagination was possible, it proved weaker compared to directly observing the linking event in the NIT. A week later, participants accurately recalled the link in the MAT, forced-choice recognition, and displayed enhanced memory for linked events in free recall, regardless of their insight mode. Interestingly, those who gained insight through imagination recalled more details for both linked and non-linked events. Notably, the vividness of imagination correlated positively with the average number of details recalled. At the neural level, imagining the linking event reduced insight-driven activity increases in the caudate nucleus, dorsolateral prefrontal (dlPFC), and orbitofrontal cortices, and reduced activity increases for non-linked events in the anterior cingulate. Strikingly, the increase in neural dissimilarity between linked events in the anterior hippocampus was abolished when insight was imagined. Interestingly, similar regions were more engaged during imagination: the hippocampus showed increased activity and coupling with the striatum.

2.2.4. Conclusion

Consistent with everyday examples, gaining insight via imagination is possible but comes with significant changes compared to direct experience. Insight via imagination came at the cost of lower immediate insight and an impeded representational change in the anterior hippocampus. Conversely, linking via imagination increased hippocampal activity and connectivity, possibly hindering necessary neural changes for mnemonic integration but facilitating long-term memory formation, aligning with previous research on the memory advantages of imagination (Bower, 1970; Hockley & Christi, 1996). Together, these results shed light on the outcomes of insight gained via imagination, highlighting the advantages of direct observation and the memory benefits of imaginative processes.

2.3. Study 3: The role of the angular gyrus

Grob, A.-M., Heinbockel, H., Milivojevic, B., Doeller, C., & Schwabe, L. (2023). Causal role of the angular gyrus in insight-driven memory reconfiguration. *bioRxiv*, https://doi.org/10.1101/2023.08.18.553803 – Appendix C

2.3.1. Background

The hippocampus does not act in isolation to accomplish mnemonic integration (Backus et al., 2016; Spalding et al., 2018). Yet, our grasp of neural mechanisms beyond the hippocampus remains limited, primarily relying on correlational insights. One potential candidate that may causally contribute to insight-driven memory reconfiguration is the angular gyrus distinguished by its extensive connectivity, including connections with the hippocampus (Uddin et al., 2010). With its central role in memory and imagination (Bonnici et al., 2018;

Thakral et al., 2017), the angular gyrus could potentially facilitate the integration of (imagination-based) insights into long-term memory by buffering (Humphreys et al., 2021) and integrating initially separate events into coherent narratives. Thus, this study aims to investigate whether angular gyrus inhibition through cTBS before gaining insight into the relationship between previously separate events reduces the impact of insight on memory and disrupts the insight-driven memory reconfiguration.

2.3.2. Methods

We tested sixty-five healthy individuals in a single day. Participants completed an adapted narrative-insight task (NIT; Milivojevic et al., 2015) while their electroencephalography (EEG) was recorded. During the NIT, they watched three video events (A, B, and X; pre-phase), which were subsequently either linked into a narrative (A and B) or not (X) during an insight-phase. All participants gained insight through imagination (I) for half of the stories and through video observation (L) for the other half. Critically, before the insight-phase, we administered inhibitory cTBS targeting the left angular gyrus to one group and sham stimulation to the other group. After the insight-phase, participants completed a free recall. Next, the same video events (A, B, and X) were presented in the post-phase to examine insight-driven representational changes. Following this, participants completed a multi-arrangements task (MAT) and a forced-choice recognition task. To examine the angular gyrus's role in episodic memory integration, we combined behavioral analysis with representational similarity analysis (RSA) of EEG frequency data.

2.3.3. Results

All participants gained insight in the NIT and recalled this insight accurately in the MAT, the forced-choice recognition, and with more details for linked events in free recall. Crucially, angular gyrus inhibition before insight reduced this memory boost for linked events and for the linking events, particularly with strong electric field stimulation. On a neural level, angular gyrus inhibition abolished insight-induced increases in theta similarity for events linked via imagination and induced representational changes for non-linked events in the theta band resembling the sham group's pattern for events linked via imagination. Moreover, angular gyrus inhibition abolished decreases in theta similarity for events linked via observation and induced neural similarity decreases for non-linked events, resembling the pattern for linked events. However, these latter findings for observation-based insight may have been driven by pre-existing group differences. In addition, angular gyrus inhibition reduced theta coupling between centro-temporal and frontal regions for events linked via imagination.

2.3.4. Conclusion

Inhibiting the angular gyrus curtailed the memory boost for the integrated narrative, suggesting a causal role in prioritizing the integrated narrative in memory. Importantly, angular gyrus inhibition abolished representational changes in the theta band for imagination-based linked events, pointing to disrupted mnemonic integration. Altogether, the angular gyrus emerges as a causal player in memory reconfiguration when gaining (imagination-based) insight and in prioritizing integrated narratives in memory.

3. General Discussion

Maintaining an accurate model of the world requires the dynamic updating of our memories in light of new information. This process of mnemonic integration, which underlies fundamental behaviors (Fernandez et al., 2023; Shohamy & Wagner, 2008; Zeithamova et al., 2012), may efficiently integrate new information with existing memory by weaving previously separate events into a coherent episode through a unified narrative (Collin et al., 2015; Milivojevic et al., 2015; Tulving, 1983). Given its implications in pattern completion and separation processes (Horner & Burgess, 2014; Yassa & Stark, 2011), the hippocampus has emerged as a key player in mnemonic integration (Collin et al., 2015; Schlichting et al., 2015). However, despite its importance to various behaviors, the factors facilitating or inhibiting this fundamental process of mnemonic integration have remained largely unknown.

Based on the disruptive impact of acute stress on hippocampal function and memory (He et al., 2023; Kim & Diamond, 2002; Schwabe & Wolf, 2012), *Study 1* aimed to investigate whether acute stress disrupts mnemonic integration. Although stress improved recognition performance one week later, it diminished medial temporal lobe activity, hindered an increase in this region, and, strikingly, abolished the insight-induced representational change in the anterior hippocampus. These results highlight the disruptive impact of acute stress on the neural underpinnings of mnemonic integration, while simultaneously demonstrating the recognition memory enhancing effects of stress. Furthermore, considering the common role of gaining insight via imagination in daily life and its shared reliance with mnemonic integration on the anterior hippocampus (Collin et al., 2015; Zeidman & Maguire, 2016), *Study 2* explored the behavioral and neural consequences of this process. We observed a remarkable tradeoff: immediate insight was worse when gained through imagination, but there was an overall memory enhancement one week later. Yet, imagination-based insight suppressed a representational change in the anterior hippocampus, likely due to increased hippocampal activity and connectivity with the striatum during the imagination-based linking process. In *Study* 3, we aimed to investigate the previously unexplored causal role of the angular gyrus in mnemonic integration, given its implications in both memory and imagination (Thakral et al., 2017). Our findings showed that inhibiting the angular gyrus before gaining insight reduced a memory boost for the integrated narrative. Strikingly, angular gyrus inhibition eliminated representational changes in the theta band for events linked via imagination. These results point to impaired memory integration following inhibition of the angular gyrus, underscoring, for the first time, its causal role in this process. Consistently, across all three studies, we observed improved memory for the integrated narrative, aligning with the concept that the brain stores episodic memories as coherent narratives (Tulving, 1983).

3.1. Linking events into a cohesive narrative

As expected, all participants gained insight into which events became part of the same narrative. Importantly, this insight was not influenced by visual similarity or semantic properties as the assignment of which videos were linked was counterbalanced across participants. However, immediate insight into which events became part of the same narrative was less successful when the linking event was imagined (*Study* 2). This outcome may be attributed to the potentially higher cognitive demands of imagination (Albers et al., 2013; Baddeley & Andrade, 2000) and its weaker neural signal compared to direct observation (Grossman & Blake, 2001; Naselaris et al., 2009). Importantly, this disadvantage of gaining insight via imagination did not manifest in *Study* 3, which differed from *Study* 2 in multiple ways. *Study* 3 employed a within-group design, where all participants gained insight through both imagination and observation, included a shared insight-phase for all stories, and applied cTBS targeting the angular gyrus prior to the insight-phase.

These factors may have collectively raised attention levels, potentially mitigating lower immediate insight through imagination. Another factor that could have counteracted initial reductions in immediate insight in *Study* 3 is the timing of free recall, which occurred immediately after the insight phase. This timing could potentially have bolstered memory through active retrieval practice (Karpicke & Blunt, 2011; Roediger III & Karpicke, 2006).

At the neural level, gaining insight into the relationship between previously separate events increased activity in specific brain regions. The first two studies consistently found increased activity in the dorsal striatum, encompassing the putamen and the caudate nucleus, following insight. This region's connection to processing integrated episodes and associative learning (Ben-Yakov & Dudai, 2011; Mattfeld & Stark, 2015) may underscore its role in mnemonic integration. Crucially, these increases were disrupted by acute stress (*Study* 1) and imagination (*Study* 2). Both acute stress and imagination-based insight further reduced orbitofrontal activity, which is closely associated with reward processing (Kringelbach, 2005; Oh et al., 2020). One might speculate that this diminished orbitofrontal activation hints at a decreased sense of reward when gaining insight under stressful or imaginative conditions. We also noted variations in brain regions between the two studies, which may have been due to the different group comparisons. In *Study 1*, the parahippocampus, linked to processing (spatial) associations (Epstein & Kanwisher, 1998; Faivre et al., 2019), displayed increased activity, which was disrupted by acute stress, in line with previous findings showing the parahippocampus's sensitivity to stress (Meyer et al., 2013; Shields et al., 2019; Wirz et al., 2017). Conversely, dorsolateral prefrontal activity increases were diminished when gaining insight via imagination. This region is known for its role in processing relational memory and insight (Long et al., 2010; Tik et al., 2018), which appears to be essential for mnemonic integration. Importantly, this region is also associated with working memory (Barbey et al., 2013; Wagner, 1999), which may have been more taxed when insight was gained through imagination.

Additionally, imagination-based insight reduced anterior cingulate activity for the non-linked events. This region is associated with conflict monitoring (Botvinick et al., 2004), possibly implying diminished attention to events outside the integrated narrative as potential sources of conflict. The specificity of this region's reduction to imagination-based insight may stem from the increased demands of imaginative processes (Albers et al., 2013).

3.2. Insight-driven neural memory reconfigurations

To elucidate how insight impacts memory representations, we examined representational changes within the anterior hippocampus (*Studies* 1 and 2), crucial to mnemonic integration (Collin et al., 2015), and in the theta frequency (*Study* 3), known for its role in memory binding (Clouter et al., 2017). Our results revealed that direct observation of the linking event resulted in insight-triggered increased dissimilarity within the anterior hippocampus (*Studies* 1 and 2), an effect specific to this region (*Study* 2). These results align with prior research underlining the anterior hippocampus's centrality in mnemonic integration (Hannula et al., 2013; Schlichting et al., 2015) and its involvement in processing spatial context and novelty detection (Brunec et al., 2018; Bunzeck & Düzel, 2006). Strikingly these insight-induced representational changes were abolished by both acute stress (*Study* 1) and imagination-based insight (*Study* 2). The disrupted mnemonic reconfiguration in the anterior hippocampus by acute stress aligns with a substantial body of research illustrating the impact of stress on hippocampal processing (Kim & Diamond, 2002; Pruessner et al., 2008; Vogel et al., 2018b). Consistent with a previous study showing that cortisol interfered with the integration of new information into memory (Kluen et al., 2017), we found that higher cortisol levels were associated with diminished representational changes. Interestingly, the disruption of representational change in the anterior hippocampus when gaining insight through imagination hints at the potentially interfering nature of imaginative processes, possibly due to their reliance on the anterior hippocampus (Zeidman & Maguire, 2016).

In contrast to previous findings of increased representational similarity (Collin et al., 2015; Schlichting et al., 2015), our study revealed increased representational dissimilarity for integrated events. This discrepancy may be attributed to differences in video presentation durations and the introduction of titles, potentially prompting distinct cognitive strategies compared to previous research (Collin et al., 2015). The increase in representational dissimilarity can be interpreted as a pattern separation mechanism, facilitating inferences across events (Molitor et al., 2021), in line with previous studies that consistently associated increased neural dissimilarity with improved memory performance (Chanales et al., 2017; Favila et al., 2016; Koolschijn et al., 2019). Indeed, the results from *Study 1* and *Study 2* demonstrate a link between post-insight neural dissimilarities and subsequent memory. What boundary conditions could have contributed to the differing results in representational changes? Some studies indicate increasingly similar anterior hippocampal patterns over time (Audrain & McAndrews, 2020; Chang et al., 2021; Dandolo & Schwabe, 2016), while others report more dissimilar anterior hippocampal patterns both on the same day and overnight (Ezzyat et al., 2018). In addition to time, a likely factor influencing the direction of representational change is the degree of neural overlap among co-activated memory representations. A recent framework suggests that moderate co-activations of memory representations may lead to increased dissimilarity, which may have been the case here (Wammes et al., 2022).

In *Study 3*, consistent with the representational changes in the first two studies, we observed increased theta band similarity between events linked via imagination. This finding aligns with previous research highlighting the role of theta activity in memory retrieval, encoding, and information integration (Cavanagh & Frank, 2014; Düzel et al., 2010). Recent studies also suggest that low-frequency theta oscillations aid in integrating various elements into memory (Clouter et al., 2017; Wang et al., 2018), with hippocampal theta activity predicting successful memory integration (Backus et al., 2016). These results are further consistent with other work showing increased theta activity during the integration of new information into existing memory (Nicolás et al., 2021). Mechanistically, hippocampal theta oscillations enhance memory integration by facilitating the accurate reinstatement of stimulus-specific information from the events being linked (Pacheco Estefan et al., 2021). Critically, inhibiting the angular gyrus before gaining insight abolished this increase in theta similarity for events linked via imagination, indicating a failure in mnemonic integration and emphasizing the angular gyrus's causal role herein. In addition, angular gyrus inhibition induced representational changes for non-linked events resembling the patterns observed in the sham group for linked events, underscoring its crucial role in effectively distinguishing integrated and non-integrated events. Moreover, events linked via direct observation showed reduced theta pattern similarity after angular gyrus inhibition, further underscoring its role in mnemonic integration. However, caution is warranted in interpreting observation-based results due to potential pre-existing group differences.

While we observed increased anterior hippocampal dissimilarity for linked events in *Study* 1 and 2, *Study* 3 revealed increased theta similarity. Notably, the neuroimaging techniques varied across these studies: the first two studies used fMRI to correlate blood oxygenation level dependent (BOLD) activity patterns, resulting in spatial (dis)similarity, while *Study* 3 employed EEG to correlate theta oscillation patterns over time, resulting in temporal (dis)similarity. Therefore, the first two studies reveal where insight-driven representational changes occur in the brain, while the third study indicates when and at what frequency these changes appear. Overall, we observed increased anterior hippocampal dissimilarity for linked events, which was disrupted by acute stress and imagination-based insight, and increased theta similarity for events linked via imagination, abolished by angular gyrus inhibition before gaining insight.

3.3. Gaining insight into the narrative

What might drive the disruption in representational changes observed from *Study* 1 to 3? To shed light on potential alterations, we investigated neural changes during the insight-phase. Acute stress reduced hippocampal activity while gaining insight into which events were part of the same narrative (*Study* 1), in line with a proposed stress-induced shift away from hippocampal 'cognitive' processing (Schwabe & Wolf, 2012). This downregulation of hippocampal activity during insight acquisition may have impeded the representational change in the anterior hippocampus, as such changes likely depend on hippocampal capacity for memory reactivations to successfully weave events into a cohesive narrative (Wammes et al., 2022; Zeithamova et al., 2012). In line with this idea, recent research showed that hippocampal activity indeed increases while gaining insight (Becker et al., 2023). Consequently, this stress-induced shift away from hippocampal processing may have limited hippocampal capacity for these reactivations during insight, potentially preventing the differentiation of hippocampal memory representations for linked events.

While acute stress decreased hippocampal activity, we observed increased anterior hippocampal activity while gaining insight via imagination in *Study* 2, in line with prior research demonstrating the crucial role of the anterior hippocampus in imaginative processes (Addis et al., 2009; Hassabis et al., 2007b; Zeidman & Maguire, 2016). This increased hippocampal activity while gaining insight via imagination may have bound hippocampal capacities for memory reactivations, probably due to retrieving elements for constructing elaborate events (Reagh & Ranganath, 2023), and, as a result, hindered a representational change in the anterior hippocampus. In addition to increased hippocampal activity, imagining the linking event also increased hippocampal connectivity with the caudate nucleus, potentially binding hippocampal capacities even more, which may have further interfered with a representational change in the anterior hippocampus. Notably, increased connectivity between the hippocampus and the caudate nucleus, rather than increased hippocampal activity per se, was associated with better subsequent memory, in line with previous work (Faul et al., 2020; Müller et al., 2018).

Whereas altered hippocampal activity during insight acquisition likely hindered a hippocampal representational change in the first two studies, the insight-phase in *Study* 3 was also of critical importance: inhibiting the angular gyrus prior to gaining insight abolished a representational change for events linked via imagination in the theta frequency. This is particularly interesting, as recent evidence has specifically linked the theta rhythm to insight acquisition (Bieth et al., 2021), emphasizing its role during the insight-phase and potentially explaining the absence of a representational theta change when the angular gyrus was inhibited at the theta frequency with cTBS. Given the proposed role of theta oscillations in reinstating stimulus-specific information (Pacheco Estefan et al., 2021), it is conceivable that the inhibition of the angular gyrus before gaining insight hindered the detailed reactivation of memory representations (Ramanan et al., 2018b). Thus, the abolished representational change highlights the causal role of the angular gyrus in integrating insights, specifically through imagination, into memory.

Altogether, while gaining insight into the relationship between previously separate events, we observed stress-induced downregulations as well as imagination-driven upregulations of hippocampal activity (and connectivity). These changes in hippocampal activity may have disrupted memory reconfiguration within the anterior hippocampus, suggesting that the hippocampus may need to be accessible during this phase to facilitate these changes effectively. Beyond the hippocampus's importance for insight acquisition, angular gyrus inhibition before insight acquisition nullified a representational change at theta frequency, highlighting its causal role in integrating new insights with pre-existing memory.

3.4. Translation of insight into long-term memory

How did the process of gaining insight into the relationship between previously separate events translate into memory? To address this question, participants completed a comprehensive assessment of their memory either on the same day (*Study* 3) or a week later (*Study* 1 and 2). They not only excelled at recreating the narrative structure in the multi-arrangements task (MAT), but we further observed a consistent memory boost for the integrated narrative in the free recall across all three studies. Prioritizing the detailed retention of integrated narratives in memory aligns with prior research (Cohn-Sheehy et al., 2021; Wang et al., 2015) and the classic idea that the brain stores episodic memories as coherent narratives (Tulving, 1983). Interestingly, a greater representational change in the anterior hippocampus was associated with recalling fewer details for the non-linked event (*Study* 2), indicating an even stronger focus on the integrated narrative. This principle of organizing episodic memories into narratives was shown to extend to recollecting less coherent events as more narrative-like (Raykov et al., 2023), and even seems to persist into old age (Delarazan et al., 2023).

Crucially, this memory boost for the integrated narrative was impaired when the angular gyrus was inhibited prior to gaining insight (*Study* 3), suggesting not only its causal involvement in memory reconfiguration but also in prioritizing the detailed retention of the integrated narrative in memory. Furthermore, angular gyrus inhibition impaired the recall of the linking events themselves, indicating a causal role of the angular gyrus in integrating newly acquired information into pre-existing memory, aligning with a recent study showing that angular gyrus inhibition during a reading-based task impaired the integration of contextual information (Branzi et al., 2021). Additionally, it is consistent with evidence demonstrating the involvement of the angular gyrus in integrating new information into schema memory (van Buuren et al., 2014; Vogel et al., 2018a, 2018b). Interestingly, angular gyrus activity during the integration of new information with pre-existing memory has been shown to be predictive of later memory performance (van der Linden et al., 2017), highlighting the angular gyrus's role in prioritizing the integrated narrative within memory. Recent research has proposed the angular gyrus as a spatiotemporal buffering region for integrating the ongoing stream of experiences (Humphreys et al., 2021), thus supporting its causal role in binding new information with pre-existing memory into a detailed narrative. Consequently, inhibiting the angular gyrus may have interfered with the reactivation and maintenance of initially separate event representations while gaining insight, potentially at theta frequency (Bieth et al., 2021), impeding the critical binding process required for the observed memory boost. As a result, the diminished memory reconfiguration in the theta band was related to diminished memory for the linking events.

Despite the lower immediate insight and an absent representational change in the anterior hippocampus, we observed a general memory boost in free recall when insight was gained via imagination (*Study* 2). This general memory enhancement aligns with previous studies that highlight the efficacy of imagination as a mnemonic strategy (Bower, 1970; Hockley & Christi, 1996; Wagner et al., 2021). Indeed, our findings reveal a direct positive relationship between imagination strength and the average number of details recalled. One plausible explanation for this effect could be deeper processing, known to improve memory (Bertsch et al., 2007; Craik & Lockhart, 1972), possibly facilitated by increased engagement through imagination. However, if this effect resulted from active engagement, it seemed to enhance memory for all events rather than being exclusive to the integrated narrative. Interestingly, this effect was not observed in *Study* 3. This difference could be attributed to the presence of a one-week delay in *Study* 2, allowing for memory consolidation, possibly necessary for the emergence of this general memory boost (Berres & Erdfelder, 2021; Weber et al., 2014). Furthermore, the benefit of actively retrieving memory representations during imagination may become more pronounced with longer retention intervals (Roediger III & Karpicke, 2006; Rowland, 2014), suggesting that a single-day design may not have allowed sufficient time to observe this effect.

While acute stress reduced hippocampal activity during insight acquisition and eliminated a representational change in the anterior hippocampus, it improved recognition memory one week later (*Study* 1). Consistent with previous findings demonstrating that stress prior to encoding may enhance recognition memory for emotional associations (Goldfarb et al., 2019; Sep et al., 2019), our results show that acute stress before encoding improves recognition memory for events linked via a narrative. It is tempting to speculate that this memory boost in stressed participants may be attributed to delayed cortisol effects (Schwabe et al., 2022; van Ast et al., 2013), potentially facilitating the processing of the stressful episode by promoting executive functioning.

3.5. Process model of mnemonic integration

Together, these three studies provide valuable insights into mnemonic integration, which will be synthesized into a process model of mnemonic integration, highlighting the intricate mechanisms during the insight-phase in this section. First, our findings demonstrated that the angular gyrus plays a causal role in reconfiguring theta representations of linked events and prioritizing the detailed memory of the integrated narrative. Expanding upon previous research that underscores the angular gyrus's involvement in memory integration (Vogel et al., 2018a; Wagner et al., 2015) and its proposed buffering function (Humphreys et al., 2021), it is hypothesized that maintaining the linking information triggers the reactivation and buffering of detailed memory representations within the angular gyrus (Fig. 4A). This hypothesis can be tested by using multi-voxel pattern analysis (MVPA) on the angular gyrus to extract specific elements (Bonnici et al., 2016; Liu et al., 2022) from the memory representations while new information is presented. It is further anticipated that theta oscillations, known for their role in integrating elements into memory (Clouter et al., 2017;

Wang et al., 2018), will facilitate the integration of new information with existing memory. This may be tested by assessing theta oscillations during insight and relating these oscillations to the decoded evidence for distinct elements of memory representations in the angular gyrus while new information is presented. Given the angular gyrus's role in prioritizing integrated narratives in memory, it is expected that concurrent buffering of new information and memory representations enhances memory retention for the integrated narrative. This hypothesis can be explored by analyzing the association between the decoded evidence of concurrent buffering and subsequent memory of the integrated narrative.

Second, the (anterior) hippocampus has emerged as a central player in gaining insight into the relationships between previously separate events, consistent with prior work (Collin et al., 2015). When hippocampal activity is altered during insight acquisition (Becker et al., 2023), whether downregulated due to acute stress or upregulated during imagination, hippocampal reconfiguration is impaired. This raises an intriguing question: is there an optimal hippocampal state that facilitates the insight-induced representational changes during mnemonic integration? Here, an optimal range of hippocampal activity during insight is hypothesized, with moderate activity levels facilitating representational change, potentially by allowing for better memory reactivation of the previously separate events (Zeithamova et al., 2012; Fig. 4B). To test this hypothesis, different strategies could be employed to manipulate hippocampal activity during insight acquisition, such as modulating it via other brain regions or using neuro-feedback (Paret & Hendler, 2020; Thakral et al., 2020). To quantify memory reconfiguration in the anterior hippocampus, an RSA approach (Kriegeskorte et al., 2008) is recommended. Next, an inverted U-shaped relationship between modulated hippocampal activity levels and representational changes within the anterior hippocampus should be explored. Given the divergent findings in these studies and prior work regarding the direction of representational change, it is hypothesized that the direction of such change depends on the level of neural overlap during memory co-activation (Wammes et al., 2022). Manipulating this overlap may involve altering the visual similarity of events or directly quantifying it through decoding neural activity during insight acquisition (Liu et al., 2022; Schönauer et al., 2017). In addition, our work uncovered a stress-induced boost in recognition memory, potentially due to delayed cortisol effects, and a general memory boost linked to hippocampo-caudal connectivity during imagination. Since these effects likely depend on processes other than altered hippocampal activity or memory co-activation, they fall outside the scope of this process model of mnemonic integration.

In conclusion, this model converges and extends potential neural mechanisms underpinning mnemonic integration. The angular gyrus is posited as a buffer for new linking information, facilitating memory recollection and concurrent buffering at theta frequency, thereby enhancing the detailed retention of the integrated narrative. This model posits an optimal range of hippocampal activity during insight, promoting reconfiguration of memory representations in the anterior hippocampus, contingent upon the extent of neural overlap during memory co-activation. Yet, an uncharted aspect is the relationship between the angular gyrus and the hippocampus, warranting future research. One plausible scenario is that the angular gyrus serves as input to the hippocampus, triggering the hippocampal reactivation of the memory representations (Fig. 4). This model, by combining neural mechanisms of mnemonic integration, lays a foundation for future research and may provide a framework for understanding the etiology of disorders characterized by memory fragmentation.

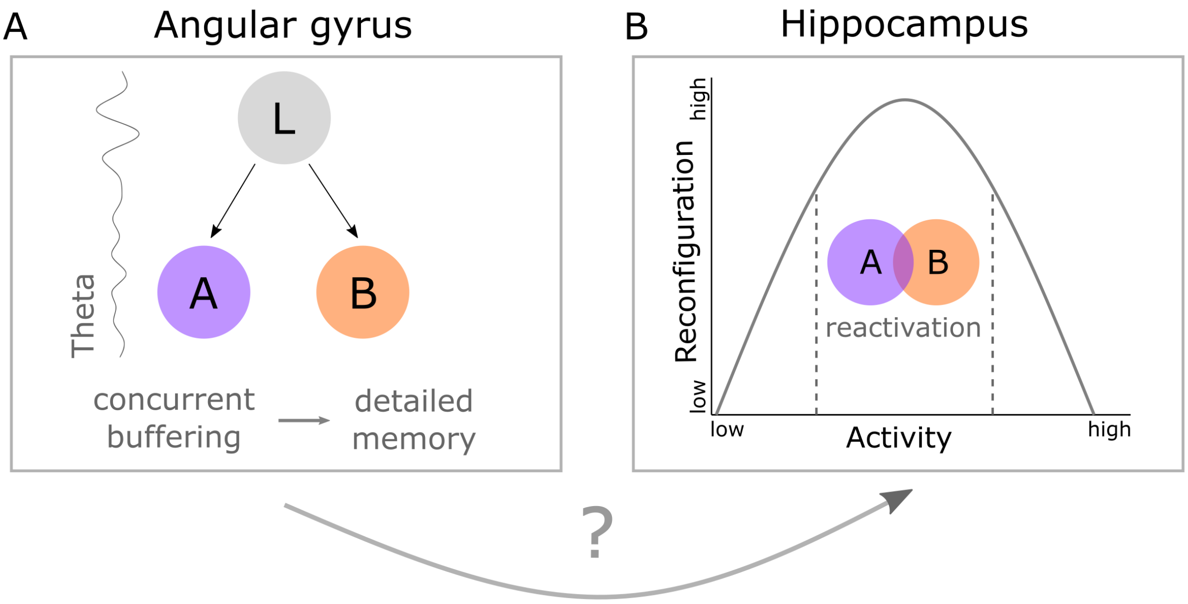


Figure 4. Process model of mnemonic integration. **A**, The angular gyrus maintains the linking information (L), which triggers the reactivation of the memory representations of A and B. This concurrent buffering, likely at the theta rhythm, results in detailed memory for the integrated narrative. **B**, An optimal range of hippocampal activity suggests that moderate activity levels during insight acquisition, possibly required for memory reactivation of A and B, promote representational change. The extent of neural overlap between these reactivated memory representations likely determines whether they increase in neural similarity or dissimilarity. The interaction between these two regions is currently unclear. However, a plausible scenario could be that the angular gyrus, with its suggested buffering function, serves as input region to the hippocampus.

3.6. Limitations and future directions

While these findings advance our understanding of the factors modulating mnemonic integration, certain aspects require further clarification. Specifically, the exact influence of the angular gyrus on representational changes in events linked through observation, due to pre-existing group differences, remains unclear and warrants future exploration. Additionally, disentangling whether the memory enhancement observed in imagination-based linking results from the act of imagination itself or from deeper cognitive processing proved challenging within our experimental design. To address this, future research could incorporate an active control group into the experimental paradigm. In addition, determining whether this effect depends on memory consolidation prompts a question for future research, which could be addressed by varying the time window between initial encoding and subsequent memory tests. Due to differences in neuroimaging techniques, directly linking hippocampal reconfigurations in the first two studies with theta reconfiguration in the third study was not feasible. Future research should bridge this gap by using methods such as MEG.

On a broader scale, an important question in the field of mnemonic integration emerges: does the relationship between hippocampal activity and insight-triggered hippocampal memory reconfiguration follow an inverted U-shaped pattern? Establishing this relationship would substantially advance our understanding of the hippocampus’s role in mnemonic integration, explaining the absence of memory reconfigurations at both low and high hippocampal activity levels during insight acquisition and pave the way for potential therapeutic interventions by optimizing hippocampal activity. Additionally, the discovery of a more distinct neural representation in the anterior hippocampus following insight, consistent with recent findings on the hippocampus's role in encoding episode-specific information (Reagh & Ranganath, 2023) but contrary to prior research (Collin et al., 2015), raises questions about the conditions underpinning such distinct or integrated reconfigurations. Future research might explore whether the direction of this effect depends on the degree of neural overlap between hippocampal memory representations (Wammes et al., 2022). Lastly, given the central roles of both the hippocampus and the angular gyrus in mnemonic integration, future work should explore the interaction between these regions. This investigation may particularly focus on examining whether the angular gyrus, known for its buffering function, triggers hippocampal reactivation of memory representations.

3.7. Conclusion

Considering the introductory example, our three studies offer a nuanced understanding of the factors influencing mnemonic integration. When acute stress precedes insight acquisition, such as observing an armed person, neural activity shifts away from the hippocampus, likely hindering the representational change in the anterior hippocampus, although recognition memory may improve a week later. Gaining insight through imagination, like reading the newspaper headline, not only results in lower immediate insight but also disrupts mnemonic reconfiguration in the anterior hippocampus, potentially due to increased hippocampal activity and connectivity during imagination. Interestingly, a week later, your recollection may include more details, both related and unrelated to the bank robbery. Moreover, the angular gyrus plays a causal role in insight acquisition. Inhibiting it during this phase may impede mnemonic reconfiguration in the theta band, consequently disrupting mnemonic integration, and resulting in less detailed memory of the integrated narrative of the bank robbery. Collectively, our findings shed light on the impact of acute stress on mnemonic integration, the dynamics of gaining insight via imagination, and the causal role of the angular gyrus during insight acquisition. To integrate these findings, a theoretical process model of mnemonic integration is proposed, centering on the accessibility of the hippocampus and angular gyrus while gaining insight into the relationship between previously separate events. These results not only advance our grasp of fundamental memory processes but also hold potential insights into the origins of fragmented memories in conditions like PTSD.

References

Addis, D. R., Pan, L., Vu, M.-A., Laiser, N., & Schacter, D. L. (2009). Constructive episodic simulation of the future and the past: Distinct subsystems of a core brain network mediate imagining and remembering. *Neuropsychologia*, 47(11), 2222–2238. https://doi.org/10.1016/j.neuropsychologia.2008.10.026

Addis, D. R., Wong, A. T., & Schacter, D. L. (2007). Remembering the past and imagining the future: Common and distinct neural substrates during event construction and elaboration. *Neuropsychologia*, 45(7), 1363–1377. https://doi.org/10.1016/j.neuropsychologia.2006.10.016

Ahmed, S., Irish, M., Loane, C., Baker, I., Husain, M., Thompson, S., Blanco-Duque, C., Mackay, C., Zamboni, G., Foxe, D., Hodges, J. R., Piguet, O., & Butler, C. (2018). Association between precuneus volume and autobiographical memory impairment in posterior cortical atrophy: Beyond the visual syndrome. *NeuroImage: Clinical*, 18, 822–834. https://doi.org/10.1016/j.nicl.2018.03.008

Albers, A. M., Kok, P., Toni, I., Dijkerman, H. C., & de Lange, F. P. (2013). Shared Representations for Working Memory and Mental Imagery in Early Visual Cortex. *Current Biology*, 23(15), 1427–1431. https://doi.org/10.1016/j.cub.2013.05.065

Amir, N., Stafford, J., Freshman, M. S., & Foa, E. B. (1998). Relationship Between Trauma Narratives and Trauma Pathology. *Journal of Traumatic Stress*, 11(2), 385–392. https://doi.org/10.1023/A:1024415523495

Arnsten, A. F. T. (2009). Stress signalling pathways that impair prefrontal cortex structure and function. *Nature Reviews Neuroscience*, 10(6), 410–422. https://doi.org/10.1038/nrn2648

van Ast, V. A., Cornelisse, S., Meeter, M., Joëls, M., & Kindt, M. (2013). Time-Dependent Effects of Cortisol on the Contextualization of Emotional Memories. *Biological Psychiatry*, 74(11), 809–816. https://doi.org/10.1016/j.biopsych.2013.06.022

Audrain, S., & McAndrews, M. P. (2020). *Schemas provide a scaffold for neocortical integration at the cost of memory specificity over time*. bioRxiv. https://doi.org/10.1101/2020.10.11.335166

Backus, A. R., Bosch, S. E., Ekman, M., Grabovetsky, A. V., & Doeller, C. F. (2016). Mnemonic convergence in the human hippocampus. *Nature Communications*, 7(1), 11991. https://doi.org/10.1038/ncomms11991

Backus, A. R., Schoffelen, J.-M., Szebényi, S., Hanslmayr, S., & Doeller, C. F. (2016). Hippocampal-Prefrontal Theta Oscillations Support Memory Integration. *Current Biology*, 26(4), 450–457. https://doi.org/10.1016/j.cub.2015.12.048

Baddeley, A. D., & Andrade, J. (2000). Working memory and the vividness of imagery. *Journal of Experimental Psychology: General*, 129(1), 126–145. https://doi.org/10.1037/0096-3445.129.1.126

Banks, W. A. (2012). Brain Meets Body: The Blood-Brain Barrier as an Endocrine Interface. *Endocrinology*, 153(9), 4111–4119. https://doi.org/10.1210/en.2012-1435

Barbey, A. K., Koenigs, M., & Grafman, J. (2013). Dorsolateral prefrontal contributions to human working memory. *Cortex*, 49(5), 1195–1205. https://doi.org/10.1016/j.cortex.2012.05.022

Barry, D. N., Barnes, G. R., Clark, I. A., & Maguire, E. A. (2019). The Neural Dynamics of Novel Scene Imagery. *Journal of Neuroscience*, 39(22), 4375–4386. https://doi.org/10.1523/JNEUROSCI.2497-18.2019

Bartlett, F. (1932). *Remembering Cambridge, England*. Cambridge Univ. Press.

Becker, M., Sommer, T., & Cabeza, R. (2023). *Neural Mechanisms of Creative Problem Solving: From Representational Change to Memory Formation*. bioRxiv. https://doi.org/10.1101/2023.06.13.544774

Benoit, R. G., & Schacter, D. L. (2015). Specifying the core network supporting episodic simulation and episodic memory by activation likelihood estimation. *Neuropsychologia*, *75*, 450–457. https://doi.org/10.1016/j.neuropsychologia.2015.06.034

Ben-Yakov, A., & Dudai, Y. (2011). Constructing Realistic Engrams: Poststimulus Activity of Hippocampus and Dorsal Striatum Predicts Subsequent Episodic Memory. *Journal of Neuroscience*, *31*(24), 9032–9042. https://doi.org/10.1523/JNEUROSCI.0702-11.2011

Berntsen, D., Willert, M., & Rubin, D. C. (2003). Splintered memories or vivid landmarks? Qualities and organization of traumatic memories with and without PTSD. *Applied Cognitive Psychology*, *17*(6), 675–693. https://doi.org/10.1002/acp.894

Berres, S., & Erdfelder, E. (2021). The sleep benefit in episodic memory: An integrative review and a meta-analysis. *Psychological Bulletin*, *147*(12), 1309–1353. https://doi.org/10.1037/bul0000350

Berryhill, M. E., Picasso, L., Arnold, R., Drowos, D., & Olson, I. R. (2010). Similarities and differences between parietal and frontal patients in autobiographical and constructed experience tasks. *Neuropsychologia*, *48*(5), 1385–1393. https://doi.org/10.1016/j.neuropsychologia.2010.01.004

Bertsch, S., Pesta, B. J., Wiscott, R., & McDaniel, M. A. (2007). The generation effect: A meta-analytic review. *Memory & Cognition*, *35*(2), 201–210. https://doi.org/10.3758/BF03193441

Bieth, T., Ovando-Tellez, M., Lopez-Persem, A., Garcin, B., Hugueville, L., Lehongre, K., Levy, R., George, N., & Volle, E. (2021). *Time course of EEG power during creative problem-solving with insight or remote thinking*. bioRxiv. https://doi.org/10.1101/2021.11.26.470102

Bisby, J. A., Burgess, N., & Brewin, C. R. (2020). Reduced Memory Coherence for Negative Events and Its Relationship to Posttraumatic Stress Disorder. *Current Directions in Psychological Science*, *29*(3), 267–272. https://doi.org/10.1177/0963721420917691

Bonnici, H. M., Cheke, L. G., Green, D. A. E., FitzGerald, T. H. M. B., & Simons, J. S. (2018). Specifying a Causal Role for Angular Gyrus in Autobiographical Memory. *Journal of Neuroscience*, *38*(49), 10438–10443. https://doi.org/10.1523/JNEUROSCI.1239-18.2018

Bonnici, H. M., Richter, F. R., Yazar, Y., & Simons, J. S. (2016). Multimodal Feature Integration in the Angular Gyrus during Episodic and Semantic Retrieval. *Journal of Neuroscience*, *36*(20), 5462–5471. https://doi.org/10.1523/JNEUROSCI.4310-15.2016

Boorman, E. D., Sweigart, S. C., & Park, S. A. (2021). Cognitive maps and novel inferences: A flexibility hierarchy. *Current Opinion in Behavioral Sciences*, *38*, 141–149. https://doi.org/10.1016/j.cobeha.2021.02.017

Borders, A. A., Aly, M., Parks, C. M., & Yonelinas, A. P. (2017). The hippocampus is particularly important for building associations across stimulus domains. *Neuropsychologia*, *99*, 335–342. https://doi.org/10.1016/j.neuropsychologia.2017.03.032

Bosch, S. E., Jehee, J. F. M., Fernández, G., & Doeller, C. F. (2014). Reinstatement of Associative Memories in Early Visual Cortex Is Signaled by the Hippocampus. *Journal of Neuroscience*, 34(22), 7493–7500. https://doi.org/10.1523/JNEUROSCI.0805-14.2014

Botvinick, M. M., Cohen, J. D., & Carter, C. S. (2004). Conflict monitoring and anterior cingulate cortex: An update. *Trends in Cognitive Sciences*, 8(12), 539–546. https://doi.org/10.1016/j.tics.2004.10.003

Bower, G. H. (1970). Imagery as a relational organizer in associative learning. *Journal of Verbal Learning and Verbal Behavior*, 9(5), 529–533. https://doi.org/10.1016/S0022-5371(70)80096-2

Bower, G. H., & Clark, M. C. (1969). Narrative stories as mediators for serial learning. *Psychonomic Science*, 14(4), 181–182. https://doi.org/10.3758/BF03332778

Branzi, F. M., Pobric, G., Jung, J., & Lambon Ralph, M. A. (2021). The Left Angular Gyrus Is Causally Involved in Context-dependent Integration and Associative Encoding during Narrative Reading. *Journal of Cognitive Neuroscience*, 33(6), 1082–1095. https://doi.org/10.1162/jocn_a_01698

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

Brunec, I. K., Robin, J., Olsen, R. K., Moscovitch, M., & Barense, M. D. (2020). Integration and differentiation of hippocampal memory traces. *Neuroscience & Biobehavioral Reviews*, 118, 196–208. https://doi.org/10.1016/j.neubiorev.2020.07.024

Buckner, R. L., & Carroll, D. C. (2007). Self-projection and the brain. *Trends in Cognitive Sciences*, 11(2), 49–57. https://doi.org/10.1016/j.tics.2006.11.004

Bunzeck, N., & Düzel, E. (2006). Absolute Coding of Stimulus Novelty in the Human Substantia Nigra/VTA. *Neuron*, 51(3), 369–379. https://doi.org/10.1016/j.neuron.2006.06.021

van Buuren, M., Kroes, M. C. W., Wagner, I. C., Genzel, L., Morris, R. G. M., & Fernández, G. (2014). Initial Investigation of the Effects of an Experimentally Learned Schema on Spatial Associative Memory in Humans. *Journal of Neuroscience*, 34(50), 16662–16670. https://doi.org/10.1523/JNEUROSCI.2365-14.2014

Cavanagh, J. F., & Frank, M. J. (2014). Frontal theta as a mechanism for cognitive control. *Trends in Cognitive Sciences*, 18(8), 414–421. https://doi.org/10.1016/j.tics.2014.04.012

Chanales, A. J. H., Oza, A., Favila, S. E., & Kuhl, B. A. (2017). Overlap among Spatial Memories Triggers Repulsion of Hippocampal Representations. *Current Biology*, 27(15), 2307-2317.e5. https://doi.org/10.1016/j.cub.2017.06.057

Chang, C. H. C., Lazaridi, C., Yeshurun, Y., Norman, K. A., & Hasson, U. (2021). Relating the Past with the Present: Information Integration and Segregation during Ongoing Narrative Processing. *Journal of Cognitive Neuroscience*, 33(6), 1106–1128. https://doi.org/10.1162/jocn_a_01707

Clouter, A., Shapiro, K. L., & Hanslmayr, S. (2017). Theta Phase Synchronization Is the Glue that Binds Human Associative Memory. *Current Biology*, 27(20), 3143-3148.e6. https://doi.org/10.1016/j.cub.2017.09.001

Cohn-Sheehy, B. I., Delarazan, A. I., Crivelli-Decker, J. E., Reagh, Z. M., Mundada, N. S., Yonelinas, A. P., Zacks, J. M., & Ranganath, C. (2021). Narratives bridge the divide between distant events in episodic memory. *Memory & Cognition*. https://doi.org/10.3758/s13421-021-01178-x

Collin, S. H. P., Milivojevic, B., & Doeller, C. F. (2015). Memory hierarchies map onto the hippocampal long axis in humans. *Nature Neuroscience*, 18(11), 1562–1564. https://doi.org/10.1038/nn.4138

Collin, S. H. P., Milivojevic, B., & Doeller, C. F. (2017). Hippocampal hierarchical networks for space, time, and memory. *Current Opinion in Behavioral Sciences*, 17, 71–76. https://doi.org/10.1016/j.cobeha.2017.06.007

Coutanche, M. N., Gianessi, C. A., Chanales, A. J. H., Willison, K. W., & Thompson-Schill, S. L. (2013). The role of sleep in forming a memory representation of a two-dimensional space. *Hippocampus*, 23(12), 1189–1197. https://doi.org/10.1002/hipo.22157

Craik, F. I. M., & Lockhart, R. S. (1972). Levels of processing: A framework for memory research. *Journal of Verbal Learning and Verbal Behavior*, 11(6), 671–684. https://doi.org/10.1016/S0022-5371(72)80001-X

Dandolo, L. C., & Schwabe, L. (2016). Stress-induced cortisol hampers memory generalization. *Learning & Memory*, 23(12), 679–683. https://doi.org/10.1101/lm.042929.116

D'Argembeau, A., & van der Linden, M. (2004). Phenomenal characteristics associated with projecting oneself back into the past and forward into the future: Influence of valence and temporal distance. *Consciousness and Cognition*, 13(4), 844–858. https://doi.org/10.1016/j.concog.2004.07.007

de Kloet, E. R., Joëls, M., & Holsboer, F. (2005). Stress and the brain: From adaptation to disease. *Nature Reviews Neuroscience*, 6(6), 463–475. https://doi.org/10.1038/nrn1683

de Quervain, D., Schwabe, L., & Roozendaal, B. (2017). Stress, glucocorticoids and memory: Implications for treating fear-related disorders. *Nature Reviews Neuroscience*, 18(1), 7–19. https://doi.org/10.1038/nrn.2016.155

Delarazan, A. I., Ranganath, C., & Reagh, Z. M. (2023). Aging impacts memory for perceptual, but not narrative, event details. *Learning & Memory*, 30(2), 48–54. https://doi.org/10.1101/lm.053740.122

Deuker, L., Bellmund, J. L., Navarro Schröder, T., & Doeller, C. F. (2016). An event map of memory space in the hippocampus. *eLife*, 5, e16534. https://doi.org/10.7554/eLife.16534

Düzel, E., Penny, W. D., & Burgess, N. (2010). Brain oscillations and memory. *Current Opinion in Neurobiology*, 20(2), 143–149. https://doi.org/10.1016/j.conb.2010.01.004

Eichenbaum, H. (2004). Hippocampus: Cognitive Processes and Neural Representations that Underlie Declarative Memory. *Neuron*, 44(1), 109–120. https://doi.org/10.1016/j.neuron.2004.08.028

Eichenbaum, H., & Cohen, N. J. (2014). Can We Reconcile the Declarative Memory and Spatial Navigation Views on Hippocampal Function? *Neuron*, 83(4), 764–770. https://doi.org/10.1016/j.neuron.2014.07.032

Epstein, R., & Kanwisher, N. (1998). A cortical representation of the local visual environment. *Nature*, 392(6676), 598–601. https://doi.org/10.1038/33402

Ezzyat, Y., Inhoff, M. C., & Davachi, L. (2018). Differentiation of Human Medial Prefrontal Cortex Activity Underlies Long-Term Resistance to Forgetting in Memory. *Journal of Neuroscience*, 38(48), 10244–10254. https://doi.org/10.1523/JNEUROSCI.2290-17.2018

Faivre, N., Dubois, J., Schwartz, N., & Mudrik, L. (2019). Imaging object-scene relations processing in visible and invisible natural scenes. *Scientific Reports*, 9(1). https://doi.org/10.1038/s41598-019-38654-z

Faul, L., St. Jacques, P. L., DeRosa, J. T., Parikh, N., & De Brigard, F. (2020). Differential contribution of anterior and posterior midline regions during mental simulation of counterfactual and perspective shifts in autobiographical memories. *NeuroImage*, *215*, 116843. https://doi.org/10.1016/j.neuroimage.2020.116843

Favila, S. E., Chanales, A. J. H., & Kuhl, B. A. (2016). Experience-dependent hippocampal pattern differentiation prevents interference during subsequent learning. *Nature Communications*, 7(1). https://doi.org/10.1038/ncomms11066

Fell, J., Ludowig, E., Staresina, B. P., Wagner, T., Kranz, T., Elger, C. E., & Axmacher, N. (2011). Medial Temporal Theta/Alpha Power Enhancement Precedes Successful Memory Encoding: Evidence Based on Intracranial EEG. *Journal of Neuroscience*, 31(14), 5392–5397. https://doi.org/10.1523/JNEUROSCI.3668-10.2011

Fernandez, C., Jiang, J., Wang, S.-F., Choi, H. L., & Wagner, A. D. (2023). Representational integration and differentiation in the human hippocampus following goal-directed navigation. *eLife*, 12. https://doi.org/10.7554/eLife.80281

Gaesser, B., Spreng, R. N., McLelland, V. C., Addis, D. R., & Schacter, D. L. (2013). Imagining the future: Evidence for a hippocampal contribution to constructive processing. *Hippocampus*, 23(12), 1150–1161. https://doi.org/10.1002/hipo.22152

Goldfarb, E. V., Mendelevich, Y., & Phelps, E. A. (2017). Acute Stress Time-dependently Modulates Multiple Memory Systems. *Journal of Cognitive Neuroscience*, 29(11), 1877–1894. https://doi.org/10.1162/jocn_a_01167

Goldfarb, E. V., Tompary, A., Davachi, L., & Phelps, E. A. (2019). Acute stress throughout the memory cycle: Diverging effects on associative and item memory. *Journal of Experimental Psychology. General*, 148(1), 13–29. https://doi.org/10.1037/xge0000472

Grossman, E. D., & Blake, R. (2001). Brain activity evoked by inverted and imagined biological motion. *Vision Research*, 41(10), 1475–1482. https://doi.org/10.1016/S0042-6989(00)00317-5

Guez, J., Naveh-Benjamin, M., Yankovsky, Y., Cohen, J., Shiber, A., & Shalev, H. (2011). Traumatic stress is linked to a deficit in associative episodic memory. *Journal of Traumatic Stress*, 24(3), 260–267. https://doi.org/10.1002/jts.20635

Hagmann, P., Cammoun, L., Gigandet, X., Meuli, R., Honey, C. J., Wedeen, V. J., & Sporns, O. (2008). Mapping the Structural Core of Human Cerebral Cortex. *PLOS Biology*, 6(7). https://doi.org/10.1371/journal.pbio.0060159

Hannula, D. E., Libby, L. A., Yonelinas, A. P., & Ranganath, C. (2013). Medial temporal lobe contributions to cued retrieval of items and contexts. *Neuropsychologia*, 51(12), 2322–2332. https://doi.org/10.1016/j.neuropsychologia.2013.02.011

Hassabis, D., Kumaran, D., & Maguire, E. A. (2007a). Using Imagination to Understand the Neural Basis of Episodic Memory. *Journal of Neuroscience*, 27(52), 14365–14374. https://doi.org/10.1523/JNEUROSCI.4549-07.2007

Hassabis, D., Kumaran, D., Vann, S. D., & Maguire, E. A. (2007b). Patients with hippocampal amnesia cannot imagine new experiences. *Proceedings of the National Academy of Sciences*, 104(5), 1726–1731. https://doi.org/10.1073/pnas.0610561104

He, Q., Beveridge, E. H., Vargas, V., Salen, A., & Brown, T. I. (2023). Effects of Acute Stress on Rigid Learning, Flexible Learning, and Value-Based Decision-Making in Spatial Navigation. *Psychological Science*, 34(5), 552–567. https://doi.org/10.1177/09567976231155870

He, Q., Liu, J. L., Beveridge, E. H., Eschapasse, L., Vargas, V., & Brown, T. I. (2022). Episodic memory integration shapes value-based decision-making in spatial navigation. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 48(8), 1098–1109. https://doi.org/10.1037/xlm0001133

Hockley, W. E., & Christi, C. (1996). Tests of the differential encoding of item and associative information. *Memory & Cognition*, 24, 202–216.

Horner, A. J., Bisby, J. A., Bush, D., Lin, W.-J., & Burgess, N. (2015). Evidence for holistic episodic recollection via hippocampal pattern completion. *Nature Communications*, 6(1), 1–11. https://doi.org/10.1038/ncomms8462

Horner, A. J., & Burgess, N. (2014). Pattern Completion in Multielement Event Engrams. *Current Biology*, 24(9), 988–992. https://doi.org/10.1016/j.cub.2014.03.012

Horner, A. J., & Doeller, C. F. (2017). Plasticity of hippocampal memories in humans. *Current Opinion in Neurobiology*, 43, 102–109. https://doi.org/10.1016/j.conb.2017.02.004

Horner, A. J., Gadian, D. G., Fuentemilla, L., Jentschke, S., Vargha-Khadem, F., & Duzel, E. (2012). A Rapid, Hippocampus-Dependent, Item-Memory Signal that Initiates Context Memory in Humans. *Current Biology*, 22(24), 2369–2374. https://doi.org/10.1016/j.cub.2012.10.055

Hsieh, L.-T., Gruber, M. J., Jenkins, L. J., & Ranganath, C. (2014). Hippocampal Activity Patterns Carry Information about Objects in Temporal Context. *Neuron*, 81(5), 1165–1178. https://doi.org/10.1016/j.neuron.2014.01.015

Humphreys, G. F., Lambon Ralph, M. A., & Simons, J. S. (2021). A Unifying Account of Angular Gyrus Contributions to Episodic and Semantic Cognition. *Trends in Neurosciences*, 44(6), 452–463. https://doi.org/10.1016/j.tins.2021.01.006

Hupbach, A., Gomez, R., Hardt, O., & Nadel, L. (2007). Reconsolidation of episodic memories: A subtle reminder triggers integration of new information. *Learning & Memory*, 14(1–2), 47–53. https://doi.org/10.1101/lm.365707

Irish, M., Halena, S., Kamminga, J., Tu, S., Hornberger, M., & Hodges, J. R. (2015). Scene construction impairments in Alzheimer's disease – A unique role for the posterior cingulate cortex. *Cortex*, 73, 10–23. https://doi.org/10.1016/j.cortex.2015.08.004

Joëls, M., & Baram, T. Z. (2009). The neuro-symphony of stress. *Nature Reviews Neuroscience*, 10(6). https://doi.org/10.1038/nrn2632

Joëls, M., Fernandez, G., & Roozendaal, B. (2011). Stress and emotional memory: A matter of timing. *Trends in Cognitive Sciences*, 15(6), 280–288. https://doi.org/10.1016/j.tics.2011.04.004

Karpicke, J. D., & Blunt, J. R. (2011). Retrieval practice produces more learning than elaborative studying with concept mapping. *Science*, 331(6018), 772–775. https:// doi.org/10.1126/science.1199327

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

Kim, J. J., Lee, H. J., Han, J.-S., & Packard, M. G. (2001). Amygdala Is Critical for Stress-Induced Modulation of Hippocampal Long-Term Potentiation and Learning. *Journal of Neuroscience*, 21(14), 5222–5228. https://doi.org/10.1523/JNEUROSCI.21-14-05222.2001

Kirschbaum, C., Pirke, K.-M., & Hellhammer, D. H. (1993). The ‘Trier Social Stress Test’ – A Tool for Investigating Psychobiological Stress Responses in a Laboratory Setting. *Neuropsychobiology*, 28(1–2), 76–81. https://doi.org/10.1159/000119004

Kluen, L. M., Nixon, P., Agorastos, A., Wiedemann, K., & Schwabe, L. (2017). Impact of Stress and Glucocorticoids on Schema-Based Learning. *Neuropsychopharmacology*, 42(6), 1254–1261. https://doi.org/10.1038/npp.2016.256

Koolschijn, R. S., Emir, U. E., Pantelides, A. C., Nili, H., Behrens, T. E. J., & Barron, H. C. (2019). The Hippocampus and Neocortical Inhibitory Engrams Protect against Memory Interference. *Neuron*, *101*(3), 528-541. https://doi.org/10.1016/j.neuron.2018.11.042

Kriegeskorte, N., & Mur, M. (2012). Inverse MDS: Inferring Dissimilarity Structure from Multiple Item Arrangements. *Frontiers in Psychology*, 3, 1-13. https://doi.org/10.3389/fpsyg.2012.00245

Kriegeskorte, N., Mur, M., & Bandettini, P. A. (2008). Representational similarity analysis—Connecting the branches of systems neuroscience. *Frontiers in Systems Neuroscience*, 2. https://doi.org/ 10.3389/neuro.06.004.2008

Kringelbach, M. L. (2005). The human orbitofrontal cortex: Linking reward to hedonic experience. *Nature Reviews Neuroscience*, 6(9). https://doi.org/10.1038/nrn1747

Kumaran, D., Summerfield, J. J., Hassabis, D., & Maguire, E. A. (2009). Tracking the Emergence of Conceptual Knowledge during Human Decision Making. *Neuron*, 63(6), 889–901. https://doi.org/10.1016 /j.neuron.2009.07.030

Kwon, S., Richter, F. R., Siena, M. J., & Simons, J. S. (2022). Episodic Memory Precision and Reality Monitoring Following Stimulation of Angular Gyrus. *Journal of Cognitive Neuroscience*, 1–12. https://doi.org/ 10.1162/jocn_a_01814

van der Linden, M., Berkers, R. M. W. J., Morris, R. G. M., & Fernández, G. (2017). Angular Gyrus Involvement at Encoding and Retrieval Is Associated with Durable But Less Specific Memories. *Journal of Neuroscience*, 37(39), 9474–9485. https://doi.org/10.1523/JNEUROSCI.3603-16.2017

Liu, Y., Nour, M. M., Schuck, N. W., Behrens, T. E. J., & Dolan, R. J. (2022). Decoding cognition from spontaneous neural activity. *Nature Reviews Neuroscience*, 23(4). https://doi.org/10.1038/s41583-022-00570-z

Long, N. M., Öztekin, I., & Badre, D. (2010). Separable Prefrontal Cortex Contributions to Free Recall. *Journal of Neuroscience*, 30(33), 10967–10976. https://doi.org/10.1523/JNEUROSCI.2611-10.2010

Maguire, E. A., & Mullally, S. L. (2013). The hippocampus: A manifesto for change. *Journal of Experimental Psychology: General*, 142(4), 1180. https://doi.org/10.1037/a0033650

Maguire, E. A., Valentine, E. R., Wilding, J. M., & Kapur, N. (2003). Routes to remembering: The brains behind superior memory. *Nature Neuroscience*, 6(1). https://doi.org/10.1038/nn988

Marr, D. (1971). A theory of archicortical function. *Proc R Soc Lond B Biol Sci*, *262*, 23–81.

Mattfeld, A. T., & Stark, C. E. L. (2015). Functional contributions and interactions between the human hippocampus and subregions of the striatum during arbitrary associative learning and memory. *Hippocampus*, 25(8), 900–911. https://doi.org/10.1002/hipo.22411

Mayes, A. R., Holdstock, J. S., Isaac, C. l., Montaldi, D., Grigor, J., Gummer, A., Cariga, P., Downes, J. J., Tsivilis, D., Gaffan, D., Gong, Q., & Norman, K. A. (2004). Associative recognition in a patient with selective hippocampal lesions and relatively normal item recognition. *Hippocampus*, 14(6), 763–784. https://doi.org/10.1002/hipo.10211

McClelland, J. L., & Goddard, N. H. (1996). Considerations arising from a complementary learning systems perspective on hippocampus and neocortex. *Hippocampus*, 6(6), 654–665. https://doi.org/10.1002/(SICI)1098-1063(1996)6:6<654::AID-HIPO8>3.0.CO;2-G

McEwen, B. S., de Kloet, E. R., & Rostene, W. (1986). Adrenal steroid receptors and actions in the nervous system. *Physiological Reviews*, 66(4), 1121–1188. https://doi.org/10.1152/physrev.1986.66.4.1121

McKenzie, S., & Eichenbaum, H. (2011). Consolidation and Reconsolidation: Two Lives of Memories? *Neuron*, 71(2), 224–233. https://doi.org/10.1016/j.neuron.2011.06.037

McNaughton, B. L., & Nadel, L. (1990). Hebb-marr networks and the neurobiological representation of action in space. In: M. A. Gluck & D. E. Rumelhart (Eds), *Neuroscience and connectionist theory* (pp. 1–63). Hillsdale, NJ: Lawrence Erlbaum Associates.

Menon, V. (2023). 20 years of the default mode network: A review and synthesis. *Neuron*, 111(16), 2469–2487. https://doi.org/10.1016/j.neuron.2023.04.023

Meyer, T., Smeets, T., Giesbrecht, T., Quaedflieg, C. W. E. M., & Merckelbach, H. (2013). Acute stress differentially affects spatial configuration learning in high and low cortisol-responding healthy adults. *European Journal of Psychotraumatology*, 4(1). https://doi.org/10.3402/ejpt.v4i0.19854

Milivojevic, B., Vicente-Grabovetsky, A., & Doeller, C. F. (2015). Insight Reconfigures Hippocampal-Prefrontal Memories. *Current Biology*, 25(7), 821–830. https://doi.org/10.1016/j.cub.2015.01.033

Molitor, R. J., Sherrill, K. R., Morton, N. W., Miller, A. A., & Preston, A. R. (2021). Memory Reactivation during Learning Simultaneously Promotes Dentate Gyrus/CA $_{2,3}$ Pattern Differentiation and CA $_{1}$ Memory Integration. *The Journal of Neuroscience*, 41(4), 726–738. https://doi.org/10.1523/JNEUROSCI.0394-20.2020

Müller, N. C. J., Konrad, B. N., Kohn, N., Muñoz-López, M., Czisch, M., Fernández, G., & Dresler, M. (2018). Hippocampal–caudate nucleus interactions support exceptional memory performance. *Brain Structure and Function*, 223(3), 1379–1389. https://doi.org/10.1007/s00429-017-1556-2

Nadel, L., Hupbach, A., Gomez, R., & Newman-Smith, K. (2012). Memory formation, consolidation and transformation. *Neuroscience & Biobehavioral Reviews*, 36(7), 1640–1645. https://doi.org/10.1016/j.neubiorev.2012.03.001

Nakazawa, K., Quirk, M. C., Chitwood, R. A., Watanabe, M., Yeckel, M. F., Sun, L. D., Kato, A., Carr, C. A., Johnston, D., Wilson, M. A., & Tonegawa, S. (2002). Requirement for Hippocampal CA3 NMDA Receptors in Associative Memory Recall. *Science*, 297, 211-218. https://doi.org/10.1126/science.1071795

Naselaris, T., Prenger, R. J., Kay, K. N., Oliver, M., & Gallant, J. L. (2009). Bayesian Reconstruction of Natural Images from Human Brain Activity. *Neuron*, 63(6), 902–915. https://doi.org/10.1016/j.neuron.2009.09.006

Ngo, C. T., Michelmann, S., Olson, I. R., & Newcombe, N. S. (2021). Pattern separation and pattern completion: Behaviorally separable processes? *Memory & Cognition*, 49(1), 193–205. https://doi.org/10.3758/s13421-020-01072-y

Nicolás, B., Sala-Padró, J., Cucurell, D., Santurino, M., Falip, M., & Fuentemilla, L. (2021). Theta rhythm supports hippocampus-dependent integrative encoding in schematic/semantic memory networks. *NeuroImage*, 226, 117558. https://doi.org/10.1016/j.neuroimage.2020.117558

Nielson, D. M., Smith, T. A., Sreekumar, V., Dennis, S., & Sederberg, P. B. (2015). Human hippocampus represents space and time during retrieval of real-world memories. *Proceedings of the National Academy of Sciences*, 112(35), 11078–11083. https://doi.org/10.1073/pnas.1507104112

Oh, Y., Chesebrough, C., Erickson, B., Zhang, F., & Kounios, J. (2020). An insight-related neural reward signal. *NeuroImage*, 214, 116757. https://doi.org/10.1016/j.neuroimage.2020.116757

O'Keefe, J., & Nadel, L. (1979). Précis of O'Keefe & Nadel's The hippocampus as a cognitive map. *Behavioral and Brain Sciences*, 2(4), 487–494. https://doi.org/10.1017/S0140525X00063949

Pacheco Estefan, D., Zucca, R., Arsiwalla, X., Principe, A., Zhang, H., Rocamora, R., Axmacher, N., & Verschure, P. F. M. J. (2021). Volitional learning promotes theta phase coding in the human hippocampus. *Proceedings of the National Academy of Sciences*, 118(10). https://doi.org/10.1073/pnas.2021238118

Paret, C., & Hendler, T. (2020). Live from the "regulating brain": Harnessing the brain to change emotion. *Emotion*, 20(1), 126–131. https://doi.org/10.1037/emo0000674

Patel, P. D., Lopez, J. F., Lyons, D. M., Burke, S., Wallace, M., & Schatzberg, A. F. (2000). Glucocorticoid and mineralocorticoid receptor mRNA expression in squirrel monkey brain. *Journal of Psychiatric Research*, 34(6), 383–392. https://doi.org/10.1016/S0022-3956(00)00035-2

Pearson, J. (2019). The human imagination: The cognitive neuroscience of visual mental imagery. *Nature Reviews Neuroscience*, 20(10). https://doi.org/10.1038/s41583-019-0202-9

Pehrs, C., Zaki, J., Taruffi, L., Kuchinke, L., & Koelsch, S. (2018). Hippocampal-Temporopolar Connectivity Contributes to Episodic Simulation During Social Cognition. *Scientific Reports*, 8(1). https://doi.org/10.1038/s41598-018-24557-y

Petit, L., Ali, K. M., Rheault, F., Boré, A., Cremona, S., Corsini, F., De Benedictis, A., Descoteaux, M., & Sarubbo, S. (2023). The structural connectivity of the human angular gyrus as revealed by microdissection and diffusion tractography. *Brain Structure and Function*, 228(1), 103–120. https://doi.org/10.1007/s00429-022-02551-5

Pitman, R. K., Rasmusson, A. M., Koenen, K. C., Shin, L. M., Orr, S. P., Gilbertson, M. W., Milad, M. R., & Liberzon, I. (2012). Biological studies of post-traumatic stress disorder. *Nature Reviews Neuroscience*, 13(11). https://doi.org/10.1038/nrn3339

Pruessner, J. C., Dedovic, K., Khalili-Mahani, N., Engert, V., Pruessner, M., Buss, C., Renwick, R., Dagher, A., Meaney, M. J., & Lupien, S. (2008). Deactivation of the Limbic System During Acute Psychosocial Stress: Evidence from Positron Emission Tomography and Functional Magnetic Resonance Imaging Studies. *Biological Psychiatry*, 63(2), 234–240. https://doi.org/10.1016/j.biopsych.2007.04.041

Race, E., Keane, M. M., & Verfaellie, M. (2011). Medial Temporal Lobe Damage Causes Deficits in Episodic Memory and Episodic Future Thinking Not Attributable to Deficits in Narrative Construction. *Journal of Neuroscience*, 31(28), 10262–10269. https://doi.org/10.1523/JNEUROSCI.1145-11.2011

Ramanan, S., Alaeddin, S., Goldberg, Z., Strikwerda-Brown, C., Hodges, J. R., & Irish, M. (2018a). Exploring the contribution of visual imagery to scene construction – Evidence from Posterior Cortical Atrophy. *Cortex*, *106*, 261–274. https://doi.org/10.1016/j.cortex.2018.06.016

Ramanan, S., Piguet, O., & Irish, M. (2018b). Rethinking the Role of the Angular Gyrus in Remembering the Past and Imagining the Future: The Contextual Integration Model. *The Neuroscientist*, 24(4), 342–352. https://doi.org/10.1177/1073858417735514

Ranganath, C., Heller, A., Cohen, M. X., Brozinsky, C. J., & Rissman, J. (2005). Functional connectivity with the hippocampus during successful memory formation. *Hippocampus*, 15(8), 997–1005. https://doi.org/10.1002/hipo.20141

Raykov, P. P., Varga, D., & Bird, C. M. (2023). False memories for ending of events. *Journal of Experimental Psychology: General*. https://psycnet.apa.org/record/2024-03333-001

Reagh, Z. M., & Ranganath, C. (2023). Flexible reuse of cortico-hippocampal representations during encoding and recall of naturalistic events. *Nature Communications*, 14(1). https://doi.org/10.1038/s41467-023-36805-5

Reul, J. M. H. M., & de Kloet, E. R. D. (1985). Two Receptor Systems for Corticosterone in Rat Brain: Microdistribution and Differential Occupation. *Endocrinology*, 117(6), 2505–2511. https://doi.org/10.1210/endo-117-6-2505

Richmond, A. S., Cummings, R., & Klapp, M. (2008). Transfer of the Method of Loci, Pegword, and Keyword Mnemonics in the Eighth Grade Classroom. *Researcher*, *21*(2), 1-13

Ritchey, M., & Cooper, R. A. (2020). Deconstructing the Posterior Medial Episodic Network. *Trends in Cognitive Sciences*, 24(6), 451–465. https://doi.org/10.1016/j.tics.2020.03.006

Roediger III, H. L., & Karpicke, J. D. (2006). The power of testing memory: Basic research and implications for educational practice. *Perspectives on Psychological Science*, 1(3), 181–210. https://doi.org/10.1111/j.1745-6916.2006.0001

Rolls, E. T. (2016). Pattern Completion and Pattern Separation Mechanisms in the Hippocampus. In P. A. Jackson, A. A. Chiba, R. F. Berman, & M. E. Ragozzino (Eds.), *The Neurobiological Basis of Memory*: A

System, Attribute, and Process Analysis (pp. 77–113). Springer International Publishing. https://doi.org/10.1007/978-3-319-15759-7_4

Rolls, E. T., & Kesner, R. P. (2006). A computational theory of hippocampal function, and empirical tests of the theory. *Progress in Neurobiology*, 79(1), 1–48. https://doi.org/10.1016/j.pneurobio.2006.04.005

Rowland, C. A. (2014). The effect of testing versus restudy on retention: A meta-analytic review of the testing effect. *Psychological Bulletin*, 140(6), 1432–1463. https://doi.org/10.1037/a0037559

Sandi, C., & Pinelo-Nava, M. T. (2007). Stress and Memory: Behavioral Effects and Neurobiological Mechanisms. *Neural Plasticity*, 2007(078970). https://doi.org/10.1155/2007/78970

Schacter, D. L., Addis, D. R., & Buckner, R. L. (2007). Remembering the past to imagine the future: The prospective brain. *Nature Reviews Neuroscience*, 8(9). https://doi.org/10.1038/nrn2213

Schlichting, M. L., Mumford, J. A., & Preston, A. R. (2015). Learning-related representational changes reveal dissociable integration and separation signatures in the hippocampus and prefrontal cortex. *Nature Communications*, 6(1), 8151. https://doi.org/10.1038/ncomms9151

Schlichting, M. L., & Preston, A. R. (2015). Memory integration: Neural mechanisms and implications for behavior. *Current Opinion in Behavioral Sciences*, 1, 1–8. https://doi.org/10.1016/j.cobeha.2014.07.005

Schlichting, M. L., & Preston, A. R. (2017). The Hippocampus and Memory Integration: Building Knowledge to Navigate Future Decisions. In D. E. Hannula & M. C. Duff (Eds.), *The Hippocampus from Cells to Systems: Structure, Connectivity, and Functional Contributions to Memory and Flexible Cognition* (pp. 405–437). Springer International Publishing. https://doi.org/10.1007/978-3-319-50406-3_13

Schönauer, M., Alizadeh, S., Jamalabadi, H., Abraham, A., Pawlizki, A., & Gais, S. (2017). Decoding material-specific memory reprocessing during sleep in humans. *Nature Communications*, 8(1). https://doi.org/10.1038/ncomms15404

Schonhaut, D. R., Ramayya, A. G., Solomon, E. A., Herweg, N. A., Fried, I., & Kahana, M. J. (2020). *Single neurons throughout human memory regions phase-lock to hippocampal theta*. bioRxiv. https://doi.org/10.1101/2020.06.30.180174

Schwabe, L. (2017). Memory under stress: From single systems to network changes. *European Journal of Neuroscience*, 45(4), 478–489. https://doi.org/10.1111/ejn.13478

Schwabe, L., Hermans, E. J., Joëls, M., & Roozendaal, B. (2022). Mechanisms of memory under stress. *Neuron*, 110, 1450-1467. https://doi.org/10.1016/j.neuron.2022.02.020

Schwabe, L., Joëls, M., Roozendaal, B., Wolf, O. T., & Oitzl, M. S. (2012). Stress effects on memory: An update and integration. *Neuroscience & Biobehavioral Reviews*, 36(7), 1740–1749. https://doi.org/10.1016/j.neubiorev.2011.07.002

Schwabe, L., Oitzl, M. S., Philippsen, C., Richter, S., Bohringer, A., Wippich, W., & Schachinger, H. (2007). Stress modulates the use of spatial versus stimulus-response learning strategies in humans. *Learning & Memory*, 14(1–2), 109–116. https://doi.org/10.1101/lm.435807

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 & Psychiatry*, 20(1), 11–21. https://doi.org/10.1136/jnnp.20.1.11

Seghier, M. L. (2013). The Angular Gyrus: Multiple Functions and Multiple Subdivisions. *The Neuroscientist*, 19(1), 43–61. https://doi.org/10.1177/1073858412440596

Sep, M. S. C., van Ast, V. A., Gorter, R., Joëls, M., & Geuze, E. (2019). Time-dependent effects of psychosocial stress on the contextualization of neutral memories. *Psychoneuroendocrinology*, *108*, 140–149. https://doi.org/10.1016/j.psyneuen.2019.06.021

Shields, G. S., McCullough, A. M., Ritchey, M., Ranganath, C., & Yonelinas, A. P. (2019). Stress and the medial temporal lobe at rest: Functional connectivity is associated with both memory and cortisol. *Psychoneuroendocrinology*, 106, 138–146. https://doi.org/10.1016/j.psyneuen.2019.04.001

Shields, G. S., Sazma, M. A., McCullough, A. M., & Yonelinas, A. P. (2017). The effects of acute stress on episodic memory: A meta-analysis and integrative review. *Psychological Bulletin*, 143(6), 636. https://doi.org/10.1037/bul0000100

Shohamy, D., & Daw, N. D. (2015). Integrating memories to guide decisions. *Current Opinion in Behavioral Sciences*, 5, 85–90. https://doi.org/10.1016/j.cobeha.2015.08.010

Shohamy, D., & Wagner, A. D. (2008). Integrating Memories in the Human Brain: Hippocampal-Midbrain Encoding of Overlapping Events. *Neuron*, 60(2), 378–389. https://doi.org/10.1016/j.neuron.2008.09.023

Shulman, G. L., Corbetta, M., Buckner, R. L., Fiez, J. A., Miezin, F. M., Raichle, M. E., & Petersen, S. E. (1997). Common Blood Flow Changes across Visual Tasks: I. Increases in Subcortical Structures and Cerebellum but Not in Nonvisual Cortex. *Journal of Cognitive Neuroscience*, 9(5), 624–647. https://doi.org/10.1162/jocn.1997.9.5.624

Simon-Kutscher, K., Wanke, N., Hiller, C., & Schwabe, L. (2019). Fear Without Context: Acute Stress Modulates the Balance of Cue-Dependent and Contextual Fear Learning. *Psychological Science*, 30(8), 1123–1135. https://doi.org/10.1177/0956797619852027

Spalding, K. N., Schlichting, M. L., Zeithamova, D., Preston, A. R., Tranel, D., Duff, M. C., & Warren, D. E. (2018). Ventromedial Prefrontal Cortex Is Necessary for Normal Associative Inference and Memory Integration. *Journal of Neuroscience*, 38(15), 3767–3775. https://doi.org/10.1523/JNEUROSCI.2501-17.2018

Squire, L. R., van der Horst, A. S., McDuff, S. G. R., Frascino, J. C., Hopkins, R. O., & Mauldin, K. N. (2010). Role of the hippocampus in remembering the past and imagining the future. *Proceedings of the National Academy of Sciences*, 107(44), 19044–19048. https://doi.org/10.1073/pnas.1014391107

Squire, L. R., & Zola-Morgan, S. (1991). The Medial Temporal Lobe Memory System. *Science*, 253(5026), 1380–1386. https://doi.org/10.1126/science.1896849

Staresina, B. P., Henson, R. N. A., Kriegeskorte, N., & Alink, A. (2012). Episodic Reinstatement in the Medial Temporal Lobe. *Journal of Neuroscience*, 32(50), 18150–18156. https://doi.org/10.1523/JNEUROSCI.4156-12.2012

Summerfield, J. J., Hassabis, D., & Maguire, E. A. (2010). Differential engagement of brain regions within a 'core' network during scene construction. *Neuropsychologia*, 48(5), 1501–1509. https://doi.org/10.1016/j.neuropsychologia.2010.01.022

Szpunar, K. K., & McDermott, K. B. (2008). Episodic future thought and its relation to remembering: Evidence from ratings of subjective experience. *Consciousness and Cognition*, 17(1), 330–334. https://doi.org/10.1016/j.concog.2007.04.006

Thakral, P. P., Madore, K. P., Kalinowski, S. E., & Schacter, D. L. (2020). Modulation of hippocampal brain networks produces changes in episodic simulation and divergent thinking. *Proceedings of the National Academy of Sciences*, 117(23), 12729–12740. https://doi.org/10.1073/pnas.2003535117

Thakral, P. P., Madore, K. P., & Schacter, D. L. (2017). A Role for the Left Angular Gyrus in Episodic Simulation and Memory. *Journal of Neuroscience*, 37(34), 8142–8149. https://doi.org/10.1523/JNEUROSCI.1319-17.2017

Thakral, P. P., Madore, K. P., & Schacter, D. L. (2019). Content-specific phenomenological similarity between episodic memory and simulation. *Memory*, 27(3), 417–422. https://doi.org/10.1080/09658211.2018.1510528

Tibon, R., Fuhrmann, D., Levy, D. A., Simons, J. S., & Henson, R. N. (2019). Multimodal Integration and Vividness in the Angular Gyrus During Episodic Encoding and Retrieval. *Journal of Neuroscience*, 39(22), 4365–4374. https://doi.org/10.1523/JNEUROSCI.2102-18.2018

Tik, M., Sladky, R., Luft, C. D. B., Willinger, D., Hoffmann, A., Banissy, M. J., Bhattacharya, J., & Windischberger, C. (2018). Ultra-high-field fMRI insights on insight: Neural correlates of the Aha!-moment. *Human Brain Mapping*, 39(8), 3241–3252. https://doi.org/10.1002/hbm.24073

Tomasi, D., & Volkow, N. D. (2011). Functional connectivity hubs in the human brain. *NeuroImage*, 57(3), 908–917. https://doi.org/10.1016/j.neuroimage.2011.05.024

Tulving, E. (1983). *Elements of Episodic Memory*. Oxford University Press.

Uddin, L. Q., Supekar, K., Amin, H., Rykhlevskaia, E., Nguyen, D. A., Greicius, M. D., & Menon, V. (2010). Dissociable Connectivity within Human Angular Gyrus and Intraparietal Sulcus: Evidence from Functional and Structural Connectivity. *Cerebral Cortex*, 20(11), 2636–2646. https://doi.org/10.1093/cercor/bhq011

Vogel, S., Fernández, G., Joëls, M., & Schwabe, L. (2016). Cognitive Adaptation under Stress: A Case for the Mineralocorticoid Receptor. *Trends in Cognitive Sciences*, 20(3), 192–203. https://doi.org/10.1016/j.tics.2015.12.003

Vogel, S., Kluen, L. M., Fernández, G., & Schwabe, L. (2018a). Stress affects the neural ensemble for integrating new information and prior knowledge. *NeuroImage*, 173, 176–187. https://doi.org/10.1016/j.neuroimage.2018.02.038

Vogel, S., Kluen, L. M., Fernández, G., & Schwabe, L. (2018b). Stress leads to aberrant hippocampal involvement when processing schema-related information. *Learning & Memory*, 25(1), 21–30. https://doi.org/10.1101/lm.046003.117

Wagner, A. D. (1999). Working Memory Contributions to Human Learning and Remembering. *Neuron*, 22(1), 19–22. https://doi.org/10.1016/S0896-6273(00)80674-1

Wagner, I. C., Konrad, B. N., Schuster, P., Weisig, S., Repantis, D., Ohla, K., Kühn, S., Fernández, G., Steiger, A., Lamm, C., Czisch, M., & Dresler, M. (2021). Durable memories and efficient neural coding through mnemonic training using the method of loci. *Science Advances*, 7(10). https://doi.org/10.1126/sciadv.abc7606

Wagner, I. C., van Buuren, M., Kroes, M. C., Gutteling, T. P., van der Linden, M., Morris, R. G., & Fernández, G. (2015). Schematic memory components converge within angular gyrus during retrieval. *eLife*, 4. https://doi.org/10.7554/eLife.09668

Wammes, J., Norman, K. A., & Turk-Browne, N. (2022). Increasing stimulus similarity drives nonmonotonic representational change in hippocampus. *eLife*, 11. https://doi.org/10.7554/eLife.68344

Wang, D., Clouter, A., Chen, Q., Shapiro, K. L., & Hanslmayr, S. (2018). Single-Trial Phase Entrainment of Theta Oscillations in Sensory Regions Predicts Human Associative Memory Performance. *Journal of Neuroscience*, 38(28), 6299–6309. https://doi.org/10.1523/JNEUROSCI.0349-18.2018

Wang, J. X., Rogers, L. M., Gross, E. Z., Ryals, A. J., Dokucu, M. E., Brandstatt, K. L., Hermiller, M. S., & Voss, J. L. (2014). Targeted enhancement of cortical-hippocampal brain networks and associative memory. *Science*, 345(6200), 1054–1057. https://doi.org/10.1126/science.1252900

Wang, Q., Bui, V.-K., & Song, Q. (2015). Narrative organisation at encoding facilitated children’s long-term episodic memory. *Memory*, 23(4), 602–611. https://doi.org/10.1080/09658211.2014.914229

Wanjia, G., Favila, S. E., Kim, G., Molitor, R. J., & Kuhl, B. A. (2021). Abrupt hippocampal remapping signals resolution of memory interference. *Nature Communications*, 12(1). https://doi.org/10.1038/s41467-021-25126-0

Weber, F. D., Wang, J.-Y., Born, J., & Inostroza, M. (2014). Sleep benefits in parallel implicit and explicit measures of episodic memory. *Learning & Memory*, 21(4), 190–198. https://doi.org/10.1101/lm.033530.113

Wirz, L., Bogdanov, M., & Schwabe, L. (2018). Habits under stress: Mechanistic insights across different types of learning. *Current Opinion in Behavioral Sciences*, 20, 9–16. https://doi.org/10.1016/j.cobeha.2017.08.009

Wirz, L., Reuter, M., Wacker, J., Felten, A., & Schwabe, L. (2017). A Haplotype Associated with Enhanced Mineralocorticoid Receptor Expression Facilitates the Stress-Induced Shift from “Cognitive” to “Habit” Learning. *eNeuro*, 4(6). https://doi.org/10.1523/ENEURO.0359-17.2017

Yarkoni, T., Poldrack, R. A., Nichols, T. E., Van Essen, D. C., & Wager, T. D. (2011). Large-scale automated synthesis of human functional neuroimaging data. *Nature Methods*, 8(8). https://doi.org/10.1038/nmeth.1635

Yassa, M. A., & Stark, C. E. L. (2011). Pattern separation in the hippocampus. *Trends in Neurosciences*, 34(10), 515–525. https://doi.org/10.1016/j.tins.2011.06.006

Yesavage, J. A., & Rose, T. L. (1984). Semantic elaboration and the method of loci: A new trip for older learners. *Experimental Aging Research*, 10(3), 155–159. https://doi.org/10.1080/03610738408258560

Zeidman, P., & Maguire, E. A. (2016). Anterior hippocampus: The anatomy of perception, imagination and episodic memory. *Nature Reviews Neuroscience*, 17(3), 173-182. https://doi.org/10.1038/nrn.2015.24

Zeidman, P., Mullally, S. L., & Maguire, E. A. (2015). Constructing, Perceiving, and Maintaining Scenes: Hippocampal Activity and Connectivity. *Cerebral Cortex*, 25(10), 3836–3855. https://doi.org/10.1093/cercor/bhu266

Zeithamova, D., Dominick, A. L., & Preston, A. R. (2012). Hippocampal and Ventral Medial Prefrontal Activation during Retrieval-Mediated Learning Supports Novel Inference. *Neuron*, 75(1), 168–179. https://doi.org/10.1016/j.neuron.2012.05.010

Zou, F., Wanjia, G., Allen, E. J., Wu, Y., Charest, I., Naselaris, T., Kay, K., Kuhl, B. A., Hutchinson, J. B., & DuBrow, S. (2023). Re-expression of CA1 and entorhinal activity patterns preserves temporal context memory at long timescales. *Nature Communications*, 14(1). https://doi.org/10.1038/s41467-023-40100-8

Appendix A: Study 1

Grob, A.-M., Milivojevic, B., Alink, A., Doeller, C. F., & Schwabe, L. (2023). Stress disrupts insight-driven mnemonic reconfiguration in the medial temporal lobe. *NeuroImage*, 265, 119804. https://doi.org/10.1016/j.neuroimage.2022.119804

NeuroImage 265 (2023) 119804

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Stress disrupts insight-driven mnemonic reconfiguration in the medial temporal lobe

Anna-Maria Grob[a], Branka Milivojevic[b], Arjen Alink[c,g], Christian F. Doeller[d,e,f], Lars Schwabe[a,*]

[a] *Department of Cognitive Psychology, Institute of Psychology, Universität Hamburg, Von-Melle-Park 5, Hamburg 20146, Germany*
[b] *Donders Institute for Brain, Cognition and Behaviour, Radboud University, Nijmegen 6525 AJ, the Netherlands*
[c] *Department of General Psychology, Institute of Psychology, Universität Hamburg, Hamburg 20146, Germany*
[d] *Max-Planck-Institute for Human Cognitive and Brain Sciences, Leipzig 04103, Germany*
[e] *Kavli Institute for Systems Neuroscience, Centre for Neural Computation, The Egil and Pauline Braathen and Fred Kavli Centre for Cortical Microcircuits, Jebsen Centre for Alzheimer's Disease, Norwegian University of Science and Technology, Trondheim 7491, Norway*
[f] *Wilhelm Wundt Institute of Psychology, Leipzig University, Leipzig 04109, Germany*
[g] *Institute of Systems Neuroscience, University Medical Center Hamburg-Eppendorf, Hamburg, 20246, Germany*

ARTICLE INFO

Keywords:
Episodic memory
Mnemonic integration
Anterior hippocampus
Insight
PTSD

ABSTRACT

Memories are not stored in isolation. Insight into the relationship of initially unrelated events may trigger a flexible reconfiguration of the mnemonic representation of these events. Such representational changes allow the integration of events into coherent episodes and help to build up-to-date-models of the world around us. This process is, however, frequently impaired in stress-related mental disorders resulting in symptoms such as fragmented memories in PTSD. Here, we combined a real life-like narrative-insight task, in which participants learned how initially separate events are linked, with fMRI-based representational similarity analysis to test if and how acute stress interferes with the insight-driven reconfiguration of memories. Our results showed that stress reduced the activity of medial temporal and prefrontal areas when participants gained insight into the link between events. Moreover, stress abolished the insight-related increase in representational dissimilarity for linked events in the anterior part of the hippocampus as well as its association with measures of subsequent memory that we observed in non-stressed controls. However, memory performance, as assessed in a forced-choice recognition test, was even enhanced in the stress group. Our findings suggest that acute stress impedes the neural integration of events into coherent episodes but promotes long-term memory for these integrated narratives and may thus have implications for understanding memory distortions in stress-related mental disorders.

1. Introduction

When watching a movie, we often experience a *plot twist*, a moment when we realize how earlier, seemingly unrelated scenes are connected. As we gain insight into the relationship between initially unrelated events, we integrate formerly separate memory representations into coherent episodes (Schlichting and Preston, 2017). Inferring which events to integrate and which to keep separate is a fundamental mechanism of memory and requires an intricate interplay of pattern completion and separation processes (Horner and Burgess, 2014; Marr, 1971; Nakazawa et al., 2002a; Norman and O'Reilly, 2003; Rolls and Kesner, 2006). Given its prominent role in both pattern completion and separation processes, it is not surprising that the medial temporal lobe, including the hippocampus, has been identified as a key region for mnemonic integration (Brunec et al., 2020; Collin et al., 2015; Horner et al., 2015; Huffman and Stark, 2014; Marr, 1971; Schapiro et al., 2017; Schlichting et al., 2015). The hippocampus, however, appears not to be functionally homogeneous and previous studies suggested a functional hierarchy along the hippocampal long axis: anterior portions were more related to memory integration, whereas posterior areas were more associated with memory separation, resulting in memory representations with different granularity (Brunec et al., 2020; Collin et al., 2017; Collin et al., 2015; Eichenbaum, 2004; Milivojevic et al., 2015; Morton et al., 2017; Schlichting et al., 2015). Accumulating evidence shows that mnemonic integration processes are altered in stress-related disorders, such as post-traumatic-stress disorder (PTSD), resulting in fragmented memories (Amir et al., 1998; Berntsen et al., 2003). In light of these clinical implications, the key question arises as to which factors modulate the capacity to integrate events into coherent episodes.

Acute stress is known to have a major impact on learning and memory (Joëls et al., 2011; Sandi and Pinelo-Nava, 2007; Schwabe et al.,

---

[*] Corresponding author.
E-mail address: Lars.Schwabe@uni-hamburg.de (L. Schwabe).

https://doi.org/10.1016/j.neuroimage.2022.119804.
Received 26 August 2022; Received in revised form 5 December 2022; Accepted 7 December 2022
Available online 9 December 2022.
1053-8119/© 2022 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license
(http://creativecommons.org/licenses/by-nc-nd/4.0/)

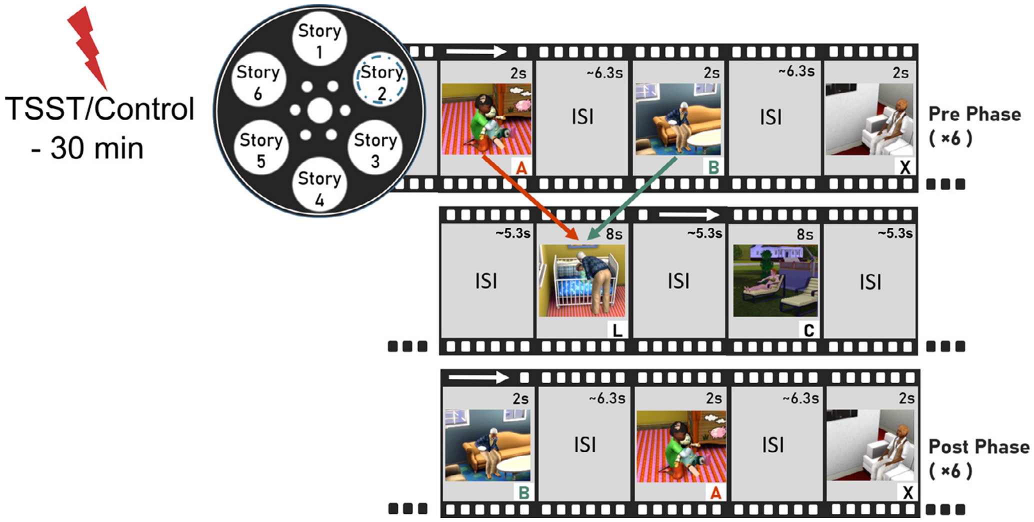


Fig. 1. Narrative-insight task (NIT). The videos (A, B, and X) from each of six story lines could either be integrated (events A and B) into narratives during the linking phase or not (A and X) and were each repeated six times. Between the different phases there was a short break to collect saliva samples.

2012a; Schwabe et al., 2022; Shields et al., 2017). These stress effects are mediated by the action of stress mediators, such as glucocorticoids (mainly cortisol in humans), on prefrontal and medial temporal areas. Converging lines of evidence from cellular to neuroimaging studies show that stress and glucocorticoids may have differential effects on hippocampal neuroplasticity and functioning, depending, for instance, on the timing of the stressor (Diamond et al., 2007; Joëls et al., 2011; Kim and Diamond, 2002). Stress unrelated to learning is generally thought to reduce hippocampal activity and hippocampus-dependent memory processes (Kim and Diamond, 2002; Lupien and Lepage, 2001; Schwabe and Wolf, 2012; Vogel et al., 2018). Beyond the well-known effects of stress and glucocorticoids on hippocampal memory formation and retrieval (de Quervain et al., 1998; Joëls et al., 2011; Schwabe et al., 2012b), stress may bias the engagement of multiple, anatomically and functionally distinct memory systems from ‘relational’ hippocampus-dependent memory towards rather habit-like forms of memory that depend, for example, on the dorsal striatum (Goodman et al., 2012; Schwabe, 2017; Vogel et al., 2016). Thus, in contrast to hippocampus-dependent memory, dorsal striatum dependent stimulus-stimulus memory is often enhanced after stress (Kim et al., 2001; Schwabe et al., 2007; VanElzakker et al., 2011). The reduced medial temporal lobe involvement after stress might translate into a reduced capacity to integrate separate events into a coherent episode, thus contributing to the mnemonic integration deficit in stress-related disorders. However, whether and how stress may affect this process of dynamic memory integration remains unknown.

In this study, we tested the hypothesis that acute stress interferes with integration processes during insight-driven reconfiguration of memory representations. To this end, we combined fMRI, neuroendocrinology, and representational similarity analysis with a life-like narrative-insight task (Milivojevic et al., 2015; Fig. 1). One week after encoding, we performed a comprehensive behavioral analysis of correctness, detailedness as well as memory representation. The delayed memory test included a standard free recall, a multidimensional arrangement task, and a forced-choice recognition test, and thus provided insights into which memory processes were altered by stress. Because the anterior part of the hippocampus appears to be particularly relevant for mnemonic integration (Collin et al., 2015; Schlichting et al., 2015), we predicted a change in the neural representation of linked events specifically in the anterior part of the hippocampus from pre- to post-insight. As task-unrelated stress is thought to interfere with hippocampal functioning, we hypothesized that acute stress would impair this insight-driven mnemonic reconfiguration in the anterior hippocampus.

2. Methods

2.1. Participants

Fifty-nine right-handed, healthy individuals (30 males, 29 females, age: M = 24.66 years, SD = 4.06 years) with normal or corrected-to-normal vision volunteered to participate in this study. Participants were screened with a standardized interview for exclusion criteria, which encompassed a history of neurological and psychiatric disorders, medication intake and drug abuse, cardiovascular-, thyroid- or kidney-related diseases, body-mass index below 19 and over 26 kg/m^2, any signs for COVID-19 infection or exposure, as well as any contraindications for MRI scanning. We tested only women who did not use hormonal contraceptives and who were not currently menstruating at the first day of the experiment, since these factors are known to influence their endocrine stress response (Kudielka and Kirschbaum, 2005). Two hours prior to the experiment participants were asked to refrain from physical exercise, caffeine and alcohol intake as well as fatty meals. All participants provided informed consent before participation and received a monetary compensation (50€) at the end of the experiment. Procedures were approved by the local ethical review committee (Faculty of Psychology and Human Movement Science, Universität Hamburg, Hamburg, Germany, AZ: 2017_143 Schwabe) and adhered to the Declaration of Helsinki. The sample size is based on an a priori calculation using G*Power, indicating that a sample size of $N = 60$ is sufficient to detect a medium-sized group × link effect ($f = .30$) with a power of .80.

We implemented a mixed-design including the within-subject factors link (linked vs. non-linked events) and session (pre- vs. post-link) and the between-subjects factor group (stress/control). Participants were pseudo-randomly assigned to one of the two groups to balance male and female participants per group. The stress group included 30 participants (15 females) and the control group consisted of 29 participants (14 females).

2.2. Procedure

Testing was conducted on two days, one week apart. All experiments took place in the afternoon or early evening (between 12 and 6 p.m.) to account for the diurnal rhythm of the stress hormone cortisol. Before starting the first day of the experiment, participants completed questionnaires assessing trait-anxiety (STAI-T; Laux et al., 1981), depressive symptoms (BDI; Hautzinger et al., 2006), chronic stress (TICS; Schulz and Schlotz, 1999), personality dimensions (BFI-

2; Danner et al., 2016), and chronotypical morningness and eveningness (MEQ; Adan and Almirall, 1991). After verification of eligibility for MRI measurements by a radiologist, participants gave informed consent and completed a state-anxiety questionnaire (STAI-S; Laux et al., 1981) and sleep quality questionnaire (PSQI; Buysse et al., 1989). Thereafter, they performed a training run and a baseline measurement of a working memory task (N-back; Kirchner, 1958) to control for effects due to stress-related impairments in working memory. Next, they completed a training session of the modified narrative-insight task (NIT; Milivojevic et al., 2015), a life-like video-based task that probes the integration of initially distinct events into coherent episodes. Participants then underwent the stress induction or control manipulation and completed the second N-back task and three runs of the modified narrative-insight task in the MRI scanner. One week later, to assess episodic memory integration, participants performed a free recall, a forced-choice recognition test and a multidimensional arena task (MAT; Kriegeskorte and Mur, 2012).

2.2.1. Day 1: Stress manipulation and manipulation check

In order to experimentally manipulate acute stress before the narrative-insight task, which assesses mnemonic integration, participants underwent either the Trier Social Stress Test (TSST; Kirschbaum et al., 1993) or a control manipulation. During the TSST, participants were requested to give a 5-min free speech, after a 3-min preparation period, about their qualification for a job tailored to their interests. Following this, participants had to perform a 5-min mental arithmetic task (counting backwards from 2043 in steps of 17). Both tasks were performed in front of a panel (one man and one woman), dressed in white lab coats. The panel was introduced as experts in behavioral analysis and was instructed to act in a rather cold, non-reinforcing manner, non-responding to questions of the participant. In addition, participants were video-taped during the TSST. In the control condition, participants engaged in two tasks of the same duration. The first task included a free speech about a topic of their choice (e.g. the last book they read). In the second task, participants counted forward (in steps of 15). Importantly, there was no panel present and no video was recorded.

To assess the effectiveness of the stress manipulation, subjective mood ratings, blood pressure, pulse and saliva samples were taken at several time points throughout the experiment. Mood changes were measured via a German mood scale (MDBF; Steyer et al., 1997). MDBF measures were obtained before and after the stress manipulation as well as after participants were removed from the MRI scanner (i.e., -5, +20, +110 min relative to treatment onset). Blood pressure and pulse (arm cuff: Omron Healthcare Europe BV) were measured before, during, and after the stress manipulation as well as after participants were removed from the scanner (i.e., -5, +8, +20, +110 min relative to treatment onset). Saliva samples were collected before and after the experimental treatment, twice in the MRI scanner and after participants were removed from the MRI scanner (i.e., -5, +20, +60, +80, +110 min relative to treatment onset) using Salivette collection devices (Sarstedt, Germany). Saliva samples were stored at -18°C and after completion of data collection, salivary cortisol levels were analyzed using a luminescence assay (IBL, International, Hamburg, Germany).

2.2.2. Day 1: Working memory control task

To control for potential stress effects on working memory, two measurements of working memory performance were obtained before and after the TSST and control manipulation, respectively. The second assessment of working memory took place approximately 20 min after stress induction, before the narrative-insight task began. Working memory was assessed with an N-back task (Kirchner, 1958). In this task, participants were presented with single-digit numbers from 0 to 9 and were asked whether the number on the screen (“target”) was the same number as the number presented n-trials before (“cue”). Working memory load was manipulated by using two complexity levels: 3-and 4-back trials. In addition to these two load levels, participants performed a control task (0-back), in which they had to indicate whether the current number was a zero. Responses were given either by pressing the left button (“no”) or by pressing the right button (“yes”), if the target number was different or identical to the cue, respectively. The selected response was highlighted. In total, participants were presented with six pseudo-randomized blocks consisting of two blocks from each level (0, 3 and 4 back). All blocks consisted of 20 numbers in random order. Numbers were presented for 500 ms and separated by a delay of 1.5 s. The blocks were separated by 5 s outside the scanner on the baseline assessment and by 13 s inside the scanner on the second assessment. Prior to each block, participants were informed of the type of the upcoming cognitive task (0-, 3-, or 4-back).

2.2.3. Day 1: Narrative-insight task

Approximately 30 min after treatment onset, when cortisol levels were expected to peak (Kirschbaum et al., 1993; Vogel and Schwabe, 2016), participants completed a modified version of the narrative-insight task (NIT; Milivojevic et al., 2015), while functional images were collected in the MRI scanner. In this task, participants were presented with life-like videos from the computer game *The Sims 3* that belonged to multiple different story lines. In total, participants saw 6 different story lines. The videos from each story line could either be integrated (events A and B) into narratives or not (A and X; see Fig. 1). Unbeknownst to the participant, each narrative had 2 possible versions to control for nonspecific stimulus effects and visual similarity. The 2 narrative versions comprised an identical event A, but different events B and linking event (L). Control event X from one version served as event B in the other version. Therefore, all participants saw the same events A, B, and X but 32 participants linked events A and X, while 27 participants linked events A and B.

Each story was presented in three phases: pre-insight phase, linking phase, and post-insight phase (Fig. 1). In the *pre-insight phase*, participants were presented with events A, B, and X for 2 s each, separated by inter-stimulus intervals of 1, 4 or 11 s (ISIs; ~5.3 s on average). Each video was presented six times in a pseudorandom order, such that each video was shown before the next round of presentations began and the same video was not presented on two consecutive trials. After the pre-insight phase, participants had to indicate on a scale from not at all (1) to very much (4) how much they thought the events belonged together. In the subsequent *linking phase*, participants viewed the linking video event (L) intertwined with a control video event (C), each presented for 8s and repeated six times (ISIs of 1, 4 or 11 s; ~5.3 s on average). The linking video (L) showed the main characters from videos A and B interacting with each other, whereas the control video (C) showed only an unknown character engaged in an unrelated activity (e.g. a man walking his dog). After the linking phase, participants completed several ratings regarding the understanding of the link and adherence to instructions on a scale ranging from not at all (1) to very much (4). In the final *post-insight phase*, participants again saw events A, B and X presented for 2 s each, repeated six times and separated by inter-stimulus intervals of 1, 4 or 11 s (ISIs; ~5.3 s on average). This phase was mainly used to assess changes in the neural representation of the events A and B, after learning that they were linked. After the post-phase, participants had to indicate again how much they thought that the events belonged together on a scale from not at all (1) to very much (4). Although the process of linking events is thought to occur in the linking phase, the successful linking of the events A and B is operationalized by the ratings of belonging after the linking phase compared to before the linking phase. Events in the post-insight phase were also presented in a pseudo-random order to reduce potential sequence effects. Participants received visual feedback when they entered an answer by highlighting the selected response. In addition to presenting A, B, and X events in the pre- and post-insight-phases, we also presented target events to which participants responded by pressing a button with the index finger of their right hand. These target events accounted for 11% of trials of the pre- and post-insight phases and consisted of a 2 s animated video of a girl on a pink scooter. These target trials were recorded to ensure that participants remained attentive throughout the experiment.

2.2.4. Day 2: Free recall

To measure the detailedness of memory one week after encoding, participants were instructed to recall the events presented on day 1 in as much detail as possible. During free recall, they were voice recorded for a maximum of 15 min. To assess the level of detailedness of the integrated episodes, audio recordings from free recall were scored according to how many details of the different video events (A, B, X, L, and C) were remembered from day one. The rating scheme was such, that it allowed for separate coding of details remembered for the A, B, and X events as well as for the events from the linking phase (L and C). The raters were instructed to assign details only to events where it was clear that they belonged exclusively to that event, so that there was no confusion of details between different events. Two raters rated the first half of the data and the other two raters rated the second half. All raters were blinded with regard to experimental conditions. To assess inter-rater reliability, all raters rated the first 5 participants and on average these ratings correlated highly with each other (*mean correlation* = .83, *SD* = .06). To obtain a better estimate of inter-subjectivity, the ratings were averaged. The details for the different event types (A, B, and X) were summed across stories to give an overall rating of event detail.

2.2.5. Day 2: Multidimensional arena task

To assess the representational structure of episodic memory, participants were asked to arrange representative images of the video events (A, B and X) of each story according to their relatedness on a two-dimensional circular arena in a multidimensional arena (MA) task (Kriegeskorte and Mur, 2012; Fig. S1). They were asked to bring the pictures that had been linked (A and B) one week earlier closer together than the pictures that had not been linked (A and X, B and X) by dragging and dropping them with the computer mouse within a white circular arena on the computer screen. All trials were self-paced and could be ended by the participant by pressing “Done”. On the first trial, participants had to arrange all images by similarity and were instructed to do so carefully. Subsequent trials consisted of subsets of the first trial selected based on an adaptive procedure aimed at minimizing uncertainty and better approximating the high-dimensional perceptual representational space. This procedure is based on an algorithm optimized to provide optimal evidence for the dissimilarity estimates (Kriegeskorte and Mur, 2012). Distances in this MA task were computed by initially computing the squared on-screen distance (Euclidian distance) between all items in the first trial to produce a roughly estimated representative dissimilarity matrix (RDM) and by iteratively updating this RDM by the weighted average of scaled trial estimates. This MA task took 10 min to complete.

2.2.6. Day 2: Forced-choice recognition test

In addition to the free recall test, we administered a forced-choice recognition test. In this test, participants completed a matching task in a forced-choice format. They were presented with an image of event A at the top of the computer screen and had to indicate whether the image of B or X in the bottom half of the screen belonged to A. Participants were presented with these forced-choice options for each of the stories they had seen a week before. After indicating for a story which event belonged to event A, they had to rate how confident they were in their answer. Confidence was rated on a scale from not at all (1) to very sure (4). This was repeated for each of the six stories. Participants were presented with the forced-choice question and the confidence rating for 5.5s each, separated by inter-stimulus intervals of 1, 4 or 11 sec (ISIs; ~5.3 s on average). Participants received visual feedback when they entered a rating question by highlighting the selected response. The forced-choice recognition test lasted about 2 to 3 min.

2.3. Analysis

2.3.1. Behavioral and physiological data analysis

Mood ratings were analyzed by means of a mixed 2 × 2 ANOVA with the between-subjects factor group (stress/control) and the within-subject factor time (-5/+20/+110 min relative to treatment onset). Blood pressure and pulse were analyzed using a mixed 2 × 2 ANOVA with the between-subjects factor group and the within-subject factor time (-5/+3/+20/+110 min relative to treatment onset). Finally, salivary cortisol levels were analyzed by means of a mixed 2 × 2 ANOVA with the between-subjects factor group and the within-subject factor time (-5/+20/+60/+80/+110 min relative to treatment onset).

To assess the degree of insight-dependent mental reorganization, the ratings for the event duplets of interest (AB and AX) from the pre- and post-insight-phase were entered into a mixed 2 × 2 × 2 ANOVA with the between-subjects factor group and the within-subject factors time (pre/post) and link (link/non-link). To evaluate the long-term representation of the integrated events, performance in the forced-choice recognition test was assessed by computing the proportion of correct answers. These performance measures (in %) were then entered into a Welch two-sample t-test with the between-subjects factor group. In order to check for confidence in the forced-choice recognition test, confidence ratings were averaged over the six stories and entered into a Welch two-sample t-test with the between-subjects factor group (Fig. S2). To analyze the representational structure of memory, Euclidian dissimilarity estimates from the multidimensional arena task were extracted for linked (AB) and for non-linked events (AX), averaged over stories, and, thereafter, entered into a mixed 2 × 2 ANOVA with the between-subjects factor group and the within-subject factor link (link/non-link). Details from free recall were entered into a mixed 2 × 2 ANOVA with the between-subjects factor group and the within-subject factor link (link/non-link).

All analyses were performed in R version 4.0.4 (https://www.r-project.org/). In case of violated sphericity, as indicated by Mauchly’s test, Greenhouse-Geisser corrected degrees of freedom and *p*-values are reported. Before analyses data were checked for outliers. Outliers were defined as mean +/- 2.5 SD. For the analysis of the narrative-insight task (NIT), four outliers were identified and excluded (two from the stress group and two from the control group). For the analysis of the forced-choice recognition test, one outlier was identified and excluded (stress group). For the analysis of the multidimensional arena task, two outliers were identified and excluded (one from the stress group and one from the control group). For the free recall analysis, three outliers were identified and excluded (two from the stress group and one from the control group). For the representational similarity analysis (RSA) of the anterior hippocampus, four outliers were identified and excluded (two in the stress group and two in the control group). For the additional RSA of the posterior hippocampus, one outlier was identified and excluded (stress group).

Imaging data were acquired on a 3T Siemens PRISMA scanner (Siemens, Germany) using a 64-channel head coil. Data was collected on three functional runs, separated by short breaks in which saliva samples were collected. We used a custom 3D echo-planar imaging (EPI) pulse sequence acquiring interleaved slices with the following parameters: TR = 2000 ms; TE = 30 ms; flip angle = 60°; volume resolution = 2 mm^3; slices = 62; approx. 530 volumes per run; field of view (FoV) = 224 mm; acceleration factor PE = 2. Additionally, a structural T1-weighted image was acquired using a MPRAGE-grappa sequence with the following parameters: TR = 2500 ms; TE = 2.06 ms; flip angle = 9°; voxel resolution = 0.8 mm^3; slices = 256; field of view (FoV) = 244 mm; 3D acceleration factor = 1 at the end of the MRI session.

2.3.2. fMRI data preprocessing

Preprocessing and analysis of the fMRI data were performed using custom scripts based on MATLAB (The Mathworks, Inc, Natick, US) and SPM 12 (Wellcome Trust Centre for Neuroimaging, London, UK). To allow for magnetic field (T1) equilibration, the first three functional scans were discarded. First, functional images were spatially realigned and slice-time corrected. Thereafter, functional images were co-registered to the structural image by co-registering the structural image to the mean EPI. To check for differences in motion between the groups, we ran a control analysis and found that there were no group differences on these movement parameters (all $p_{corr} > .120$). Moreover, we controlled for individual head movement by including the motion regressors in our generalized linear model (GLM). For the multivariate analysis (see below), the images were not preprocessed further. For the univariate analysis (see below), the functional images were normalized to the MNI template and subsequently smoothed using a 6 mm^3 full-width at half maximum (FWHM) Gaussian kernel.

Results of the neural analyses were considered significant at a family-wise error (FWE) corrected threshold of $p < .050$. To test our hypotheses, we performed, in addition to more explorative whole-brain analyses, ROI analyses with a-priori defined ROIs using small-volume correction (SVC; $p < .050$, FWE corrected) with an initial threshold of $p < .001$ uncorrected. Based on previous findings in the mnemonic integration and stress literature (Milivojevic et al., 2015; Schlichting et al., 2015; Schwabe et al., 2012a; Wirz et al., 2018), we focused on the following ROIs: amygdala, hippocampus, parahippocampal cortex, and orbitofrontal cortex. The hippocampus was split into posterior and anterior sub-regions, as these have been found to be differentially implicated in mnemonic integration and separation processes (Collin et al., 2015; Dandolo and Schwabe, 2018; Robin and Moscovitch, 2017). We used hippocampal masks built by dividing a hippocampal mask into three parts with approximately equal lengths along the long axis, using the WFU pick-atlas: pHC from $Y = -40$ to -30, mHC from $Y = -29$ to -19, and aHC from $Y = -18$ to -4 (Collin et al., 2015; Dandolo and Schwabe, 2018). With the exception of the hippocampal sub-regions all other anatomical masks were derived from the Harvard-Oxford cortical and subcortical atlas using a probability threshold of 50%. We corrected for the number of ROIs in the specific analyses by applying Bonferroni correction (p_{corr}). The resulting estimates were extracted using the MarsBar Toolbox (Brett et al., 2002) to correlate the neural activity with behavioral outcomes.

2.3.3. Univariate fMRI analysis

For the univariate fMRI analysis, data from all three runs were concatenated to allow estimation of neural responses using all acquired data. The concatenated time series was analyzed using a generalized linear model (GLM) as implemented in SPM12. This model included one regressor per event type (A, B, and X) during each phase (pre- and post-link). Each of these six event regressors of interest modelled 36 trials (six different stories). Each model also included the following task nuisance regressors: regressors for the link video and control video in the link phase, and one regressor for the 24 target events (girl on the pink scooter). All task regressors and the nuisance task regressors of no interest were convolved with the canonical hemodynamic response function, producing a modelled time-course of neural activity. All analyses further contained six concatenated nuisance regressors to control for head movement as well as three run constants. A high-pass filter of 128 s was used to remove low-frequency drifts and serial correlations in the time series were accounted for using an autoregressive AR(1)-model. To analyze the neural basis of the change from pre- to post-insight we computed a contrast comparing post link events to pre link events ($AB_{post} > AB_{pre}$). These contrast images were analyzed on the group level using a two-sample t-test. To rule out that the differences found between this contrast are due to time, we also computed a contrast comparing post non-link events to pre non-link events ($X_{post} > X_{pre}$).

2.3.4. Univariate fMRI adaptation in linking phase

To measure insight-related changes during the linking phase, we set up another model contrasting link and control events. This model was adjusted for effects of lag between the presentation of link and control events due to fMRI adaptation. Functional images from all three runs were concatenated to allow for estimation of neural responses using a GLM. This model included single regressors for all event types (A, B, X, L, C) in each story separately. Essentially, to measure the insight-related response that is adjusted for fMRI adaptation processes, six parametric regressors were included that reflect the time between events during the linking phase. To assess the degree of fMRI adaptation, the regressors were defined as –log (time since last presentation of link [linking event to linking event] or control event [control event to control event]). These lags were calculated as the difference between the onsets of the events of interest (e.g. linking event to linking event or control event to control event) and could take on values of 18s, 21s, 24s, 28s, 31s, or 38s. We used log lags according to a previous paper using the same paradigm (Milivojevic et al., 2015) since other studies suggested that adaptation effects are not automatically linear at longer lags between events (Weiner et al., 2010; Zhou et al., 2018). Each model also included the following nuisance variables: one regressor for the 24 target events, six concatenated nuisance regressors to control for head movement as well as three run constants. All task regressors and the regressor for target events were convolved with the canonical hemodynamic response function, producing a modelled time-course of neural activity. A high-pass filter of 128 s was used to remove low-frequency drifts and serial correlations in the time series were accounted for using an autoregressive AR(1)-model. For each subject contrast images collapsed across the six stories were calculated (Link > Control) and were then taken to the second-level group analysis. On the second level, analyses were performed using two-sample t-tests.

2.3.5. Multivariate analysis

In order to assess changes in neural patterns induced by insight into the narrative structure of events, we conducted a Representational Similarity Analysis (RSA, Kriegeskorte et al., 2008) using the rsatoolbox (Nili et al., 2014). We focused on the hippocampal long axis, since its subcomponents have been differentially associated with memory integration as well as segregation – two processes that are critical to episodic memory integration (Brunec et al., 2018; Collin et al., 2017; Dandolo and Schwabe, 2018; Milivojevic et al., 2015; Robin and Moscovitch, 2017; Schlichting et al., 2015). On the first level, functional images from all three runs were concatenated to allow for estimation of neural responses using a GLM. Only un-normalized and un-smoothed images entered the GLM. This model included single regressors for each of the event types and each phase (A_{pre}, B_{pre}, X_{pre}, L, C, A_{post}, B_{post}, X_{post}) in each of the 6 story lines separately. Thus, each event-regressor modeled 6 trials. Each model also included the following additional nuisance regressors: one regressor for the 24 target events, six concatenated nuisance regressors to control for head movement as well as three run constants. All task regressors and the regressor for target events were convolved with the canonical hemodynamic response function, producing a modelled time-course of neural activity. Voxel-wise beta estimates resulting from the regressors of interest (A_{pre}, B_{pre}, X_{pre}, A_{post}, B_{post}, X_{post}) were further transformed into t-statistics to account for noise induced unreliability (Walther et al., 2016). In a second analysis step, we back-transformed the ROIs from MNI space to subject-space for each participant individually. The computation of Representational Dissimilarity Matrices (RDMs) for each ROI and each subject was, thus, performed in native space of each participant. The resulting t-images from the regressors of interest were used to create vectors of activity pattern for each event, separately for each ROI. These activity patterns were used to calculate the dissimilarity between two trials by correlation distances (1-r, Pearson's rank order correlation). Thereafter, the dissimilarities for each combination were entered into a 36×36 Representational Dissimilarity Matrix (RDM). The dissimilarities for linked (AB_{pre}, AB_{post}) and non-linked events (AX_{pre}, AX_{post}) pre- and post-insight were extracted for each story and averaged over stories for each participant. These averaged dissimilarities were then entered into a mixed $2 \times 2 \times 2$ ANOVA in R version 4.0.4 (https://www.r-project.org/) with the between-subjects factor group (stress vs. control) and the within-subject factors time (pre

Table 1
Subjective mood ratings.

	Stress			Control		
	-5	+20	+110	-5	+20	+110
MDBF	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)
Positive mood	33.40 (4.77)	27.57^{***} (6.61)	31.40^{*} (5.59)	32.89 (5.34)	33.75 (5.27)	34.21 (4.66)
Calmness	31.07 (5.90)	26.10^{**} (6.53)	31.53 (5.66)	30.14 (5.86)	31.21 (5.95)	33.71 (3.65)
Wakefulness	29.67 (5.47)	28.67 (5.60)	**24.07** (6.82)	31.00 (5.48)	30.89 (5.80)	**25.04** (6.72)

The subjective mood scale MDBF with its sub-scales valence, arousal, and wakefulness was rated on a Likert scale ranging from *not at all* (1) to *very much* (5) five minutes prior to treatment onset, 20 min after treatment onset, and 110 min after treatment onset. Data represents means (SD); significant between-subjects effects are indicated by: $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$; significant within-subjects effects are highlighted in bold.

vs. post) and link (link vs. non-Link). We corrected for the number of ROIs by applying Bonferroni correction (p_{corr}).

2.3.6. Correlations with cortisol

To relate our behavioral, univariate and multivariate results to cortisol measures, we calculated the *area under the curve with respect to increase* (AUC_I), as this measure has been shown to operationalize a critical aspect of cortisol release: AUC_I is related to the sensitivity of the system and shows changes over time (Pruessner et al., 2003).

2.3.7. Regression analysis

To directly assess the relation between neural dissimilarity measures and perceived dissimilarity in the multidimensional arena task, we calculated a linear regression model and compared it to a quadratic regression model using the likelihood ratio test for the stress and control groups separately. To further probe whether potential group differences were significant, we built a basic model that did not include interaction effects with group and an interaction model that included these interaction effects. We determined which model better fit the data by testing these two models against each other implementing the likelihood ratio test. These analyses were performed in R version 4.0.4 (https://www.r-project.org/).

3. Results

3.1. Successful stress induction

Approximately 30 min before participants completed the narrative-insight task (Fig. 1) in the MRI scanner, they underwent either a psychosocial stressor (Trier Social Stress Test, TSST; $n = 30$) or a non-stressful control manipulation ($n = 29$). Significant changes in subjective mood as well as in blood pressure and salivary cortisol confirmed the successful stress induction by the TSST. Negative mood increased significantly in response to the TSST but not after the control manipulation (*time* × *group* interaction: $F_{(1.96,\ 111.78)} = 14.75$, $p < .001$, $\eta_G = .059$). Post-hoc t-tests showed significantly higher negative mood ratings in the stress group compared to the control group after the experimental manipulation ($t_{(55.23)} = 3.82$, $p < .001$, $d = .99$), as well as at the end of the experiment ($t_{(55.55)} = 2.09$, $p = .041$, $d = .54$), whereas there was no difference at baseline ($t_{(56.07)} = -.04$, $p = .682$, $d = -.11$). There was also a significant increase in restlessness in the stress condition but not in the control condition (*time* × *group* interaction: $F_{(1.99,\ 113.63)} = 9.81$, $p < .001$, $\eta_G = .045$). Post-hoc comparisons revealed significantly higher restlessness ratings after the experimental manipulation in the stress group (vs. control; $t_{(56.81)} = 3.02$, $p = .004$, $d = .78$) and a similar trend at the end of the experiment (vs. control; $t_{(49.30)} = 1.78$, $p = .081$, $d = .46$), while groups did not differ at baseline ($t_{(56.99)} = -.63$, $p = .528$, $d = -.17$). Furthermore, there was an increase in tiredness across the experiment, irrespective of the experimental group ($F_{(1.50,\ 85.22)} = 56.03$, $p < .001$, $\eta_G = .172$; Table 1).

Systolic blood pressure increased significantly in stressed participants but not in the control group (*time* × *group* interaction: $F_{(2.41,\ 132.45)} = 22.66$, $p < .001$, $\eta_G = .057$; see Fig. 2). Post-hoc t-tests showed significantly higher systolic blood pressure in the stress group compared to the control group during the experimental manipulation ($t_{(52.32)} = -4.06$, $p < .001$, $d = 1.07$). There was no significant difference at the other time points of measurement (in minutes relative to treatment onset: -5 min (baseline): $t_{(56.90)} = -.02$, $p = .984$, $d = .01$; +20 min: $t_{(55.85)} = -1.49$, $p = .141$, $d = .39$; +110 min: $t_{(55.44)} = -.97$, $p = .339$, $d = .25$). Likewise, diastolic blood pressure increased in response to the TSST but not to the control manipulation (*time* × *group* interaction: $F_{(2.46,\ 135.44)} = 29.15$, $p < .001$, $\eta_G = .088$; see Fig. 2). Post-hoc t-tests indicated significantly higher diastolic blood pressure in the stress group compared to the control group during the experimental manipulation ($t_{(48.54)} = -4.70$, $p < .001$, $d = 1.23$; all other time points of measurement in minutes relative o treatment onset: -5 min (baseline): $t_{(56.99)} = 1.07$, $p = .291$, $d = -.28$; +20 min: $t_{(55.83)} = -1.17$, $p = .246$, $d = -.31$; +110 min: $t_{(56.84)} = .19$, $p = .848$, $d = -.06$). Furthermore, participants' pulse increased significantly in the stress but not the control group (*time* × *group* interaction: $F_{(2.17,\ 119.09)} = 13.19$, $p < .001$, $\eta_G = .049$; see Fig. 2). Post-hoc t-tests showed again significantly higher pulse in stressed participants compared to controls during the experimental manipulation ($t_{(45.56)} = -3.64$, $p < .001$, $d = .95$; all other time points of measurement in minutes relative to treatment onset: -5 min: $t_{(56.68)} = .10$, $p = .923$, $d = -.03$; +20 min: $t_{(55.98)} = -.66$, $p = .513$, $d = .17$; +110 min: $t_{(56.62)} = -.76$, $p = .452$, $d = .20$).

Finally, salivary cortisol increased significantly in stressed participants but not in controls (*time* × *group* interaction: $F_{(2.64,\ 150.54)} = 9.88$, $p < .001$, $\eta_G = .050$; see Fig. 2). While groups did not differ in baseline cortisol concentrations ($t_{(46.12)} = -.73$, $p = .470$, $d = .18$), stressed participants had significantly higher salivary cortisol concentrations compared to controls after the experimental manipulation, with peak levels at the start of the narrative-insight task ($t_{(35.34)} = -4.35$, $p < .001$, $d = 1.12$), which remained elevated throughout the task (+60 min: $t_{(55.84)} = -3.20$, $p = .002$, $d = .83$; +80 min: $t_{(54.88)} = -2.45$, $p = .018$, $d = .64$; end of the experiment: $t_{(56.98)} = -1.70$, $p = .096$, $d = .44$).

3.2. Superior memory for linked vs. non-linked events

In order to examine stress effects on mnemonic integration, we used a modified narrative-insight task (Fig. 1). In this task, participants first repeatedly watched three videos showing specific episodes (pre-insight phase). Thereafter, a new (linking) event (L) was presented that linked two of the previously seen events (A and B) but left the third event non-linked (control event X; linking phase). Finally, the now linked or non-linked events were presented again to examine insight-driven representational changes (post-insight phase; Fig. 4). In all of these phases, we included target stimuli to which participants should respond, thus controlling for their attention during the task. Participants responded to 94.92% ($SD = 14.04\%$) of the target presentations, without any differences between groups ($t_{(38.117)} = -.81$, $p = .423$, $d = -.21$), indicating that stress did not affect attention during the task.

In the narrative-insight task, all participants gained – as expected – insight into the relationship of the initially separate events, as

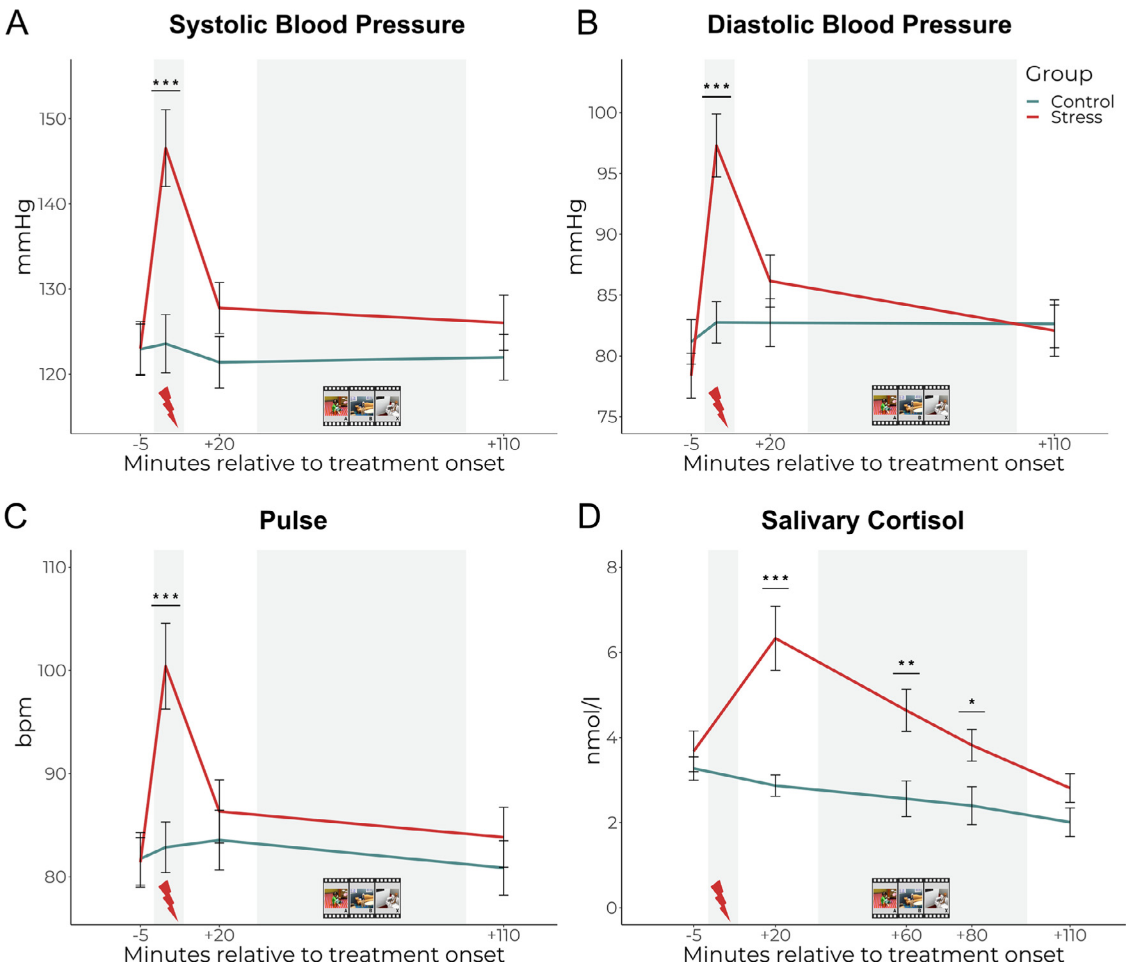


Fig. 2. Physiological stress responses. (A) Significant increases in systolic (mmHG) and (B) diastolic blood pressure (mmHG) and (C) pulse (bpm). (D) as well as in concentrations of salivary cortisol (nmol/l) confirmed the successful stress induction by the Trier Social Stress Test (TSST). Grey shades indicate periods of the TSST and control procedure, respectively, (red flash) and the narrative insight task (film roll). Data represents means (+/- SE); $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$.

reflected in significantly increased assessments of belonging after the linking phase for linked than non-linked events (*time* × *link* interaction: $F_{(1,\ 53)} = 745.21$, $p < .001$, $\eta_G = .626$, Fig. 4). Importantly, groups did not differ in these assessments of belonging, indicating that stress did not affect the basic insight into the relationship of events. In addition to the initial linking of events on day 1, which required connection and integration of the initially unrelated events, we also examined memory for this insight, one week later. The findings of day 1 were also reflected in the multidimensional arena task one week after encoding of the events. In this task, in which participants placed events that belong together closer to each other, participants performed very well (multidimensional arena task: *mean distance for linked events* = .02, *SD* = .01; *mean distance for non-linked events* = .05, *SD* = .02; Fig. 4). Again, there were no significant differences between stressed and control participants (multidimensional arena task: *link:* $F_{(1,\ 50)} = 89.35$, $p < .001$, $\eta_G = .324$), thus indicating that both groups remembered the basic association between events. In line with this view, those in both groups who rated the linked events as more closely related after insight also arranged the linked events more closely in the multidimensional arena task one week later ($r = -.49$, $t_{(50)} = -3.96$, $p < .001$). In addition, those in both groups who distinguished more between linked and non-linked events after insight (link - nonlink) arranged the linked events closer together in the multidimensional arena task ($r = -.30$, $t_{(46)} = -2.14$, $p = .038$). However, we found that the increase in cortisol over time (AUC_I) in the stress group was associated with closer distances for non-linked events (A and X), whereas this was not the case in the control group (stress: $r = -.43$, $t_{(23)} = -2.26$, $p = .034$; control: $r = .08$, $t_{(24)} = .41$, $p = .683$; stress vs. control: $z = -1.91$, $p = .028$; Fig. 3).

Strikingly, whether events were linked or not during encoding had a significant impact on the memory for these events, as assessed one week after encoding in the free recall test: participants recalled linked events (averaged A and B) in significantly more detail than non-linked events (X; *item:* $F_{(1,\ 53)} = 48.27$, $p < .001$, $\eta_G = .243$; Figs. 4D and S5). This enhanced memory for linked vs. non-linked events was observed in both groups (stress: $t_{(26)} = 4.79$, $p < .001$, $d_{repeated\ measures} = -.86$; control: $t_{(27)} = 5.05$, $p < .001$, $d_{repeated\ measures} = -.79$; *group* × *item:* $F_{(1,\ 53)} = .32$, $p = .575$, $\eta_G = .002$). Although the stress group seemed to recall more details on a descriptive level, there was no significant effect of group in the free recall test (*group:* $F_{(1,\ 53)} = 1.96$, $p = .167$, $\eta_G = .023$). We also found that those in both groups who recalled more details for linked events also arranged the linked events closer together in the multidimensional arena task ($r = -.32$, $t_{(49)} = -2.39$, $p = .021$).

In addition to the free recall test, we administered also a forced-choice recognition test, which involves lower memory search demands. Overall, performance in the forced-choice recognition test was very high ($M = 79.95\%$; $SD = 22.17\%$). Interestingly, stressed participants performed better than controls in this task (forced-choice recognition test: $t_{(46.79)} = -2.17$, $p = .035$, $d = -.58$). Moreover, we found a positive relationship between post-insight link ratings and delayed forced-choice recognition test performance across both groups ($r = .48$, $t_{(55)} = 4.01$, $p < .001$), suggesting that those participants who gained better insight into which events were linked on day 1 also performed better in the

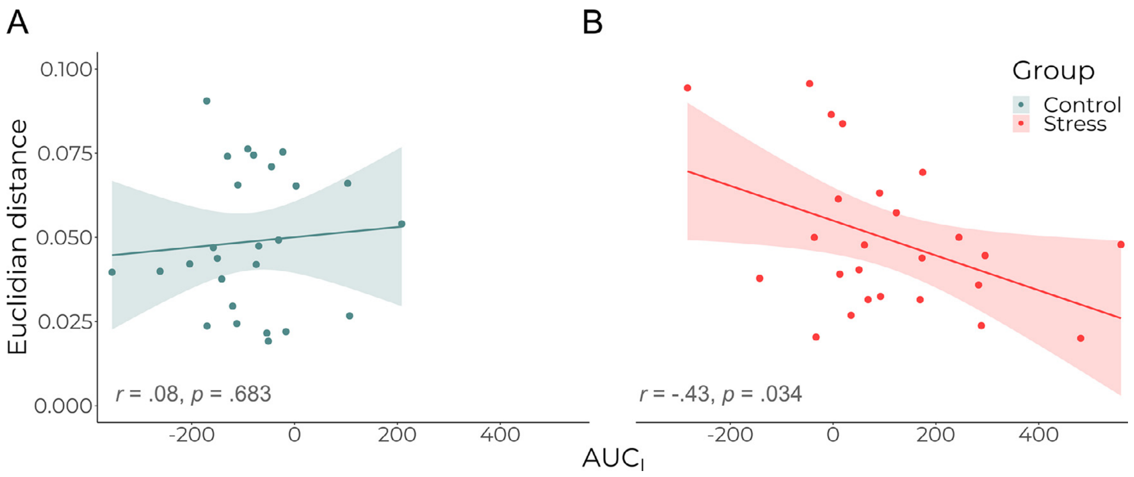


Fig. 3. Association between cortisol and multidimensional arena task. (A) Non-significant correlation between the increase in cortisol release over time (AUC_I) and Euclidian distance for non-linked events (A and X) in the multidimensional arena task in controls. (B) Significant correlation between the increase in cortisol release over time (AUC_I) and Euclidian distance for non-linked events (A and X) in the multidimensional arena task.

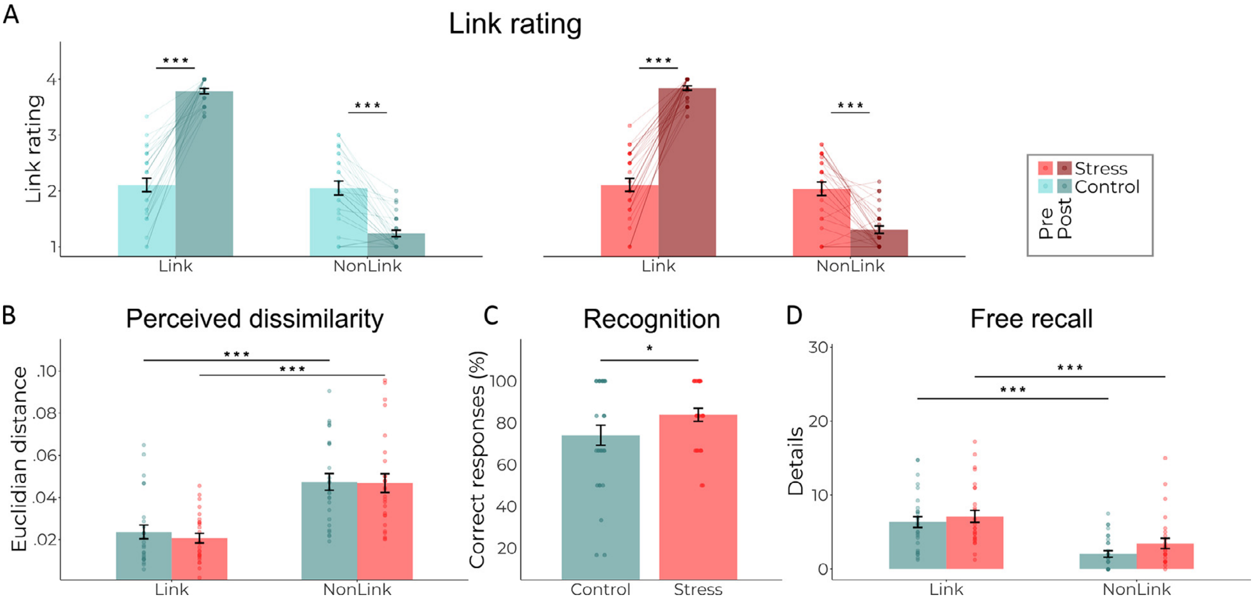


Fig. 4. Behavioral measures of insight and memory performance. (A) Significant increases in ratings of belonging for linked events and significant decreases in ratings of belonging for non-linked events in the control group (left) and in the stress group (right). (B) Significant differences between linked and non-linked events in the multidimensional arena task (Euclidian distance) for the control and stress group. (C) High performance (correct responses (%)) in the forced-choice recognition test for both groups. (D) Significant differences between linked (A and B) and non-linked events (X) events in the free recall for the stress and control group. Data represents means (+/- SE); * $p < .05$, $^{***}p < .001$.

forced-choice recognition test. We further obtained that those in both groups who differentiated better between linked and non-linked events post-insight also performed better in the forced-choice recognition test ($r = .32$, $t_{(51)} = 2.44$, $p = .018$). Participants in both groups who arranged the linked events closer together in the multidimensional arena task also performed better on the forced-choice recognition test ($r = -.59$, $t_{(49)} = -5.17$, $p < .001$).

3.3. Stress lowers medial temporal lobe activity during linking of events

To shed light on the insight-related neural processes underlying episodic integration, we measured BOLD-activity using fMRI during the linking phase, when participants learned about the relationship of the initially unrelated events A and B through a linking video (L), which was interleaved with an unrelated control video (C). We compared the neural activity of the linking event (L) with control events (C; Link > Control; Fig. 5) and accounted for fMRI adaptation processes by including parametric regressors that reflect the time between events during the linking phase. We used log lags since previous studies suggested that adaptation effects are not automatically linear at longer lags between events (Weiner et al., 2010; Zhou et al., 2018). This analysis revealed that stress (vs. control) lowered linking-related activity in the left hippocampus (SVC peak level: $x = -28$, $y = -10$, $z = -20$; $t_{(1,57)} = 4.49$, p_{corr}(FWE) = .012, $k = 23$) extending into the left amygdala (SVC peak level: $x = -26$, $y = -8$, $z = -20$; $t_{(1,57)} = 4.25$, p_{corr}(FWE) = .012, $k = 13$). In an exploratory analysis, we found a correlation suggesting that participants in the stress group with higher amygdala activity during linking also recalled more details for non-linked events ($r = .37$, $t(26) = 2.05$, $p = .051$). As this correlation did not reach statistical significance, this association should be interpreted with caution though.

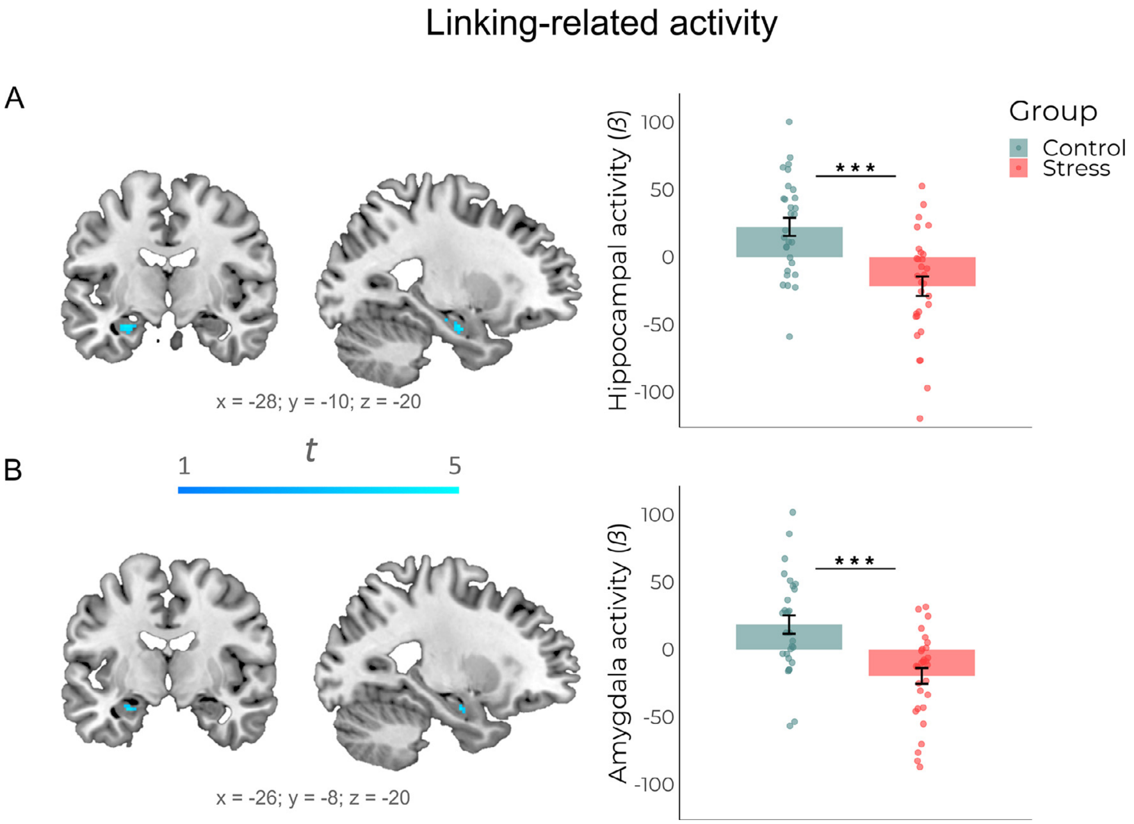


Fig. 5. Neural activity during linking phase (stress vs control group). (A) Significant decreases in stressed participants (vs. controls; Link > Control) in left hippocampus (SVC peak level: $x = -28$, $y = -10$, $z = -20$). Only masked ROI is displayed. Coronal and sagittal sections are shown, superimposed on a T1-template image. Depicted next to this is the peak voxel activity of the left hippocampus (HC) for stressed participants and controls during linking. Data represents means (+/- SE); $^{***}p < .001$. (B) Significant decreases in stressed participants (vs. controls; Link > Control) extended into the left amygdala (SVC peak level: $x = -26$, $y = -8$, $z = -20$). Only masked ROI is displayed. Coronal and sagittal sections are shown, superimposed on a T1-template image. Depicted next to this is the peak voxel activity of the left amygdala (AMY) for stressed participants and controls during linking. Data represents means (+/- SE); $^{***}p < .001$ and left amygdala when accounted for fMRI adaptation processes.

3.4. *Stress hinders insight-related increase in medial temporal lobe activity*

To assess neural changes associated with insight induced during the linking phase, we compared BOLD-activity changes for events that were linked (A and B) from the pre- with the post-insight-phase ($AB_{post} > AB_{pre}$). Our initial whole-brain analysis revealed a decrease in neural activity from pre- to post-insight in stressed participants (vs. controls) in the right putamen (whole-brain cluster-level: $x = 18$, $y = 14$, $z = -8$; $t_{(1,57)} = 4.95$, p_{corr}(FWE) = .005, $k = 215$; Fig. S4 in supplementary material). Focusing on our regions of interest, we found decreases from pre- to post-insight in neural activity in stressed participants (vs. controls) in the right orbitofrontal cortex (OFC: SVC peak level: $x = 34$, $y = 28$, $z = -8$; $t_{(1,57)} = 4.25$, p_{corr}(FWE) = .036, $k = 4$; Fig. 6), and in the bilateral parahippocampal cortices (left PHC: SVC peak level: $x = -24$, $y = 0$, $z = -30$; $t_{(1,57)} = 4.30$, p_{corr}(FWE) = .012, $k = 22$; Fig. 6; right PHC: SVC peak level: $x = 20$, $y = -16$, $z = -28$; $t_{(1,57)} = 4.67$, p_{corr}(FWE) = .004, $k = 19$). We performed an exploratory analysis to relate this result to the behavioral level and found that across both groups, those who had a greater increase from pre to post insight for linked events in the right parahippocampus tended to remember fewer details for the non-linked event ($r = -.26$, t(54) = -1.96, $p = .055$); yet this results needs to be interpreted with caution as the correlation did not reach statistical significance. To rule out that these differences for linked events were only due to the passage of time, we also compared activity changes for non-linked events from the pre- with the post-insight-phase and found no differences between the groups (left OFC: SVC peak level: $x = -16$, $y = 22$, $z = -24$; $t_{(1,57)} = 3.68$, p_{corr}(FWE) = .120, $k = 3$; left PHC: SVC peak level: $x = -26$, $y = -2$, $z = -32$; $t_{(1,57)} = 3.45$, p_{corr}(FWE) = .133, $k = 1$), thus suggesting that the above activity changes were specific to the insight into the link between initially unrelated events. Interestingly, we found that the change in the right orbitofrontal cortex from pre- to post-insight was negatively associated with the cortisol increase (AUC_I) over both groups ($r = -.37$, $t_{(55)} = -3.00$, $p = .004$).

3.5. *Stress disrupts insight-related change in event representations*

Finally, to examine the representational change induced by insight into the relationship of initially unrelated events, we compared multivariate voxel patterns pre- and post-insight by performing a ROI-based representational similarity analysis (RSA). We focused primarily on the longitudinal long axis of the hippocampus, since hippocampal sub-regions have been differentially implicated in integration and segregation of events in general (Cohn-Sheehy et al., 2021b; Dandolo and Schwabe, 2018; Lohnas et al., 2018; Schlichting et al., 2015) and mnemonic integration across initially unrelated events in particular (Collin et al., 2015; Milivojevic et al., 2015). In this analysis, representational dissimilarity matrices (RDMs) were computed for the anterior and the posterior portion of the hippocampal long axis. Thereafter, we extracted the neural dissimilarities averaged over stories for linked and non-linked events pre- and post-insight from these RDMs for each participant (Fig. 7B) and compared them in a mixed analysis of variance. Interestingly, we found that while control partici-

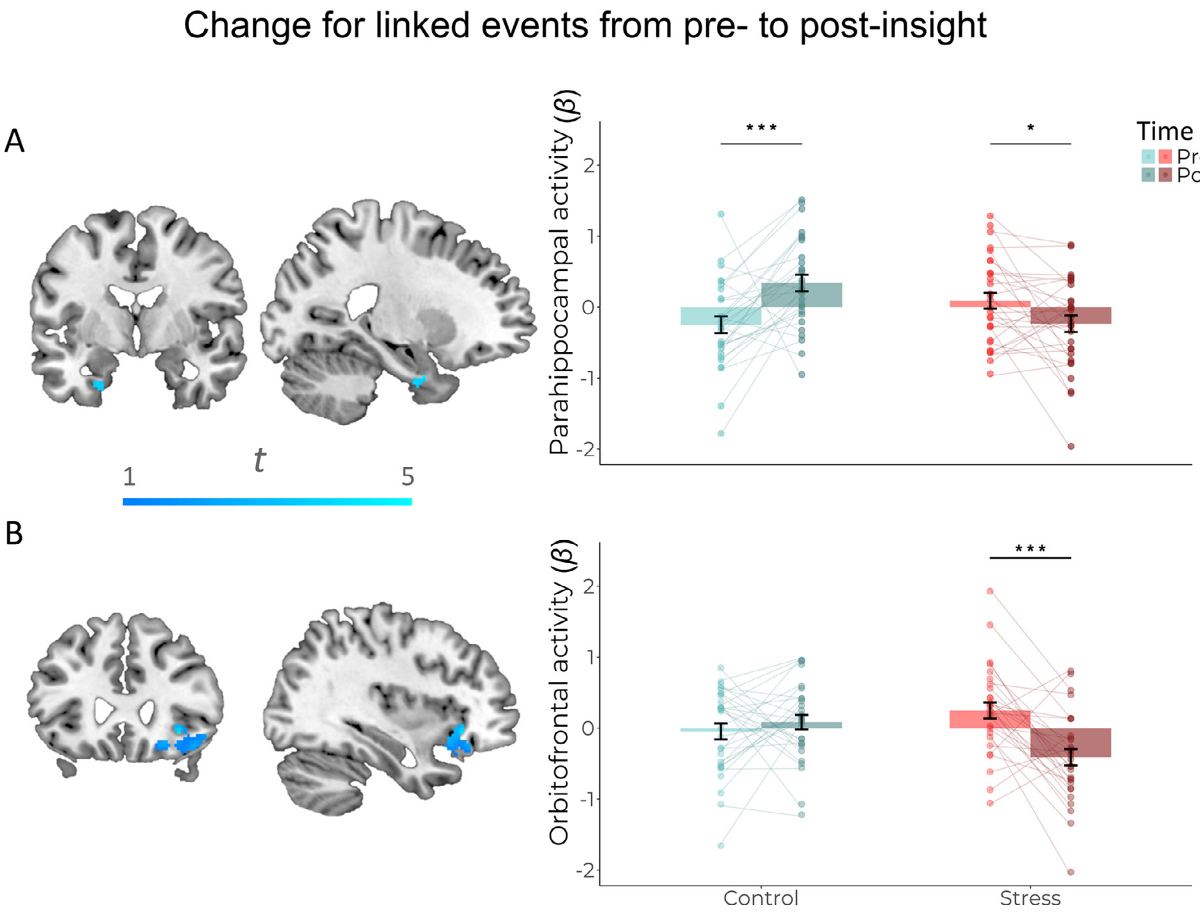


Fig. 6. Change in neural activity from pre- to post-insight. (A) Significant decreases in stressed participants (vs. controls; Linkpost > Linkpre) from pre to post insight in left parahippocampus (SVC peak level: x = -24; y = 0; z = -30). Only masked ROI is displayed. Coronal and sagittal sections are shown, superimposed on a T1-template image. (B) Peak voxel activity of the left parahippocampal cortex (PHC) for stressed participants and controls pre- and post-insight. Data represents means (+/- SE); $^{*}p < .05$, $^{***}p < .001$. (C) Significant decreases in stressed participants (vs. controls; Linkpost > Linkpre) in orbitofrontal cortex (SVC peak level: x = 34; y = 28; z = -8). Only masked ROI is displayed. Coronal and sagittal sections are shown, superimposed on a T1-template image. (D) Peak voxel activity of the right orbitofrontal cortex (OFC) for stressed participants and controls pre- and post-insight. Data represents means (+/- SE); $^{***}p < .001$.

pants exhibited a significant increase in representational dissimilarity for linked events from pre to post insight in the right anterior hippocampus, stress abolished this insight-related change in anterior hippocampal representations (*group* × *time* × *link* interaction: $F_{(1,\,53)} = 6.20$, $p_{\text{corr}} = .032$, $\eta_G = .017$; Fig. 7C). For the posterior hippocampus, there was no such change (*group* x *time* × *link* interaction: $F_{(1,\,56)} = 1.03$, $p_{corr} = .626$, $\eta_G = .002$; Fig. S3), in line with previous studies suggesting that the anterior but not the posterior part of the hippocampus is involved in mnemonic integration (Collin et al., 2015; Dandolo and Schwabe, 2018; De Shetler and Rissman, 2017; Duncan and Schlichting, 2018; Morton et al., 2017; Robin and Moscovitch, 2017). We performed a follow-up analysis of the interaction in the anterior hippocampus and found that controls showed a significant increase in representational dissimilarity from pre to post specifically for linked events ($t_{(26)} = -2.13$, $p = .043$, $d_{\text{repeated measures}} = .41$; Fig. 7C) but no increase in representational dissimilarity from pre to post for non-linked events ($t_{(26)} = .05$, $p = .620$, $d_{\text{repeated measures}} = -.10$; *time* × *link* interaction: $F_{(1,\,26)} = 4.51$, $p = .043$, $\eta_G = .027$). After stress, the change in representational dissimilarity for linked events was eliminated (*time* × *link* interaction: $F_{(1,\,27)} = 2.09$, $p = .160$, $\eta_G = .011$). The representational dissimilarity for linked events in the right anterior hippocampus post-insight was negatively related to the increase in cortisol release over time (AUC_I) across both groups, which was not the case for the representational dissimilarity pre-insight in the right anterior hippocampus (pre: $r = .06$, $t_{(53)} = .42$, $p = .678$; post: $r = -.31$, $t_{(53)} = -2.34$, $p = .023$; pre vs. post: $z = 1.90$, $p = .029$).

To further elucidate the behavioral relevance of the neural representational changes and their abolishment by stress, we first tested for a potential linear relationship between representational dissimilarity in the right anterior hippocampus post-insight for linked events and distances between linked events in the multidimensional arena task. In this analysis, however, we observed no significant effect ($R^2 = -.02$, $F_{(1,\,24)} = .44$, $p = .514$). Since recent studies indicated that there might be a non-linear, quadratic relationship between memory processes and changes in representational similarity (Wammes et al., 2022), we tested also for a potential quadratic relationship and indeed obtained not only a better model fit for the quadratic compared to the linear relationship ($\chi^2_{(1)} = 15.21$, $p < .001$) but also a significant quadratic association between representational dissimilarity in the right anterior hippocampus post-insight for linked events and linked events in the multidimensional arena task in controls ($R^2 = .41$, $F_{(2,\,23)} = 9.52$, $p < .001$; Fig. 6D). Importantly, this association was abolished by acute stress: neither the linear ($R^2 = -.02$, $F_{(1,\,23)} = .54$, $p = .472$), nor the quadratic model ($R^2 = .06$, $F_{(2,\,22)} = 1.78$, $p = .192$; linear vs. quadratic model: $\chi^2_{(1)} = 3.18$, $p = .075$; Fig. 6D) provided a significant fit in stressed participants. The significant interaction effect dissimilarity^2 × group in the interaction model, which showed a better fit compared to the basic model ($\chi^2_{(2)} = 10.83$, $p = .004$), indicated that the groups differed significantly from each other regarding

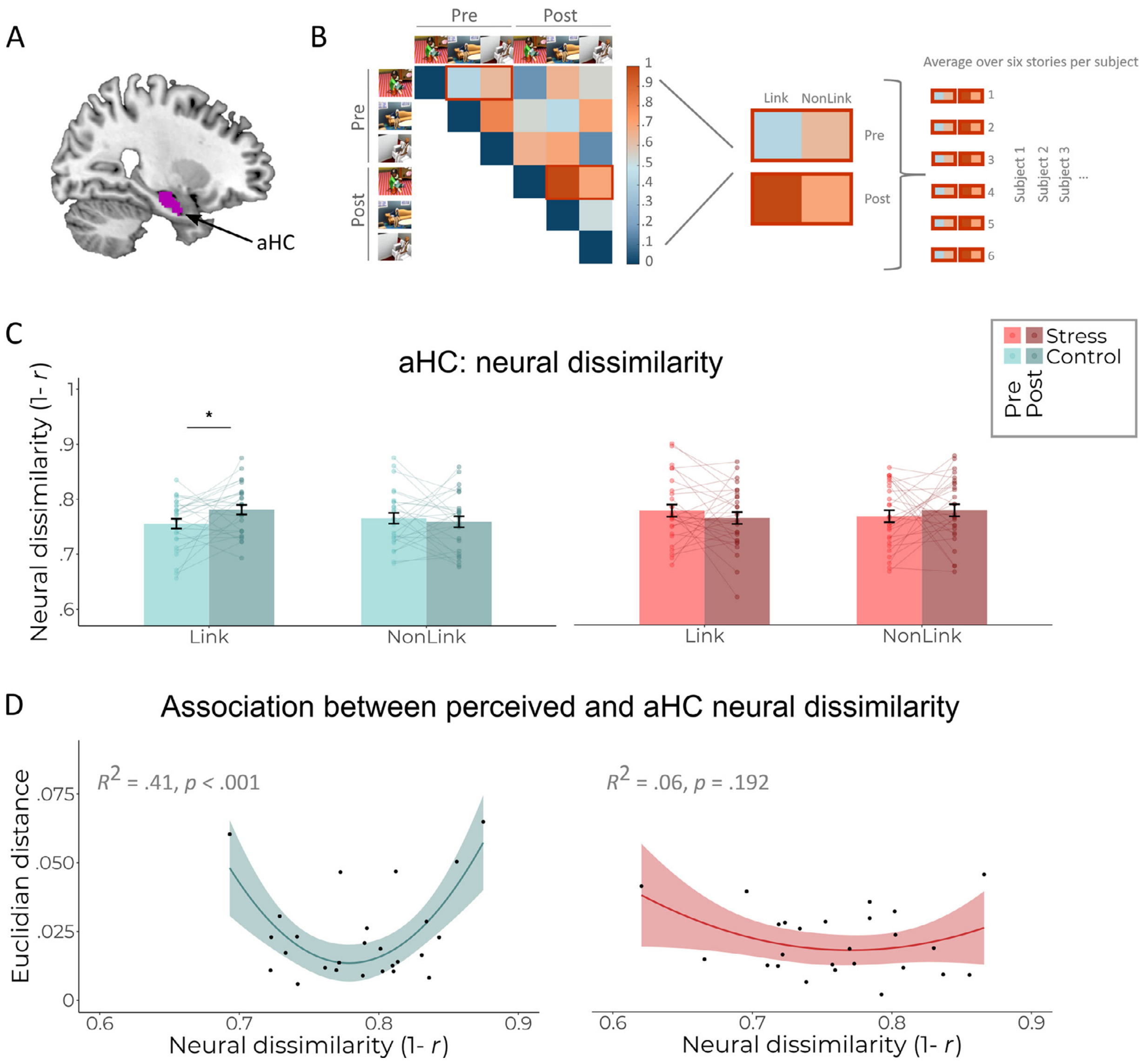


Fig. 7. Conceptual RSA and results for anterior hippocampus (aHC). (A) Masked right anterior hippocampus. (B) Conceptual neural dissimilarity matrix from right anterior hippocampus. Dissimilarities for linked and non-linked events were extracted and averaged across six stories for each participant resulting in average dissimilarities for link and non-link pre- and post-insight. (C) Significant difference between pre- and post-insight for linked events in the right anterior hippocampus in controls as well as non-significant differences in the stress group. Data represents means (+/- SE); $^*p < .05$. (D) Significant quadratic regression between neural dissimilarity post-insight in right aHC and perceived dissimilarity from MA-task (in Euclidian distance) for control group and non-significant quadratic regression for stress group. Each point represents one participants. Fitted quadratic regression line with shaded 95% confidence interval.

the fit of the quadratic model (Table 2). We further found confirmation of the behavioral relevance of neural dissimilarities post-insight, as higher dissimilarities were related to greater distances between non-linked events in the multidimensional arena task ($r = .31$, $t_{(51)} = 2.29$, $p = .026$). Furthermore, those who had higher post-insight neural dissimilarities for linked events also differentiated better between linked and non-linked events in the multidimensional arena task ($r = -.30$, $t_{(49)} = -2.23$, $p = .031$).

3.6. Control variables

To rule out the possibility that the stress and control groups differed in terms of trait-anxiety (STAI-T), state-anxiety (STAI-S), sleep quality (PSQI), chronic stress (TICS), depressive symptoms (BDI), personality dimensions (BFI-2), and chronotype (MEQ), participants completed corresponding questionnaires before the experiment. There were no differences between the groups on any of these measures (all $p > .10$; see Table 3; for MEQ: Fisher´s exact test, $p = .358$).

Furthermore, there was no difference between participants in their working memory capacity, as measured by an N-back task, neither at baseline nor before the task (see Table 4). Thus, it is unlikely that stress effects during the narrative insight task (or in the retention test 1 week later) were influenced by mere group differences in working memory.

4. Discussion

Integrating initially unrelated events into coherent episodes in light of new information is a fundamental memory process. This process may, however, be impaired in stress-related disorders, such as PTSD (Balderston et al., 2017; Berntsen et al., 2003; Lange et al., 2017). Therefore, we tested here the hypothesis that acute stress interferes with the insight-driven reconfiguration of memory. Our results show that, compared to a control manipulation, acute stress reduced medial tempo-

Table 2
Regression models for the prediction of distances for linked events in the multidimensional arena task.

Model	Variable	B	95% CI	β	t	p	R^2 adjusted
Basic	Constant	.99	[.41, 1.56]	-.32	-2.02	.049*	.15
	Dissimilarity	-2.53	[-4.02, -1.03]	.11	.79	.434	
	Dissimilarity^2	1.65	[.67, 2.63]	.33	3.40	.001**	
	Group	-.00	[-.01, .00]	-.14	-1.03	.310	
IA	Constant	2.89	[1.59, 4.18]	-.46	-2.99	.005**	.29
	Dissimilarity	-7.38	[-10.70, -4.06]	-.07	-.52	.608	
	Dissimilarity^2	4.74	[2.62, 6.85]	.57	4.76	<.001***	
	Group	-2.34	[-3.78, -.90]	.15	.99	.329	
	Dissimilarity × Group	6.00	[2.29, 9.72]	.09	.68	.502	
	Dissimilarity^2 × Group	-3.85	[-6.23, -1.46]	-.39	-3.24	.002**	

Note. Basic: basic model without interaction terms; IA: interaction model including the group interaction effects; CI = confidence interval for B; β coefficients are standardized. $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$.

Table 3
Control variables.

	Stress		Control		
Measure	M	SD	M	SD	p
STAI-T	37.47	9.26	35.90	8.87	.509
STAI-S	36.90	6.90	35.72	7.35	.534
PSQI	6.07	3.25	5.44	2.10	.402
TICS	25.77	8.57	25.21	9.05	.808
BDI	7.13	7.93	4.79	4.44	.167
BFI-2 E	42.50	6.51	40.76	6.69	.315
BFI-2 N	31.03	7.59	28.62	9.23	.278
BFI-2 O	44.03	5.75	43.17	9.00	.665
BFI-2 C	39.83	7.80	43.31	7.95	.096
BFI-2 A	45.87	4.42	47.07	6.78	.400

Note. The questionnaires (STAI-T, BDI, BFI-2 all dimensions) were completed via an online-link before participants came in for day 1 and STAI-S and PSQI were completed at the beginning of the experiment. No significant difference between the groups were observed on these measures. Data represents means (+/- SD).

Table 4
N-back task.

	Stress		Control		
N-back	M	SD	M	SD	p
Pre					
3-back Acc	79.75%	11.91%	79.40%	10.93%	.906
3-back RT	780.57 ms	164.01 ms	729.20 ms	164.91 ms	.235
4-back Acc	78.33%	9.20%	77.24%	11.52%	.690
4-back RT	765.27 ms	144.87 ms	722.75 ms	206.18 ms	.365
Post					
3-back Acc	80.58%	13.17%	80.00%	15.40%	.877
3-back RT	782.96 ms	182.44 ms	795.93 ms	211.56 ms	.802
4-back Acc	76.25%	12.71%	76.81%	15.25%	.879
4-back RT	779.51 ms	162.71 ms	797.09 ms	194.50 ms	.708

Note. Participants completed the N-back task before stress induction at baseline and after stress induction before they completed the narrative-insight task in the scanner. Groups did not differ on N-back measures pre- or post-stress or –control manipulation. Data represents means (+/- SD).

ral activity when learning about the link between initially unrelated events as well as the increase in medial temporal activity from pre- to post-insight for linked events. Moreover, stress abolished the change in the neural representation of linked events in the anterior hippocampus that we observed in a non-stressed control group. These stress-induced changes in the neural implementation of the integration across initially unrelated events were directly linked to subsequent mnemonic measures of insight. Control analyses showed that these effects of acute stress could not be explained by group differences in chronic stress, anxiety, depressive mood or working memory capacity.

Across groups, our behavioral data revealed a memory benefit for linked compared to non-linked events, suggesting that narrative coherence may promote memory longevity. This finding is in line with the notion that the brain stores episodic memories as coherent narratives (Tulving, 1983) and with recent findings suggesting that integrated episodes can be recalled more easily (Cohn-Sheehy et al., 2021a; Wang et al., 2015). This memory advantage of integrated episodes over non-linked events might be due to a pattern completion process, which allows cueing of an entire episode with a single element (Gardner-Medwin, 1976; Horner and Burgess, 2014; Nakazawa et al., 2002b; Rolls, 2013). Although events A and B were not repeated during the linking phase, the linking events may have induced a reactivation of these events, which may further have contributed to the differences in detail recall for linked and non-linked events. Notably, the basic insight into the relationship between linked and non-linked events was not affected by stress, most likely because the task was designed to result in high insight performance. In line with this view, performance in the insight task was near-ceiling for both groups.

While performance in the multidimensional arrangement test was comparable between groups, the stress group outperformed the control group in the forced-choice recognition test. A similar, but non-significant trend was observed in the free recall test; the lack of significance in the free recall test may be due to factors such as task sensitivity or differences in task difficulty. Compared to free recall, the forced-choice recognition test is cognitively less demanding as it requires only a limited search process. In accordance with previous work, that has shown that stress prior encoding led to improved recognition performance for high-arousal pairings (Goldfarb et al., 2019) and congruent pairings of faces and scenes one day after encoding (Sep et al., 2019), we show that stress prior encoding one week later led to improved recognition performance of events that were linked through a narrative compared to non-linked events. This memory boost in stressed participants may have been due to delayed cortisol effects that have been suggested to boost memory consolidation processes and to potentially counteract initial impairments of memory updating (Schwabe et al., 2022; van Ast et al., 2013).

At the neural level, however, stress led to a significant reduction of insight-related increases of activity in the parahippocampus, orbitofrontal cortex, and putamen. The finding that parahippocampal activity increased after having learned which scenes belong together is generally in line with reports suggesting that the parahippocampus encodes spatial settings, such as scenes (Epstein and Kanwisher, 1998; Faivre et al., 2019), as well as non-spatial associations (Aminoff et al., 2007; Bar et al., 2008). The orbitofrontal cortex and the putamen have been associated with reward processing and goal orientation (Basu et al., 2021; Porcelli et al., 2012; Rudebeck and Rich, 2018), pointing to a role in monitoring which events were linked into episodes and which were not.

Most strikingly, non-stressed control participants showed an increase from pre- to post-insight in neural dissimilarity in the anterior hippocampus for linked events. This finding is consistent with studies highlighting the anterior hippocampus as key region for mnemonic integration (Collin et al., 2015; Hannula et al., 2013; Schlichting et al., 2015). Because the anterior hippocampus is also critical for representing both (spatial) context (Brunec et al., 2018; Collin et al., 2015; Fritch et al., 2020), novelty (Bunzeck and Düzel, 2006; Cowan et al., 2021; Kaplan et al., 2014), and repulsion between overlapping representations (Chanales et al., 2017, 2021) may explain why we observed an increase in dissimilarity particularly in this region after participants learned that two of the events were linked via another event, resulting in an integrated episode. Critically, however, this insight-driven change in neural representations disappeared in stressed participants. Consistent with this stress effect, the more cortisol increased over time, the smaller the insight-related neural reconfiguration in the right anterior hippocampus. In light of evidence suggesting that stress might impair processes of pattern completion and separation (Balderston et al., 2017; Berntsen et al., 2003; Esterling et al., 1999; Leal et al., 2014), it is tempting to speculate that acute stress disrupted these processes which are likely mechanisms allowing representational dissimilarity to change (Muller and Kubie, 1987).

Interestingly, we observed an increase in dissimilarity in the anterior hippocampus, but not an increase in similarity, as observed in some earlier studies (Collin et al., 2015; Dimsdale-Zucker et al., 2018; Hannula et al., 2013; Schlichting et al., 2015) or an increase in similarity for linked events and a decrease in similarity for non-linked events, as observed in the posterior hippocampus in previous work (Milivojevic et al., 2015). Importantly, our design differs from previous work (Milivojevic et al., 2015) that used the narrative-insight task in terms of video length: the events during the pre- and post-phase were presented for 2 sec while events in the linking phase were presented for 8 sec for technical reasons. In addition, our design differs from this previous work in that we used a control event (C) during the linking phase to which the linking event (L) was compared to obtain only the linking-related activity. It has also been suggested that hippocampal similarity may increase when events share item as well as context associations but not when events shared either context (scene) or item (people) information (Libby et al., 2019), which may have been the case in the present study. This was, however, also the case in a previous study using the same paradigm in which increased similarity for linked events was found in the anterior hippocampus (Collin et al., 2015). Further evidence suggests that memory representations that have been moderately co-activated, result in increased dissimilarity (Wammes et al., 2022). Increases in dissimilarity between related memories might be interpreted as a pattern separation mechanism allowing inferences across events (Molitor et al., 2021). Indeed, increased dissimilarity has been associated with better memory performance in several previous studies (Chanales et al., 2017; Dandolo and Schwabe, 2018; Favila et al., 2016; Hulbert and Norman, 2015; Koolschijn et al., 2019). In line with these findings, we also found a link between neural dissimilarity post-insight and memory performance (in the multidimensional arena task) in controls. Here, medium dissimilarity values were related to the smallest distance between linked events, whereas low and high dissimilarities resulted in worse performance. Although Wammes et al. (2022) found that the co-activation of memories is non-monotonically related to a resulting increase or decrease in dissimilarity, our results even suggest that the resulting representational dissimilarity is related to a behavioral outcome in a quadratic manner. Wammes et al. (2022) show that low levels of co-activation resulted in no change regarding the dissimilarity between memories and that high levels of co-activation led to decreased dissimilarity. Moderate levels of co-activation, however, – where one memory is strongly activated and the unique parts of the other memory are moderately active – resulted in increased dissimilarity and, thus, less competition between these memories, which might have been the case in the present study. Again, the link between hippocampal reconfiguration and subsequent memory was abolished by acute stress.

Beyond the insight-driven reconfiguration of memory representations, acute stress did also affect the neural processes involved in the linking of initially unrelated events itself. During the linking phase, stress particularly reduced medial temporal lobe activity, in line with the proposed stress-induced shift of multiple memory systems at the expense of a ‘cognitive’, medial temporal lobe-based system (Goodman et al., 2012; Kim et al., 2001; Schwabe, 2017; Schwabe and Wolf, 2012; Vogel et al., 2016; Wirz et al., 2017). Linking two previously unrelated events together requires a neural substrate that can integrate these memories into a novel unified mnemonic representation, and the hippocampus has been found to be specifically relevant to this function (Bowman and Zeithamova, 2018; Griffiths and Fuentemilla, 2020; Schlichting et al., 2015). Here, it should be noted that linking previously separate events into a coherent narrative requires several sub-processes, such as the successful retrieval of the previously encoded events, the inference of their link, and their mnemonic integration, all of which are relevant and likely dependent on the hippocampus but can hardly be dissociated during the linking process. In addition to the hippocampus, we observed increased amygdala activity in controls during link vs. control events, which was directly associated with insight manifestations one week later. Given the well-documented role of the amygdala in both positive and negative affect (LeDoux, 2007; Phelps and LeDoux, 2005; Weymar and Schwabe, 2016), it is tempting to speculate that the insight into the link between previously unrelated events comes with an (presumably positive) affective response, which may facilitate the subsequent memory of the gained insight. Indeed, there is abundant evidence that emotion-related amygdala activation may modulate mnemonic processing in other brain areas, such as the hippocampus, to promote memory consolidation (Roozendaal et al., 2009; Roozendaal and McGaugh, 2011).

In sum, our findings show that acute stress comes with significant changes in the neural integration of initially separated events into coherent episodes. Specifically, stress reduced medial temporal activity when learning about the links between events and hindered an increase in medial temporal activity from pre- to post-insight. Moreover, stress abolished the insight-driven representational reconfiguration in the anterior hippocampus, which was directly linked to the subsequent memory of the linked events. Although stress reduced the neural changes associated with insight, it enhanced long-term memory, most likely due to the facilitating effect of glucocorticoids on memory consolidation. Together, the present findings shed light on how acute stress impacts mnemonic integration across separate events and may aid our understanding of disintegrated, fragmented memories in stress-related disorders, such as PTSD (Amir et al., 1998; Bisby et al., 2020; Esterling et al., 1999).

Data and code availability

Code and data reported in this manuscript are available from the first author’s GitHub repository under https://github.com/an-ma-grob/EpInt_Stress. The RSA analyses were performed using the rsatoolbox (Nili et al., 2014), which can be found under https://git.fmrib.ox.ac.uk/hnili/rsa.

Ethics

Human subjects: University of Hamburg approved the study. All participants gave informed consent to participate in this study.

Declaration of Competing Interest

The authors declare no competing interests

Credit authorship contribution statement

Anna-Maria Grob: Methodology, Formal analysis, Validation, Investigation, Data curation, Writing – original draft, Visualization, Project administration. **Branka Milivojevic:** Methodology, Formal analysis, Validation, Writing – review & editing. **Arjen Alink:** Methodology, Resources, Writing – review & editing. **Christian F. Doeller:** Conceptualization, Methodology, Validation, Resources, Writing – review & editing, Funding acquisition. **Lars Schwabe:** Conceptualization, Methodology, Validation, Writing – original draft, Supervision, Project administration, Funding acquisition.

Data availability

Code and data reported in this manuscript are available from the first author's GitHub repository under https://github.com/anma-grob/EpInt_Stress.

Funding

This project was funded by the German Research Foundation (DFG; grant SCHW1357/22 to LS and CFD.). CFD's research is supported by the Max Planck Society, the European Research Council (ERC-CoG GEOCOG 724836), the Kavli Foundation, the Jebsen Foundation, Helse Midt Norge and The Research Council of Norway (223262/F50; 197467/F50).

Acknowledgement

We gratefully acknowledge the assistance of Carlo Hiller with programming the task, Hamed Nili for his support during data analysis, and Anica Koslowski, Dania Al Darwich, Merve Tural, Carlotta Reinhardt, Sophie Lutter, Mihriban Sahin, and Dewi Soetjipto for their assistance during data collection.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2022.119804.

References

Adan, A., Almirall, H., 1991. Horne & Östberg morningness-eveningness questionnaire: a reduced scale. Pers. Individ. Differ. 12 (3), 241–253. doi:10.1016/0191-8869(91)90110-W.

Aminoff, E., Gronau, N., Bar, M., 2007. The parahippocampal cortex mediates spatial and nonspatial associations. Cereb. Cortex 17 (7), 1493–1503. doi:10.1093/cercor/bhl078.

Amir, N., Stafford, J., Freshman, M.S., Foa, E.B., 1998. Relationship between trauma narratives and trauma pathology. J. Trauma Stress 11 (2), 385–392. doi:10.1023/A:1024415523495.

Balderston, N.L., Mathur, A., Adu-Brimpong, J., Hale, E.A., Ernst, M., Grillon, C., 2017. Effect of anxiety on behavioural pattern separation in humans. Cogn. Emot. 31 (2), 238–248. doi:10.1080/02699931.2015.1096235.

Bar, M., Aminoff, E., Schacter, D.L., 2008. Scenes Unseen: the parahippocampal cortex intrinsically subserves contextual associations, not scenes or places per se. J. Neurosci. 28 (34), 8539–8544. doi:10.1523/JNEUROSCI.0987-08.2008.

Basu, R., Gebauer, R., Herfurth, T., Kolb, S., Golipour, Z., Tchumatchenko, T., Ito, H.T., 2021. The orbitofrontal cortex maps future navigational goals. Nature 599 (7885), 7885. doi:10.1038/s41586-021-04042-9, Article.

Berntsen, D., Willert, M., Rubin, D.C., 2003. Splintered memories or vivid landmarks? Qualities and organization of traumatic memories with and without PTSD. Appl. Cogn. Psychol. 17 (6), 675–693. doi:10.1002/acp.894.

Bisby, J.A., Burgess, N., Brewin, C.R., 2020. Reduced memory coherence for negative events and its relationship to posttraumatic stress disorder. Curr. Dir. Psychol. Sci. 29 (3), 267–272. doi:10.1177/0963721420917691.

Bowman, C.R., Zeithamova, D., 2018. Abstract memory representations in the ventromedial prefrontal cortex and hippocampus support concept generalization. J. Neurosci. 38 (10), 2605–2614. doi:10.1523/JNEUROSCI.2811-17.2018.

Brett, M., Anton, J.L., Valabregue, R., Poline, J.B., 2002. Region of interest analysis using an SPM toolbox. In: Proceedings of the 8th International Conference on Functional Mapping of the Human Brain, 16, p. 497.

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. Curr. Biol. 28 (13), 2129–2135. doi:10.1016/j.cub.2018.05.016, e6.

Brunec, I.K., Robin, J., Olsen, R.K., Moscovitch, M., Barense, M.D., 2020. Integration and differentiation of hippocampal memory traces. Neurosci. Biobehav. Rev. 118, 196–208. doi:10.1016/j.neubiorev.2020.07.024.

Bunzeck, N., Düzel, E., 2006. Absolute coding of stimulus novelty in the human substantia Nigra/VTA. Neuron 51 (3), 369–379. doi:10.1016/j.neuron.2006.06.021.

Buysse, D., Reynolds, C., Monk, T., Berman, S., Kupfer, D., 1989. The pittsburgh sleep quality index—a new instrument for psychiatric practice and research. Psychiatry Res. 28 (2), 193–213. doi:10.1016/0165-1781(89)90047-4.

Chanales, A.J.H., Oza, A., Favila, S.E., Kuhl, B.A., 2017. Overlap among spatial memories triggers repulsion of hippocampal representations. Curr. Biol. 27 (15), 2307–2317. doi:10.1016/j.cub.2017.06.057, e5.

Chanales, A.J.H., Tremblay-McGaw, A.G., Drascher, M.L., Kuhl, B.A., 2021. Adaptive repulsion of long-term memory representations is triggered by event similarity. Psychol. Sci. 32 (5), 705–720. doi:10.1177/0956797620972490.

Cohn-Sheehy, B.I., Delarazan, A.I., Crivelli-Decker, J.E., Reagh, Z.M., Mundada, N.S., Yonelinas, A.P., Zacks, J.M., Ranganath, C., 2021a. Narratives bridge the divide between distant events in episodic memory. Mem. Cognit. doi:10.3758/s13421-021-01178-x.

Cohn-Sheehy, B.I., Delarazan, A.I., Reagh, Z.M., Crivelli-Decker, J.E., Kim, K., Barnett, A.J., Zacks, J.M., Ranganath, C., 2021b. The hippocampus constructs narrative memories across distant events. Curr. Biol. 31 (22), 4935–4945. doi:10.1016/j.cub.2021.09.013, e7.

Collin, S.H.P., Milivojevic, B., Doeller, C.F., 2015. Memory hierarchies map onto the hippocampal long axis in humans. Nat. Neurosci. 18 (11), 1562–1564. doi:10.1038/nn.4138.

Collin, S.H.P., Milivojevic, B., Doeller, C.F., 2017. Hippocampal hierarchical networks for space, time, and memory. Curr. Opin. Behav. Sci. 17, 71–76. doi:10.1016/j.cobeha.2017.06.007.

Cowan, E.T., Fain, M., O'Shea, I., Ellman, L.M., Murty, V.P, 2021. VTA and anterior hippocampus target dissociable neocortical networks for post-novelty enhancements. J. Neurosci. 41 (38), 8040–8050. doi:10.1523/JNEUROSCI.0316-21.2021.

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

Danner, D., Rammstedt, B., Bluemke, M., Treiber, L., Berres, S.,Soto, C., & John, O. P. (2016).Die deutsche Version des Big Five Inventory 2 (BFI-2). Zusammenstellung sozialwissenschaftlicher Items und Skalen [German version of the Big Five Inventory 2 (BFI-2)]. Mannheim, Germany: GESIS. https://doi.org/10.6102/zis247

de-Quervain, D.J.F., Roozendaal, B., McGaugh, J.L., 1998. Stress and glucocorticoids impair retrieval of long-term spatial memory. Nature 394 (6695), 787–790. doi:10.1038/29542.

De Shetler, N.G., Rissman, J., 2017. Dissociable profiles of generalization/discrimination in the human hippocampus during associative retrieval. Hippocampus 27 (2), 115–121. doi:10.1002/hipo.22684.

Diamond, D.M., Campbell, A.M., Park, C.R., Halonen, J., Zoladz, P.R., 2007. The temporal dynamics model of emotional memory processing: a synthesis on the neurobiological basis of stress-induced amnesia, flashbulb and traumatic memories, and the yerkes-dodson law. Neural Plast. 2007, e60803. doi:10.1155/2007/60803.

Dimsdale-Zucker, H.R., Ritchey, M., Ekstrom, A.D., Yonelinas, A.P., Ranganath, C., 2018. CA1 and CA3 differentially support spontaneous retrieval of episodic contexts within human hippocampal subfields. Nat. Commun. 9 (1), 294. doi:10.1038/s41467-017-02752-1.

Duncan, K.D., Schlichting, M.L., 2018. Hippocampal representations as a function of time, subregion, and brain state. Neurobiol. Learn. Mem. 153, 40–56. doi:10.1016/j.nlm.2018.03.006.

Eichenbaum, H., 2004. Hippocampus: cognitive processes and neural representations that underlie declarative memory. Neuron 44 (1), 109–120. doi:10.1016/j.neuron.2004.08.028.

Epstein, R., Kanwisher, N., 1998. A cortical representation of the local visual environment. Nature 392 (6676), 598–601. doi:10.1038/33402.

Esterling, B.A., L'Abate, L., Murray, E.J., Pennebaker, J.W., 1999. Empirical foundations for writing in prevention and psychotherapy: mental and physical health outcomes. Clin. Psychol. Rev. 19 (1), 79–96. doi:10.1016/S0272-7358(98)00015-4.

Faivre, N., Dubois, J., Schwartz, N., Mudrik, L., 2019. Imaging object-scene relations processing in visible and invisible natural scenes. Sci. Rep. 9 (1), 1. doi:10.1038/s41598-019-38654-z, Article.

Favila, S.E., Chanales, A.J.H., Kuhl, B.A., 2016. Experience-dependent hippocampal pattern differentiation prevents interference during subsequent learning. Nat. Commun. 7 (1), 1. doi:10.1038/ncomms11066, Article.

Fritch, H.A., MacEvoy, S.P., Thakral, P.P., Jeye, B.M., Ross, R.S., Slotnick, S.D., 2020. The anterior hippocampus is associated with spatial memory encoding. Brain Res. 1732, 146696. doi:10.1016/j.brainres.2020.146696.

Gardner-Medwin, A.R., 1976. The recall of events through the learning of associations between their parts. Proc. R. Soc. Lond. B. Biol. Sci. 194 (1116), 375–402. doi:10.1098/rspb.1976.0084.

Goldfarb, E.V., Tompary, A., Davachi, L., Phelps, E.A., 2019. Acute stress throughout the memory cycle: diverging effects on associative and item memory. J. Exp. Psychol. Gen. 148 (1), 13–29. doi:10.1037/xge0000472.

Goodman, J., Leong, K.C., Packard, M.G., 2012. Emotional modulation of multiple memory systems: Implications for the neurobiology of post-traumatic stress disorder. Rev. Neurosci. 23 (5), 627–643. doi:10.1515/revneuro-2012-0049, –6.

Griffiths, B.J., Fuentemilla, L., 2020. Event conjunction: how the hippocampus integrates episodic memories across event boundaries. Hippocampus 30 (2), 162–171. doi:10.1002/hipo.23161.

Hannula, D.E., Libby, L.A., Yonelinas, A.P., Ranganath, C., 2013. Medial temporal lobe contributions to cued retrieval of items and contexts. Neuropsychologia 51 (12), 2322–2332. doi:10.1016/j.neuropsychologia.2013.02.011.

Hautzinger, M., Keller, F., Kühner, C., 2006. *Beck Depressions-Inventar (BDI-II). Revision.* Frankfurt/Main: Harcourt Test Services.

Horner, A.J., Bisby, J.A., Bush, D., Lin, W.J., Burgess, N., 2015. Evidence for holistic episodic recollection via hippocampal pattern completion. Nat. Commun. 6 (1), 1–11. doi:10.1038/ncomms8462.

Horner, A.J., Burgess, N., 2014. Pattern Completion in Multielement Event Engrams. Curr. Biol. 24 (9), 988–992. doi:10.1016/j.cub.2014.03.012.

Huffman, D.J., Stark, C.E.L., 2014. Multivariate pattern analysis of the human medial temporal lobe revealed representationally categorical cortex and representationally agnostic hippocampus. Hippocampus 24 (11), 1394–1403. doi:10.1002/hipo.22321.

Hulbert, J.C., Norman, K.A., 2015. Neural differentiation tracks improved recall of competing memories following interleaved study and retrieval practice. Cereb. Cortex 25 (10), 3994–4008.

Joëls, M., Fernandez, G., Roozendaal, B., 2011. Stress and emotional memory: a matter of timing. Trends Cogn. Sci. 15 (6), 280–288. doi:10.1016/j.tics.2011.04.004.

Kaplan, R., Horner, A.J., Bandettini, P.A., Doeller, C.F., Burgess, N., 2014. Human hippocampal processing of environmental novelty during spatial navigation. Hippocampus 24 (7), 740–750. doi:10.1002/hipo.22264.

Kim, J.J., Diamond, D.M., 2002. The stressed hippocampus, synaptic plasticity and lost memories. Nat. Rev. Neurosci. 3 (6), 453–462. doi:10.1038/nrn849.

Kim, J.J., Lee, H.J., Han, J.S., Packard, M.G., 2001. Amygdala is critical for stress-induced modulation of hippocampal long-term potentiation and learning. J. Neurosci. 21 (14), 5222–5228. doi:10.1523/JNEUROSCI.21-14-05222.2001.

Kirchner, W.K., 1958. Age differences in short-term retention of rapidly changing information. J. Exp. Psychol. 55 (4), 352–358. doi:10.1037/h0043688.

Kirschbaum, C., Pirke, K.M., Hellhammer, D.H., 1993. The 'Trier Social Stress Test' – a tool for investigating psychobiological stress responses in a laboratory setting. Neuropsychobiology 28 (1), 76–81. doi:10.1159/000119004, –2.

Koolschijn, R.S., Emir, U.E., Pantelides, A.C., Nili, H., Behrens, T.E.J., Barron, H.C., 2019. The hippocampus and neocortical inhibitory engrams protect against memory interference. Neuron 101 (3), 528–541. doi:10.1016/j.neuron.2018.11.042, e6.

Kriegeskorte, N., Mur, M., 2012. Inverse MDS: inferring dissimilarity structure from multiple item arrangements. Front. Psychol. 3. doi:10.3389/fpsyg.2012.00245.

Kriegeskorte, N., Mur, M., Bandettini, P.A., 2008. Representational similarity analysis—connecting the branches of systems neuroscience. Front. Syst. Neurosci. 2. doi:10.3389/neuro.06.004.2008.

Kudielka, B.M., Kirschbaum, C., 2005. Sex differences in HPA axis responses to stress: a review. Biol. Psychol. 69 (1), 113–132. doi:10.1016/j.biopsycho.2004.11.009.

Lange, I., Goossens, L., Michielse, S., Bakker, J., Lissek, S., Papalini, S., Verhagen, S., Leibold, N., Marcelis, M., Wichers, M., Lieverse, R., van Os, J., van Amelsvoort, T., Schruers, K., 2017. Behavioral pattern separation and its link to the neural mechanisms of fear generalization. Soc. Cogn. Affect. Neurosci. 12 (11), 1720–1729. doi:10.1093/scan/nsx104.

Laux, L., Glanzmann, P., Schaffner, P., Spielberger, C.D., Laux, L., Glanzmann, P., Schaffner, P., Spielberger, C.D., 1981. State-trait anxiety inventory—manual of the German version. Beltz.

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. doi:10.1002/hipo.22298.

LeDoux, J., 2007. The amygdala. Curr. Biol. 17 (20), R868–R874.

Libby, L.A., Reagh, Z.M., Bouffard, N.R., Ragland, J.D., Ranganath, C., 2019. The hippocampus generalizes across memories that share item and context information. J. Cogn. Neurosci. 31 (1), 24–35. doi:10.1162/jocn_a_01345.

Lohnas, L.J., Duncan, K., Doyle, W.K., Thesen, T., Devinsky, O., Davachi, L., 2018. Time-resolved neural reinstatement and pattern separation during memory decisions in human hippocampus. Proc. Natl Acad. Sci. 115 (31), E7418–E7427. doi:10.1073/pnas.1717088115.

Lupien, S.J., Lepage, M., 2001. Stress, memory, and the hippocampus: can't live with it, can't live without it. Behav. Brain Res. 127 (1), 137–158. doi:10.1016/S0166-4328(01)00361-8.

Marr, D., 1971. A theory of archicortical function. Proc. R. Soc. Lond. B Biol. Sci. 262, 23–81.

Milivojevic, B., Vicente-Grabovetsky, A., Doeller, C.F., 2015. Insight reconfigures hippocampal-prefrontal memories. Curr. Biol. 25 (7), 821–830. doi:10.1016/j.cub.2015.01.033.

Molitor, R.J., Sherrill, K.R., Morton, N.W., Miller, A.A., Preston, A.R., 2021. Memory reactivation during learning simultaneously promotes dentate Gyrus/CA $_{2,3}$ pattern differentiation and CA $_{1}$ memory integration. J. Neurosci. 41 (4), 726–738. doi:10.1523/JNEUROSCI.0394-20.2020.

Morton, N.W., Sherrill, K.R., Preston, A.R., 2017. Memory integration constructs maps of space, time, and concepts. Curr. Opin. Behav. Sci. 17, 161–168. doi:10.1016/j.cobeha.2017.08.007.

Muller, R.U., Kubie, J.L., 1987. The effects of changes in the environment on the spatial firing of hippocampal complex-spike cells. J. Neurosci. 7 (7), 1951–1968. doi:10.1523/JNEUROSCI.07-07-01951.1987.

Nakazawa, K., Quirk, M.C., Chitwood, R.A., Watanabe, M., Yeckel, M.F., Sun, L.D., Kato, A., Carr, C.A., Johnston, D., Wilson, M.A., Tonegawa, S., 2002a. Requirement for hippocampal CA3 NMDA receptors in associative memory recall. Science doi:10.1126/science.1071795.

Nakazawa, K., Quirk, M.C., Chitwood, R.A., Watanabe, M., Yeckel, M.F., Sun, L.D., Kato, A., Carr, C.A., Johnston, D., Wilson, M.A., Tonegawa, S., 2002b. Requirement for hippocampal CA3 NMDA receptors in associative memory recall. Science 297 (5579), 211–218. doi:10.1126/science.1071795, (New York, N.Y.).

Nili, H., Wingfield, C., Walther, A., Su, L., Marslen-Wilson, W., Kriegeskorte, N., 2014. A toolbox for representational similarity analysis. PLoS Comput. Biol. 10 (4), e1003553. doi:10.1371/journal.pcbi.1003553.

Norman, K.A., O'Reilly, R.C, 2003. Modeling hippocampal and neocortical contributions to recognition memory: A complementary-learning-systems approach. Psychol. Rev. 110 (4), 611–646. doi:10.1037/0033-295X.110.4.611.

Phelps, E.A., LeDoux, J.E., 2005. Contributions of the amygdala to emotion processing: from animal models to human behavior. Neuron 48 (2), 175–187. doi:10.1016/j.neuron.2005.09.025.

Porcelli, A.J., Lewis, A.H., Delgado, M.R., 2012. Acute stress influences neural circuits of reward processing. Front. Neurosci. 6, 157.

Pruessner, J.C., Kirschbaum, C., Meinlschmid, G., Hellhammer, D.H., 2003. Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. Psychoneuroendocrinology 28 (7), 916–931. doi:10.1016/S0306-4530(02)00108-7.

Robin, J., Moscovitch, M., 2017. Details, gist and schema: hippocampal–neocortical interactions underlying recent and remote episodic and spatial memory. Curr. Opin. Behav. Sci. 17, 114–123. doi:10.1016/j.cobeha.2017.07.016.

Rolls, E., 2013. The mechanisms for pattern completion and pattern separation in the hippocampus. Front. Syst. Neurosci. 7. https://www.frontiersin.org/article/10.3389/fnsys.2013.00074.

Rolls, E.T., Kesner, R.P., 2006. A computational theory of hippocampal function, and empirical tests of the theory. Prog. Neurobiol. 79 (1), 1–48. doi:10.1016/j.pneurobio.2006.04.005.

Roozendaal, B., McEwen, B.S., Chattarji, S., 2009. Stress, memory and the amygdala. Nat. Rev. Neurosci. 10 (6), 423–433. doi:10.1038/nrn2651.

Roozendaal, B., McGaugh, J.L., 2011. Memory modulation. Behav. Neurosci. 125 (6), 797–824. doi:10.1037/a0026187.

Rudebeck, P.H., Rich, E.L., 2018. Orbitofrontal cortex. Curr. Biol. 28 (18), R1083–R1088. doi:10.1016/j.cub.2018.07.018.

Sandi, C., Pinelo-Nava, M.T., 2007. Stress and memory: behavioral effects and neurobiological mechanisms. Neural Plast. 2007, e78970. doi:10.1155/2007/78970.

Schapiro, A.C., Turk-Browne, N.B., Botvinick, M.M., Norman, K.A., 2017. Complementary learning systems within the hippocampus: a neural network modelling approach to reconciling episodic memory with statistical learning. Philos. Trans. R. Soc. B Biol. Sci. 372 (1711), 20160049. doi:10.1098/rstb.2016.0049.

Schlichting, M.L., Mumford, J.A., Preston, A.R., 2015. Learning-related representational changes reveal dissociable integration and separation signatures in the hippocampus and prefrontal cortex. Nat. Commun. 6 (1), 1–10. doi:10.1038/ncomms9151.

Schlichting, M.L., Preston, A.R, 2017. The hippocampus and memory integration: building knowledge to navigate future decisions. In: Hannula, D.E., Duff, M.C. (Eds.), The Hippocampus from Cells to Systems: Structure, Connectivity, and Functional Contributions to Memory and Flexible Cognition. Springer International Publishing, pp. 405–437. doi:10.1007/978-3-319-50406-3_13.

Schulz, P., Schlotz, W., 1999. Trierer Inventar zur Erfassung von chronischem Sre (TICS): Skalenkonstruktion, teststatistische Überprüfung und Validierung der Skala Arbeitsüberlastung, [The Trier Inventory for the Assessment of Chronic Stress (TICS), Scale construction, statistical testing, and validation of the scale work overload]. Diagnostica 45 (1), 8–19. doi:10.1026//0012-1924.45.1.8.

Schwabe, L., 2017. Memory under stress: from single systems to network changes. Eur. J. Neurosci. 45 (4), 478–489. doi:10.1111/ejn.13478.

Schwabe, L., Hermans, E.J., Joëls, M., Roozendaal, B., 2022. Mechanisms of memory under stress. Neuron doi:10.1016/j.neuron.2022.02.020.

Schwabe, L., Joëls, M., Roozendaal, B., Wolf, O.T., Oitzl, M.S., 2012a. Stress effects on memory: an update and integration. Neurosci. Biobehav. Rev. 36 (7), 1740–1749. doi:10.1016/j.neubiorev.2011.07.002.

Schwabe, L., Oitzl, M.S., Philippsen, C., Richter, S., Bohringer, A., Wippich, W., Schachinger, H., 2007. Stress modulates the use of spatial versus stimulus-response learning strategies in humans. Learn. Mem. 14 (1), 109–116. doi:10.1101/lm.435807, –2.

Schwabe, L., Tegenthoff, M., Höffken, O., Wolf, O.T., 2012b. Simultaneous glucocorticoid and noradrenergic activity disrupts the neural basis of goal-directed action in the human brain. J. Neurosci. 32 (30), 10146–10155. doi:10.1523/JNEUROSCI.1304-12.2012.

Schwabe, L., Wolf, O.T., 2012. Stress modulates the engagement of multiple memory systems in classification learning. J. Neurosci. 32 (32), 11042–11049. doi:10.1523/JNEUROSCI.1484-12.2012.

Sep, M.S.C., van Ast, V.A., Gorter, R., Joëls, M., Geuze, E., 2019. Time-dependent effects of psychosocial stress on the contextualization of neutral memories. Psychoneuroendocrinology 108, 140–149. doi:10.1016/j.psyneuen.2019.06.021.

Shields, G.S., Sazma, M.A., McCullough, A.M., Yonelinas, A.P., 2017. The effects of acute stress on episodic memory: a meta-analysis and integrative review. Psychol. Bull. 143 (6), 636.

Steyer, R., Schwenkmezger, P., Notz, P., Eid, M., 1997. Der Mehrdimensionale Befindlichkeitsfragebogen. Hogrefe.

Tulving, E., 1983. Elements of episodic memory. Oxford University Press.

van Ast, V.A., Cornelisse, S., Meeter, M., Joëls, M., Kindt, M., 2013. Time-dependent effects of cortisol on the contextualization of emotional memories. Biol. Psychiatry 74 (11), 809–816. doi:10.1016/j.biopsych.2013.06.022.

VanElzakker, M., Zoladz, P., Thompson, V., Park, C., Halonen, J., Spencer, R., Diamond, D., 2011. Influence of pre-training predator stress on the expression of c-fos mRNA in the hippocampus, amygdala, and striatum following long-term spatial memory retrieval. Front. Behav. Neurosci. 5. https://www.frontiersin.org/articles/10.3389/fnbeh.2011.00030.

Vogel, S., Fernández, G., Joëls, M., Schwabe, L., 2016. Cognitive adaptation under stress: a case for the mineralocorticoid receptor. Trends Cogn. Sci. 20 (3), 192–203. doi:10.1016/j.tics.2015.12.003.

Vogel, S., Kluen, L.M., Fernández, G., Schwabe, L., 2018. Stress leads to aberrant hippocampal involvement when processing schema-related information. Learn. Mem. 25 (1), 21–30. doi:10.1101/lm.046003.117.

Vogel, S., Schwabe, L., 2016. Stress in the zoo: Tracking the impact of stress on memory formation over time. Psychoneuroendocrinology 71, 64–72. doi:10.1016/j.psyneuen.2016.04.027.

Walther, A., Nili, H., Ejaz, N., Alink, A., Kriegeskorte, N., Diedrichsen, J., 2016. Reliability of dissimilarity measures for multi-voxel pattern analysis. Neuroimage 137, 188–200. doi:10.1016/j.neuroimage.2015.12.012.

Wammes, J., Norman, K.A., Turk-Browne, N., 2022. Increasing stimulus similarity drives nonmonotonic representational change in hippocampus. ELife 11, e68344. doi:10.7554/eLife.68344.

Wang, Q., Bui, V.K., Song, Q., 2015. Narrative organisation at encoding facilitated children's long-term episodic memory. Memory 23 (4), 602–611. doi:10.1080/09658211.2014.914229.

Weiner, K.S., Sayres, R., Vinberg, J., Grill-Spector, K., 2010. fMRI-adaptation and category selectivity in human ventral temporal cortex: regional differences across time scales. J. Neurophysiol. 103 (6), 3349–3365. doi:10.1152/jn.01108.2009.

Weymar, M., Schwabe, L., 2016. Amygdala and emotion: the bright side of It. Front. Neurosci. 10. https://www.frontiersin.org/article/10.3389/fnins.2016.00224.

Wirz, L., Bogdanov, M., Schwabe, L., 2018. Habits under stress: mechanistic insights across different types of learning. Curr. Opin. Behav. Sci. 20, 9–16. doi:10.1016/j.cobeha.2017.08.009.

Wirz, L., Wacker, J., Felten, A., Reuter, M., Schwabe, L., 2017. A deletion variant of the α2b-adrenoceptor modulates the stress-induced shift from “Cognitive” to “Habit” memory. J. Neurosci. 37 (8), 2149–2160. doi:10.1523/JNEUROSCI.3507-16.2017.

Zhou, J., Benson, N.C., Kay, K.N., Winawer, J., 2018. Compressive temporal summation in human visual cortex. J. Neurosci. 38 (3), 691–709. doi:10.1523/JNEUROSCI.1724-17.2017.

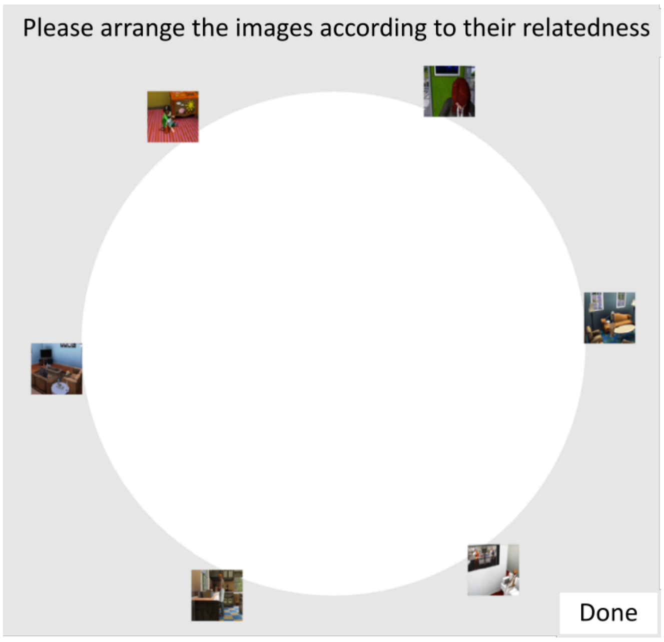
Supplementary material

Stress disrupts insight-driven mnemonic reconfiguration in the medial temporal lobe

Anna-Maria Grob[1], Branka Milivojevic[2], Arjen Alink[3], Christian F. Doeller[4,5,6], Lars Schwabe[1]

[1]Department of Cognitive Psychology, Institute of Psychology, Universität Hamburg, 20146 Hamburg, Germany; [2]Radboud University, Donders Institute for Brain, Cognition and Behaviour, 6525 AJ Nijmegen, the Netherlands; [3]Department of General Psychology, Institute of Psychology, Universität Hamburg, 20146 Hamburg, Germany; [4]Max-Planck-Insitute for Human Cognitive and Brain Sciences, 04103 Leipzig, Germany, Germany; [5]Kavli Institute for Systems Neuroscience, Centre for Neural Computation, The Egil and Pauline Braathen and Fred Kavli Centre for Cortical Microcircuits, Jebsen Centre for Alzheimer's Disease, Norwegian University of Science and Technology, 7491 Trondheim, Norway; [6]Wilhelm Wundt Institute of Psychology, 04109 Leipzig University, Leipzig, Germany

Corresponding author: Lars.Schwabe@uni-hamburg.de



Please arrange the images according to their relatedness

Fig. S1. Multiple arrangements task. Participants were instructed to arrange representative images of the video events (A, B, and X) of each story according to their relatedness on a two-dimensional circular arena in a multiple arrangements task (Kriegeskorte & Mur, 2012). They were asked to bring the pictures that had been linked (A and B) one week earlier closer together than the pictures that had not been linked (A and X, B and X) by dragging and dropping them with the computer mouse within a white circular arena on the computer screen.

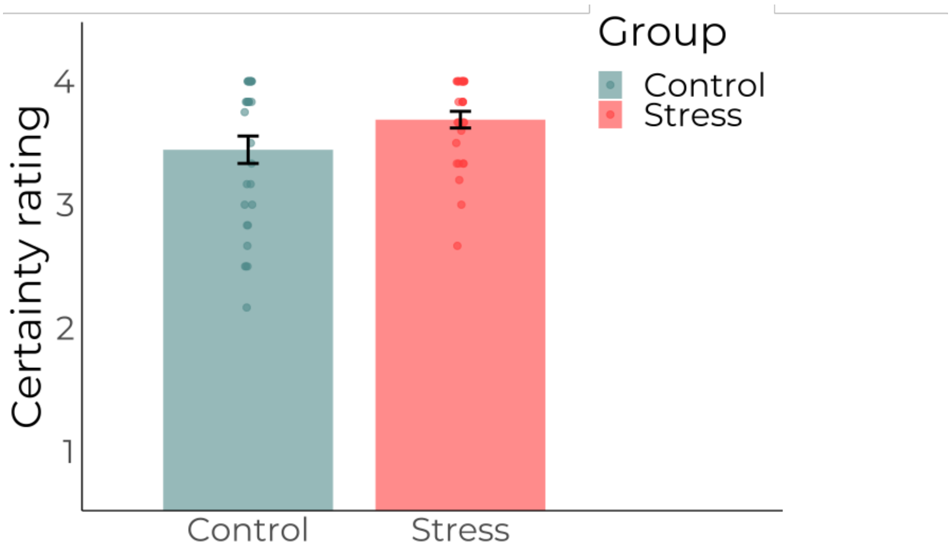


Fig. S2. Certainty ratings in cued recall. High certainty in the cued recall for both groups. Data represents means (+/- SE).

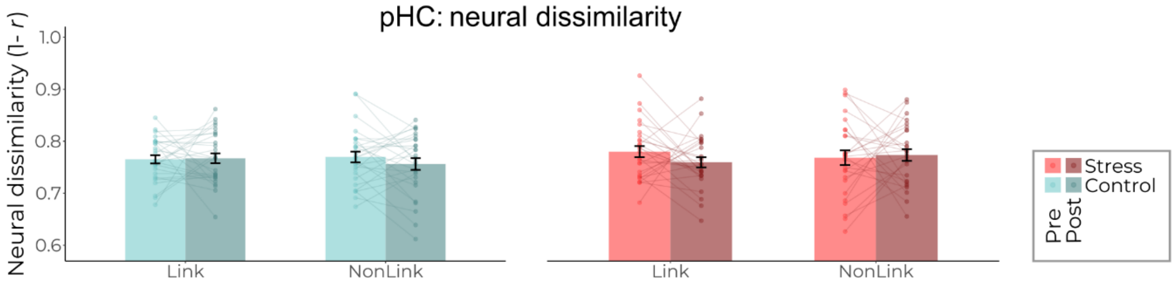


Fig. S3. RSA results for posterior hippocampus (pHC). Non-significant differences between pre- and post-insight for linked and non-linked events in the right posterior hippocampus in controls and the stress group. Data represents means (+/- SE).

Table S1. T-tests for motion regressors overall and for each block.

	Stress		Control		
Motion	*M*	*SD*	*M*	*SD*	p_{corr}
Overall					
Trans_X	-.00	.15	0.03	0.14	1.00
Trans_Y	.17	0.31	0.17	0.31	1.00
Trans_Z	0.09	0.50	0.27	0.62	1.00
Rot_Pitch	0.00	0.01	0.00	0.01	1.00
Rot_Roll	-0.00	0.00	-0.00	0.00	1.00
Rot_Yaw	-0.00	0.00	0.00	0.00	.156
Block 1					
Trans_X	0.01	0.18	0.04	0.16	1.00
Trans_Y	0.22	0.39	0.26	0.35	1.00
Trans_Z	-0.06	0.66	-0.02	1.09	1.00
Rot_Pitch	0.01	0.01	0.01	0.01	1.00
Rot_Roll	0.00	0.00	-0.00	0.01	1.00
Rot_Yaw	-0.00	0.00	0.00	0.00	.120
Block 2					
Trans_X	0.02	0.18	0.04	0.17	1.00
Trans_Y	0.14	0.56	0.23	0.48	1.00
Trans_Z	0.23	0.74	0.48	0.99	1.00
Rot_Pitch	0.00	0.01	0.00	0.02	1.00
Rot_Roll	0.00	0.01	0.00	0.01	1.00
Rot_Yaw	-0.00	0.00	0.00	0.00	.540

Block 3					
Trans_X	-0.03	0.23	0.02	0.16	1.00
Trans_Y	0.16	0.42	0.02	0.33	1.00
Trans_Z	0.11	0.82	0.37	0.76	1.00
Rot_Pitch	0.00	0.02	-0.00	0.01	1.00
Rot_Roll	-0.00	0.00	-0.00	0.00	1.00
Rot_Yaw	-0.00	0.01	0.00	0.00	.888

Note. Translational motion (Trans_X, Trans_Y, Trans_Z) and rotational motion (Rot_Pitch, Rot_Roll, Rot_Yaw) relative to first MR image averaged for each participant. Motion data averaged over total scanning time, over first block, over second block, and over third block. P_{corr} values from t-tests are provided. Data represents means (+/- SD).

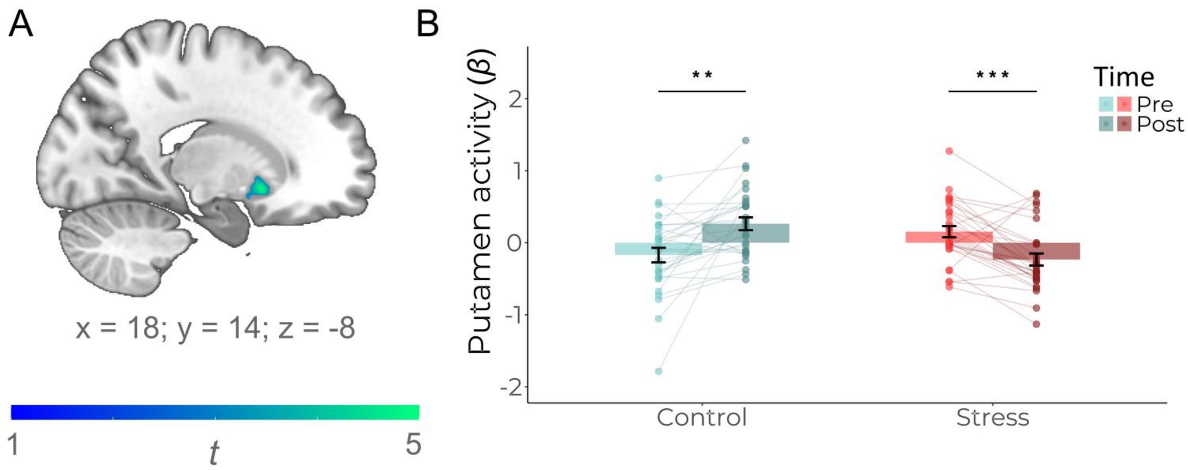


Fig. S4. Change in putamen activity. **A**, Significant decreases in stressed participants (vs. controls; $\text{Link}_{post} > \text{Link}_{pre}$) from pre to post insight in the right putamen (whole-brain cluster-level: x = 18, y = 14, z = -8; $t_{(1,57)} = 4.95$, $p_{corr}(\text{FWE}) = .005$, $k = 215$). Only cluster of interest is displayed in sagittal view, superimposed on a T_1-template image. **B**, Cluster activity of the right putamen for stressed participants and controls pre- and post-insight. Data represents means (+/- SE); $^{**}p < .01$, $^{***}p < .001$.

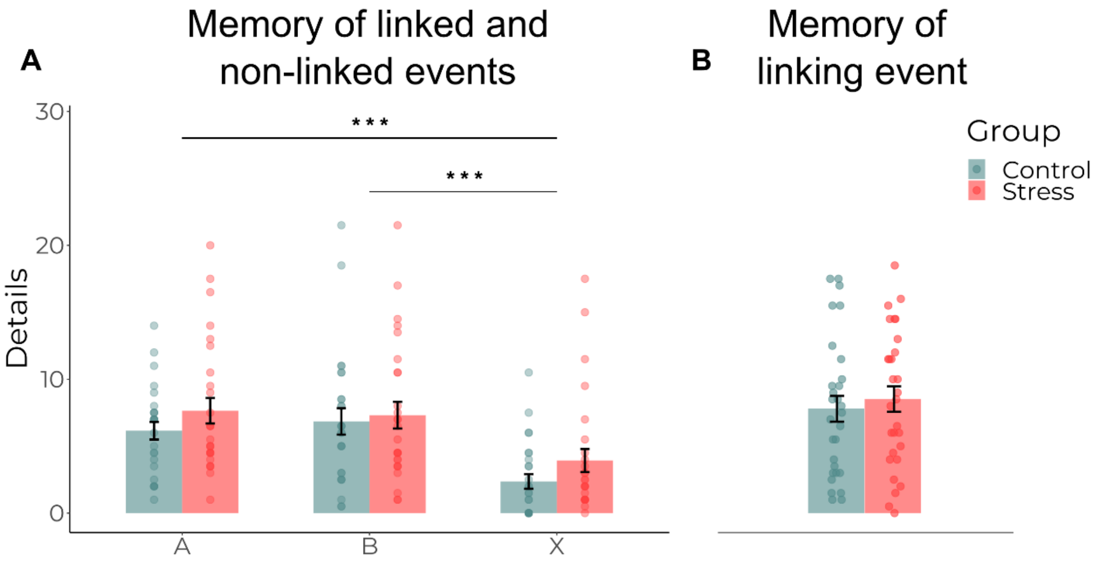


Fig. S5. Details from free recall. **A**, Significant differences between details recalled for A and X and B and X for both, the stress and the control group. **B**, Details recalled for the link event (L). There were no differences between the groups. Data represents means (+/- SE); ***p < .001.

Appendix B: Study 2

Grob, A.-M., Milivojevic, B., Alink, A., Doeller, C. F., & Schwabe, L. (2023). Imagining is not seeing: lower insight-driven memory reconfiguration when imagining the link between separate events. *Cerebral Cortex*, 33(12), 7409–7427, https://doi.org/10.1093/cercor/bhad048

Cerebral Cortex, 2023, **33**, 7409–7427
https://doi.org/10.1093/cercor/bhad048
Advance access publication date 25 March 2023
Original Article

Imagining is not seeing: lower insight-driven memory reconfiguration when imagining the link between separate events

Anna-Maria Grob[1], Branka Milivojevic[2], Arjen Alink[3,4], Christian F. Doeller[5,6,7], Lars Schwabe[1,*]

[1]Department of Cognitive Psychology, Institute of Psychology, Universität Hamburg, Hamburg 20146, Germany,
[2]Donders Institute for Brain, Cognition and Behaviour, Radboud University, Nijmegen 6525AJ, The Netherlands,
[3]Department of General Psychology, Institute of Psychology, Universität Hamburg, Hamburg 20146, Germany,
[4]Department of Systems Neuroscience, University Medical Center Hamburg-Eppendorf, Hamburg 20246, Germany,
[5]Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig 04103, Germany,
[6]Kavli Institute for Systems Neuroscience, Centre for Neural Computation, The Egil and Pauline Braathen and Fred Kavli Centre for Cortical Microcircuits, Jebsen Centre for Alzheimer's Disease, Norwegian University of Science and Technology, Trondheim 7491, Norway,
[7]Wilhelm Wundt Institute of Psychology, Leipzig University, Leipzig 04109, Germany

*Corresponding author: Department of Cognitive Psychology, Universität Hamburg, Institute of Psychology, Von-Melle-Park 5, Hamburg 20146, Germany.
Email: Lars.Schwabe@uni-hamburg.de

Gaining insight into the relationship between previously separate events allows us to combine these events into coherent episodes. This insight may occur via observation or imagination. Although much of our reasoning occurs in the absence of direct sensory stimuli, how mnemonic integration is accomplished via imagination has remained completely unknown. Here, we combined fMRI with representational similarity analysis and a real-life-like narrative-insight task (NIT) to elucidate the behavioral and neural effects of insight through imagination (vs. observation). Healthy participants performed the NIT in the MRI scanner and underwent memory testing one week later. Crucially, participants in the observation group gained insight through a video, while participants in the imagination group gained insight through an imagination instruction. Although we show that insight via imagination was weaker than insight via direct observation, the imagination group showed better detail memory. Moreover, the imagination group showed no representational change in the anterior hippocampus or increases in frontal and striatal activity for the linked events, as was the case in the observation group. However, the hippocampus and striatum were more activated during linking via imagination, which might indicate that their increased recruitment during imagination impedes concurrent mnemonic integration but may facilitate long-term memory.

Key words: fMRI; imagination; insight; memory integration; hippocampus; striatum; prefrontal cortex.

Our memories are highly dynamic and can be recombined with remarkable flexibility. When we gain insight into how two seemingly separate events are connected, we are able to flexibly integrate these initially discrete events into coherent episodes. These new, overlapping memory representations occur when new learning experiences share a common element with preexisting memory traces, thus prompting the integration of novel information into the existing memory network (Schlichting and Preston 2017). For instance, when we watch a movie, we sometimes experience a "plot twist," a moment when we realize how earlier, seemingly unrelated scenes are actually connected. This fundamental process of mnemonic integration is thought to underlie a variety of flexible behavior, ranging from decision-making (Wimmer and Shohamy 2012; Shohamy and Daw 2015) or inferring novel relationships (Eichenbaum et al. 1999; Zeithamova and Preston 2010; Zeithamova et al. 2012) to spatial navigation (Gupta et al. 2010; He et al. 2022). In daily life, the relationship of two seemingly unrelated events is often not directly observed but is imagined. For instance, instead of watching a movie, we can also read the book and gain insight into the plot and possible twists through our own imagination. Gaining insight via imagination bears particular importance in educational settings, where existing discrete units of knowledge are brought together by imagination, triggered by reading or hearing about an event, rather than by direct sensory experience. Imaginative techniques, such as the loci method, have been repeatedly shown to benefit memory in early research (Bower 1970; Yesavage and Rose 1984; Hockley and Christi 1996) and have proven valuable from educational settings to memory championships (Maguire et al. 2003; Richmond et al. 2008). Moreover, previous research demonstrated a memory advantage for deep versus shallow (i.e. perception-based) encoding (Craik and Lockhart 1972; Kapur et al. 1994; Otten et al. 2001; Ritchey et al. 2011). However, despite the importance of imagination for the integration of event knowledge in educational settings and its importance as a mnemonic strategy, previous research on memory integration has focused almost exclusively on integration through direct experience by presenting the unknown connection directly to the observer. Thus, to date, it remains largely unclear exactly how mnemonic integration is accomplished through imagination.

The ability to imagine future or novel scenarios appears to be intimately linked to episodic memory. Studies in patients with medial temporal lobe (in particular, hippocampal) damage revealed that many of these patients lost not only their episodic memory but also their ability to imagine future events

Received: November 24, 2022. **Revised:** February 1, 2023. **Accepted:** February 2, 2023
© The Author(s) 2023. Published by Oxford University Press. All rights reserved. For permissions, please e-mail: journals.permission@oup.com

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

(Tulving 1985; Hassabis et al. 2007; Squire et al. 2010; Race et al. 2011). Likewise, neuroimaging studies showed similar brain activity during recollection and imagination, encompassing brain regions such as the hippocampus (Addis et al. 2009; Benoit and Schacter 2015; Bellana et al. 2017; Benedek et al. 2018). These data led to the "prospective brain" hypothesis, which postulates that the brain uses stored information to imagine, plan, and predict future events (Schacter et al. 2007). The capacity to construct a scene, whether remembered or imagined, depends on the hippocampus, which continuously constructs event representations beyond concrete perception (Gaesser et al. 2013; Maguire and Mullally 2013; Zeidman and Maguire 2016; Barry et al. 2019; Clark et al. 2019).

Beyond imagination, the hippocampus is also critically implicated in mnemonic integration (Collin et al. 2015; Schlichting et al. 2015). To accomplish mnemonic integration, the hippocampus can separate patterns of activity which reduce interference between memory representations, (Marr 1971; McClelland et al. 1995; Norman and O'Reilly 2003; Huffman and Stark 2014; Libby et al. 2019; Brunec et al. 2020) as well as combine related memories into integrated memory representations (Collin et al. 2015; Horner et al. 2015; Milivojevic et al. 2015; Schlichting et al. 2015; Schapiro et al. 2017; Brunec et al. 2020). These opposed processes of pattern separation and completion seem to depend on different parts of the hippocampus, as previous findings suggest a functional division along its longitudinal axis. While the anterior hippocampus has been associated with memory integration, the posterior hippocampus has been more implicated in memory separation (Collin et al. 2015, 2017; Milivojevic et al. 2015; Schlichting et al. 2015; Brunec et al. 2020). Thus, previous research suggests that the hippocampus plays a critical role in both imagination and memory integration, raising the question of whether memory integration can still be fully accomplished when the hippocampus is at least partially occupied by imagination. Until now, however, it remains completely unknown how insight into the relationship between two initially unrelated events comes about through imagination and what neural mechanisms are involved in imagination-based mnemonic integration.

Therefore, the present study aimed to elucidate the neural mechanisms and behavioral consequences of linking initially unrelated events through imagination. To this end, we combined fMRI with multivariate representational similarity analysis (RSA) and a modified life-like narrative-insight task (NIT; Milivojevic et al. 2015; Fig. 1). In this task, participants were first presented a series of unrelated events and then either saw or were asked to imagine how some of these events were linked. One week after encoding, we performed a comprehensive behavioral analysis of the memory for the linked (and nonlinked) events. These delayed memory tests included a free recall and a forced-choice recognition test as well as a multidimensional arena task (MAT) in which participants indicated how related they thought the events were. We hypothesized that insight through imagination is possible but is more difficult to achieve than insight through observation. Because the hippocampus has repeatedly been shown to be relevant to imaginative processes (Maguire and Mullally 2013; Zeidman and Maguire 2016), we predicted greater hippocampal involvement during the imagination relative to the presentation of a linking event. We further assumed that the hippocampal recruitment during imagination might affect its capacity to reconfigure the representation of the now linked events. Finally, we tested how these neural changes associated with imagination-based mnemonic integration would affect subsequent memory for the linked (vs. nonlinked) events.

Materials and methods

Participants

Fifty-six healthy, right-handed individuals (29 males, 27 females, age: $M = 25.68$ years, $SD = 3.97$ years) with normal or corrected-to-normal vision volunteered to participate in this study. Participants were screened using a standardized interview for exclusion criteria that included a history of neurological and psychiatric disease; medication use and substance abuse; cardiovascular, thyroid, or renal disease; body mass index <19 and >26 kg/m^2; evidence of COVID-19 infection or exposure; and contraindications to MRI examination. It was also ensured that every participant was proficient in the German language. All participants gave informed consent before participation and received a moderate monetary compensation (50€) at the end of the experiment. The procedures were approved by the local ethics committee (Faculty of Psychology and Human Movement Science, Universität Hamburg, Hamburg, Germany, 2017_143 Schwabe) and adhered to the Declaration of Helsinki. The sample size is in line with previous studies on imaginative processes and subsequent memory (Devitt and Schacter 2020) and is further corroborated by an a priori calculation using G*Power, indicating that a sample size of $n = 54$ is sufficient to detect a medium-sized effect ($f = 0.25$) for the crucial group × link effect with a power of 0.95.

We implemented a mixed-design including the within-subject factors link (linked vs. nonlinked events) and session (pre- vs. post-link) and the between-subjects factor group (imagination vs. observation). Participants were pseudorandomly assigned to one of the two groups to achieve a comparable number of men and women per group and a balanced assignment to the imagination and observation groups. However, this resulted in slightly different group sizes. The imagination group comprised 27 participants (13 females) and the observation group consisted of 29 participants (14 females).

Procedure

The experiment included two days, one week apart. All experiments took place in the afternoon or early evening (between 12 and 6 pm). Before the start of the first experimental day, participants completed questionnaires assessing imagination (FFIS; Zabelina and Condon 2019), trait-anxiety (STAI-T; Laux et al. 1981), depressive symptoms (BDI; Hautzinger et al. 2006), chronic stress (TICS; Schulz and Schlotz 1999), and personality dimensions (BFI-2; Danner et al. 2016). After verification of eligibility for MRI measurements by a radiologist, participants gave informed consent and completed a state-anxiety questionnaire (STAI-S; Laux et al. 1981) and sleep quality questionnaire (PSQI; Buysse et al. 1989). They then performed a training run, which was immediately followed by the measurement of a working memory task (*N*-back; Kirchner 1958) to control for differences in working memory. Next, they completed a training session of the modified NIT (Milivojevic et al. 2015; Fig. 1), a life-like video-based task that tests the integration of originally separate events into coherent episodes. Participants then completed three runs of the modified NIT in the MRI scanner. One week later, to assess episodic memory integration, participants performed a free recall, a forced-choice recognition test, and a MAT (Kriegeskorte and Mur 2012).

Day 1: working memory control task

To check for possible group differences in working memory, a measurement of working memory performance was performed before participants entered the MRI scanner. Working memory

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

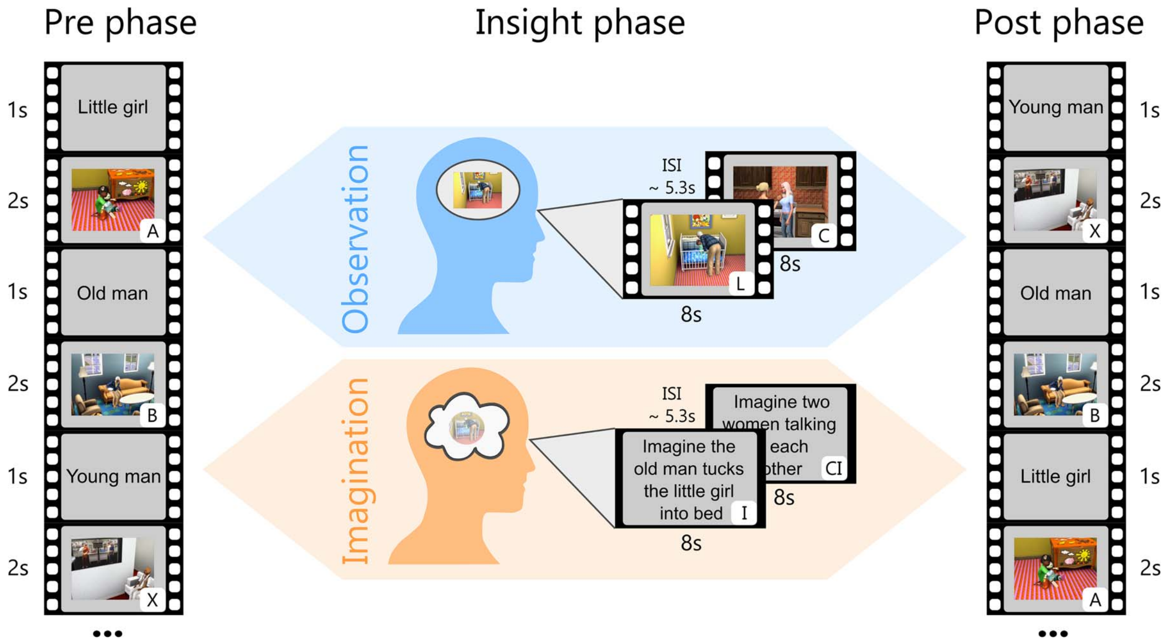


Fig. 1. Modified NIT. In a pre-insight phase, video events (A, B, and X) from each of 6 story lines were each preceded by a title (1 s) and repeated for 6 times. The ISI in the pre phase between an event and the next title was ∼5.3 s. In a subsequent insight phase, some events could be integrated (events A and B) into narratives. Critically, while some participants saw a linking video (L) intertwined with a control video (C; observation group), others saw a written imagination instruction (I) intertwined with a control imagination instruction (CI; imagination group). The other event (X) was left nonlinked. In a post-insight phase, all video events were presented in exactly the same manner as in the pre-insight phase. Please note that texts were presented in German during the experiment and are translated here.

was measured with an *N*-back task (Kirchner 1958). In this task, participants were presented with single-digit numbers from 0 to 9 and were asked whether the number on the screen ("target") was the same number as the number presented in *n*-trials before ("cue"). Working memory load was manipulated by using two levels of complexity: 3- and 4-back trials. In addition to these two load levels, participants executed a control task (0-back) in which they had to indicate whether the current number was a 0. Responses were made either by pressing the left button ("no") or by pressing the right button ("yes") if the target number was identical to or different from the cue. The selected response was highlighted. In total, participants were shown six pseudorandomized blocks consisting of two blocks from each level (0, 3, and 4 back). All blocks consisted of 20 numbers in random order. The numbers were presented for 500 ms and were separated by a delay of 1.5 s. The blocks were separated by 5 s. Before each block, participants were informed of the type of cognitive task ahead (0-, 3-, or 4-back).

Day 1: modified NIT

In the MRI scanner, participants underwent a modified version of the NIT (Milivojevic et al. 2015), while functional images were recorded. In this task, participants were presented with videos of life-like events from the computer game *The Sims* 3 that belonged to several different storylines. In total, participants saw six different storylines. The videos from each storyline could either be integrated (events A and B) into narratives or not (A and X; see Fig. 1). Unbeknownst to the participant, each narrative had two possible versions to control for nonspecific stimulus effects and visual similarity. The two narrative versions comprised an identical event A, but different events B. Control event X from one version served as event B in the other version. Therefore, all participants saw the same events A, B, and X, but 30 participants linked events A and X, while 26 participants linked events A and B. In the following, the linked events will always be referred to as events A and B, whereas the nonlinked events will be referred to as A and X. To elucidate the underlying mechanisms of mnemonic integration, two different insight conditions were introduced into the task: imagination and observation.

Each story was presented in three phases: pre-insight phase, insight phase, and post-insight phase (Fig. 1). In the *pre-insight phase*, all participants were presented with events A, B, and X for 2 s each, separated by interstimulus intervals (ISIs) of 1, 4, or 11 s (∼5.3 s on average). Each video was preceded by a short title (1 s) and was presented 6 times in a pseudorandom order such that each video was shown before the next round of presentations began and the same video was not presented on two consecutive trials. After the pre-insight phase, participants had to indicate on a scale from not at all (1) to very much (4) how much they thought the events belonged together. In the subsequent *insight phase*, the task differed according to whether participants were in the imagination or the observation condition. Participants in the observation condition viewed the linking video event (L) intertwined with a control video event (C), each presented for 8 s and repeated six times (ISIs of 1, 4, or 11 s, ∼5.3 s on average). Participants in the imagination condition, however, were presented with an instruction (I) to imagine a specific linking scene using the titles from each video to indicate which person was meant, interleaved with a control instruction (CI), each presented for 8 s and repeated six times (ISIs of 1, 4, or 11 s, ∼5.3 s on average). Participants were instructed to imagine specific scenes only when specifically asked to do so; otherwise, they were told to simply relax and watch the videos or answer the rating questions. In the observation condition, the linking video (L) showed the main characters from videos A and B interacting with each other, while the control video (C) showed only an unknown character engaged in an unrelated activity (e.g. two women talking to each other). In the imagination

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

condition, the linking instruction (I) instructed them to imagine the main characters from videos A and B interacting with each other, while the control instruction (CI) asked them to imagine an unknown character engaged in an unrelated activity (e.g. two women talking to each other). After the insight phase, participants completed several ratings regarding the understanding of the link and adherence to instructions on a scale ranging from not at all (1) to very much (4). In the final *post-insight phase*, all participants were again presented with events A, B, and X presented for 2 s each, repeated six times, and separated by ISIs of 1, 4, or 11 s (~5.3 s on average). Each video was again preceded by a short title (1 s). Events in the post-insight phase were also presented in a pseudorandom order to reduce potential sequence effects. The main purpose of this phase was to assess the changes in the neural representation of events A and B after they learned that they were linked. After the post phase, participants had to indicate again how much they thought that the events belonged together on a scale from not at all (1) to very much (4). Participants received visual feedback when they entered a rating question by highlighting the selected response. In addition to presenting A, B, and X events in the pre- and post-insight phases, we also presented target events to which participants responded by pressing a button with the index finger of their right hand. These target events accounted for 11% of trials in the pre- and post-insight phases and consisted of a 2 s animated video of a girl on a pink scooter. These target trials were recorded to ensure that participants remained vigilant throughout the experiment.

Day 2: free recall

To assess the detailedness of memory one week after encoding, participants were instructed to recall the events presented on day 1 in as much detail as possible. During free recall, they were voice recorded for a maximum of 15 min. To assess the level of detailedness of the integrated episodes, audio recordings from free recall were scored according to how much detail of the different video events (A, B, and X) were recalled from day 1. The rating scheme was such that it allowed for separate coding of details remembered for the A, B, and X events. The video events (A, B, and X) from the different stories did not differ in how many details could be named (*event*: $F(1.67, 8.37) = 2.93$, $P = 0.114$, $\eta_G = 0.296$; mean A = 21.83; *SD* A = 4.62; mean B = 19.17; *SD* B = 3.71; mean X = 25.50; *SD* X = 4.76). The raters were instructed to assign details only to events where it was clear that they belonged exclusively to that event so that there was no confusion of details between different events. Two raters scored the first half of the data and another two raters scored the second half. All raters were blinded to the experimental conditions. To assess the interrater reliability, all raters rated the first five participants, and on average, these ratings were highly correlated with each other (*mean correlation* = 0.83, *SD* = 0.06). To obtain a better estimate of intersubjectivity, these ratings were averaged. The details for the different event types (A, B, and X) were summed across stories to obtain an overall rating of event details. The mean of the linked events (A and B) was then calculated to obtain a measure of linked events. The nonlinked event (X) was left as it was.

Day 2: MAT

To estimate the representational structure of episodic memory, participants were asked to arrange representative images of the video events (A, B, and X) of each story according to their relatedness on a 2D circular arena in a MAT (Kriegeskorte and Mur 2012; Supplementary Fig. S1). They were asked to bring the pictures that had been linked (A and B) one week earlier closer together than the pictures that had not been linked (A and X) by dragging and dropping them with the computer mouse inside a white circular arena on the computer screen. Thus, participants were instructed to group the events according to the extent to which they were related in the NIT. The images were large enough on the computer screen to be recognized by all participants. All trials were self-paced and could be completed by the participants by pressing "Done". In the first trial, participants had to order all pictures by similarity and were instructed to do so carefully. Subsequent trials consisted of subsets of the first trial selected based on an adaptive procedure aimed at minimizing uncertainty and better approximating the high-dimensional perceptual representational space. This procedure is based on an algorithm optimized to provide optimal evidence for the dissimilarity estimates (Kriegeskorte and Mur 2012). The distances in this MA task were calculated by first computing the squared screen distance (Euclidean distance) between all elements in the first trial to create a roughly estimated representative dissimilarity matrix (RDM) and by iteratively updating this RDM by the weighted average of the scaled trial estimates. This MA task took 10 min to complete.

Day 2: forced-choice recognition test

To also have an estimate of correct recollection for linked versus nonlinked events, participants completed a forced-choice matching task. They were presented with an image of event A at the top of the computer screen and had to indicate whether the image of B or X in the bottom half of the screen belonged to A. Participants were presented with these forced-choice options for each of the stories they had seen a week before. After indicating for a story which event belonged to event A, they had to rate how confident they were in their answer. Confidence was rated on a scale from not at all (1) to very sure (4). This was repeated for each of the six stories. Participants were presented with the forced-choice question and the confidence rating for 5.5 s each, which were separated by ISIs of 1, 4, or 11 s (~5.3 s on average). Participants received visual feedback when they entered a rating question by highlighting the selected response. The forced-choice recognition test lasted for approximately 2–3 min.

Analysis

Behavioral and physiological data analysis

To assess the degree of insight-related mental reorganization, the ratings for the event duplets of interest (AB and AX) from the pre- and post-insight phases were entered into a mixed 2 × 2 × 2 ANOVA with the between-subjects factor group and the within-subject factors time (pre/post) and link (link/nonlink). To evaluate the long-term representation of the integrated events, performance in forced-choice recognition was assessed by calculating the proportion of correct answers. These performance measures (in %) were then entered into a two-sample *t*-test with the between-subjects factor group. To analyze the representational structure of memory, Euclidian dissimilarity estimates were extracted from the MAT for linked (AB) and nonlinked events (AX), averaged across stories, and then entered into a mixed 2 × 2 ANOVA with the between-subjects factor group and the within-subject factor link (link/nonlink). Details from free recall were entered into a mixed 2 × 2 ANOVA with the between-subjects factor group and the within-subject factor item (link/nonlink).

All analyses were performed in R version 4.0.4 (https://www.r-project.org/). In case of violation of sphericity, as indicated by the Mauchly test, Greenhouse–Geisser corrected degrees of freedom and *P*-values are reported. Prior to analysis, data were checked for outliers. Outliers were defined as median +/−3 *SD*. For the

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

analysis of the modified NIT, four outliers were identified and excluded (two from the imagination and two from the observation group). For the analysis of the MAT, two outliers were identified and excluded (one from the imagination and one from the observation group). For the free recall analysis, two outliers were identified and excluded (one from the imagination and one from the observation group). For the RSA, one outlier was identified and removed (observation group). These outliers consisted of eight different individuals, as one individual was an outlier in both the NIT and the MAT. Presumably, those identified here as outliers did not understand the tasks as well compared to the other participants.

MRI acquisition and analysis

Imaging data were acquired on a 3T Siemens PRISMA scanner (Siemens, Germany) with a 64-channel head coil. Data were collected on three functional runs, which were separated by short pauses. We used a custom 3D echo-planar imaging (EPI) pulse sequence acquiring interleaved slices with the following parameters: TR = 2,000 ms; TE = 30 ms; flip angle = 60°; volume resolution = 2 mm^3; slices = 62; approx. 530 volumes per run; field of view (FoV) = 224 mm; acceleration factor PE = 2. Additionally, a structural T1-weighted image was acquired using a MPRAGE-grappa sequence with the following parameters: TR = 2,500 ms; TE = 2.06 ms; flip angle = 9°; voxel resolution = 0.8 mm^3; slices = 256; FoV = 244 mm; 3D acceleration factor = 1 at the end of the MRI session.

fMRI data preprocessing

Preprocessing and analysis of the fMRI data were performed using functions of the SPM 12 toolbox (Wellcome Trust Centre for Neuroimaging, London, UK) and custom scripts. To allow for magnetic field (T1) equilibration, the first three functional scans were discarded. First, the functional images were spatially realigned and were slice-time corrected. Then, the functional images were coregistered with the structural image by coregistering the structural image to the mean EPI. For multivariate analysis (see below), images were not preprocessed further. For univariate analysis (see below), functional images were normalized to the MNI template and were then smoothed with a 6-mm^3 full-width at half maximum Gaussian kernel.

The results of the neural analyses were considered as significant at a family-wise error (FWE)-corrected threshold of $P < 0.050$. To test our hypotheses, we performed, in addition to more explorative whole-brain analyses, region of interest (ROI) analyses with a priori-defined ROIs using small-volume correction (SVC; $P < 0.050$, FWE-corrected) with an initial threshold of $P < 0.001$ as uncorrected. As the hippocampus has been found to be involved in imaginative processes (Addis et al. 2009; Benoit and Schacter 2015; Zeidman and Maguire 2016; Barry et al. 2019), we focused on the hippocampus for our ROI analyses. The hippocampus was split into posterior and anterior subregions, as these have been found to be differentially implicated in mnemonic integration and separation processes (Collin et al. 2015; Robin and Moscovitch 2017; Dandolo and Schwabe 2018). Our hippocampal masks were derived from previous work using the WFU pick-atlas: pHC from $Y = -40$ to -30, and aHC from $Y = -18$ to -4 (Collin et al. 2015; Dandolo and Schwabe 2018). We corrected for the number of ROIs in the specific analyses by applying Bonferroni correction (P_{corr}).

Univariate fMRI analysis

For univariate fMRI analysis, data from all three runs were concatenated to allow estimation of neural responses using all acquired data. The concatenated time series were analyzed using a generalized linear model (GLM) as implemented in SPM12. This model included one regressor per event type (A, B, and X) during each phase (pre- and postlink). Each of these six event regressors of interest modeled 36 trials (six trials per each of the six different stories). Each model also included the following nuisance regressors: regressors for the link videos and control videos or the imagination instructions and the CIs in the insight phase, and one regressor for the 24 target events (girl on the pink scooter). All analyses also included six concatenated nuisance regressors to control for head movement as well as three run constants. All task regressors and the nuisance task regressors of no interest were convolved with the canonical hemodynamic response function to obtain a modeled time course of neuronal activity. A high-pass filter of 128 s was used to remove low-frequency drifts, and serial correlations in the time series were accounted for using an autoregressive AR(1)-model. To analyze the neural basis of the change from pre- to post-insight, we computed a contrast comparing postlink events with prelink events ($AB_{post} > AB_{pre}$) and a contrast comparing post nonlink events with pre nonlink events ($X_{post} > X_{pre}$). These contrast images were analyzed at the group level using a two-sample *t*-test.

Univariate fMRI analysis: insight phase

For the analysis of the insight phase, data from all three runs were concatenated to allow estimation of neural responses using a GLM. This model included individual regressors for all event types (A, B, X, L/I, and C/CI). Critically, to measure the strength of insight during the insight phase, we also included two parametric modulators reflecting the information gained through the link video (or instruction) or the control video (or instruction). To assess the level of insight, the parametric regressor was defined as: decreasing values from the first repetition (6) to the last repetition (1) for both link events (L/I) and control events (C/CI). Critically, this model with its decreasing parametric modulation was set up to focus on the insight gained, which should be greatest at the beginning, as well as to counteract potential repetition effects in the imagination condition (Mulukom et al. 2013). Each model also included the following nuisance variables: one regressor for the 24 target events, six concatenated nuisance regressors to control for head movement as well as three run constants. All task regressors and the nuisance task regressors of no interest were convolved with the canonical hemodynamic response function to obtain a modeled time course of neuronal activity. A high-pass filter of 128 s was used to remove low-frequency drifts, and serial correlations in the time series were accounted for using an autoregressive AR(1)-model. For each participant, contrast images across the six stories were calculated for the insight phase in general, which were then taken to the second-level group analysis. Two-sample *t*-test analyses were performed at the second level.

Functional connectivity analysis

To analyze the crosstalk of the brain areas identified in the previous analyses with other brain areas related to the processes underlying episodic integration during linking, we performed a psychophysiological interaction (PPI) analysis to measure task-dependent connectivity using the bilateral caudate nuclei as seed regions, as the caudate nucleus yielded the highest univariate increases from pre- to post-insight for linked events in the observation group compared to the imagination group. Furthermore, higher connectivity between the caudate and the hippocampus has been linked to better imagination and memory performance

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

in previous studies (Müller et al. 2018; Faul et al. 2020). Hence, the first eigenvariate of the activity time course of the specific ROI for the link contrast (Link Events > Control Events) was extracted using an anatomical mask and included as a seed in the PPI. A first-level model was set up, including the seed region, a vector coding the contrast of interest and an interaction term, which was computed as an element-by-element product of the first two regressors. The resulting interaction contrasts were brought to the second level to test whether functional connectivity between regions differed between the imagination and observation groups.

We further analyzed the connectivity for the change contrast in the nonlinked event by performing a PPI analysis using the bilateral dorsolateral prefrontal cortex (dlPFC), as this region has been shown to be important in a previous univariate analysis and to be important for relational memory and insight (Murray and Ranganath 2007; Long et al. 2010; Blumenfeld et al. 2011; Tik et al. 2018). Thus, the first eigenvariate of the activity time course of the specific ROI for the nonlink contrast ($X_{post} > X_{pre}$) was extracted using an anatomical mask and included as a seed in the PPI. A first-level model was set up, including the seed region, a vector coding the contrast of interest and an interaction term, which was computed as an element-by-element product of the first two regressors. The resulting interaction contrasts were brought to the second level to test whether functional connectivity between regions differed between the imagination and observation groups.

The results of both PPI analyses were corrected by a Bonferroni correction of four ROIs. In addition to the anterior and posterior hippocampus, we also corrected for the seed regions of both PPIs: the caudate nucleus and the dlPFC.

Multivariate analysis

To assess the changes in neural patterns induced by insight into the narrative structure of events and the modulation thereof by the mode of linking, we performed an RSA (Kriegeskorte et al. 2008) using the rsatoolbox (Nili et al. 2014). We focused on the hippocampal long axis since its subregions have been differentially associated with memory integration as well as segregation — two processes that are critical for episodic memory integration (Milivojevic et al. 2015; Schlichting et al. 2015; Collin et al. 2017; Robin and Moscovitch 2017; Brunec et al. 2018; Dandolo and Schwabe 2018). At the first level, functional images from all three runs were concatenated to allow for the estimation of neural responses using a GLM. The analysis was performed in native space and, thus, only nonnormalized and nonsmoothed images were included in the GLM. This model included individual regressors for each event type by phase (A_{pre}, B_{pre}, X_{pre}, L, C, A_{post}, B_{post}, and X_{post}) in each of the six storylines separately. Thus, each event-regressor modeled six trials. Each model also included the following additional nuisance regressors: one regressor for the 24 target events, six concatenated nuisance regressors to control for head movement as well as three run constants. All task regressors and the nuisance task regressors of no interest were convolved with the canonical hemodynamic response function, resulting in a modeled time course of neuronal activity. Voxel-wise beta estimates resulting from the regressors of interest (A_{pre}, B_{pre}, X_{pre}, A_{post}, B_{post}, and X_{post}) were further transformed into t-statistics to account for the unreliability caused by noise (Walther et al. 2016). In a second analysis step, we back-transformed the ROIs from MNI space to subject-space for each participant individually. The computation of representational dissimilarity matrices (RDMs) for each ROI and each subject was, thus, performed in the native space of each participant. The resulting t-images from the regressors of interest were used to create vectors of activity pattern for each event, separately for each ROI. These activity patterns were used to calculate the dissimilarity between two trials by correlation distances ($1-r$, Pearson's rank order correlation). Dissimilarities for each combination were then entered into a 36 × 36 RDM. Dissimilarities for linked (AB_{pre} and AB_{post}) and nonlinked events (AX_{pre} and AX_{post}) pre- and post-insight were extracted for each story and were averaged across stories for each participant. These averaged dissimilarities were then entered into a mixed 2 × 2 × 2 × 2 ANOVA in R version 4.0.4 (https://www.r-project.org/) with the between-subjects factor group (imagination vs. observation) and the within-subject factors time (pre- vs. post), link (link vs. nonlink), and hippocampus (anterior vs. posterior). In addition, we performed an exploratory ROI RSA focused on the medial prefrontal cortex, as this region is of interest during mnemonic integration (Milivojevic et al. 2015), using the same approach as for the hippocampal long axis.

To shed light on possible representational changes beyond the hippocampus, we also performed an RSA using a whole-brain searchlight approach with the rsatoolbox (Nili et al. 2014). For this purpose, we used the same GLM as for the ROI RSA, i.e. we performed the searchlight RSA in the native space of each participant. The resulting t-images from the regressors of interest (A_{pre}, B_{pre}, X_{pre}, A_{post}, B_{post}, and X_{post}) were used to create vectors of activity patterns for each event. We then calculated the correlation (Pearson's rank order correlation) between the activity patterns within each searchlight consisting of a minimum of 30 voxels and measuring three voxels in radius and a theoretical model operationalizing the increase in dissimilarity for linked events as found in the ROI RSA for the right anterior hippocampus. The resulting statistics for a single individual were mapped back on the central voxel of each sphere, producing a neural similarity map for a single individual. After normalization and smoothing with a Gaussian kernel of 6 mm^3, these neural similarity maps were taken to the second-level group analysis. Two-sample t-test analyses were performed at the second level and FWE-corrected P-values are reported.

Correlational analysis

To relate the findings from univariate analyses to the behavioral results, we extracted the peak voxel contrast values of interest in each ROI using the MarsBar toolbox (Brett et al. 2002). Subsequently, the correlation between the extracted neural peak activity of each ROI and behavioral outcomes was estimated by correlating neural activity with behavioral outcomes for the imagination and the observation groups separately and then testing these correlations against each other (Eid et al. 2017).

Results

Imagination results in weaker insight, but stronger memory than observation

To investigate the effects of the mode of insight on mnemonic integration, we used a modified NIT (Fig. 1). In this task, participants first watched three videos showing specific episodes (pre-insight phase). Then, participants were either presented a new (linking) event (L) that linked two of the previously viewed events (A and B) but left the third event unrelated (event X; *observation group*) or received a written instruction (I) to imagine the linking of these events (*imagination group*). Finally, the now linked or nonlinked events were presented again to examine the insight-related changes in representation (post-insight phase). In all these phases, participants were presented with target stimuli to which they were asked to respond, thus controlling

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

for attention during the task. Participants responded on average to 94.64% ($SD = 14.10\%$) of the target presentations without any group differences ($t_{(33.113)} = 0.94$, $P = 0.352$, $d = -0.26$). The groups adhered well to their instructions as participants in the imagination group indicated that they imagined the linking event very well ($M = 3.34$, $SD = 0.55$), while participants in the observation group indicated that they understood the presented linking event very well ($M = 3.34$, $SD = 0.43$). Participants in the imagination group also rated their imagination as rather depictive ($M = 3.31$, $SD = 0.61$), and participants in the observation group indicated that the link they saw made sense to them ($M = 3.37$, $SD = 0.43$). Participants in the imagination group engaged significantly more in imagination ($M = 3.34$, $SD = 0.62$) than did participants in the observation group ($M = 2.61$, $SD = 0.90$; observation vs. imagination: $t_{(49.788)} = -3.54$, $P < 0.001$, $d = 0.94$).

In the NIT, participants in the observation group showed better insight into the relationship between the originally separate events than did participants in the imagination group, thus revealing an immediate advantage of gaining insight via observation over gaining insight via imagination (group × time × link interaction: $F(1, 50) = 5.16$, $P = 0.027$, $\eta_G = 0.012$; Fig. 2A). A follow-up test indicated that the imagination group had lower link ratings for linked items post-insight compared to participants in the observation group ($t_{(33.104)} = -2.07$, $P = 0.046$, $d = 0.60$), while the imagination group tended to rate the nonlinked items post-insight as more related than the observation group ($t_{(34.065)} = 1.76$, $P = 0.088$, $d = -0.50$), pre-insight, there were no group differences (link: $t_{(48.074)} = 0.20$, $P = 0.844$, $d = 0.06$; nonlink: $t_{(48.643)} = 0.13$, $P = 0.893$, $d = 0.04$).

One week later, the performance in the free recall test showed that participants remembered those events that were linked one week before (A and B) in more detail than the event that remained nonlinked (X; item: $F(1, 52) = 29.35$, $P < 0.001$, $\eta_G = 0.150$), suggesting a memory advantage of linked over nonlinked events. Moreover, participants in the imagination group remembered overall more details than those in the observation group in the free recall (group: $F(1, 52) = 5.40$, $P = 0.024$, $\eta_G = 0.067$; group × item: $F(1, 52) = 1.04$, $P = 0.314$, $\eta_G = 0.006$; Fig. 2B), indicating a memory advantage for all events after linking via imagination compared to linking via observation. Consistent with the memory advantage of the imagination group, those in the imagination group who indicated that they imagined the linking event more strongly, while prompted to do so, also recalled more details about the events (average of A, B, and X) a week later ($r = 0.47$, $t_{(22)} = 2.52$, $P = 0.020$; Fig. 2C). While the imagination group outperformed the observation group in the free recall, there were neither group differences in the forced-choice recognition test ($M = 75.89\%$; $SD = 24.40\%$; $t_{(53.92)} = 0.56$, $P = 0.580$, $d = -0.15$; Fig. 2D) nor did the groups differ on the MAT (mean distance for linked events = 0.02, $SD = 0.02$; mean distance for nonlinked events = 0.05, $SD = 0.02$; link: $F(1, 50) = 138.63$, $P < 0.001$, $\eta_G = 0.297$;Fig. 2E). Interestingly, across both groups, those who recalled more details for linked events in the free recall also grouped the linked events in the MAT closer together ($r = -0.49$, $t_{(48)} = -3.92$, $P < 0.001$; Fig. 2F). The forced-choice recognition test and the MAT are, compared to the free recall, less demanding and capture memory per se, while the free recall captures detailedness of memory.

Imagination reduces insight-related activity in striatal and frontal regions

In order to assess neural changes associated with insight brought about during the insight phase, we compared BOLD activity changes for events that were linked (A and B) from the pre- to the post-insight phase ($AB_{post} > AB_{pre}$). Our whole-brain analysis revealed that the imagination group showed less activation compared to the observation group in the caudate nucleus (whole-brain cluster-level: $t_{(1, 54)} = -5.07$, $p_{corr}(FWE) = 0.046$, $k = 133$, peak: $x = 16$, $y = -8$, $z = 22$; Fig. 3A), the dlPFC (whole-brain cluster-level: $t_{(1, 54)} = -4.93$, $p_{corr}(FWE) < 0.001$, $k = 576$, peak: $x = 40$, $y = 46$, $z = 26$; Fig. 3B), and the orbitofrontal cortex (whole-brain cluster-level: $t_{(1, 54)} = -4.50$, $p_{corr}(FWE) = 0.040$, $k = 138$, peak: $x = 22$, $y = 56$, $z = -6$; Fig. 3C). Interestingly, we found a positive correlation between the change in orbitofrontal activity from pre- to post-insight and the differentiation between linked and nonlinked events in free recall for the imagination but not for the observation group (observation: $r = -0.10$, $t_{(26)} = -0.52$, $P = 0.607$; imagination: $r = 0.50$, $t_{(24)} = 2.87$, $P = 0.009$; observation vs. imagination: $z = 2.28$, $P = 0.011$; Fig. 4). This suggests that a minimal increase in orbitofrontal activity is necessary for differentiation in free recall to occur; smaller increases or even decreases appear to be linked to a reduced differentiation in memory for linked versus nonlinked events. To further shed light on the changes induced by the insight phase, we also compared BOLD activity changes for events that remained nonlinked (X) across the pre- with the post-insight phase ($X_{post} > X_{pre}$). Our whole-brain analysis revealed that the imagination group showed a decrease from pre- to post-insight in the anterior cingulate cortex, whereas there was no such change in the observation group (whole-brain cluster-level: $t_{(1, 54)} = -6.15$, p_{corr} (FWE) = 0.013, $k = 163$, peak: $x = -8$, $y = 34$, $z = 2$; Fig. 5).

Imagination prevents insight-induced representational change

To further shed light on the neural changes induced by the different types of insight—imagination versus observation—we compared multivariate voxel patterns pre- and post-insight by performing a ROI-based representational similarity analysis (RSA; Fig. 6A). We focused exclusively on the hippocampus in this analysis because the hippocampus has been shown to play a crucial role in the imagination processes (Addis et al. 2007; Mullally and Maguire 2014) and is also of paramount importance for mnemonic integration (Collin et al. 2015; Schlichting et al. 2015). To get more than a coarse picture of what is transpiring in the hippocampus, we divided the hippocampus along its long axis, as anterior regions have been found to be more relevant to mnemonic integration, whereas posterior regions are thought to be more involved in mnemonic segregation (Collin et al. 2015; Milivojevic et al. 2015; Schlichting et al. 2015; Brunec et al. 2018). For this analysis, RDMs were computed for the anterior and the posterior portions of the hippocampal long axis. Next, we extracted the neural dissimilarities averaged across stories for linked and nonlinked events pre- and post-insight from these RDMs for each participant and compared them in a mixed ANOVA (Fig. 6A). We found that while the observation group showed an increase in representational dissimilarity for linked events from pre- to post-insight in the right anterior hippocampus, the imagination group did not show such a reconfiguration (group × time × axis × link interaction: $F(1, 53) = 9.28$, $p_{corr} = 0.008$, $\eta_G = 0.005$; Fig. 6B). To further follow up on this effect, we performed post hoc tests, showing that this effect was only found for linked events (group × time × axis interaction: $F(1, 53) = 6.85$, $p_{corr} = 0.024$, $\eta_G = 0.012$) but not for nonlinked events (group × time × axis interaction: $F(1, 53) = 0.81$, $p_{corr} = 0.746$, $\eta_G = 0.001$). The increase in representational dissimilarity was only observed in the observation group (time × axis interaction: $F(1, 27) = 5.92$, $p_{corr} = 0.044$ $\eta_G = 0.028$) but not for the imagination group (time × axis interaction: $F(1, 26) = 1.56$,

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

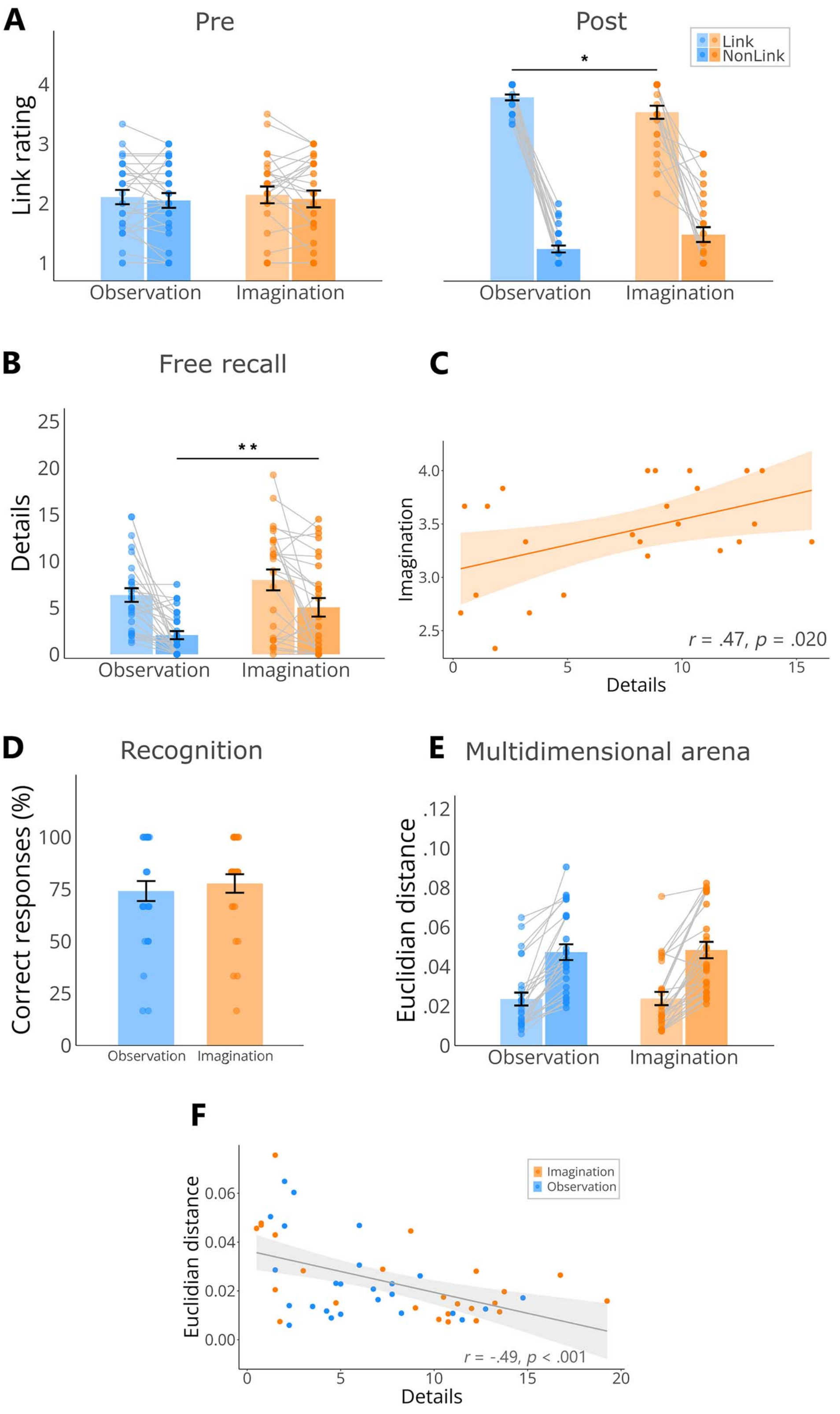


Fig. 2. Behavioral measures of insight and memory performance. A) No differences between the imagination and the observation group pre-insight for linked and nonlinked events, but lower ratings for linked events for the imagination group compared with the observation group post-insight, whereas there were no differences for nonlinked events. B) No difference in free recall between the groups for linked (A and B) events, but more details remembered in the imagination group for nonlinked events compared to the observation group. C) Significant positive correlation between the average strength of imagination during the insight phase and the remembered details on average (A, B, and X) one week later. D) High performance (correct responses (%)) in the forced-choice recognition test for both groups. E) Significant differences between linked and nonlinked events in the MAT (Euclidian distance) for the imagination and observation group. F) Significant negative correlation between the Euclidian distance between linked events in the MAT and the recalled details for linked events in the free recall. Data represent mean (+/−SE); $^{*}P < 0.05$, $^{**}P < 0.01$.

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

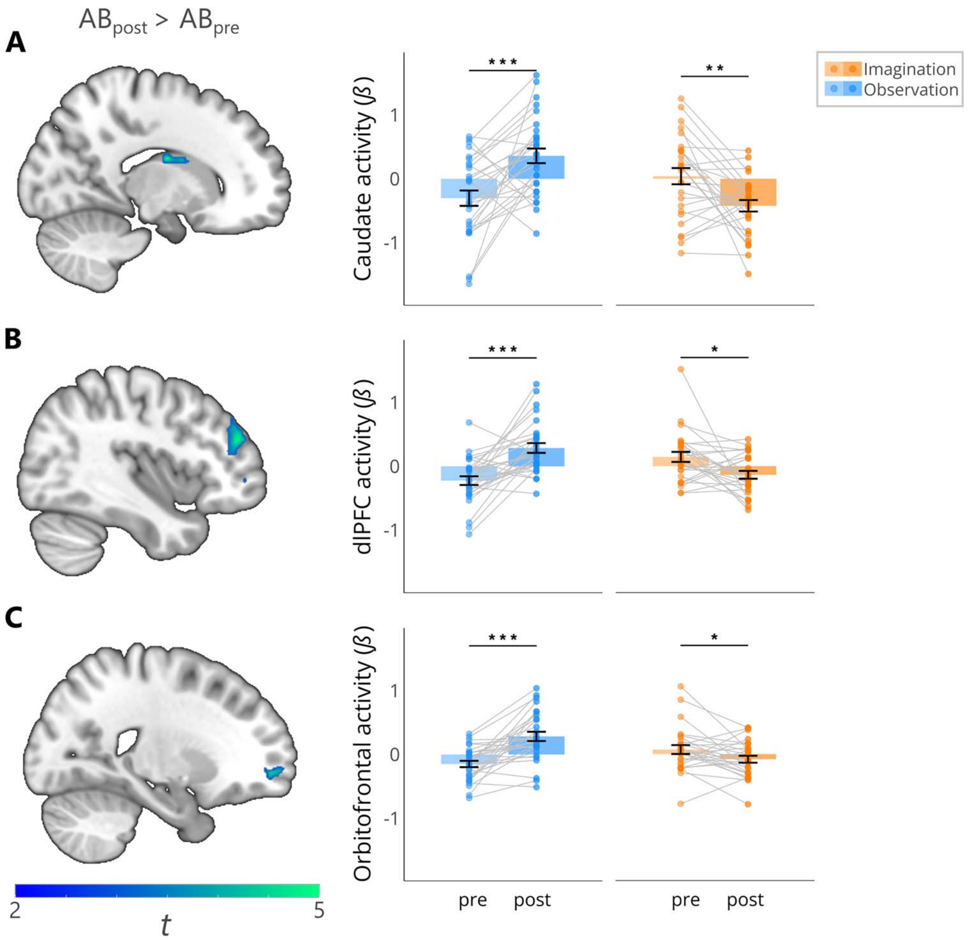


Fig. 3. Neural change for linked events. A) Masked caudate nucleus cluster on sagittal T1 image. Extracted beta values from caudate nucleus cluster for pre- and post-insight linked events, separately for the observation and the imagination group. B) Masked dlPFC cluster on sagittal T1 image. Extracted beta values from dlPFC cluster for pre- and post-insight linked events, separately for the observation and the imagination group. C) Masked orbitofrontal cortex cluster on sagittal T1 image. Extracted beta values from orbitofrontal cortex cluster for pre- and post-insight linked events, separately for the observation and the imagination group. Data represent mean (+/−SE); *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

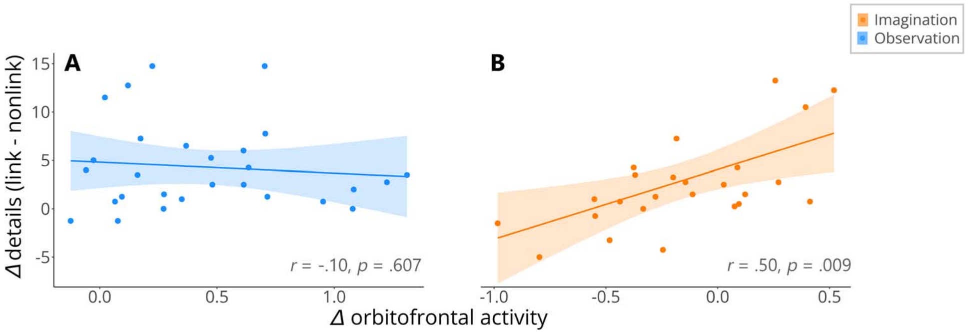


Fig. 4. Association between change in orbitofrontal activity and memory performance. A) Nonsignificant positive correlation between change in orbitofrontal activity from pre- to post-insight and the difference in free recall between linked and nonlinked events (linked events – nonlinked events) in the observation group. B) Significant correlation between change in orbitofrontal activity from pre- to post-insight and the difference in free recall between linked and nonlinked events (linked events – nonlinked events) in the imagination group.

$p_{\mathrm{corr}} = 0.446$, $\eta_G = 0.004$). Follow-up tests showed a strong trend for a change in representational pattern dissimilarity from pre- to post-insight in the right anterior hippocampus ($t_{(27)} = -2.30$, $p_{\mathrm{corr}} = 0.060$, $d_{\mathrm{repeated\ measures}} = -0.43$) but not in the right posterior hippocampus ($t_{(27)} = 0.25$, $p_{\mathrm{corr}} = 1$, $d_{\mathrm{repeated\ measures}} = -0.05$) of the observation group. Interestingly, over both groups, those with higher dissimilarity in the right anterior hippocampus post-insight also differentiated better between linked and nonlinked events in the MAT by arranging those events that were linked much closer together than those that were nonlinked ($r = -0.31$, $t_{(49)} = -2.32$, $P = 0.025$; Fig. 6F). Moreover, over both groups, those with more representational change from pre- to post-insight also recalled less details for the nonlinked event ($r = -0.27$, $t_{(51)} = -2.01$, $P = 0.049$; Fig. 6F), suggesting that they focused less on the nonlinked event. Furthermore, we performed an exploratory ROI-based RSA focusing on the medial prefrontal cortex, as

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

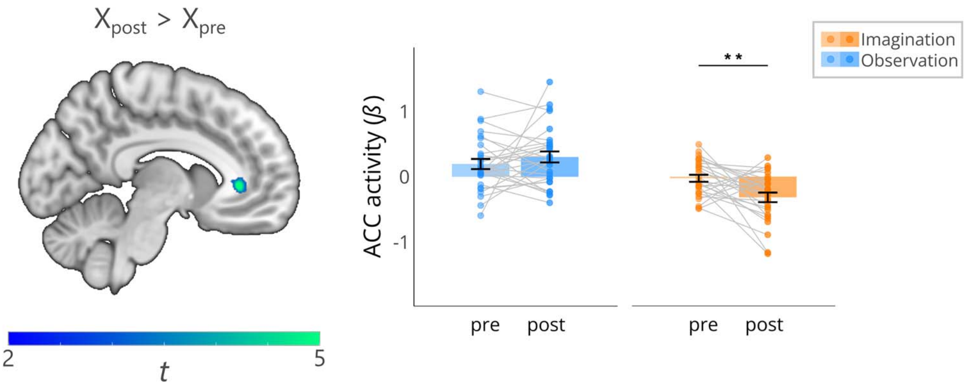


Fig. 5. Neural change for the nonlinked event. Masked anterior cingulate cluster on sagittal T1 image. Extracted beta values from anterior cingulate cluster for pre- and post-insight linked events, separately for the observation and the imagination group. Data represent mean (+/−SE); $^{**}P < 0.01$.

previous research has highlighted its importance for episodic memory integration (Milivojevic et al. 2015). We found a trend for an increase in neural dissimilarity from pre- to post-insight for linked events, which is similar to the representational change in the right anterior hippocampus, which was not the case for nonlinked events (time × link interaction: $F(1, 54) = 3.92$, $P = 0.053$, $\eta_G = 0.013$; Supplementary Fig. S2). Follow-up *t*-tests, however, yielded no significant effects (all $Ps > 0.139$). In addition, we performed a whole-brain searchlight RSA with a theoretical model operationalizing the increase in dissimilarity from pre- to post-insight to explore possible representational changes beyond the hippocampus. This searchlight analysis, however, yielded no significant representational patterns (whole-brain cluster-level: all $p_{corr}(FWE) > 0.719$; whole-brain peak-level: all $p_{corr}(FWE) > 0.572$).

Higher striato-hippocampal coupling during linking via imagination

To finally assess the underlying neural processes while gaining insight through imagination versus presentation, we measured BOLD activity using fMRI while participants learned that two initially unrelated events were actually linked (A and B) through a linking video (L) or a linking instruction (I) interleaved with a control video (C) or control instruction (CI). Our initial whole-brain analysis revealed that, during the insight phase, participants in the imagination group exhibited higher activity in the supplementary motor area (whole-brain cluster-level: $t_{(1, 54)} = -5.20$, $p_{corr}(FWE) = 0.002$, $k = 260$, peak: $x = -4$, $y = 0$, $z = 60$) and in the lingual gyrus (whole-brain cluster-level: $t_{(1, 54)} = 4.43$, $p_{corr}(FWE) < 0.001$, $k = 1097$, peak: $x = 8$, $y = -76$, $z = 0$). Interestingly, we found that those in the imagination group with higher activation of the lingual gyrus during the insight phase also rated linked events post-insight as belonging more together and nonlinked events as belonging less together ($r = 0.42$, $t_{(23)} = 2.22$, $P = 0.036$). Activation in these two areas provides a further validation of the condition participants were in: both the supplementary motor area and the lingual gyrus have been found to be active during reading (Mechelli et al. 2000; Cummine et al. 2017), which was required while the imagination instructions were shown. In addition, the lingual gyrus was found to be implicated in visuospatial working memory (Ragland et al. 2002; Schmidt et al. 2007; Gutiérrez-Garralda et al. 2014), suggesting that participants might have manipulated internal visuospatial layouts. The observation group further showed, compared to the imagination group, increased activity in the lateral occipital cortex (whole-brain cluster-level: $t_{(1, 54)} = -7.68$, $p_{corr}(FWE) < 0.001$, $k = 4138$, peak: $x = 50$, $y = -72$, $z = 0$), the occipital pole (whole-brain cluster-level: $t_{(1, 54)} = -7.16$, $p_{corr}(FWE) < 0.001$, $k = 1777$, peak: $x = -16$, $y = -102$, $z = 10$) as well as the parietal operculum (whole-brain cluster-level: $t_{(1, 54)} = -4.71$ $p_{corr}(FWE) = 0.042$, $k = 144$, peak: $x = 62$, $y = -38$, $z = 20$). These findings are in line with other studies reporting stronger activation in these lower visual, occipital regions during perception compared to imagination (Kosslyn et al. 1997; Ganis et al. 2004; Stokes et al. 2009). Beyond these whole-brain differences that are directly linked to sensory aspects of the presentation form, we found increased activity in the imagination group compared to the observation group in the bilateral anterior hippocampi (left anterior HC: SVC peak level: $x = -18$, $y = -4$, $z = -22$; $t_{(1, 54)} = 3.93$, p_{corr} $(FWE) = 0.024$; right anterior HC: SVC peak level: $x = 22$, $y = -2$, $z = -20$; $t_{(1, 54)} = 3.76$, p_{corr} $(FWE) = 0.040$). Interestingly, those in the observation group with more activity in the right anterior hippocampus during linking also showed a greater increase from pre- to post-insight in representational dissimilarity for linked events in the right anterior hippocampus; however, this appeared to be less the case for the imagination group (observation: $r = 0.43$, $t_{(26)} = -2.47$, $P = 0.021$; imagination: $r = 0.20$, $t_{(25)} = 1.00$, $P = 0.326$; observation vs. imagination: $z = -0.94$, $P = 0.175$; Supplementary Fig. S3).

In a next step, we assessed changes in the functional connectivity of the areas identified in the previous analyses during the linking of initially unrelated events using a PPI analysis (Fig. 7). We focused on the caudate nuclei as seed regions, as these yielded the highest univariate increase from pre- to post-insight for linked events in the observation group compared to the imagination group. Moreover, higher connectivity between the caudate and the hippocampus has been linked to better imagination and memory performance in previous studies (Müller et al. 2018; Faul et al. 2020). When comparing the link event with the control event (Link > Control), we found that participants in the imagination group showed, at the whole-brain level, higher functional connectivity than the observation group between the left caudate (seed) and the intracalcarine cortex (whole-brain cluster-level: $t_{(1, 54)} = 4.78$; $p_{corr}(FWE) < 0.001$, $k = 941$, peak: $x = -2$, $y = -86$, $z = 2$). We further found higher functional connectivity between the right caudate (seed) and the occipital pole in the imagination relative to the observation group (whole-brain cluster-level: $t_{(1, 54)} = 4.92$; $p_{corr}(FWE) = 0.003$, $k = 232$, peak: $x = 16$, $y = -98$, $z = 6$). Interestingly, when focusing on our ROIs, we also found higher coupling between the left caudate and the left hippocampus in the imagination compared to the observation group (SVC peak level: $x = -30$, $y = -30$, $z = -8$; $t_{(1, 54)} = 4.40$; $p_{corr}(FWE) = 0.016$, $k = 22$;

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

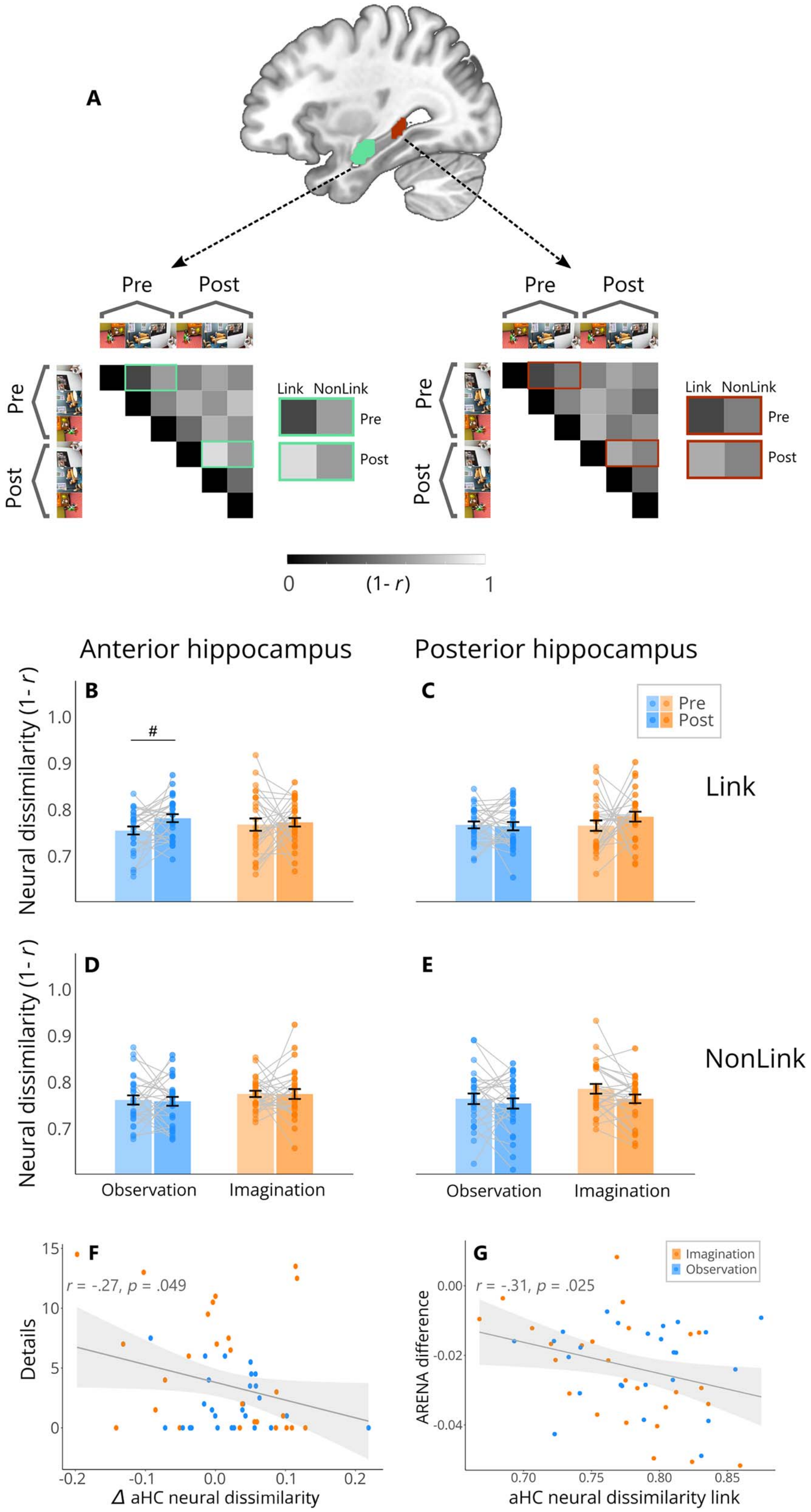


Fig. 6. Conceptual RSA and results for RSA. A) Masked right anterior and posterior hippocampus with conceptual RDMs for each region. Dissimilarities pre- and post-insight were extracted per region and averaged over six stories per participants before they were entered into an ANOVA. B) Trending difference between pre- and post-insight for linked events in the right anterior hippocampus in the observation and nonsignificant difference in the imagination group. C) Nonsignificant pre- and post-insight neural dissimilarities for linked events in the right posterior hippocampus for the observation and the imagination group. D) Nonsignificant pre- and post-insight neural dissimilarities for nonlinked events in the right anterior hippocampus for the observation and the imagination group. E) Nonsignificant pre- and post-insight neural dissimilarities for nonlinked events in the right posterior hippocampus for the observation and the imagination group. F) Significant negative correlation between representational change in the right anterior hippocampus (aHC; post – pre) and recalled details for the nonlinked event in free recall. G) Significant negative correlation between the neural dissimilarity for linked events in the right anterior hippocampus (aHC) and the difference in the MAT between linked and nonlinked events (link – nonlink). Data represent mean (+/−*SE*); # $P_{\mathrm{corr}} = 0.06$.

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

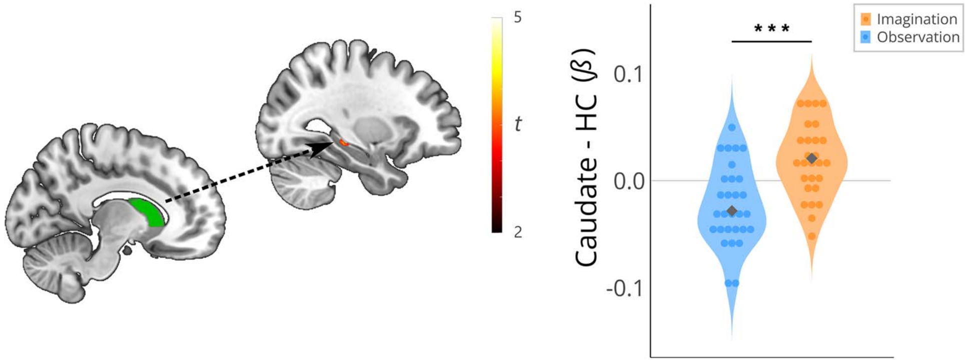


Fig. 7. PPI results with seed from caudate nucleus. Masked left caudate nucleus seed on sagittal T1 image and masked left hippocampal connectivity. Violin distribution of extracted connectivity beta values from left hippocampus ($x = -30$, $y = -30$, $z = -8$) for the observation and imagination groups separately. Within-group mean: gray rectangle. ***$P < 0.001$.

Table 1. Control variables.

Measure	Imagination		Observation		
	M	SD	M	SD	P
FFIS-C	23.59	3.92	22.24	5.60	.298
FFIS-D	18.74	4.91	16.69	4.51	.110
FFIS-E	14.30	6.58	14.90	5.74	.718
FFIS-F	26.26	8.56	25.03	10.27	.629
STAI-T	37.19	6.27	35.90	8.87	.531
STAI-S	34.13	6.22	35.72	7.35	.395
PSQI	5.17	2.88	4.41	1.31	.245
TICS	27.48	7.91	25.21	9.05	.320
BDI	6.30	5.91	4.79	4.44	.290
BFI-2 E	39.81	8.29	40.76	6.69	.643
BFI-2 N	28.96	6.15	28.62	9.23	.870
BFI-2 O	44.93	7.88	43.17	9.00	.441
BFI-2 C	40.93	7.09	43.31	7.95	.241
BFI-2 A	47.07	5.76	47.07	6.28	.997

Note. The questionnaires FFIS with its dimensions: FFIS-C (complexity of imagination), FFIS-D (directedness of imagination), FFIS-E (emotional valence of imagination), and FFIS-F (frequency of imagination); STAI-T; BDI; BFI-2 with its dimensions: BFI-2 E (extraversion), BFI-2 N (neuroticism), BFI-2 O (openness to experience), BFI-2 C (conscientiousness), and BFI-2 A (agreeableness), and TICS (Trier Inventory of Chronic Stress) were completed via an online link before participants came in for day 1, and STAI-S and PSQI were completed at the beginning of the experiment. No significant differences between the groups were observed on these measures. Data represent means (+/−SD).

Fig. 7). Accordingly, those in both groups, who had higher functional connectivity between the left caudate and the left hippocampus, also recalled more details on average one week later ($r = 0.27$, $t_{(52)} = 2.02$, $P = 0.048$).

We further performed a PPI for the change from pre to post for the nonlinked event with the bilateral dlPFC as seed regions since these regions have also been found to be implicated in a change from pre to post in a previous analysis. When comparing the increase from pre to post for the nonlinked event ($X_{\text{post}} > X_{\text{pre}}$), we found that participants in the imagination group tended to show a lower functional connectivity increase between the left dlPFC and the right anterior hippocampus than participants in the observation group (SVC peak level: $x = 30$, $y = -4$, $z = -26$; $t_{(1,\,54)} = 3.89$, p_{corr} (FWE) $= 0.068$; $k = 5$). Furthermore, participants in the imagination group tended to show a lower functional connectivity increase between the right dlPFC and the right anterior hippocampus (SVC peak level: $x = 30$, $y = -4$, $z = -26$; $t_{(1,\,54)} = 3.92$, p_{corr} (FWE) $= 0.060$; $k = 3$).

Control variables

To rule out the possibility that the imagination and observation groups differed in terms of trait imagination capacity (FFIS), trait-anxiety (STAI-T), state-anxiety (STAI-S), sleep quality (PSQI), chronic stress (TICS), depressive symptoms (BDI), and personality dimensions (BFI-2), participants completed corresponding questionnaires before the experiment. There were no differences between the groups on any of these measures (all $Ps > 0.110$; see Table 1).

Furthermore, there was no difference between groups in their working memory capacity, as measured by an *N*-back task at baseline (all $Ps > 0.180$; see Table 2). Thus, it is unlikely that differences during the NIT (or in the retention test one week later) were influenced by mere group differences in working memory.

Discussion

Gaining insight into the relationship of initially separate events often comes with an insight-induced memory reconfiguration (Collin et al. 2015; Milivojevic et al. 2015), enabling the integration of memories. This process of memory integration is fundamental to many cognitive processes, such as decision-making (Gupta et al. 2010; Zeithamova et al. 2012; Shohamy and Daw 2015). Gaining insight into the relationship of events is a fundamental memory process and is also highly important for educational settings. Notably, in educational contexts, the integration of knowledge is often achieved by reading. To this point, however, mnemonic

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

Table 2. *N*-back task.

	Imagination		Observation		
N-back	*M*	*SD*	*M*	*SD*	*P*
3-back Acc	75.09%	12.74%	79.40%	10.93%	.182
3-back RT	789.91 ms	169.03 ms	729.20 ms	164.91 ms	.180
4-back Acc	75.37%	10.18%	77.24%	11.52%	.522
4-back RT	768.43 ms	145.96 ms	722.75 ms	206.18 ms	.341

Note. Participants completed the *N*-back task before they went into the scanner. Groups did not differ on these *N*-back measures. Data represent means (+/−SD).

integration has been investigated exclusively by presenting participants a linking event as a direct experience, while it has remained understudied how insight can come about through imagining that link. Therefore, in the present study, we aimed to elucidate the behavioral and neural consequences of linking previously unrelated events via imagination and contrasted these with the mechanisms and effects of linking through direct observation. Our results show that it is possible to gain insight through imagination, although this insight is weaker than the insight gained via presentation of videos of the linking event. Dovetailing these behavioral findings, we also found lower insight-related increases in the frontal and striatal activities as well as an absence of representational change in the anterior hippocampus when gaining insight via imagination. Interestingly, very similar regions were more strongly recruited while linking via imagination: The anterior hippocampus showed increased activity, and we also found increased coupling between the striatum and the hippocampus when participants imagined the link between initially unrelated events. These findings suggest that these regions may have been more occupied by the process of imagination and may, thus, not have been able to accomplish these insight-induced changes, as was the case when linking via observation. Although immediate insight was weaker in the imagination group, we found an overall memory enhancement one week later.

All participants gained insight into which events were linked and which were left nonlinked, demonstrating that gaining insight is possible through both imagination and observation. However, insight was stronger with observation than with imagination of the linking event, which may be explained by the fact that imagination is a more demanding process, given its neural overlap with working memory and association with visual working memory performance (Baddeley and Andrade 2000; Keogh and Pearson 2011; Albers et al. 2013; Christophel et al. 2015). Imagination could further be viewed as a weak form of perception with a reversed information flow compared to perception (Grossman and Blake 2001; Naselaris et al. 2009; Breedlove et al. 2020; Dijkstra et al. 2020), which could also explain why actual perception (i.e. observation) led to stronger insight. One might also argue that the imagination group showed lower insight because they first had to read the instruction, recall the video events (A and B), and then imagine the linking event, whereas the observation group gained insight immediately while only watching the video. Although this alternative explanation can hardly be ruled out, we consider this alternative rather unlikely because the linking event presentation was long and repeated for six times, which may have also led to recognition of the event descriptions and hence speeded up the reading process. In line with this view, participants indicated that they could imagine the linking events well. Another factor that may have contributed to the lower insight in the imagination group is the higher activity of the anterior hippocampus during linking. Compared to the posterior hippocampus, the anterior hippocampus has not only been shown to be a hub for imaginative scene construction in previous research (Mullally and Maguire 2014; Zeidman and Maguire 2016) but to be also of pivotal importance for mnemonic integration (Collin et al. 2015; Schlichting et al. 2015). Thus, imagining the link may have interfered with gaining insight in the imagination group.

Beyond the differential insight into the links between initially unrelated events, we obtained also significant differences between the imagination and observation groups in the insight-driven neural reconfiguration of memory representations. Specifically, we observed a representational change from pre- to post-insight in the right anterior hippocampus for linked events in the observation group. The anterior hippocampus is known to be involved not only in mnemonic integration (Collin et al. 2015; Schlichting et al. 2015) but also in processing of spatial context (Fritch et al. 2020) and novelty detection (Bunzeck and Düzel 2006), which are both features that may have been at play here: Spatial layouts were processed while viewing the events (A, B, and X), and novelty processing may have been required when discovering that the events A and B belong together. We found an increase in dissimilarity in the right anterior hippocampus but no increase in similarity as reported in some previous studies (Collin et al. 2015; Schlichting et al. 2015; Dimsdale-Zucker et al. 2018). This change in neural dissimilarity appeared to be rather specific to the anterior hippocampus, as we observed only a trend for a similar pattern in the medial prefrontal cortex but no similar representational changes elsewhere in the brain. It has been presumed that hippocampal similarity may increase when events share item as well as context associations but not when events share either context (scene) or item (people) information (Libby et al. 2019), which may have been the case in the present study. However, this was equally the case in a previous study using the same paradigm which found increased similarity for linked events in the anterior hippocampus (Collin et al. 2015). However, the present study also deviated from previous work in that titles were shown prior to the presentation of each video (A, B, and X), which may have elicited a different strategy than that found in previous work with this task (Collin et al. 2015; Milivojevic et al. 2015). Further evidence suggests that memory representations that have been moderately coactivated, result in increased dissimilarity (Wammes et al. 2022). Increases in dissimilarity between related memories might be interpreted as a pattern separation mechanism allowing inferences across events (Molitor et al. 2021). Indeed, increased dissimilarity has been associated with better memory performance in several previous studies (Hulbert and Norman 2015; Favila et al. 2016; Chanales et al. 2017; Dandolo and Schwabe 2018; Koolschijn et al. 2019). In line with these findings, we also found a positive association between neural dissimilarity post-insight in the right anterior hippocampus and memory performance across groups. Therefore, it seems likely that the remapping of neural codes

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

we observed was actually hippocampal pattern separation—a process that is necessary to distinguish memories from one another (Muller and Kubie 1987; Leutgeb et al. 2007; Yassa and Stark 2011). Importantly, the change in anterior hippocampal representational dissimilarity from pre- to post-insight was only observed in the observation group but not in participants who imagined the link between events, which dovetails the weaker immediate insight in the imagination group on a behavioral level.

Beyond the hippocampus, the observation group also showed an increased activity from pre- to post-insight in the caudate nucleus and the dorsolateral prefrontal and orbitofrontal cortices for linked events. Previous studies have shown that dorsal striatal regions were involved in the processing of integrated episodes, prediction-error based learning, and associative learning (Ben-Yakov and Dudai 2011; Mattfeld and Stark 2015; Pine et al. 2018), which may all be processes directly underlying mnemonic integration. Furthermore, dorsolateral prefrontal regions have been found to be important for relational memory (Murray and Ranganath 2007; Long et al. 2010; Blumenfeld et al. 2011) and insight per se (Tik et al. 2018). Whereas, orbitofrontal regions have been found to be involved in the processing of reward experiences in general (Kringelbach 2005; Salimpoor et al. 2011; Kringelbach et al. 2012) and in an insight-related reward signal in particular (Oh et al. 2020). All of these processes are important for mnemonic integration, as relational memory of events must be updated via the insight gained, which in turn can be rewarding.

However, the imagination group showed smaller increases or even decreases in activity for linked events in these regions, which is again consistent with weaker immediate insight in the imagination group. Interestingly, those in the imagination group with less increase or a decrease in orbitofrontal activity for linked events from pre- to post-insight also recalled less details for linked events and more details for nonlinked events, indicating that the increase in orbitofrontal activity at encoding plays a specific role in discriminating between memories for linked and nonlinked events one week later. We further found an increased connectivity between the bilateral dorsolateral prefrontal regions and the right anterior hippocampus in the observation group. The connectivity between the dlPFC and the hippocampus has been previously found to be linked to spatial working memory (Bähner et al. 2015), and successful updating of already existing memories (Kluen et al. 2019), which may have especially been the case here.

In addition to these increases for linked events in the observation group, we found decreased activity in the anterior cingulate from pre- to post-insight for nonlinked events in the imagination group. The anterior cingulate has been found to be important during conflict monitoring (Botvinick et al. 2001, 2004) and is part of a salience network, which appears to be tasked with detecting salient events and thus contributes to behavioral control (Uddin 2015; Seeley 2019; Becker et al. 2020). The decrease in anterior cingulate activity observed in the imagination group from pre- to post-insight for nonlinked events might, therefore, suggest that the nonlinked event was less monitored as an event that provoked conflict and became less salient compared to the observation group. This, however, remains speculative as our design did not allow a distinction of different levels of saliency.

How may the imagination of the linking event have reduced the insight into the link between initially unrelated events and the neural mechanisms associated herewith? To address this question, we focused on the insight phase. We hypothesized that the hippocampus would be more involved in linking via imagination than in linking via presentation because the hippocampus has been shown to play an important role in imagination (Addis et al. 2009; Mullally and Maguire 2014; Zeidman and Maguire 2016). We further assumed that this hippocampal recruitment during imagination could hinder mnemonic integration, as this process is also highly hippocampus-dependent (Collin et al. 2015; Schlichting et al. 2015). Indeed, we found stronger activation of the anterior hippocampus during the insight phase in the imagination group compared to the observation group, i.e. in the same area that appeared to be implicated in the mnemonic reconfiguration in the observation group. In addition to our univariate analyses, we also analyzed connectivity during linking and found higher coupling between the left caudate and the left hippocampus in the imagination group specifically for the link event compared to a control event during the insight phase. Higher connectivity between the hippocampus and the caudate nucleus has been associated with better imagination as well as better memory performance (Müller et al. 2018; Faul et al. 2020). Indeed, those with higher connectivity between the hippocampus and the caudate nucleus recalled more details one week later. Notably, the imagination group also showed a reduced increase in the caudate nucleus from pre- to post-insight for linked events compared to the observation group. This could suggest that resources required for linking were occupied by the imagination, which might have prevented the insight-induced increase in caudate activity, as observed in the observation group.

Beyond the immediate insight gained during the insight phase, insight also manifested in memory. Although participants showed near-ceiling performance in the forced-choice recognition test and were able to arrange events according to whether they were linked or nonlinked in the MAT, both groups also showed a memory advantage for details of linked versus nonlinked events, suggesting that narrative coherence promotes prioritization in memory. This finding dovetails with the assumption that the brain stores episodic memories as coherent narratives (Tulving 1983) and with more recent findings that integrated episodes can be recalled more easily (Wang et al. 2015; Cohn et al. 2021). The greater accessibility of these integrated episodes may be attributed to the fact that any element of the episode can be used as a cue for the entire episode (Nakazawa et al. 2002; Horner et al. 2015).

However, there was also an overall memory advantage for the imagination group in the number of details recalled, suggesting that memory in general, rather than specifically the effect of insight on memory, was enhanced by imagining the link. Consistent with this memory enhancement through imagination, there was even a positive relationship between the strength of imagination and the number of details remembered by the imagination group for linked events. This result is also consistent with studies that used imagination as a mnemonic technique and showed that it led to better memory performance (Bower 1970; Hockley and Christi 1996) and also with other results that showed that learning via imagination has a lasting effect on behavioral and neural outcomes (Reddan et al. 2018; Greening et al. 2022). As a result of the increased engagement of the imagination group during the linking phase, the results could also be due to a deeper processing effect (Craik and Lockhart 1972). It is well known that active engagement with the encoding material, as was the case in the imagination group, improves memory compared to passive viewing (Slamecka and Graf 1978; Johns and Swanson 1988; Bertsch et al. 2007). Interestingly, however, we observed here a memory boost both for linked events and for nonlinked events, i.e. the memory boost was not limited to the actually imagined event but occurred for all events that were presented on day 1. Thus, if there was an effect of active engagement, it was a more general

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

and no specific effect. With the current design, it was not possible to distinguish whether the general memory boost observed in the imagination group was due to active engagement with the task or to imagining the linking instruction. Future studies might investigate this aspect further using a more active control group to disentangle imagination and active engagement effects. Overall, it seems that, although direct insight decreased in the imagination group, memory performance increased and that insight through imagination appears to result in a trade-off: lower direct insight, but better memory performance.

In line with many everyday examples, our data show that gaining insight into the relationship between events is possible not only through direct experience but also through imagining the link between those events. Gaining insight via imagination, however, came at the cost of a diminished immediate insight and an impeded representational change in the anterior hippocampus. Linking via imagination resulted in higher hippocampal activity and connectivity with the striatum during linking, which may have impeded the neural changes required for mnemonic integration on the one hand but may have facilitated long-term memory formation on the other hand. Together, our data shed light on how initially unrelated events can be integrated when the link between them is either directly observed or mentally constructed, and could lead to an emphasis on the benefits of hands-on experiences for gaining knowledge in educational settings, while using imaginative techniques to promote long-term memory.

Acknowledgments

We gratefully acknowledge the assistance of Carlo Hiller with programming the task; Hamed Nili for his support during data analysis; and Anica Koslowski, Dania Al Darwich, Merve Tural, Carlotta Reinhardt, Sophie Lutter, Mihriban Sahin, and Dewi Soetjipto for their assistance during data collection.

Supplementary material

Supplementary material is available at *Cerebral Cortex* online.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon request.

Funding

This project was funded by the German Research Foundation (DFG; grant SCHW1357/22 to LS and CFD.). CFD's research is supported by the Max Planck Society, the European Research Council (ERC-CoG GEOCOG 724836), the Kavli Foundation, the Jebsen Foundation, Helse Midt Norge, and the Research Council of Norway (223262/F50 and 197467/F50).

Conflict of interest statement: None declared.

References

Addis DR, Wong AT, Schacter DL. Remembering the past and imagining the future: common and distinct neural substrates during event construction and elaboration. *Neuropsychologia*. 2007:45(7):1363–1377. https://doi.org/10.1016/j.neuropsychologia.2006.10.016.

Addis DR, Pan L, Vu M-A, Laiser N, Schacter DL. Constructive episodic simulation of the future and the past: distinct subsystems of a core brain network mediate imagining and remembering. *Neuropsychologia*. 2009:47(11):2222–2238. https://doi.org/10.1016/j.neuropsychologia.2008.10.026.

Albers AM, Kok P, Toni I, Dijkerman HC, de Lange FP. Shared representations for working memory and mental imagery in early visual cortex. *Curr Biol*. 2013:23(15):1427–1431. https://doi.org/10.1016/j.cub.2013.05.065.

Baddeley AD, Andrade J. Working memory and the vividness of imagery. *J Exp Psychol Gen*. 2000:129(1):126–145Scopus 10.1037/0096-3445.129.1.126.

Bähner F, Demanuele C, Schweiger J, Gerchen MF, Zamoscik V, Ueltzhöffer K, Hahn T, Meyer P, Flor H, Durstewitz D, et al. Hippocampal–dorsolateral prefrontal coupling as a species-conserved cognitive mechanism: a human translational imaging study. *Neuropsychopharmacology*. 2015:40(7):Article 7. https://doi.org/10.1038/npp.2015.13.

Barry DN, Barnes GR, Clark IA, Maguire EA. The neural dynamics of novel scene imagery. *J Neurosci*. 2019:39(22):4375–4386. https://doi.org/10.1523/JNEUROSCI.2497-18.2019.

Becker M, Sommer T, Kühn S. Verbal insight revisited: FMRI evidence for early processing in bilateral insulae for solutions with AHA! Experience shortly after trial onset. *Hum Brain Mapp*. 2020:41(1):30–45. https://doi.org/10.1002/hbm.24785.

Bellana B, Liu Z-X, Diamond NB, Grady CL, Moscovitch M. Similarities and differences in the default mode network across rest, retrieval, and future imagining. *Hum Brain Mapp*. 2017:38(3):1155–1171. https://doi.org/10.1002/hbm.23445.

Benedek M, Schües T, Beaty RE, Jauk E, Koschutnig K, Fink A, Neubauer AC. To create or to recall original ideas: brain processes associated with the imagination of novel object uses. *Cortex*. 2018:99:93–102. https://doi.org/10.1016/j.cortex.2017.10.024.

Benoit RG, Schacter DL. Specifying the core network supporting episodic simulation and episodic memory by activation likelihood estimation. *Neuropsychologia*. 2015:75:450–457. https://doi.org/10.1016/j.neuropsychologia.2015.06.034.

Ben-Yakov A, Dudai Y. Constructing realistic engrams: poststimulus activity of hippocampus and dorsal striatum predicts subsequent episodic memory. *J Neurosci*. 2011:31(24):9032–9042. https://doi.org/10.1523/JNEUROSCI.0702-11.2011.

Bertsch S, Pesta BJ, Wiscott R, McDaniel MA. The generation effect: a meta-analytic review. *Mem Cogn*. 2007:35(2):201–210. https://doi.org/10.3758/BF03193441.

Blumenfeld RS, Parks CM, Yonelinas AP, Ranganath C. Putting the pieces together: the role of dorsolateral prefrontal cortex in relational memory encoding. *J Cogn Neurosci*. 2011:23(1):257–265. https://doi.org/10.1162/jocn.2010.21459.

Botvinick MM, Braver TS, Barch DM, Carter CS, Cohen JD. Conflict monitoring and cognitive control. *Psychol Rev*. 2001:108:624–652. https://doi.org/10.1037/0033-295X.108.3.624.

Botvinick MM, Cohen JD, Carter CS. Conflict monitoring and anterior cingulate cortex: an update. *Trends Cogn Sci*. 2004:8(12):539–546. https://doi.org/10.1016/j.tics.2004.10.003.

Bower GH. Imagery as a relational organizer in associative learning. *J Verbal Learn Verbal Behav*. 1970:9(5):529–533. https://doi.org/10.1016/S0022-5371(70)80096-2.

Breedlove JL, St-Yves G, Olman CA, Naselaris T. Generative feedback explains distinct brain activity codes for seen and mental images. *Curr Biol*. 2020:30(12):2211–2224.e6. https://doi.org/10.1016/j.cub.2020.04.014.

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

Brett, M., Anton, J.-L., Valabregue, R., & Poline, J.-B. (2002, June 2-6). Region of interest analysis using an SPM toolbox [abstract]. *Presented at the 8th International Conferance on Functional Mapping of the Human Brain*, Sendai, Japan. *Available on CD-ROM in NeuroImage*, 2002:16:(2), abstract 497.

Brunec IK, Bellana B, Ozubko JD, Man V, Robin J, Liu Z-X, Grady C, Rosenbaum RS, Winocur G, Barense MD, et al. Multiple scales of representation along the hippocampal anteroposterior axis in humans. *Curr Biol*. 2018:28(13):2129–2135.e6. https://doi.org/10.1016/j.cub.2018.05.016.

Brunec IK, Robin J, Olsen RK, Moscovitch M, Barense MD. Integration and differentiation of hippocampal memory traces. *Neurosci Biobehav Rev*. 2020:118:196–208. https://doi.org/10.1016/j.neubiorev.2020.07.024.

Bunzeck N, Düzel E. Absolute coding of stimulus novelty in the human substantia nigra/VTA. *Neuron*. 2006:51(3):369–379. https://doi.org/10.1016/j.neuron.2006.06.021.

Buysse D, Reynolds C, Monk T, Berman S, Kupfer D. The Pittsburgh sleep quality index—a new instrument for psychiatric practice and research. *Psychiatry Res*. 1989:28(2):193–213. https://doi.org/10.1016/0165-1781(89)90047-4.

Chanales AJH, Oza A, Favila SE, Kuhl BA. Overlap among spatial memories triggers repulsion of hippocampal representations. *Curr Biol*. 2017:27(15):2307–2317.e5. https://doi.org/10.1016/j.cub.2017.06.057.

Christophel TB, Cichy RM, Hebart MN, Haynes J-D. Parietal and early visual cortices encode working memory content across mental transformations. *NeuroImage*. 2015:106:198–206. https://doi.org/10.1016/j.neuroimage.2014.11.018.

Clark IA, Hotchin V, Monk A, Pizzamiglio G, Liefgreen A, Maguire EA. Identifying the cognitive processes underpinning hippocampal-dependent tasks. *J Exp Psychol Gen*. 2019:148:1861–1881. https://doi.org/10.1037/xge0000582.

Cohn-Sheehy BI, Delarazan AI, Crivelli-Decker JE, Reagh ZM, Mundada NS, Yonelinas AP, Zacks JM, Ranganath C. Narratives bridge the divide between distant events in episodic memory. *Mem Cogn*. 2021:50:478–494. https://doi.org/10.3758/s13421-021-01178-x.

Collin SHP, Milivojevic B, Doeller CF. Memory hierarchies map onto the hippocampal long axis in humans. *Nat Neurosci*. 2015:18(11):1562–1564. https://doi.org/10.1038/nn.4138.

Collin SHP, Milivojevic B, Doeller CF. Hippocampal hierarchical networks for space, time, and memory. *Curr Opin Behav Sci*. 2017:17:71–76. https://doi.org/10.1016/j.cobeha.2017.06.007.

Craik FIM, Lockhart RS. Levels of processing: a framework for memory research. *J Verbal Learn Verbal Behav*. 1972:11(6):671–684. https://doi.org/10.1016/S0022-5371(72)80001-X.

Cummine J, Hanif W, Dymouriak-Tymashov I, Anchuri K, Chiu S, Boliek CA. The role of the supplementary motor region in overt reading: evidence for differential processing in SMA-proper and pre-SMA as a function of task demands. *Brain Topogr*. 2017:30(5):579–591. https://doi.org/10.1007/s10548-017-0553-3.

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

Danner D, Rammstedt B, Bluemke M, Treiber L, Berres S, Soto CJ, John OP. (2016). Die deutsche Version des Big Five Inventory 2 (BFI-2). *Mannheim: GESIS - Leibniz-Institut für Sozialwissenschaften*. https://doi.org/10.6102/zis247.

Devitt AL, Schacter DL. Looking on the bright side: aging and the impact of emotional future simulation on subsequent memory. *J Gerontol B*. 2020:75(9):1831–1840. https://doi.org/10.1093/geronb/gbz041.

Dijkstra N, Ambrogioni L, Vidaurre D, van Gerven M. Neural dynamics of perceptual inference and its reversal during imagery. *elife*. 2020:9:1–19.

Dimsdale-Zucker HR, Ritchey M, Ekstrom AD, Yonelinas AP, Ranganath C. CA1 and CA3 differentially support spontaneous retrieval of episodic contexts within human hippocampal subfields. *Nat Commun*. 2018:9(1):1–8.

Eichenbaum H, Dudchenko P, Wood E, Shapiro M, Tanila H. The hippocampus, memory, and place cells: Is it spatial memory or a memory space? *Neuron*. 1999:23(2):209–226. https://doi.org/10.1016/S0896-6273(00)80773-4.

Eid M, Gollwitzer M, Schmitt M. (2017). *Statistik und Forschungsmethoden* (5th ed). Weinheim, Germany: Beltz Verlag. https://www.beltz.de/produkt_detailansicht/8413-statistik-und-forschungsmethoden.html.

Faul L, St. Jacques PL, DeRosa JT, Parikh N, De Brigard F. Differential contribution of anterior and posterior midline regions during mental simulation of counterfactual and perspective shifts in autobiographical memories. *NeuroImage*. 2020:215:116843. https://doi.org/10.1016/j.neuroimage.2020.116843.

Favila SE, Chanales AJH, Kuhl BA. Experience-dependent hippocampal pattern differentiation prevents interference during subsequent learning. *Nat Commun*. 2016:7(1):Article 1. https://doi.org/10.1038/ncomms11066.

Fritch HA, MacEvoy SP, Thakral PP, Jeye BM, Ross RS, Slotnick SD. The anterior hippocampus is associated with spatial memory encoding. *Brain Res*. 2020:1732:146696. https://doi.org/10.1016/j.brainres.2020.146696.

Gaesser B, Spreng RN, McLelland VC, Addis DR, Schacter DL. Imagining the future: evidence for a hippocampal contribution to constructive processing. *Hippocampus*. 2013:23(12):1150–1161. https://doi.org/10.1002/hipo.22152.

Ganis G, Thompson WL, Kosslyn SM. Brain areas underlying visual mental imagery and visual perception: an fMRI study. *Cogn Brain Res*. 2004:20(2):226–241. https://doi.org/10.1016/j.cogbrainres.2004.02.012.

Greening SG, Lee T-H, Burleigh L, Grégoire L, Robinson T, Jiang X, Mather M, Kaplan J. Mental imagery can generate and regulate acquired differential fear conditioned reactivity. *Sci Rep*. 2022:12(1):Article 1. https://doi.org/10.1038/s41598-022-05019-y.

Grossman ED, Blake R. Brain activity evoked by inverted and imagined biological motion. *Vis Res*. 2001:41(10):1475–1482. https://doi.org/10.1016/S0042-6989(00)00317-5.

Gupta AS, van der Meer MAA, Touretzky DS, Redish AD. Hippocampal replay is not a simple function of experience. *Neuron*. 2010:65(5):695–705. https://doi.org/10.1016/j.neuron.2010.01.034.

Gutiérrez-Garralda JM, Hernandez-Castillo CR, Barrios FA, Pasaye EH, Fernandez-Ruiz J. Neural correlates of spatial working memory manipulation in a sequential Vernier discrimination task. *Neuroreport*. 2014:25(18):1418–1423. https://doi.org/10.1097/WNR.0000000000000280.

Hassabis D, Kumaran D, Vann SD, Maguire EA. Patients with hippocampal amnesia cannot imagine new experiences. *Proc Natl Acad Sci*. 2007:104(5):1726–1731. https://doi.org/10.1073/pnas.0610561104.

Hautzinger M, Keller F, Kühner C. *BDI-II. Beck depressions inventar revision—manual*. Frankfurt, Germany: Harcourt Test Services; 2006

He Q, Liu JL, Beveridge EH, Eschapasse L, Vargas V, Brown TI. Episodic memory integration shapes value-based decision-making in spatial navigation. *J Exp Psychol Learn Mem Cogn*. 2022:48(8):1098–1109. https://doi.org/10.1037/xlm0001133.

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

Hockley WE, Christi C. Tests of the differential encoding of item and associative information. *Mem Cogn*. 1996:24:202–216.

Horner AJ, Bisby JA, Bush D, Lin W-J, Burgess N. Evidence for holistic episodic recollection via hippocampal pattern completion. *Nat Commun*. 2015:6(1):1–11. https://doi.org/10.1038/ncomms8462.

Huffman DJ, Stark CEL. Multivariate pattern analysis of the human medial temporal lobe revealed representationally categorical cortex and representationally agnostic hippocampus. *Hippocampus*. 2014:24(11):1394–1403. https://doi.org/10.1002/hipo.22321.

Hulbert JC, Norman KA. Neural differentiation tracks improved recall of competing memories following interleaved study and retrieval practice. *Cereb Cortex*. 2015:25(10):3994–4008.

Johns EE, Swanson LG. The generation effect with nonwords. *J Exp Psychol Learn Mem Cogn*. 1988:14:180–190. https://doi.org/10.1037/0278-7393.14.1.180.

Kapur S, Craik FI, Tulving E, Wilson AA, Houle S, Brown GM. Neuroanatomical correlates of encoding in episodic memory: levels of processing effect. *Proc Natl Acad Sci*. 1994:91(6):2008–2011. https://doi.org/10.1073/pnas.91.6.2008.

Keogh R, Pearson J. Mental imagery and visual working memory. *PLoS One*. 2011:6(12):e29221. https://doi.org/10.1371/journal.pone.0029221.

Kirchner WK. Age differences in short-term retention of rapidly changing information. *J Exp Psychol*. 1958:55(4):352–358. https://doi.org/10.1037/h0043688.

Kluen LM, Dandolo LC, Jocham G, Schwabe L. Dorsolateral prefrontal cortex enables updating of established memories. *Cereb Cortex*. 2019:29(10):4154–4168. https://doi.org/10.1093/cercor/bhy298.

Koolschijn RS, Emir UE, Pantelides AC, Nili H, Behrens TEJ, Barron HC. The hippocampus and neocortical inhibitory engrams protect against memory interference. *Neuron*. 2019:101(3):528–541.e6. https://doi.org/10.1016/j.neuron.2018.11.042.

Kosslyn SM, Thompson WL, Alpert NM. Neural systems shared by visual imagery and visual perception: a positron emission tomography study. *NeuroImage*. 1997:6(4):320–334. https://doi.org/10.1006/nimg.1997.0295.

Kriegeskorte N, Mur M. Inverse MDS: inferring dissimilarity structure from multiple item arrangements. *Front Psychol*. 2012:3(245). https://doi.org/10.3389/fpsyg.2012.00245.

Kriegeskorte N, Mur M, Bandettini PA. Representational similarity analysis—connecting the branches of systems neuroscience. *Front Syst Neurosci*. 2008:2. https://doi.org/10.3389/neuro.06.004.2008.

Kringelbach ML. The human orbitofrontal cortex: linking reward to hedonic experience. *Nat Rev Neurosci*. 2005:6(9):Article 9. https://doi.org/10.1038/nrn1747.

Kringelbach ML, Stein A, van Hartevelt TJ. The functional human neuroanatomy of food pleasure cycles. *Physiol Behav*. 2012:106(3):307–316. https://doi.org/10.1016/j.physbeh.2012.03.023.

Laux L, Glanzmann P, Schaffner P, Spielberger CD. *State-trait anxiety inventory—manual of the German version*. Beltz: Weinheim, Germany; 1981

Leutgeb JK, Leutgeb S, Moser M-B, Moser EI. Pattern separation in the dentate gyrus and CA3 of the hippocampus. *Science*. 2007:315(5814):961–966. https://doi.org/10.1126/science.1135801.

Libby LA, Reagh ZM, Bouffard NR, Ragland JD, Ranganath C. The hippocampus generalizes across memories that share item and context information. *J Cogn Neurosci*. 2019:31(1):24–35. https://doi.org/10.1162/jocn_a_01345.

Long NM, Öztekin I, Badre D. Separable prefrontal cortex contributions to free recall. *J Neurosci*. 2010:30(33):10967–10976. https://doi.org/10.1523/JNEUROSCI.2611-10.2010.

Maguire EA, Mullally SL. The hippocampus: a manifesto for change. *J Exp Psychol Gen*. 2013:142(4):1180. https://doi.org/10.1037/a0033650.

Maguire EA, Valentine ER, Wilding JM, Kapur N. Routes to remembering: the brains behind superior memory. *Nat Neurosci*. 2003:6(1):Article 1. https://doi.org/10.1038/nn988.

Marr D. A theory of archicortical function. *Proc R Soc Lond B Biol Sci*. 1971:262:23–81.

Mattfeld AT, Stark CEL. Functional contributions and interactions between the human hippocampus and subregions of the striatum during arbitrary associative learning and memory. *Hippocampus*. 2015:25(8):900–911. https://doi.org/10.1002/hipo.22411.

McClelland JL, McNaughton BL, O'Reilly RC. Why there are complementary learning systems in the hippocampus and neocortex: insights from the successes and failures of connectionist models of learning and memory. *Psychol Rev*. 1995:102(3):419–457. https://doi.org/10.1037/0033-295X.102.3.419.

Mechelli A, Humphreys GW, Mayall K, Olson A, Price CJ. Differential effects of word length and visual contrast in the fusiform and lingual gyri during. *Proc R Soc Lond Ser B Biol Sci*. 2000:267(1455):1909–1913. https://doi.org/10.1098/rspb.2000.1229.

Milivojevic B, Vicente-Grabovetsky A, Doeller CF. Insight reconfigures hippocampal-prefrontal memories. *Curr Biol*. 2015:25(7):821–830. https://doi.org/10.1016/j.cub.2015.01.033.

Molitor RJ, Sherrill KR, Morton NW, Miller AA, Preston AR. Memory reactivation during learning simultaneously promotes dentate gyrus/CA $_{2,3}$ pattern differentiation and CA$_1$ memory integration. *J Neurosci*. 2021:41(4):726–738. https://doi.org/10.1523/JNEUROSCI.0394-20.2020.

Mullally SL, Maguire EA. Memory, imagination, and predicting the future: a common brain mechanism? *Neuroscientist*. 2014:20(3):220–234. https://doi.org/10.1177/1073858413495091.

Muller RU, Kubie JL. The effects of changes in the environment on the spatial firing of hippocampal complex-spike cells. *J Neurosci*. 1987:7(7):1951–1968. https://doi.org/10.1523/JNEUROSCI.07-07-01951.1987.

Müller NCJ, Konrad BN, Kohn N, Muñoz-López M, Czisch M, Fernández G, Dresler M. Hippocampal–caudate nucleus interactions support exceptional memory performance. *Brain Struct Funct*. 2018:223(3):1379–1389. https://doi.org/10.1007/s00429-017-1556-2.

Murray LJ, Ranganath C. The dorsolateral prefrontal cortex contributes to successful relational memory encoding. *J Neurosci*. 2007:27(20):5515–5522. https://doi.org/10.1523/JNEUROSCI.0406-07.2007.

Nakazawa K, Quirk MC, Chitwood RA, Watanabe M, Yeckel MF, Sun LD, Kato A, Carr CA, Johnston D, Wilson MA, et al. Requirement for hippocampal CA3 NMDA receptors in associative memory recall. *Science*. 2002:297(5579):211–218. https://doi.org/10.1126/science.1071795.

Naselaris T, Prenger RJ, Kay KN, Oliver M, Gallant JL. Bayesian reconstruction of natural images from human brain activity. *Neuron*. 2009:63(6):902–915. https://doi.org/10.1016/j.neuron.2009.09.006.

Nili H, Wingfield C, Walther A, Su L, Marslen-Wilson W, Kriegeskorte N. A toolbox for representational similarity analysis. *PLoS Comput Biol*. 2014:10(4):e1003553. https://doi.org/10.1371/journal.pcbi.1003553.

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

Norman KA, O'Reilly RC. Modeling hippocampal and neocortical contributions to recognition memory: a complementary-learning-systems approach. *Psychol Rev*. 2003:110(4):611–646. https://doi.org/10.1037/0033-295X.110.4.611.

Oh Y, Chesebrough C, Erickson B, Zhang F, Kounios J. An insight-related neural reward signal. *NeuroImage*. 2020:214:116757. https://doi.org/10.1016/j.neuroimage.2020.116757.

Otten LJ, Henson RNA, Rugg MD. Depth of processing effects on neural correlates of memory encoding: relationship between findings from across- and within-task comparisons. *Brain*. 2001:124(2): 399–412. https://doi.org/10.1093/brain/124.2.399.

Pine A, Sadeh N, Ben-Yakov A, Dudai Y, Mendelsohn A. Knowledge acquisition is governed by striatal prediction errors. *Nat Commun*. 2018:9:1673. https://doi.org/10.1038/s41467-018-03992-5.

Race E, Keane MM, Verfaellie M. Medial temporal lobe damage causes deficits in episodic memory and episodic future thinking not attributable to deficits in narrative construction. *J Neurosci*. 2011:31(28):10262–10269. https://doi.org/10.1523/JNEUROSCI.1145-11.2011.

Ragland JD, Turetsky BI, Gur RC, Gunning-Dixon F, Turner T, Schroeder L, Chan R, Gur RE. Working memory for complex figures: an fMRI comparison of letter and fractal n-back tasks. *Neuropsychology*. 2002:16:370–379. https://doi.org/10.1037/0894-4105.16.3.370.

Reddan MC, Wager TD, Schiller D. Attenuating neural threat expression with imagination. *Neuron*. 2018:100(4):994–1005.e4. https://doi.org/10.1016/j.neuron.2018.10.047.

Richmond AS, Cummings R, Klapp M. Transfer of the method of loci, pegword, and keyword mnemonics in the eighth grade classroom. *Researcher*. 2008:21(2):1–13.

Ritchey M, LaBar KS, Cabeza R. Level of processing modulates the neural correlates of emotional memory formation. *J Cogn Neurosci*. 2011:23(4):757–771. https://doi.org/10.1162/jocn.2010.21487.

Robin J, Moscovitch M. Details, gist and schema: hippocampal–neocortical interactions underlying recent and remote episodic and spatial memory. *Curr Opin Behav Sci*. 2017:17:114–123. https://doi.org/10.1016/j.cobeha.2017.07.016.

Salimpoor VN, Benovoy M, Larcher K, Dagher A, Zatorre RJ. Anatomically distinct dopamine release during anticipation and experience of peak emotion to music. *Nat Neurosci*. 2011:14(2):257–262.

Schacter DL, Addis DR, Buckner RL. Remembering the past to imagine the future: the prospective brain. *Nat Rev Neurosci*. 2007:8(9):Article 9. https://doi.org/10.1038/nrn2213.

Vv M, Schacter DL, Corballis MC, Addis DR. Re-imagining the future: repetition decreases hippocampal involvement in future simulation. *PLoS One*. 2013:8(7):e69596. https://doi.org/10.1371/journal.pone.0069596.

Schapiro AC, Turk-Browne NB, Botvinick MM, Norman KA. Complementary learning systems within the hippocampus: a neural network modelling approach to reconciling episodic memory with statistical learning. *Philos Trans R Soc B Biol Sci*. 2017:372(1711):20160049. https://doi.org/10.1098/rstb.2016.0049.

Schlichting ML, Preston, AR. The hippocampus and memory integration: building knowledge to navigate future decisions. In: Hannula DE, Duff MC, editors. *The hippocampus from cells to systems: structure, connectivity, and functional contributions to memory and flexible cognition*. Basel, Switzerland: Springer International Publishing; 2017. p. 405–437. https://doi.org/10.1007/978-3-319-50406-3_13.

Schlichting ML, Mumford JA, Preston AR. Learning-related representational changes reveal dissociable integration and separation signatures in the hippocampus and prefrontal cortex. *Nat Commun*. 2015:6(1):1–10. https://doi.org/10.1038/ncomms9151.

Schmidt D, Krause BJ, Weiss PH, Fink GR, Shah NJ, Amorim M-A, Müller H-W, Berthoz A. Visuospatial working memory and changes of the point of view in 3D space. *NeuroImage*. 2007:36(3): 955–968. https://doi.org/10.1016/j.neuroimage.2007.03.050.

Schulz P, Schlotz W. Trierer Inventar zur Erfassung von chronischem Sre (TICS): Skalenkonstruktion, teststatistische Überprüfung und Validierung der Skala Arbeitsüberlastung. [The Trier Inventory for the Assessment of Chronic Stress (TICS). Scale construction, statistical testing, and validation of the scale work overload.]. *Diagnostica*. 1999:45(1):8–19. https://doi.org/10.1026//0012-1924.45.1.8.

Seeley WW. The salience network: a neural system for perceiving and responding to homeostatic demands. *J Neurosci*. 2019:39(50): 9878–9882. https://doi.org/10.1523/JNEUROSCI.1138-17.2019.

Shohamy D, Daw ND. Integrating memories to guide decisions. *Curr Opin Behav Sci*. 2015:5:85–90. https://doi.org/10.1016/j.cobeha.2015.08.010.

Slamecka NJ, Graf P. The generation effect: delineation of a phenomenon. *J Exp Psychol Hum Learn Mem*. 1978:4:592–604. https://doi.org/10.1037/0278-7393.4.6.592.

Squire, LR, van der Horst, AS, McDuff, SG, Frascino, JC, Hopkins, RO, & Mauldin, KN. Role of the hippocampus in remembering the past and imagining the future. *Proc Natl Acad Sci*. 2010:107(44): 19044–19048. https://doi.org/10.1073/pnas.1014391107.

Stokes M, Thompson R, Cusack R, Duncan J. Top-down activation of shape-specific population codes in visual cortex during mental imagery. *J Neurosci*. 2009:29(5):1565–1572. https://doi.org/10.1523/JNEUROSCI.4657-08.2009.

Tik M, Sladky R, Luft CDB, Willinger D, Hoffmann A, Banissy MJ, Bhattacharya J, Windischberger C. Ultra-high-field fMRI insights on insight: neural correlates of the Aha!-moment. *Hum Brain Mapp*. 2018:39(8):3241–3252.

Tulving E. *Elements of episodic memory*. Oxford, United Kingdom: Oxford University Press; 1983

Tulving E. Memory and consciousness. *Can Psychol/Psychologie Canadienne*. 1985:26(1):1–12. https://doi.org/10.1037/h0080017.

Uddin LQ. Salience processing and insular cortical function and dysfunction. *Nat Rev Neurosci*. 2015:16:55-61. https://doi.org/10.1038/nrn3857.

Walther A, Nili H, Ejaz N, Alink A, Kriegeskorte N, Diedrichsen J. Reliability of dissimilarity measures for multi-voxel pattern analysis. *NeuroImage*. 2016:137:188–200. https://doi.org/10.1016/j.neuroimage.2015.12.012.

Wammes J, Norman KA, Turk-Browne N. Increasing stimulus similarity drives nonmonotonic representational change in hippocampus. *elife*. 2022:11:e68344. https://doi.org/10.7554/eLife.68344.

Wang Q, Bui V-K, Song Q. Narrative organisation at encoding facilitated children's long-term episodic memory. *Memory*. 2015:23(4):602–611. https://doi.org/10.1080/09658211.2014.914229.

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

Yassa MA, Stark CEL. Pattern separation in the hippocampus. *Trends Neurosci*. 2011:34(10):515–525. https://doi.org/10.1016/j.tins.2011.06.006.

Yesavage JA, Rose TL. Semantic elaboration and the method of loci: a new trip for older learners. *Exp Aging Res*. 1984:10(3):155–159. https://doi.org/10.1080/03610738408258560.

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

Zabelina DL, Condon DM. The four-factor imagination scale (FFIS): a measure for assessing frequency, complexity, emotional valence, and directedness of imagination. *Psychol Res*. 2020:84:2287-2299. https://doi.org/10.1007/s00426-019-01227-w.

Zeidman P, Maguire EA. Anterior hippocampus: the anatomy of perception, imagination and episodic memory. *Nat Rev Neurosci*. 2016:17(3):173-182. https://doi.org/10.1038/nrn.2015.24.

Zeithamova D, Preston AR. Flexible memories: differential roles for medial temporal lobe and prefrontal cortex in cross-episode binding. *J Neurosci*. 2010:30(44):14676–14684. https://doi.org/10.1523/JNEUROSCI.3250-10.2010.

Zeithamova D, Dominick AL, Preston AR. Hippocampal and ventral medial prefrontal activation during retrieval-mediated learning supports novel inference. *Neuron*. 2012:75(1):168–179. https://doi.org/10.1016/j.neuron.2012.05.010.

Downloaded from https://academic.oup.com/cercor/article/33/12/7409/7086049 by Staats- und Universitätsbibliothek Hamburg user on 25 October 2023

Supplementary material

Imagining is not seeing: Lower insight-driven memory reconfiguration when imagining the link between separate events

Anna-Maria Grob[1], Branka Milivojevic[2], Arjen Alink[3], Christian F. Doeller[4,5,6], and Lars Schwabe[1]

[1]Department of Cognitive Psychology, Institute of Psychology, Universität Hamburg, 20146 Hamburg, Germany; [2]Radboud University, Donders Institute for Brain, Cognition and Behaviour, 6525 AJ Nijmegen, the Netherlands; [3]Department of General Psychology, Institute of Psychology, Universität Hamburg, 20146 Hamburg, Germany; [4]Max-Planck-Insitute for Human Cognitive and Brain Sciences, 04103 Leipzig, Germany, Germany; [5]Kavli Institute for Systems Neuroscience, Centre for Neural Computation, The Egil and Pauline Braathen and Fred Kavli Centre for Cortical Microcircuits, Jebsen Centre for Alzheimer's Disease, Norwegian University of Science and Technology, 7491 Trondheim, Norway; [6]Wilhelm Wundt Institute of Psychology, 04109 Leipzig University, Leipzig, Germany

Corresponding author: Lars.Schwabe@uni-hamburg.de

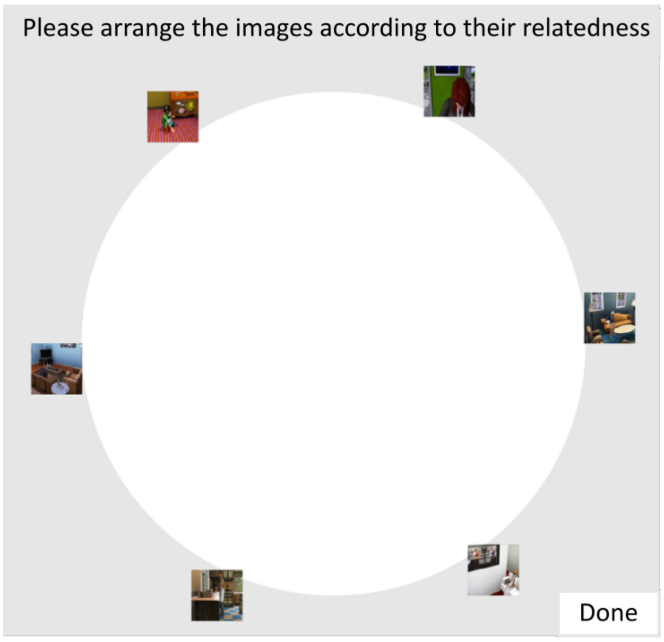


Fig. S1. Multidimensional arena task. Participants were instructed to arrange representative images of the video events (A, B, and X) of each story according to their relatedness on a two-dimensional circular arena in a multidimensional arena task (Kriegeskorte & Mur, 2012). They were asked to bring the pictures that had been linked (A and B) one week earlier closer together than the pictures that had not been linked (A and X, B and X) by dragging and dropping them with the computer mouse within a white circular arena on the computer screen. Please note that texts were presented in German and are translated here.

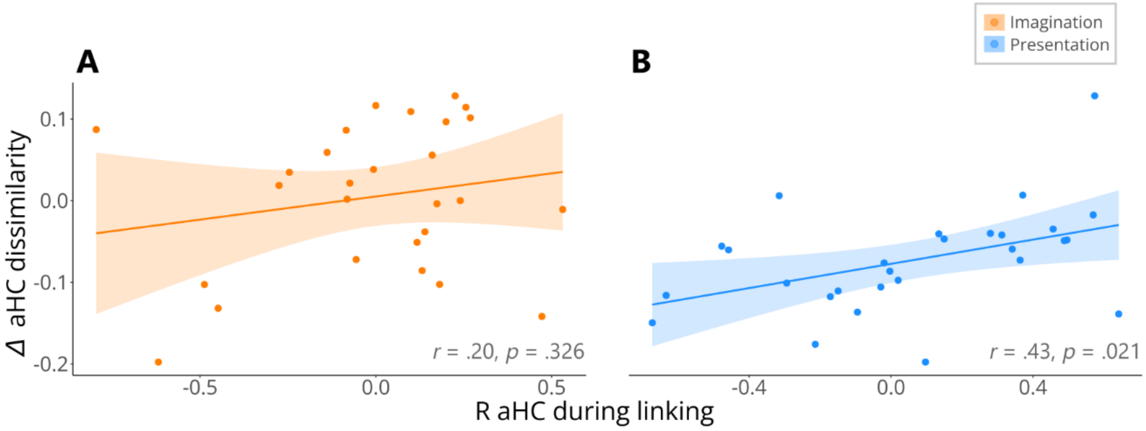


Fig. S2. Association hippocampus activity during linking and representational change from pre- to post-insight. **A**, Non-significant correlation between right anterior hippocampal activity (R aHC) during linking and pre- to post-insight change in representational dissimilarity in right anterior hippocampus (aHC) in imagination group. **B**, Significant positive correlation between right anterior hippocampal activity (R aHC) during linking and pre- to post-insight change in representational dissimilarity in right anterior hippocampus (aHC) in observation group.

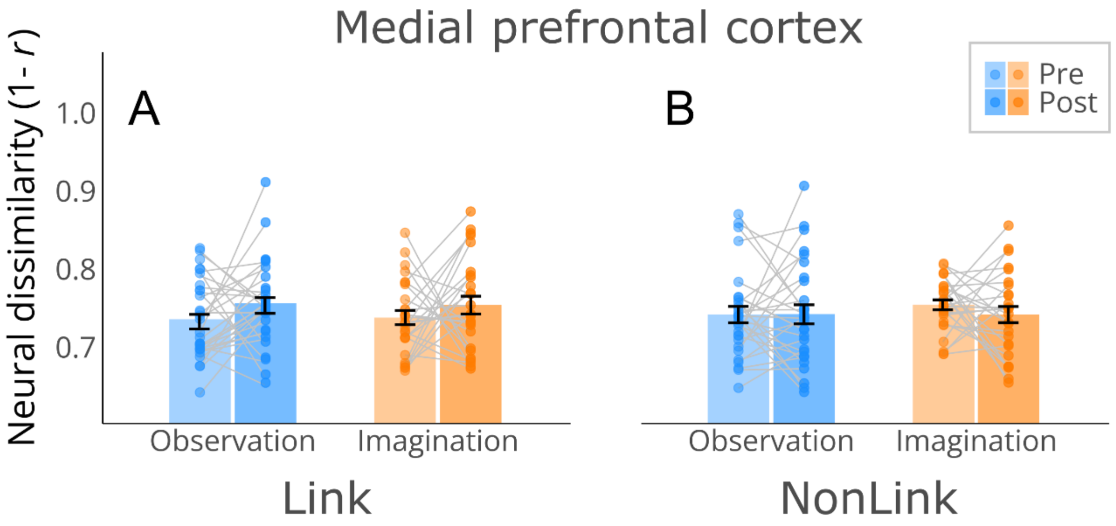


Fig. S3. Results for RSA in the medial prefrontal cortex. **A**, Non-significant difference between pre- and post-insight for linked events in the medial prefrontal cortex in the observation and non-significant difference in the imagination group. **B**, Non-significant pre- and post-insight neural dissimilarities for non-linked events in the medial prefrontal cortex for the observation and the imagination group.

Appendix C: Study 3

Grob, A.-M., Heinbockel, H., Milivojevic, B., Doeller, C., & Schwabe, L. (2023). Causal role of the angular gyrus in insight-driven memory reconfiguration. *bioRxiv*, https://doi.org/10.1101/2023.08.18.553803

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Causal role of the angular gyrus in insight-driven memory reconfiguration

Anna-Maria Grob[1], Hendrik Heinbockel[1], Branka Milivojevic[2], Christian Doeller[3,4,5], and Lars Schwabe[1]

[1]Department of Cognitive Psychology, Institute of Psychology, Universität Hamburg, 20146 Hamburg, Germany; [2]Radboud University, Donders Institute for Brain, Cognition and Behaviour, 6525 AJ Nijmegen, the Netherlands; [3]Max-Planck-Insitute for Human Cognitive and Brain Sciences, 04103 Leipzig, Germany; [4]Kavli Institute for Systems Neuroscience, Centre for Neural Computation, The Egil and Pauline Braathen and Fred Kavli Centre for Cortical Microcircuits, Jebsen Centre for Alzheimer's Disease, Norwegian University of Science and Technology, 7491 Trondheim, Norway; [5]Wilhelm Wundt Institute of Psychology, 04109 Leipzig University, Leipzig, Germany

Corresponding author: Lars.Schwabe@uni-hamburg.de

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Abstract

Maintaining an accurate model of the world relies on our ability to update memory representations in light of new information. Previous research on the integration of new information into memory mainly focused on the hippocampus. Here, we hypothesized that the angular gyrus, known to be involved in episodic memory and imagination, plays a pivotal role in the insight-driven reconfiguration of memory representations. To test this hypothesis, participants received continuous theta burst stimulation (cTBS) inhibiting the left angular gyrus or sham stimulation before gaining insight into the relationship between previously separate life-like animated events in a narrative-insight task. During this task, participants also underwent EEG recording and their memory for linked and non-linked events was assessed shortly thereafter. Our results show that cTBS to the angular gyrus decreased memory for the linking events and reduced the memory advantage for linked relative to non-linked events. At the neural level, cTBS-induced angular gyrus inhibition reduced centro-temporal coupling with frontal regions and abolished insight-induced neural representational changes for events linked via imagination, indicating impaired memory reconfiguration. Further, the cTBS group showed representational changes for non-linked events that resembled the patterns observed in the sham group for the linked events, suggesting failed pruning of the narrative in memory. Together, our findings demonstrate a causal role of the left angular gyrus in insight-related memory reconfigurations.

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Introduction

The capacity to flexibly update our memories in light of new information is fundamental to maintaining an accurate model of the world around us. This flexibility requires adaptable memory networks that can be reconfigured upon acquiring new insights. Previous research provided direct evidence for insight-induced reconfigurations of memory representations and showed that insight into the connection of initially separate events propels the integration of these events into coherent episodes (Collin et al., 2015; Milivojevic et al., 2015). Such mnemonic integration allows novel inferences (Spalding et al., 2018; Zeithamova et al., 2012) that aid efficient navigation (Coutanche et al., 2013; Fernandez et al., 2023; He et al., 2022) and decision-making (Boorman et al., 2021; Kumaran et al., 2009; Shohamy & Daw, 2015). Importantly, in everyday life, the inference about the relationship between seemingly unrelated events is often not inferred via direct observation but through imagination. For instance, when reading a book, we gain insight into the plot and possible twists through our imagination, which then prompts us to update our memory representations. Even when new insights are derived from direct observation, the integration process requires imaginative capacities to bind the previously separate memories into a coherent narrative. At the neural level, the hippocampus has been shown to play a pivotal role in (imagination-based) mnemonic integration (Cohn-Sheehy et al., 2021; Collin et al., 2015; Griffiths & Fuentemilla, 2020; Grob et al., 2023a; Milivojevic et al., 2015). However, while the hippocampus appears to be crucial for mnemonic integration, it does not act in isolation but operates in collaboration with cortical areas to accomplish this complex process (Backus et al., 2016; Milivojevic et al., 2015; Pehrs et al., 2018; Schlichting & Preston, 2015; Spalding et al., 2018). Yet, our understanding of the specific areas implicated in the insight-driven reconfiguration of memory representations, beyond the hippocampus, remains limited. Moreover, existing data on the neural underpinnings of mnemonic integration are mainly correlational in nature and which areas are causally involved in the integration of initially unrelated memories into cohesive representations is completely unknown.

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

One promising candidate that may contribute to insight-driven memory reconfiguration is the angular gyrus. The angular gyrus has extensive structural and functional connections to many other brain regions (Petit et al., 2023), including the hippocampus (Coughlan et al., 2023; Thakral et al., 2020; Uddin et al., 2010; Wang et al., 2014). Accordingly, the angular gyrus has been implicated in a myriad of cognitive functions, including mental arithmetic, visuospatial processing, inhibitory control, and theory-of-mind (Cattaneo et al., 2009; Grabner et al., 2009; Lewis et al., 2019; Schurz et al., 2014). Moreover, there is accumulating evidence pointing to a key role of the angular gyrus in long-term memory (Bellana et al., 2017; Bonnici et al., 2018; Kwon et al., 2022; Wang et al., 2014) and imagination (Ramanan et al., 2018; Thakral et al., 2017, 2020). How these putative functions of the angular gyrus relate to one another, however, remained unclear. We reasoned that these functions might be directly linked, enabling the angular gyrus to drive the integration of (imagination-related) insights into long-term memory. In line with this idea, recent theories propose that the angular gyrus acts as dynamic buffer for spatiotemporal representations (Humphreys et al., 2021), which may allow the angular gyrus to transiently maintain the initially separate events and to integrate these into cohesive narratives. This buffering function of the angular gyrus may be particularly relevant for imagination-based linking. Thus, we hypothesized that the angular gyrus plays a crucial role in integrating imagination-related insights into long-term memory and hence in the dynamic reconfiguration of memory representations in light of new information.

To test this hypothesis and determine the causal role of this area in insight-related memory reconfigurations, we conducted a preregistered study combining a life-like video-based narrative-insight task (NIT; Milivojevic et al., 2015; Fig. 1), probing insight-related reconfigurations of memory, with representational similarity analysis of EEG data and (double-blind) ‘neuro-navigated’ TMS to an area of the left angular gyrus that was implicated in imaginative processing before (Thakral et al., 2017). We predicted that cTBS to the left angular gyrus would reduce the impact of (imagination-based) insight into the link of initially unrelated events on memory performance as well as the insight-driven neural reconfiguration of linked and non-linked event representations.

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

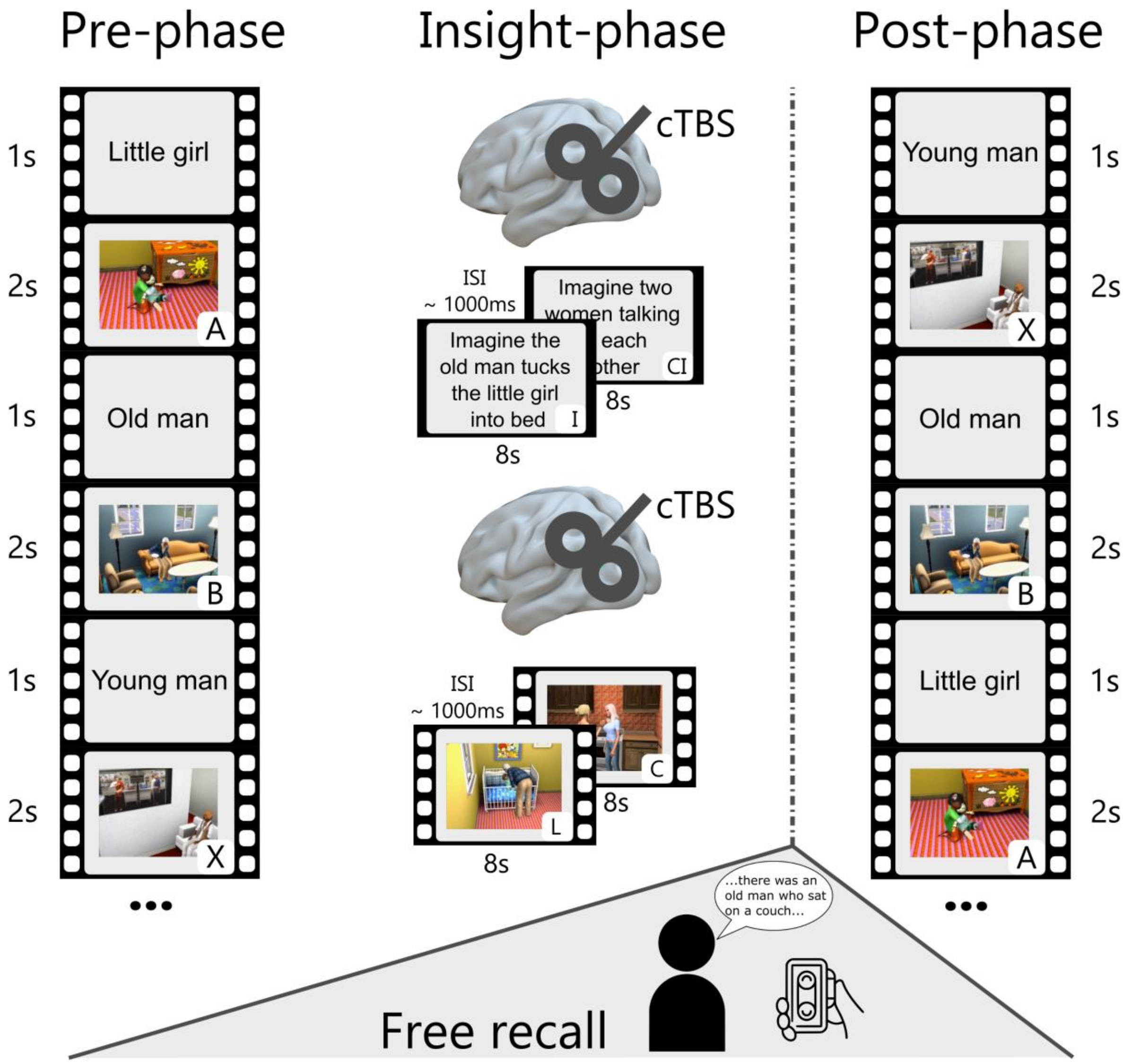


Fig. 1. Modified narrative-insight task (NIT) and procedure. During the pre-phase, participants viewed video events (A, B, and X) from ten different storylines. Each event was preceded by a title (1s) and repeated 18 times. The inter-stimulus interval (ISI) was ~ 1000 ms. The subsequent insight-phase consisted of two parts. In one part, participants gained insight through a written imagination instruction (I) interspersed with a control instruction (CI). In the other part, they gained insight through a linking video (L) interspersed with a control video (C). The order of gaining insight through imagination or video observation was counterbalanced across participants. Before each insight part, participants received, depending on the experimental group, either a sham or cTBS stimulation over the left angular gyrus (MNI: -48, -67, 30). After the insight-phase, participants had a 30-minute break and then completed a free recall for a maximum of 20 minutes in a different room. In the post-phase, all video events were presented in the same manner as the pre-phase.

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Results

Inhibition of the angular gyrus reduces insight-related memory boost

The angular gyrus has been implicated in a myriad of tasks and functions, including long-term memory (Bonnici et al., 2018; Kwon et al., 2022; Wang et al., 2014) and imagination (Ramanan et al., 2018; Thakral et al., 2017). Here we hypothesized that these functions of the angular gyrus are directly linked to one another. Specifically, we postulated that the angular gyrus plays a crucial role in the integration of imagination-related insights into long-term memory representations and that it thus represents a key player in the dynamic reconfiguration of memory in light of new information. To test this hypothesis and the causal role of the angular gyrus in insight-related memory reconfigurations, we combined the life-like video-based NIT with representational similarity analysis of EEG data and (double-blind) neuro-navigated TMS over the left angular gyrus. During the NIT, participants first saw three video events (A, B, and X; pre-phase), which were then either linked into a narrative (A and B) or not (A and X) in a subsequent insight-phase. Critically, before the insight-phase, we applied either sham stimulation (31 participants, 15 females) or inhibitory continuous theta burst stimulation (cTBS; 34 participants, 16 females) to the left angular gyrus. Following the insight-phase and a 30-minute break to mitigate potential TMS aftereffects (Huang et al., 2005; Jannati et al., 2023), participants completed a free recall task, which provided a measure of insight-related changes in subsequent memory. Thereafter, participants saw the same video events (A, B, and X) again in a post-phase. EEG was measured during all stages of the NIT. Contrasting neural representation patterns from the pre- and post-phases allowed us to assess insight-related memory reconfiguration and its modulation by angular gyrus inhibition. Due to its specific relevance in imaginative processes (Ramanan et al., 2018; Thakral et al., 2017, 2020), we expected that the angular gyrus would be particularly relevant if insight relies strongly on imagination. Therefore, participants gained insight into half of the stories by imagining the link themselves, while they observed the link as a video in the other half of the stories. Participants' ratings showed that they adhered well to these instructions during the linking phase. When linking events via imagination, they reported imagining the linking events very

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

well (M = 3.38, SD = 0.47) and their imagination as depictive (M = 3.35, SD = 0.46). When linking via observation, they reported a high level of understanding of the linking events (M = 3.37, SD = 0.51) and found the linking events meaningful (M = 3.35, SD = 0.52) on a 1-4 Likert scale. Furthermore, participants demonstrated a high level of attention throughout the NIT, responding to target stimuli with near-ceiling performance (M = 99.25 %; SD = 1.40 %) without any group differences ($t(63.00) = 0.42$, $p = 0.675$, $d = -0.10$).

Importantly, participants were unaware of the allocation to the cTBS or sham condition, as indicated by the treatment guess at the end of the experiment (Fisher's exact test; $p = 0.597$). Furthermore, TMS stimulation did not affect participants' subjective mood, wakefulness or arousal (mood: *group* × *time*: $F(1, 63) = 0.76$, $p = 0.386$, $\eta_G = 0.00$; wakefulness*: group* × *time*: $F(1, 63) = 0.01$, $p = 0.921$, $\eta_G = 0.00$; arousal*: group* × *time*: $F(1, 63) = 0.01$, $p = 0.921$, $\eta_G = 0.00$).

As expected, all participants gained insight into which events were linked in the NIT, as they rated the belongingness of linked events higher than non-linked events from pre- to post-insight, as indicated by a linear mixed model (LMM: *time* × *link*: $\beta = 2.49$, 95% CI [2.15, 2.83], $t(418.44) = 14.01$, $p < 0.001$; Figure 2 – Figure supplement 1). Post-hoc tests showed increasing belongingness ratings for linked events and decreasing belongingness ratings for non-linked events from pre- to post-insight (LMM: *link*: $\beta = 1.49$, 95% CI [1.33, 1.64], $t(418) = 24.49$, $p < 0.001$; *non-link*: $\beta = -.91$, 95% CI [-1.07, -.76], $t(418.00) = -15.03$, $p < 0.001$). This insight was further reflected in the multi-arrangements task (MAT), in which participants were instructed to arrange representative images (A, B, and X) from each story based on their relatedness. In this task, all participants arranged linked events closer together than non-linked events (MAT; LMM: *link*: $\beta = -1.33$, 95% CI [-1.59, -1.07], $t(177.00) = -9.81$, $p < 0.001$; Figure 2 – Figure supplement 2). The strong insight gained by all participants was further reflected in their near-ceiling performance in the forced-choice recognition task, in which participants were instructed to identify the event (B or X) that was linked with A. Participants accurately indicated whether B or X was linked to A (sham: M = 94.65%, SD = 9.00%; cTBS: M = 97.34%, SD = 6.10%; Figure 2 – Figure supplement 3). Importantly, there were no group

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

differences in any of these measures (LMM: NIT: *group* × *time* × *link*: β = -0.02, 95% *CI* [-0.49, 0.45], *t*(418.27) = -0.09, *p* = 0.929; LMM: MAT: *group* × *link*: β = 0.11, 95% *CI* [-0.26, 0.48], *t*(177.00) = 0.58, *p* = 0.561; LMM: Forced-choice recognition: *group*: β = 0.23, 95% *CI* [-0.26, 0.72], *t*(113.37) = 0.90, *p* = 0.368), indicating that all participants successfully gained insight into which events were linked and that the (left) angular gyrus did not play a critical role in the process of gaining insight itself.

To investigate the causal role of the left angular gyrus in insight-related episodic memory integration, the key question of this study, we first analyzed the detailedness of participants' memory for both linked and non-linked events during free recall. Across groups, linked events were generally recalled in more detail than non-linked events (LMM: *link*: β = 1.20, 95% *CI* [0.86, 1.54], *t*(406.00) = 6.75, $p < 0.001$), suggesting a memory boost for integrated narratives. Most interestingly, inhibiting the left angular gyrus through cTBS reduced this insight-related memory boost for linked events significantly (LMM: *group* × *link*: β = -0.54, 95% *CI* [-1.02, -0.06], *t*(406.00) = -2.17, *p* = 0.030; Fig. 2A). Pairwise comparisons revealed a significantly lower number of recalled details for linked events in the cTBS compared to the sham group, while there was no significant difference for non-linked events (LMM: *link*: β = -0.40, 95% *CI* [-0.79, -0.02], *t*(85.50) = -2.79, *p* = 0.033; LMM: *non-link*: β = -0.09, 95% *CI* [-0.29, 0.42], *t*(406.00) = -0.62, *p* = 0.926). Additionally, we observed that all participants showed better memory for central compared to peripheral details of the plot when recalling linked events, which was not observed to the same extent for non-linked events (LMM: *link* × *detail*: β = 0.61, 95% *CI* [0.12, 1.09], *t*(406.00) = 2.43, *p* = 0.016).

In a second step, we analyzed whether cTBS to the angular gyrus affected, in addition to memory detailedness for initially separate but now linked events, also the memory for the linking events themselves. Our results showed that cTBS (vs. sham) significantly reduced the frequency with which participants recalled the linking events (LMM: *group*: β = -0.66, 95% *CI* [-1.13, -0.18], *t*(98.13) = -2.71, *p* = 0.008; Fig. 2B). Interestingly, this TMS effect appeared to be particularly pronounced when events were linked via imagination (cTBS vs. sham: *t*(61.46) = -2.53, *p* = 0.014, *d* = -0.63) and was less prominent when they were linked via direct

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

observation (cTBS vs. sham: $t(58.59) = -1.63$, $p = 0.107$, $d = -0.40$), although it is important to note that the interaction was not significant (LMM: *group* × *mode*: $\beta = 0.30$, 95% *CI* [-0.18, 0.77], $t(62) = 1.23$, $p = 0.225$).

To assess the effect of cTBS stimulation on the angular gyrus (Pizem et al., 2022; Zhang et al., 2022), we performed electric field simulations at 80 % of the individual motor threshold, averaging the estimated field strength within a 10mm sphere centered around the angular gyrus coordinate (MNI: -48, -67, 30). In order to examine whether the behavioral effects were dependent on the simulated electric field strength (Fig. 2C), we next included electric field strength (strong vs. weak via median split) and repeated the previous linear mixed model predicting the number of details for linked events including a group factor reflecting stimulation strength (sham, low, high). This model yielded a significant *group* × *link* interaction (LMM: $\beta = -0.78$, 95% *CI* [-1.35, -0.21,], $t(399.00) = -2.63$, $p = 0.009$; Fig. 2D), suggesting a dependency of memory on stimulation strength. Pairwise comparisons for linked events confirmed that a stronger electric field induction in the angular gyrus significantly reduced the memory boost for linked events, while there was no such effect for weak cTBS stimulation (LMM: sham vs. low: $\beta = 0.05$, 95% *CI* [-0.45, 0.55], $t(87.70) = 0.28$, $p = 1.000$; sham vs. high: $\beta = 0.74$, 95% *CI* [0.25, 1.23], $t(87.7) = 4.45$, $p < 0.001$, low vs. high: $\beta = 0.69$, 95% *CI* [0.13, 1.26], $t(87.7) = 3.60$, $p = 0.007$). We further included the electric field strength (strong vs. weak via median split) and repeated the previous linear mixed model predicting the naming of the linking events including the group factor stimulation strength (sham, low, high). This analysis yielded a significant effect of *group* (LMM: $\beta = -0.92$, 95% *CI* [-1.50, -0.35], $t(97.79) = -3.11$, $p = 0.003$; Fig. 2E), suggesting that the memory for the linking events was dependent on the angular gyrus stimulation strength.

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

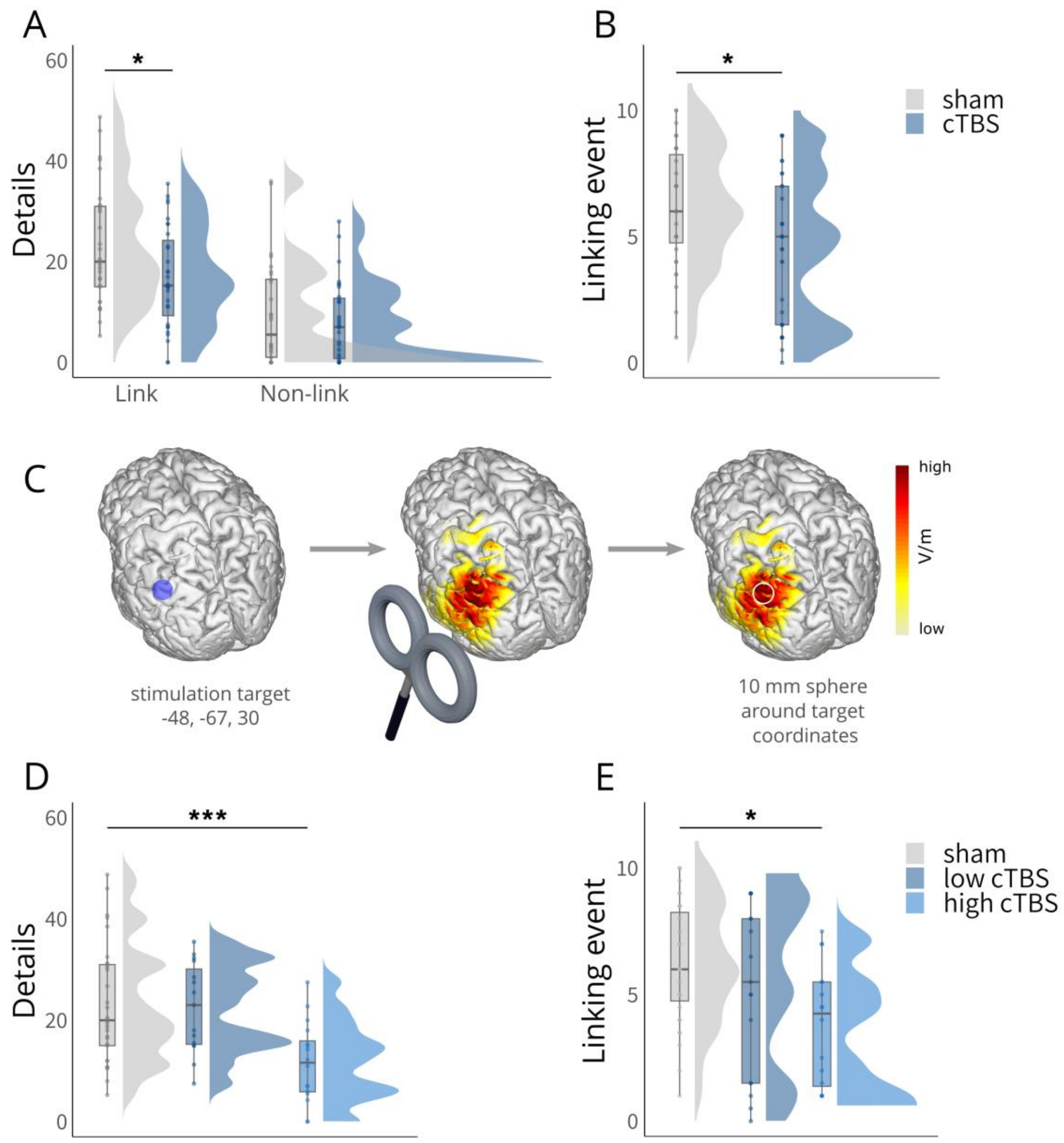


Fig 2. Behavioral results. **A**, Significantly reduced recall of details for linked events in the cTBS group compared to the sham group, with no significant difference for the non-linked events. **B**, Significantly reduced recall of the linking events in the cTBS group compared to the sham group. **C**, Schematic overview of electric field modeling: Simulation was performed for the angular gyrus coordinate (MNI: x = -48, y = -67, z = 30) using a Magstim 70mm figure-of eight coil at 80 % of individual motor thresholds, reflecting the applied setup. The resulting electric field was averaged within a 10mm spherical ROI and centered on the target coordinate and extracted for subsequent analyses. **D**, Significantly reduced number of details recalled for linked events specifically in the high cTBS group (based on a median-split on simulated electric field strengths). **E**, Significantly reduced recall of the linking events specifically in the high cTBS group (based on a median-split on simulated electric field strengths). Boxplots show the median for each group. Boxplot whiskers extend to the minimum or maximum value within 1.5 times the interquartile range. Points within the boxplot indicate individual data points per each group. Density plots indicate data distribution per group. The belongingness ratings for the linked and non-linked events are shown in Figure 2

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

– Figure supplement 1, the data of the multiple arrangements task in Figure 2 – Figure supplement 2, and the data of the forced-choice recognition test in Figure 2 – Figure supplement 3. Statistical differences stem from pairwise post-hoc tests of marginal means. $^{*}p < 0.05$, $^{***}p < 0.001$.

Angular gyrus inhibition disrupts neural pattern reconfiguration following imagination-based insight

Our behavioral data showed that cTBS to the angular gyrus reduced the insight-related memory boost. In a next step, we tested whether inhibitory stimulation of the angular gyrus may also alter the insight-related reconfiguration of neural memory representations, taking the mode of insight (i.e. imagination vs. observation) into account. To this end, we leveraged representational similarity analysis (RSA) of EEG data and compared changes in multivariate oscillatory theta power patterns for linked and non-linked events from pre- to post-insight (Fig. 3A). We focused exclusively on the theta band since theta has been shown to hold a key role in episodic memory integration (Backus et al., 2016; Nicolás et al., 2021). For this analysis, similarity maps (time × time) were computed by correlating story-specific theta frequency patterns within linked (A with B) and within non-linked (A with X) events in the pre- and post-phase, separately.

We examined insight-induced effects on neural representations for linked events by comparing the change from pre- to post-insight (post - pre) and the difference between imagination and observation (imagination – observation) between cTBS and sham groups using an independent sample cluster-based permutation t-test. This analysis yielded a negative cluster ($p = 0.032$, *ci*-range = 0.00, $SD = 0.00$) in the parieto-temporal region (electrodes: T7, Tp7, P7; Fig. 3B). Follow-up tests on the extracted similarity cluster analyzed the representational pattern change and its modulation by TMS separately for the imagination and observation condition. For stories linked via imagination, we obtained an increase in representational similarity from pre- to post-insight in the sham group ($t(30) = 3.48$, $p = 0.002$, $d_{repeated\ measures} = 0.62$), whereas there was no such increase and even a trend for a decrease in representational similarity for linked events from pre- to post-insight in the cTBS group ($t(30) = -2.01$, $p = 0.053$, $d_{repeated\ measures} = -0.36$; *group* × *time*: $F(1, 60) = 14.03$, $p < 0.001$, $\eta_G = 0.09$; Fig. 3B

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

middle panel). Interestingly, we observed that a lower change (post - pre) in representational similarity of events linked via imagination (vs. observation) was associated, across groups, with a reduced probability of recall of the linking events ($r = 0.27$, $t(59) = 2.17$, $p = 0.034$), suggesting a direct association between neural pattern reconfiguration and subsequent memory.

For stories that were linked via observation, we observed a seemingly opposite pattern (*group* × *time*: $F(1, 60) = 19.21$, $p < 0.001$, $\eta_G = 0.12$): decreased similarity in the sham group ($t(30) = -3.94$, $p < 0.001$, $d_{repeated\ measures} = -0.62$) but increased representational similarity in the cTBS group ($t(30) = 2.30$, $p = 0.029$, $d_{repeated\ measures} = 0.62$; Fig. 3B lower panel). However, these changes in representational similarity for the observation condition should be interpreted with caution, as these seemingly opposite changes appeared to be at least in part driven by group differences already in the pre-phase, before participants gained insight.

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

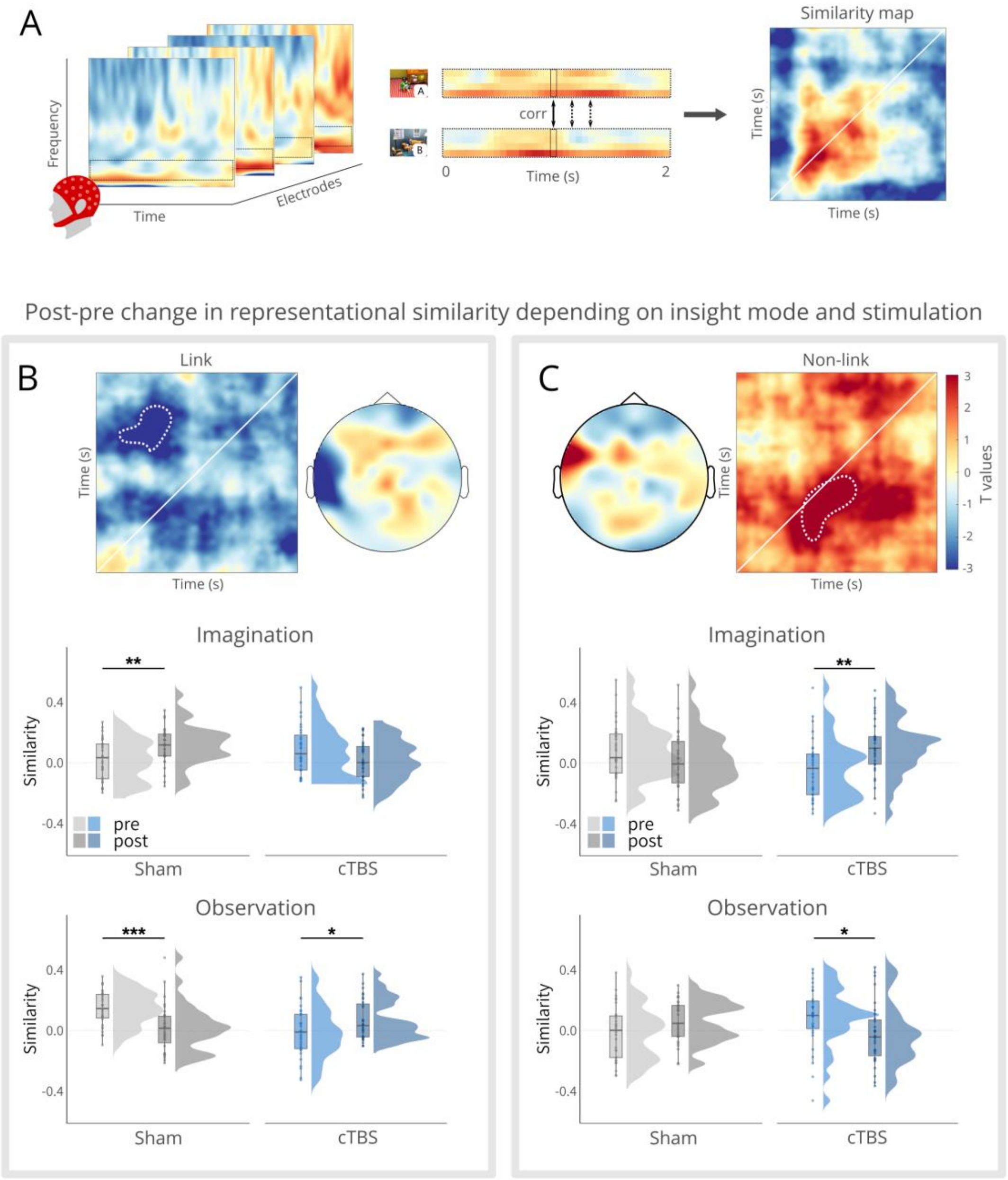


Fig 3. Representational pattern changes. **A**, Conceptual overview of the representational similarity analysis (RSA) on theta oscillations. First, time-frequency data was computed, and the theta power values (4-7 Hz) were extracted. Using these feature vectors, Pearson's correlations were computed to compare the power patterns across time points of events (here: event A and B). These correlations resulted in a time × time similarity map. **B**, Significant cluster, denoted by white dotted line for illustrative purposes, for the change from post-pre and imagination-observation between the cTBS and sham groups using an independent sample cluster-based permutation t-test for linked events (A and B). In the middle panel, follow-up tests on stories linked via imagination revealed increased similarity for the sham group, while no significant effect was observed for the cTBS group. In the lower panel, follow-up tests on stories linked via observation showed decreased similarity for the sham group and increased similarity for the cTBS group. **C**, Significant cluster, denoted by white dotted line for illustrative purposes, for the change from post-pre and imagination-observation between the cTBS and sham groups using an independent sample cluster-based

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

permutation t-test for non-linked events (A and X). In the middle panel, follow-up tests on stories linked via imagination revealed increased similarity for the cTBS group, while no significant effect was observed for the sham group. In the lower panel, follow-up tests on stories linked via observation showed decreased similarity for the cTBS group and no significant effect for the sham cTBS group. Boxplots show the median similarity for each group at each time point. Boxplot whiskers extend to the minimum or maximum value within 1.5 times the interquartile range. Points within the boxplot indicate individual data points in each group. Density plots indicate data distribution per group and time. $*p < 0.05$, $**p < 0.01$, $***p < 0.001$.

Interestingly, we observed a different pattern of insight-related representational pattern changes for non-linked events. Similarly to linked events, we compared the change from pre- to post-insight and the difference between imagination and observation between cTBS and sham using an independent sample cluster-based permutation t-test. This analysis yielded a positive cluster ($p = 0.035$, *ci*-range = 0.00, *SD* = 0.00) in a fronto-temporal region (electrode: FT7; Fig. 3C). Again, we pursued this effect with separate follow-up tests for the imagination and observation conditions. In the imagination condition, the sham group did not show any representational changes for non-linked events ($t(30) = -1.35$, $p = 0.187$; $d_{repeated\ measures} = -0.23$), while we observed increased neural similarity for non-linked events from pre- to post-insight in the cTBS group ($t(30) = 3.61$, $p = 0.001$, $d_{repeated\ measures} = 0.67$; Fig. 3C middle panel). Thus, participants who received cTBS to the angular gyrus showed a pattern of pre- to post-insight representational changes for non-linked events that resembled the pattern observed in the sham group for events linked via imagination, suggesting that angular gyrus inhibition before gaining imagination-based insight interfered with efficient pruning of the integrated narrative.

For stories linked via observation, we observed, again, a seemingly opposite pattern (*group* × *time*: $F(1, 60) = 10.32$, $p = 0.002$, $\eta_G = 0.07$): no representational change in the sham group ($t(30) = 1.65$, $p = 0.110$, $d_{repeated\ measures} = 0.34$) but decreased neural similarity for non-linked events from pre- to post-insight in the cTBS group ($t(30) = -2.40$, $p = 0.023$, $d_{repeated\ measures} = -0.42$). Again, these representational changes should be interpreted with caution, as the differences appear to be at least in part driven by group differences in the pre-insight phase.

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Inhibiting the angular gyrus diminishes fronto-temporal connectivity associated with imagination-based insight

To further elucidate the neural mechanisms involved in the changes in insight-related memory reconfiguration after cTBS to the left angular gyrus, we next examined changes in functional connectivity using the same contrast as in the previous RSA analyses. More specifically, we computed imaginary coherence for the mean theta frequency using a sliding window approach and tested the change in connectivity from pre- to post-insight for linking via imagination vs. observation between the cTBS and the sham groups using an independent sample cluster-based permutation t-test.

This analysis yielded a negative cluster (p = 0.044, *ci*-range =0 .00, SD = 0.00; time window: 1.25 – 1.75s; Fig. 4A) between centro-temporal and frontal regions (C4 – Fp1; C6 – Fp1; T8-Fp1; T8 – AF7). For stories linked via imagination, follow-up tests indicated decreased functional connectivity between these regions in the cTBS group ($t(30) = -4.25$, $p < 0.001$, $d_{repeated\ measures} = -0.70$), while there was no change in the sham group ($t(30) = 0.02$, $p = 0.987$, $d_{repeated\ measures} = 0.00$; *group* × *time*: $F(1, 60) = 8.05$, $p = 0.006$, $\eta_G = 0.050$; Fig. 4B). Interestingly, across both groups higher coherence between these areas in the post- relative to the pre-phase for stories linked via imagination relative to observation was associated with better recall of details (central and peripheral) for stories linked via imagination ($r = 0.31$, $t(59) = 2.50$, $p = 0.015$; Fig. 4C), suggesting that the reduced crosstalk between these regions was linked to impaired subsequent memory.

For stories linked via observation, we found a seemingly opposite pattern (*group* × *time*: $F(1, 60) = 12.73$, $p < .001$, $\eta_G = .080$; Fig. 4D): decreased functional connectivity for the sham group ($t(30) = -2.75$, $p = 0.010$, $d_{repeated\ measures} = -0.47$), while the cTBS group exhibited increased connectivity ($t(30) = 2.28$, $p = 0.030$, $d_{repeated\ measures} = 0.36$). Since these differences appeared to be again already present prior to gaining insight, the functional connectivity changes obtained for the observation condition should be interpreted with caution. Regarding non-linked events (X), we did not find any significant cluster in this coherence analysis (all clusters $p > 0.221$), indicating that the reported connectivity changes were specific to linked events.

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

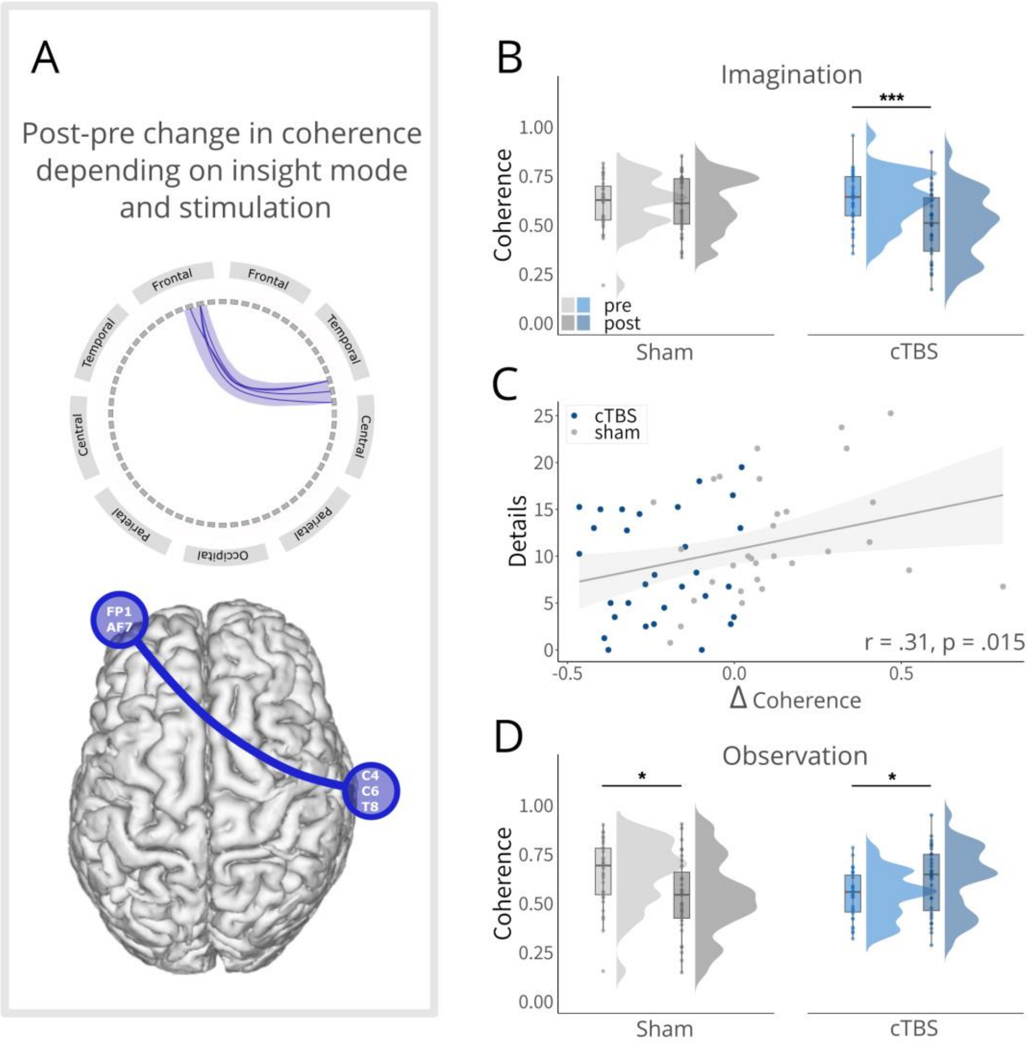


Fig 4. Connectivity change for linked events. **A**, Conceptual depiction of the negative cluster (centro-temporal and frontal). In the upper panel, the connections are presented separately for each electrode pair. The lower panel illustrates the cluster coherence based on the electrode locations relative to the brain. **B**, Follow-up tests for events linked via imagination indicated decreased coherence between centro-temporal and frontal electrodes for the cTBS group, while no change was observed for the sham group. **C**, Significant positive correlation, indicating that the less the coherence between centro-temporal and frontal electrodes changed from pre to post for imagination (vs. observation), the fewer details for linked events via imagination were recalled. Please note, that this correlation became even stronger when the outlier was removed ($r = 0.38$, $t(58) = 3.11$, $p = 0.003$). **D**, Follow-up tests for events linked via observation indicated decreased coherence centro-temporal and frontal electrodes for the sham group, while the cTBS group showed a significant increase in coherence. Boxplots show the median coherence for each group at each time point. Boxplot whiskers extend to the minimum or maximum value within 1.5 times the interquartile range. Points within the boxplot indicate individual data points in each group. Density plots indicate data distribution per group and time. $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Control variables

Overall, levels of subjective chronic stress, anxiety, and depressive mood were relatively low and not different between groups. The groups did further not differ in terms of personality traits or imagination capacity (all $p > 0.056$; see Table 1).

Table 1. Control variables.

	Sham		cTBS	
Measure	M	SD	M	SD
FFIS-C	24.06	4.24	23.59	4.64
FFIS-D	16.84	5.42	17.86	5.22
FFIS-E	13.84	7.16	15.00	7.10
FFIS-F	27.87	8.96	28.21	9.63
STAI-T	34.13	9.27	38.62	11.15
STAI-S	35.35	7.60	39.65	10.08
TICS	11.97	8.54	13.41	9.95
BDI	6.84	6.88	7.65	7.57
BFI-2 E	43.10	5.66	40.59	8.54
BFI-2 N	27.13	6.94	30.12	10.09
BFI-2 O	47.16	6.99	46.68	6.89
BFI-2 C	40.42	8.06	40.71	6.78
BFI-2 A	48.94	5.06	46.74	5.76

Note. The questionnaires FFIS with its dimensions: FFIS-C (complexity of imagination), FFIS-D (directedness of imagination), FFIS-E (emotional valence of imagination), FFIS-F (frequency of imagination); STAI-T and STAI-S; TICS; BDI; BFI-2 with its dimensions: BFI-2 E (extraversion), BFI-2 N (neuroticism), BFI-2 O (openness to experience), BFI-2 C (conscientiousness), BFI-2 A (agreeableness) were completed during the 30-minute break after the insight-phase. No significant group differences were observed on any of these measures. Data represents means (+/- *SD*).

Discussion

Updating our memory representations in light of new information is key to keeping an accurate model of the world. Given the previously described role of the angular gyrus in episodic

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

memory and imagination (Benoit & Schacter, 2015; Bonnici et al., 2018; Thakral et al., 2017), we hypothesized that this area plays a pivotal role in (imagination-based) insight-driven memory reconfiguration. To probe the causal role of the angular gyrus in insight-induced mnemonic changes and related neural pattern reconfigurations, we combined a life-like narrative insight task with cTBS to the angular gyrus. Our results show that inhibition of the angular gyrus reduced the insight-related memory boost for linked events and decreased memory for the linking events themselves. At the neural level, angular gyrus inhibition reduced the coupling between centro-temporal and frontal regions and abolished insight-induced neural representational changes for events linked via imagination, which points to impaired memory integration.

Unsurprisingly, all participants successfully gained insight into which events were linked in the NIT, as reflected in their reliable recognition of the linked events in the forced-choice recognition task and their relatedness ratings in the MAT. Importantly this insight had a direct impact on memory, with better memory for linked relative to non-linked events. This memory boost for linked events aligns with previous findings (Cohn-Sheehy et al., 2021; Grob et al., 2023a, 2023b; Wang et al., 2015) and supports the notion that the brain stores episodic memories as coherent narratives (Tulving, 1983), for which any element can cue the entire episode (Horner et al., 2015; Nakazawa et al., 2002). Crucially, while cTBS to the angular gyrus had no effect on basic insight, inhibiting the angular gyrus prior to gaining insight into the relationship of previously separate events specifically reduced this memory boost for linked events, particularly when electric field stimulation of the angular gyrus was strong. The diminished memory boost for linked events following effective angular gyrus inhibition demonstrates a causal involvement of the angular gyrus in prioritizing linked narratives in memory and, by implication, the reconfiguration of memories in light of new information.

Inhibition of the angular gyrus prior to gaining insight impaired memory not only for the linked events but also for the linking events themselves. Again, this was exclusively observed for inhibitory stimulation with a strong electric field, ensuring effective inhibition of the angular gyrus. The resulting impairment in memory for linking events following angular gyrus

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

inhibition highlights its causal role in integrating newly acquired information into pre-existing memory representations, suggesting that the linking events – whether observed or imagined – serve as binding information for creating a coherent narrative. This interpretation is in line with a recent study showing that online TMS over the angular gyrus during a reading-based task impaired the integration of contextual information (Branzi et al., 2021). Dovetailing with recent accounts proposing the angular gyrus as a spatiotemporal buffering region for integrating our continuous stream of experiences (Humphreys et al., 2021), inhibition of the angular gyrus may have disrupted the reactivation and maintenance of initially separate events A and B during the linking phase. This disruption may have impeded the binding process that is likely crucial for the observed memory boost. At the same time, the lacking reactivation and integration of previously separate events A and B during the linking phase may have diminished the significance of the linking event, leading to reduced memory for the linking event itself.

Consistent with previous neuroimaging studies demonstrating distinct representational changes associated with insight into the relationship of initially separate events (Collin et al., 2015; Milivojevic et al., 2015), we observed, in addition to insight-related memory changes, increased similarity in neural representations of events linked via imagination in the theta band from pre- to post-insight. This finding aligns with studies linking theta band activity to hippocampal involvement in memory integration (Backus et al., 2016; Herweg et al., 2020; Nicolás et al., 2021). Mechanistically, hippocampal theta oscillations may facilitate memory integration by promoting more accurate representations of stimulus-specific information while gaining insight (Pacheco Estefan et al., 2021). Critically, inhibiting the angular gyrus abolished these insight-induced changes in neural pattern similarity between linked events in the theta band, which was directly associated with reduced recall of the linking events. Beyond its causal involvement in the insight-driven neural reconfiguration of linked event representations, angular gyrus inhibition led to representational changes for non-linked events that closely resembled the changes observed in the sham group for linked events. This finding indicates that inhibition of the angular gyrus impairs the separation of linked and non-linked

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

events, suggesting its causal role in effectively pruning out events that are not part of the integrated narrative.

Given the consistent findings linking the angular gyrus to scene imagination (Addis et al., 2007; Hassabis et al., 2007; Ramanan et al., 2018; Thakral et al., 2017), our study focused on the role of the angular gyrus in imagination-based mnemonic integration. It is important to note that the neural findings discussed thus far exclusively pertain to imagination-based insight, aligning with the primary focus of our study. When gaining insight via imagination, participants had to retrieve memory representations of initially separate events to construct the linking event in their mind (Schacter et al., 2008). We assume that the retrieval and reinstatement necessary to construct the imagined linking event led to a high degree of co-activation of the neural patterns associated with each event, leading to more similar representations (Wammes et al., 2022). Most interestingly, inhibiting the angular gyrus' buffering function (Humphreys et al., 2021) disrupted the observed increase in similarity for events linked via imagination, lending further support to its causal role in imagination-based memory integration. Together, our findings demonstrate that inhibiting the angular gyrus disrupts neural pattern reconfiguration following imagination-based insight.

Although we specifically targeted the left angular gyrus and identified its causal role in insight-driven memory reconfiguration, the angular gyrus does not act in isolation. As a major connector hub, it integrates information from various brain regions, with connections including the prefrontal and parietal regions (Frey et al., 2008; Makris et al., 2005, 2007), striatum (Petit et al., 2023; Uddin et al., 2010), sensory-motor areas (Bonner et al., 2013), and the medial-temporal lobe, including the hippocampus (Uddin et al., 2010). Some of these regions play a key role in insight-induced memory reconfigurations, in particular the hippocampus and prefrontal cortex (Collin et al., 2015; Milivojevic et al., 2015). Consistent with this, inhibiting the angular gyrus resulted in decreased theta band connectivity between centro-temporal and frontal regions for events linked via imagination. Importantly, this reduction in connectivity was directly related to a subsequent memory decline. This finding, specific to linked events, aligns with prior research indicating that stronger (and inter-

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

hemispheric) functional coupling in the theta band between frontal and posterior regions is linked to enhanced associative memory (Cruzat et al., 2021; Summerfield & Mangels, 2005; Wu et al., 2007). Furthermore, in line with our finding that is specific to imagination-based linking, the importance of theta band synchronization has been highlighted in research focused on mental imagery (Li et al., 2009). These results suggest that by disrupting the angular gyrus, long-range theta synchronization for events linked via imagination is also disrupted, directly impacting memory performance for these events. This underscores the role of the angular gyrus as a connector hub, integrating information from various regions, particularly during the process of imagination-based memory integration.

To compare the angular gyrus' involvement in imagination-based linking with observation-based linking, where mental construction of linking events is not required, participants linked half of the stories by observing the linking events as videos. For events linked via observation, we found decreased pattern similarity in the theta band between linked events from the pre- to the post-phase. It may be tempting to speculate that viewing the linking event, reactivated only elements of the memory representations of A and B, resulting in a moderate co-activation of their memory representations, which typically leads to decreased similarity between events (Wammes et al., 2022) and more distinctive memory representations in line with previous studies (Grob et al., 2023a, 2023b; Heinbockel et al., 2022). Inhibition of the angular gyrus disrupted this decrease, potentially preventing full access to the original memory representation of A and B in all their detailed distinctiveness during the observation of the linking event, subsequently failing to induce a decrease in similarity (Ramanan et al., 2018). Following cTBS to the angular gyrus, we further observed decreased pattern similarity for non-linked events, resembling the pattern change observed in the sham group for linked events, which may highlight the role of the angular gyrus in representational separation during observation-based linking. Furthermore, for events linked via observation, we observed decreased theta coherence in the sham group. It may be speculated that decreased theta synchronization for events linked via observation indicated less working memory demands in line with prior research (Fell & Axmacher, 2011; Kawasaki et al., 2014; Sarnthein et al., 1998).

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Importantly, angular gyrus inhibition led to increased functional connectivity between centro-temporal and frontal regions, potentially indicating increased working memory demands. However, caution is warranted when interpreting these findings for observation-based insight because these appeared to be driven at least in part by group differences already in the pre-phase, i.e. before participants' gained insight and before the TMS manipulation.

In conclusion, our data point to a causal involvement of the angular gyrus in (imagination-based) insight-driven memory reconfiguration. These results provide novel insights into the neural mechanisms of memory integration and bridge the traditionally separate functions attributed to the angular gyrus, namely memory and imagination. Beyond their relevance for understanding fundamental memory processes, these findings may have relevant implications for promoting the integration of fragmented memories in mental disorders, such as posttraumatic stress disorder.

Materials and Methods

Preregistration

This study was preregistered before the start of data collection at the German Clinical Trials Register (DRKS-ID: DRKS00025202; https://drks.de/search/de/trial/DRKS00025202).

Participants

Sixty-five healthy right-handed individuals (34 males, 31 females, age: *M* = 24.49 years, *SD* = 4.29 years) with normal or corrected-to-normal vision volunteered to participate in this study. Participants were screened using a standardized interview for exclusion criteria that comprised a history of neurological and psychiatric disease, medication use and substance abuse, cardiovascular, thyroid, or renal disease, body mass index below 19 or above 26 kg/m^2, evidence of COVID-19 infection or exposure, and any contraindications to MRI examination or TMS. All participants gave written informed consent before participation and received a monetary compensation at the end of the experiment. The procedures were approved by the local ethics committee (Faculty of Psychology and Human Movement Science, Universität

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Hamburg, Hamburg, Germany, 2020_301 Grob Schwabe) and adhered to the Declaration of Helsinki. The sample size is in line with recent studies on episodic memory integration using the same task (Grob et al., 2023a, 2023b). Additionally, an a-priori power calculation using G*Power (Faul et al., 2007) indicates that a sample size of N = 54 is sufficient for detecting a medium-sized group × link effect (f = 0.25) with a power of 0.95.

We implemented a mixed-design including the within-subject factors link (linked vs. non-linked events), session (pre- vs. post-link), and mode (imagination vs. observation) as well as the between-subjects factor group (cTBS to the angular gyrus vs. sham). Participants were pseudo-randomly assigned to the cTBS group (n=34, 16 females) and the sham group (n = 31, 15 females) to achieve a comparable distribution of men and women in each group. Due to technical issues, three cTBS participants were excluded from EEG analyses.

Procedure

After obtaining participants' written informed consent, we determined their individual motor thresholds for transcranial magnetic stimulation (TMS). Thereafter, they completed a training session of the modified narrative-insight task (NIT; Milivojevic et al., 2015), a life-like video-based task that tests the integration of initially separate events into coherent episodes (see below). During this training, participants were equipped with electroencephalography (EEG) caps and electrodes. Following the training session, participants completed the pre-phase of the NIT. After completing a German mood questionnaire (MDBF; Steyer et al., 1997), participants underwent either sham or cTBS targeting the left angular gyrus before commencing the insight-phase, with an additional stimulation session administered before the second half of the insight-phase. Crucially, this study was double-blind, ensuring that both the participant and the experimenter were unaware of the stimulation condition. Upon completion of the insight-phase, participants transitioned to another experimental room where they were given a 30-minute break, during which they completed the German mood questionnaire (MDBF) again, along with assessments of their imagination capacity (FFIS; Zabelina & Condon, 2019), trait-anxiety (STAI-T; Laux et al., 1981), and state-anxiety (STAI-S; Laux et al., 1981), depressive symptoms (BDI; Hautzinger et al., 2006), chronic stress (TICS; Schulz &

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Schlotz, 1999), and personality dimensions (BFI-2; Danner et al., 2016). This break was crucial for minimizing potential aftereffects of TMS that could have affected performance during the post-phase and memory tasks (Huang et al., 2005; Jannati et al., 2023). After this break, participants engaged in a self-paced free recall task, after which they returned to the EEG room to complete the post-phase of the NIT. The comparison of neural activity patterns between the pre- and post-phases allowed the analysis of insight-related changes in neural memory representations. EEG recordings were obtained during the pre-, insight-, and post-phase of the NIT. Finally, participants completed a multi-arrangements task (MAT; Kriegeskorte & Mur, 2012) and a forced-choice recognition task. In total, the experiment took about 4.5 hours per participant.

Narrative-Insight Task

To examine insight-related mnemonic integration processes, participants completed a modified version of the narrative-insight task (NIT; Milivojevic et al., 2015; Fig. 1), while their brain activity was measured using EEG. The task involved watching life-like videos from the computer game *The Sims 3*, representing different storylines. Each storyline consisted of events that could either be integrated (A and B) into narratives or not (A and X). Participants were unaware that each narrative had two versions. The two versions shared event A but had different events B. Event X from one version served as event B in the other version. Thus, all participants viewed the same events A, B, and X, with 37 participants linking events A and X and 28 participants linking events A and B. Counterbalancing which events were linked over participants controlled for non-specific stimulus effects and visual similarity. Throughout this manuscript, the linked events are referred to as events A and B, while the non-linked event is referred to as X. Given the role of the angular gyrus in imagination (Benoit & Schacter, 2015; Thakral et al., 2017) and recent research highlighting distinct neural underpinnings when gaining insight via imagination vs. observation, we introduced two insight modes: imagination-based linking for half of the stories and observation-based linking for the other half.

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

The NIT consisted of three phases (Fig. 1): the pre-phase, the insight-phase, and the post-phase. The task included ten stories featuring three videos (A, B, and X) in both the pre- and post-phase, and two videos (L, C) and two imagination instructions (I, CI) in the insight-phase. In the *pre-phase*, participants viewed events A, B, and X for two seconds each, with inter-trial intervals (ITIs) between 700-1300 ms (~1000 ms). Each video was preceded by a brief title (one second) and presented 18 times in pseudorandom order. The presentation order ensured that each video appeared before the next round of presentations began, and consecutive trials did not feature the same video. Following the pre-phase, participants rated the extent to which they perceived the events as belonging together on a scale from not at all (1) to very much (4). The subsequent *insight-phase* comprised two parts. For five stories, participants viewed the linking video event (L) interspersed with a control video event (C), each presented for eight seconds and repeated nine times with ITIs between 700-1300 ms (on average ~1000 ms). For the other five stories, participants observed an instruction (I) to imagine a particular linking scene, with the video titles indicating the intended person, alternating with a control instruction (CI). Each instruction was presented for eight seconds and repeated nine times with ITIs between 700-1300 ms (~1000 ms). A total of 32 participants first linked events via imagination and later via observation, while 33 participants first linked events via observation and then via imagination. Importantly, participants were stimulated with cTBS or sham before both parts of the insight-phase to maintain the stimulation effect throughout the insight-phase. For detailed description of the TMS procedure see below.

Participants were instructed to imagine specific scenes only when specifically asked to do so; otherwise, they were told to simply relax and watch the videos or answer the rating questions. In the observation condition, the linking video (L) depicted the main characters from videos A and B interacting with each other, while the control video (C) featured an unrelated activity involving an unknown character (e.g., two women engaged in conversation). In the imagination condition, a written linking instruction (I) prompted participants to imagine the main characters from video A and B interacting with each other, while the control instruction (CI) asked them to imagine an unknown character engaged in an unrelated activity (e.g., two

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

women talking to each other). Following the insight-phase, participants provided ratings regarding their comprehension of the link and adherence to instructions on a scale ranging from 1 (not at all) to 4 (very much). After the insight-phase, participants were taken to another room for a 30-minute break, during which they completed several questionnaires. After the break, they performed the free recall task (see below). Subsequently, in the final *post-phase*, events A, B, and X were again displayed for two seconds, repeated 18 times with ITIs between 700-1300 ms (on average ~1000 ms). Each video was preceded by a one-second title. The post-phase order was pseudorandomized to minimize sequence effects. Its purpose was to examine neural representation changes for events A and B after participants learned that these were linked. Participants then rated the extent to which they perceived the events as belonging together on a scale of 1 (not at all) to 4 (very much). Participants received visual feedback in the form of highlighted selected responses when entering a rating question. In addition to the presentation of A, B, and X events in the pre- and post-phases, we included target events to ensure sustained attention throughout the experiment. These target events, accounting for 11% of pre- and post-phase trials, required participants to press a button in response to a two-second animated video of a girl on a pink scooter.

Free recall

To assess the extent to which insight into the relationship of initially unrelated events affects subsequent memory, participants performed a free recall test in which they were instructed to recall all presented events in as much detail as possible (Fig. 1). During free recall, participants were voice recorded for a maximum of 20 min. To assess the level of detailedness of the integrated episodes, audio recordings from free recall were scored according to how much detail of the different video events (A, B, and X) were recalled from day one and whether the linking events (L, and I) were named. A rating system was employed that allowed for distinct coding of details associated with each specific event (A, B, X, L, and I) and distinguished between central and peripheral details. Central details refer to elements that are crucial to the plot and directly impact the linking process. These details include significant aspects such as distinctive features of the protagonist in each event. Peripheral details encompass any

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

observable details in the video events that are not central to the plot. For example, these could include features like the presence of a carpet in a room or the color of the curtains. Importantly, there was no difference in the number of details that could be named among the video events A, B, and X across different stories (*event*: $F(1.35, 12.14) = 2.09$, $p = 0.173$). However, it is worth noting that a greater number of peripheral details could be named compared to central details (*detail*: $F(1, 9) = 83.24$, $p < 0.001$), which was expected as there were more details visible in the video events that were unrelated to the plot and, consequently, had no direct influence on the linking process. We engaged four independent raters and instructed them to assign details only to events for which it was clear that they belonged exclusively to that event, thereby avoiding any confusion between different events. The raters further scored whether the participants named the linking events or not. The scoring process involved two raters evaluating the first half of the data, while another two raters assessed the second half. All raters were blinded to the experimental conditions. To assess inter-rater reliability, all raters rated the first five participants, and on average, these ratings were highly correlated with each other (*mean correlation* = 0.80, *SD* = 0.14). To enhance inter-subjectivity, these ratings were averaged. The details of the different event types (A, B, and X) were combined across stories to generate a comprehensive rating of event details for both imagined and observed links. The average rating of the linked events (A and B) was then calculated to represent the overall measure of linked events. The non-linked event (X) remained unchanged. The naming of the linking events were combined across stories, separately for imagination and observation. Following the free recall, participants proceeded to the post-phase of the NIT.

Multi-arrangements Task

In order to ensure that participants accurately retained the structure of the events they gained insight into, we assessed their representational structure through a multi-arrangements task (MAT; Kriegeskorte & Mur, 2012). In this task, participants were instructed to arrange representative images (A, B, and X) from each story based on their relatedness. Using a computer mouse, participants dragged and dropped the images within a circular two-dimensional arena displayed on the computer screen. This task served to assess whether

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

participants could successfully bring the linked images (A and B) closer together than the non-linked images (A and X). Each trial was self-paced and could be concluded by the participant by selecting "Done". In the first trial, participants had to arrange all images by similarity and were instructed to do so carefully. Subsequent trials consisted of subsets of the first trial selected based on an adaptive procedure designed to minimize uncertainty and better approximate the high-dimensional perceptual representational space. This procedure is based on an algorithm optimized to provide optimal evidence for the dissimilarity estimates (Kriegeskorte & Mur, 2012). Distances in this MA task were computed by initially computing the squared on-screen distance (Euclidian distance) between all items in the first trial to produce a roughly estimated representative dissimilarity matrix (RDM) and by iteratively updating this RDM by the weighted average of scaled trial estimates. The completion of the MA task required approximately 15 minutes. Distances for linked (A and B) and non-linked events (A and X) were averaged across stories for both imagined and observed links.

Forced-choice recognition

To further ensure participants' accurate identification of linked and non-linked events following the NIT, a forced-choice recognition task was administered to assess participants' comprehension. They were presented with an image of event A at the top of the computer screen and had to indicate whether the image of B or X in the bottom half of the screen was linked to A. Participants were presented with these forced-choice options for each of the stories they had seen before. After indicating for a story which event was linked to event A, they had to rate how confident they were in their answer. Confidence was rated on a scale from not at all (1) to very sure (4). This process was repeated for all ten stories. Participants were presented with the forced-choice question and the confidence rating for 5.5 seconds each, with one-second inter-stimulus intervals. Participants received visual feedback when submitting their ratings, as the selected response was highlighted. The forced-choice recognition test lasted approximately five minutes. Data from the forced-choice recognition task were pooled across stories and the percentage of correct responses was calculated, separately for imagined and observed links.

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Transcranial Magnetic Stimulation

Transcranial magnetic stimulation (TMS) was applied over the left angular gyrus before participants gained insight into the relationship of initially unrelated events. We used a PowerMAG Research 100 stimulator (MAG & More GmbH, München, Germany) for stimulation, that is specifically designed for delivering repetitive transcranial magnetic stimulation (rTMS) in both clinical and research applications. Two different 70 mm figure-of-eight-shaped coils were used depending on the TMS condition: The PMD70-pCool coil with a 2T maximum field strength was used for cTBS, while the PMD70-pCool-SHAM coil, with minimal magnetic field strength, was employed for sham, providing a similar sensory experience, with stimulation pulses being scattered over the scalp.

Motor Threshold Determination

The motor threshold (MT) was assessed at the beginning of the experiment while participants were at rest, wearing an EEG cap without electrodes attached. This measurement was utilized to determine the appropriate strength of TMS required to pass through the cap. Disposable Ag/AgCL surface electromyography (EMG) electrodes were placed on the right abductor pollicis brevis (ABP) muscle, with the reference electrode on the bony landmark of the index finger and the ground electrode on the right elbow. To locate the motor hotspot, we identified the center of the head and moved 5 cm to the left and 3.5 cm forward at a 45° angle, marking it as the center point of a 9-point grid search area with each point spaced 1 cm apart from adjacent points. Starting at 40% of the maximum stimulator output (MSO), we gradually increased the intensity in 5% increments while positioning the TMS coil at a 45° angle and moving it around the search area, delivering single pulses until we identified the motor hotspot. Once the motor hotspot was located, the MT was determined at that site. It was defined as the minimum percentage of maximum stimulator output (MSO) over the left motor cortex needed to elicit motor evoked potentials (MEPs) with a peak-to-peak amplitude of 50 μV in eight out of 16 consecutive pulses.

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Neuro-navigation

Before the experimental session, we obtained individual T1-weighted structural MR images using a 3T Siemens PRISMA scanner from each participant. These images were used for neuro-navigation with the PowerMag View! System (MAG & More GmbH, München, Germany). The system utilizes two infrared cameras (Polaris Spectra) to track the positions of the participant's head and TMS coil in space. Based on the individual T1 MR images, we created 3D reconstructions of the participants' heads, allowing us to precisely locate the left angular gyrus coordinate (MNI: -48, -67, 30) derived from previous work (Thakral et al., 2017) for TMS stimulation. The coordinates were entered as TAL coordinates. Once the TAL coordinate was entered, the coil was positioned in accordance with the template provided by the neuro-navigation system, aiming for a brain-to-target distance of less than 3 cm. This procedure ensured precise coil placement tailored to the unique anatomy of each participant, while maintaining the shortest and therefore optimal distance to the cortex.

Continuous Theta Burst Stimulation

Depending on the experimental condition, we administered continuous Theta Burst Stimulation (cTBS) using either the cTBS or the sham figure-of-eight coil at 80% of the motor threshold (MT) intensity. The experiment was conducted in a double-blind manner, where neither the participant nor the experimenter were aware of the stimulation condition (cTBS vs. sham). Previous evidence has demonstrated the inhibitory effect of cTBS on the targeted brain region under stimulation (Huang et al., 2005; Jannati et al., 2023). Following the standard TBS protocol, participants received a series of bursts comprising three magnetic pulses (pulse triplets) at a frequency of 50 Hz, with the triplets repeated at a rate of five Hz (i.e., five pulse triplets per second). Each participant received a total of 600 magnetic pulses delivered over a 40-second duration. The coil was positioned tangentially on the head and mechanically fixed in a coil holder to maintain its position. Throughout the stimulation, it was ensured via neuro-navigation that the brain-to-target distance remained below 3 cm from the left angular gyrus coordinate (MNI: -48, -67, 30).

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Electric field modeling

Electric field simulations were performed in SimNIBS v4.0.1 to perform TMS simulations for the cTBS group. To assess the potential stimulation strength based on individual motor thresholds and T1 images, we segmented and meshed these MRI scans into tetrahedral head models using the SimNIBS charm pipeline. All head models were visually inspected to exclude segmentation errors. In a next step, we performed the TMS simulation at 80 % of individual motor thresholds (*M* = 54.82 %; *SD* = 12.93 %). We modeled the Magstim 70mm figure-of-eight coil placed over the left angular gyrus target coordinates (MNI: -48, -67, 30), accounting for the presence of the EEG cap during stimulation. Next, to estimate the average field strength in the region of interest (ROI), we extracted the gray matter regions and created a 10mm spherical ROI centered around the target coordinate and averaged the estimated field strength for the sphere. This approach enabled us to evaluate the potential stimulation strength and its impact on the target brain area (Pizem et al., 2022; Zhang et al., 2022).

EEG data acquisition

EEG data was recorded using a 64-electrode BioSemi ActiveTwo system (BioSemi B.V., Amsterdam, the Netherlands) following the international 10-20 system. The sampling rate was set to 1024 Hz, and a band-pass filter of 0.03-100 Hz was applied online. Additional electrodes were placed at the mastoids, above and below the orbital ridge of the right eye, and at the outer canthi of both eyes. Electrode DC offsets were kept within ± 20 µV range using the common mode sense (CMS) and driven right leg (DRL) electrodes, serving as active reference and ground, respectively.

Behavioral data analysis

To illuminate the impact of gaining insight into the relationship between initially unrelated events on subsequent memory, we subjected the number of details remembered during free recall to a linear-mixed model (LMM) implemented with the lme4 package (Bates et al., 2015) including group (cTBS/sham), mode (imagination/observation), link (link/non-link), and detail (central/peripheral) and their interactions as fixed effects, with a random intercept per participant. As a follow-up analysis, we calculated a median split on the cTBS group, based on

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

simulations of the electric field strength and re-analyzed this data with a new group variable (sham/low stim/high stim), mode (imagination/observation), link (link/non-link), and detail (central/peripheral) and their interactions as fixed effects, with a random intercept per participant. To further examine mnemonic integration based on memory of the linking phase, naming of the linking events were entered into an LMM including group (cTBS/sham), and mode (imagination/observation), and their interactions as fixed effects. Additionally, a random intercept per participant was included to account for individual variability. As a follow-up analysis, we re-analyzed this data with a new group variable (sham/low stim/high stim), mode (imagination/observation), link (link/non-link), and detail (central/peripheral) and their interactions as fixed effects, with a random intercept per participant to estimate the effect of stimulation strength on this outcome. To verify that all participants acquired insight into the relationship between events, we analyzed the ratings for the event duplets of interest (linked events AB and non-linked events AX) from the pre- and post-phase of the NIT. This analysis was conducted using a LMM including group (cTBS/sham), mode (imagination/observation), time (pre/post), and link (link/non-link) and their interactions as fixed effects and a random intercept per participant. To confirm the retention of the representational structure of the NIT in memory, Euclidean distance estimates were extracted from the multi-arrangements task for linked (AB) and non-linked events (AX), averaged across stories, and then entered into an LMM including group (cTBS/sham), mode (imagination/observation), and link (link/non-link), and their interactions as fixed effects and a random intercept per participant. Additionally, to further ensure participants' accurate identification of linked and non-linked events, we assessed performance in the forced-choice recognition task by calculating the proportion of correct answers. These performance measures (in %) were then entered into an LMM including group (cTBS/sham), and mode (imagination/observation), and their interactions as fixed effects and a random intercept per participant.

All analyses were performed in R version 4.0.4 and for all analyses standardized betas are reported. Prior to the analysis, the data were examined for outliers, defined as mean +/- 3 *SD*.

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

For the modified NIT analysis, three outliers (two from the sham and one from the cTBS group) were identified and excluded. For the analysis of the forced-choice recognition task, two outliers (one from each group) were identified and excluded. For the analysis of the multi-arrangements task, four outliers (one from the sham and three from the cTBS group) were identified and excluded. For the free recall analysis, five outliers (two from the sham and three from the cTBS group) were identified and excluded.

EEG preprocessing

The offline analysis of EEG data from the narrative-insight task (NIT) was conducted using the FieldTrip toolbox (Oostenveld et al., 2011) and custom scripts implemented in Matlab (TheMathWorks). Pre- and post-phase trials were segmented from -2 to 3 seconds relative to stimulus onset and then re-referenced to the mean average of all scalp electrodes. The data were demeaned based on the average signal of the entire trial and de-trended. To eliminate power-line noise, a discrete Fourier-Transform filter (DFT) at 50 Hz was applied. Any electrodes that did not record or exhibited constant noise were removed (max. one per participant) and interpolated using weighted neighboring electrodes. Noisy trials were removed after visual inspection, on average 2.32 (+/- *SD* 1.34) of the 540 pre-phase trials and 2.63 (+/- *SD* 1.74) of the 540 post-phase trials. Following artifact rejection, the epochs were down-sampled to 256 Hz. Next, we performed an extended infomax independent component analysis (ICA) using the 'runica' method with a stop criterion of weight change < 10^{-7} to identify and reject components associated with eye blinks and other sources of noise. In a two-step procedure, we first correlated the signals from the horizontal and vertical EOG electrodes with each independent component. Components exhibiting a correlation higher than 0.9 were immediately removed from further analysis. In a second step, the remaining components were identified through visual inspection of their time courses and corresponding brain topographies. On average, 3.32 (+/- *SD* 1.38) components were removed before back projecting the signals into electrode space.

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Representational similarity analysis

To investigate how the brain processes insight-induced changes in the relationships between unrelated events, we conducted a representational similarity analysis (RSA) at the EEG electrode level (Heinbockel et al., 2022; Pacheco Estefan et al., 2021). RSA allows us to estimate neural activity patterns associated with specific events by measuring their correlations, thus providing insights into the underlying neural processes (Kriegeskorte et al., 2008). To measure the insight-induced representational changes, we focused on assessing the similarity of linked and non-linked events before and after gaining insight, separately for events that were linked via imagination and events that were linked via observation. We performed the RSA in the theta frequency range as prior evidence highlighted the key role of theta activity in episodic memory integration (Backus et al., 2016; Nicolás et al., 2021).

To perform this analysis, we first calculated time-frequency representations utilizing spectral decomposition using sliding Hanning windows on the preprocessed EEG data. The frequency range was set from 2 Hz to 45 Hz, with 1 Hz increments and a five-cycle window. The analysis was conducted within a time interval of -2 to 3 seconds relative to stimulus onset. For each participant, single trial power estimates were then averaged across stories and baseline corrected using absolute baseline correction with a time window of -1.8 to -1 seconds relative to stimulus onset. The time-frequency data was then appended into separate data files for the pre- and post-phase, as well as for imagined and observed stories. In a second step, we utilized the time-frequency data obtained in the theta range (4-7 Hz) to conduct RSA. These theta power values were then combined to create representational feature vectors, which consisted of the power values for four frequencies (4-7 Hz) × 41 time points (0-2 seconds) × 64 electrodes. We then calculated Pearson's correlations to compare the power patterns across theta frequency between the time points of linked events (A with B), as well as between the time points of non-linked events (A with X) for the pre- and the post-phase separately, separately for stories linked via imagination and via observation. To ensure unbiased results, we took precautions not to correlate the same combination of stories twice, which prevented

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

potential inflation of the data. To facilitate statistical comparisons, we applied a Fisher z-transform to the Pearson's *rho* values at each time point. This yielded a global measure of similarity on each electrode site. We, thus, obtained time × time similarity maps for the linked events (A and B) and the non-linked events (A and X) in the pre- and post-phases, separately for insight gained through imagination and observation. In total, this analysis produced eight Representational Dissimilarity Matrices (RDMs) for each participant.

We performed statistical analyses on the RDMs using cluster-based permutation t-tests in the Fieldtrip toolbox (10.000 permutations; Oostenveld et al., 2011). This approach allows for testing statistical differences while controlling for multiple comparisons without spatial constraints (Maris & Oostenveld, 2007). The samples were clustered at a level of $\alpha_{\text{cluster}} = 0.001$ to allow for more refined clusters. Clusters with a corrected Monte Carlo *p*-value < 0.05 were considered statistically significant. The RDMs for the change from pre- to post-phase in linked events (post - pre) that were linked via imagination (vs. observation; imagination - observation) were contrasted between the cTBS (vs. the sham) groups via an independent sample cluster-based permutation t-test. Similarly, the RDMs for the change from the pre- to post-phase (post - pre) in non-linked events that were linked via imagination (vs. observation) were contrasted between the cTBS (vs. sham) groups via an independent sample cluster-based permutation t-test.

Coherence analysis

To gain a deeper understanding of the connectivity changes between linked (A and B) events before and after gaining insight, we conducted a sliding window coherence analysis in electrode-space on the same contrasts that we found in our RSA analyses. Therefore, this analysis specifically focused on the comparison between imagined and observed links, utilizing the concept of imaginary coherence (Nolte et al., 2004). Imaginary coherence quantifies the synchronization between two electrodes, accounting for phase-lag at a specific frequency and minimizing the influence of volume conduction effects. We first computed a frequency analysis focusing on the mean theta frequency (5.5 Hz; dpss-taper = 1.5 Hz). Then, we computed

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

imaginary coherence for all possible electrode combinations. To capture the temporal dynamics, we employed a sliding window approach that spanned the duration of the video display (0-2 seconds) in 500ms windows, sliding forward in steps of 50ms. By applying this sliding window analysis, we obtained a coherence spectrum matrix of 64 (electrodes) × 64 (electrodes) for each of the 31 time windows in each participant. We calculated the average coherence matrices for both A and B, resulting in a single coherence matrix that represents the connectivity patterns of the linked events. Subsequently, we focused on the same interaction that was yielded by the previous RSA by examining the changes in coherence spectra from pre- to post-phase (post - pre) for the imagined (vs. observed) linked events. To determine the statistical significance of the observed differences between groups (sham vs. cTBS), we utilized an independent sample cluster-based permutation t-test across all 31 time windows, correcting for the multiple comparisons of channels and time windows.

In order to investigate the changes in connectivity from pre- to post-phase for the non-linked event (X), we conducted a sliding window coherence analysis following the same procedure as described above. Please note that the non-linked event was treated separately and not averaged with any other event to maintain its distinct characteristics. Similar to the linked events analysis, we obtained 31 time windows representing the change from pre- to post-phase (post - pre) for the imagined (vs. observed) non-linked event, which was the same interaction as in the previous RSA. To evaluate the statistical significance of these changes between the groups (sham vs. cTBS), we employed an independent sample cluster-based permutation t-test.

Correlational analysis

To relate the findings from the RSA and the coherence analyses to the behavioral results, we extracted the significant clusters. We then proceeded to estimate the correlation between the extracted neural cluster activity and behavioral outcomes. Specifically, we correlated neural similarity and activity with behavioral outcomes separately for the cTBS and sham groups. Subsequently, we compared these correlations to determine if they differed significantly from each other (Eid et al., 2017).

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Data availability

The data generated in this study as well as all original code is available at https://doi.org/10.25592/uhhfdm.12928. For any additional information needed to reanalyze the reported data, please contact the lead researcher directly.

Author contributions

A.G.: Conceptualization, Data curation, Formal analysis, Investigation, Visualization, Methodology, Writing – original draft, Writing – review and editing; H.H.: Formal analysis, Methodology, Visualization, Writing – review and editing; B.M.: Conceptualization, Writing – review and editing; C.D.: Conceptualization, Writing – review and editing; L.S.: Funding acquisition, Conceptualization, Resources, Supervision, Writing – original draft; Writing – review and editing

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

References

Addis, D. R., Wong, A. T., & Schacter, D. L. (2007). Remembering the past and imagining the future: Common and distinct neural substrates during event construction and elaboration. *Neuropsychologia*, *45*(7), 1363–1377. https://doi.org/10.1016/j.neuropsychologia.2006.10.016

Backus, A. R., Schoffelen, J.-M., Szebényi, S., Hanslmayr, S., & Doeller, C. F. (2016). Hippocampal-Prefrontal Theta Oscillations Support Memory Integration. *Current Biology*, *26*(4), 450–457. https://doi.org/10.1016/j.cub.2015.12.048

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using **lme4**. *Journal of Statistical Software*, *67*(1). https://doi.org/10.18637/jss.v067.i01

Bellana, B., Liu, Z.-X., Diamond, N. B., Grady, C. L., & Moscovitch, M. (2017). Similarities and differences in the default mode network across rest, retrieval, and future imagining. *Human Brain Mapping*, *38*(3), 1155–1171. https://doi.org/10.1002/hbm.23445

Benoit, R. G., & Schacter, D. L. (2015). Specifying the core network supporting episodic simulation and episodic memory by activation likelihood estimation. *Neuropsychologia*, *75*, 450–457. https://doi.org/10.1016/j.neuropsychologia.2015.06.034

Bonner, M. F., Peelle, J. E., Cook, P. A., & Grossman, M. (2013). Heteromodal conceptual processing in the angular gyrus. *NeuroImage*, *71*, 175–186. https://doi.org/10.1016/j.neuroimage.2013.01.006

Bonnici, H. M., Cheke, L. G., Green, D. A. E., FitzGerald, T. H. M. B., & Simons, J. S. (2018). Specifying a Causal Role for Angular Gyrus in Autobiographical Memory. *Journal of Neuroscience*, *38*(49), 10438–10443. https://doi.org/10.1523/JNEUROSCI.1239-18.2018

Boorman, E. D., Sweigart, S. C., & Park, S. A. (2021). Cognitive maps and novel inferences: A flexibility hierarchy. *Current Opinion in Behavioral Sciences*, *38*, 141–149. https://doi.org/10.1016/j.cobeha.2021.02.017

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Branzi, F. M., Pobric, G., Jung, J., & Lambon Ralph, M. A. (2021). The Left Angular Gyrus Is Causally Involved in Context-dependent Integration and Associative Encoding during Narrative Reading. *Journal of Cognitive Neuroscience*, *33*(6), 1082–1095. https://doi.org/10.1162/jocn_a_01698

Cattaneo, Z., Silvanto, J., Pascual-Leone, A., & Battelli, L. (2009). The role of the angular gyrus in the modulation of visuospatial attention by the mental number line. *NeuroImage*, *44*(2), 563–568. https://doi.org/10.1016/j.neuroimage.2008.09.003

Cohn-Sheehy, B. I., Delarazan, A. I., Crivelli-Decker, J. E., Reagh, Z. M., Mundada, N. S., Yonelinas, A. P., Zacks, J. M., & Ranganath, C. (2021). Narratives bridge the divide between distant events in episodic memory. *Memory & Cognition*. https://doi.org/10.3758/s13421-021-01178-x

Cohn-Sheehy, B. I., Delarazan, A. I., Reagh, Z. M., Crivelli-Decker, J. E., Kim, K., Barnett, A. J., Zacks, J. M., & Ranganath, C. (2021). The hippocampus constructs narrative memories across distant events. *Current Biology*, *31*(22), 4935-4945.e7. https://doi.org/10.1016/j.cub.2021.09.013

Collin, S. H. P., Milivojevic, B., & Doeller, C. F. (2015). Memory hierarchies map onto the hippocampal long axis in humans. *Nature Neuroscience*, *18*(11), 1562–1564. https://doi.org/10.1038/nn.4138

Coughlan, G., Bouffard, N. R., Golestani, A., Thakral, P. P., Schacter, D. L., Grady, C., & Moscovitch, M. (2023). Transcranial magnetic stimulation to the angular gyrus modulates the temporal dynamics of the hippocampus and entorhinal cortex. *Cerebral Cortex*, *33*(6), 3255–3264. https://doi.org/10.1093/cercor/bhac273

Coutanche, M. N., Gianessi, C. A., Chanales, A. J. H., Willison, K. W., & Thompson-Schill, S. L. (2013). The role of sleep in forming a memory representation of a two-dimensional space. *Hippocampus*, *23*(12), 1189–1197. https://doi.org/10.1002/hipo.22157

Cruzat, J., Torralba, M., Ruzzoli, M., Fernández, A., Deco, G., & Soto-Faraco, S. (2021). The phase of Theta oscillations modulates successful memory formation at encoding. *Neuropsychologia*, *154*, 107775. https://doi.org/10.1016/j.neuropsychologia.2021.107775

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Danner, D., Rammstedt, B., Bluemke, M., Treiber, L., Berres, S., Soto, C. J., & John, O. P. (2016). *Die deutsche Version des Big Five Inventory 2 (BFI-2)*.

Eid, M., Gollwitzer, M., & Schmitt, M. (2017). *Statistik und Forschungsmethoden* (5th ed.). Beltz Verlag. https://www.beltz.de/produkt_detailansicht/8413-statistik-und-forschungsmethoden.html

Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, *39*(2), 175–191. https://doi.org/10.3758/BF03193146

Fell, J., & Axmacher, N. (2011). The role of phase synchronization in memory processes. *Nature Reviews Neuroscience*, *12*(2), Article 2. https://doi.org/10.1038/nrn2979

Fernandez, C., Jiang, J., Wang, S.-F., Choi, H. L., & Wagner, A. D. (2023). Representational integration and differentiation in the human hippocampus following goal-directed navigation. *ELife*, *12*, e80281. https://doi.org/10.7554/eLife.80281

Frey, S., Campbell, J. S. W., Pike, G. B., & Petrides, M. (2008). Dissociating the Human Language Pathways with High Angular Resolution Diffusion Fiber Tractography. *Journal of Neuroscience*, *28*(45), 11435–11444. https://doi.org/10.1523/JNEUROSCI.2388-08.2008

Grabner, R. H., Ansari, D., Koschutnig, K., Reishofer, G., Ebner, F., & Neuper, C. (2009). To retrieve or to calculate? Left angular gyrus mediates the retrieval of arithmetic facts during problem solving. *Neuropsychologia*, *47*(2), 604–608. https://doi.org/10.1016/j.neuropsychologia.2008.10.013

Griffiths, B. J., & Fuentemilla, L. (2020). Event conjunction: How the hippocampus integrates episodic memories across event boundaries. *Hippocampus*, *30*(2), 162–171. https://doi.org/10.1002/hipo.23161

Grob, A.-M., Milivojevic, B., Alink, A., Doeller, C. F., & Schwabe, L. (2023a). Imagining is not seeing: Lower insight-driven memory reconfiguration when imagining the link between separate events. *Cerebral Cortex*, bhad048. https://doi.org/10.1093/cercor/bhad048

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Grob, A.-M., Milivojevic, B., Alink, A., Doeller, C. F., & Schwabe, L. (2023b). Stress disrupts insight-driven mnemonic reconfiguration in the medial temporal lobe. *NeuroImage*, *265*, 119804. https://doi.org/10.1016/j.neuroimage.2022.119804

Hassabis, D., Kumaran, D., Vann, S. D., & Maguire, E. A. (2007). Patients with hippocampal amnesia cannot imagine new experiences. *Proceedings of the National Academy of Sciences*, *104*(5), 1726–1731. https://doi.org/10.1073/pnas.0610561104

Hautzinger, M., Keller, F., & Kühner, C. (2006). *BDI-II. Beck depressions inventar revision—Manual*. Harcourt Test Services.

He, Q., Liu, J. L., Beveridge, E. H., Eschapasse, L., Vargas, V., & Brown, T. I. (2022). Episodic memory integration shapes value-based decision-making in spatial navigation. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, No Pagination Specified-No Pagination Specified. https://doi.org/10.1037/xlm0001133

Heinbockel, H., W.E.M. Quaedflieg, C., Wacker, J., & Schwabe, L. (2022). Spatio-temporal theta pattern dissimilarity in the right centro-parietal area during memory generalization. *Brain and Cognition*, *164*, 105926. https://doi.org/10.1016/j.bandc.2022.105926

Herweg, N. A., Solomon, E. A., & Kahana, M. J. (2020). Theta Oscillations in Human Memory. *Trends in Cognitive Sciences*, *24*(3), 208–227. https://doi.org/10.1016/j.tics.2019.12.006

Horner, A. J., Bisby, J. A., Bush, D., Lin, W.-J., & Burgess, N. (2015). Evidence for holistic episodic recollection via hippocampal pattern completion. *Nature Communications*, *6*(1), 1–11. https://doi.org/10.1038/ncomms8462

Huang, Y.-Z., Edwards, M. J., Rounis, E., Bhatia, K. P., & Rothwell, J. C. (2005). Theta Burst Stimulation of the Human Motor Cortex. *Neuron*, *45*(2), 201–206. https://doi.org/10.1016/j.neuron.2004.12.033

Humphreys, G. F., Lambon Ralph, M. A., & Simons, J. S. (2021). A Unifying Account of Angular Gyrus Contributions to Episodic and Semantic Cognition. *Trends in Neurosciences*, *44*(6), 452–463. https://doi.org/10.1016/j.tins.2021.01.006

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Jannati, A., Oberman, L. M., Rotenberg, A., & Pascual-Leone, A. (2023). Assessing the mechanisms of brain plasticity by transcranial magnetic stimulation. *Neuropsychopharmacology*, *48*(1), Article 1. https://doi.org/10.1038/s41386-022-01453-8

Kawasaki, M., Kitajo, K., & Yamaguchi, Y. (2014). Fronto-parietal and fronto-temporal theta phase synchronization for visual and auditory-verbal working memory. *Frontiers in Psychology*, *5*. https://www.frontiersin.org/articles/10.3389/fpsyg.2014.00200

Kriegeskorte, N., & Mur, M. (2012). Inverse MDS: Inferring Dissimilarity Structure from Multiple Item Arrangements. *Frontiers in Psychology*, *3*. https://doi.org/10.3389/fpsyg.2012.00245

Kriegeskorte, N., Mur, M., & Bandettini, P. A. (2008). Representational similarity analysis—Connecting the branches of systems neuroscience. *Frontiers in Systems Neuroscience*, *2*. https://doi.org/10.3389/neuro.06.004.2008

Kumaran, D., Summerfield, J. J., Hassabis, D., & Maguire, E. A. (2009). Tracking the Emergence of Conceptual Knowledge during Human Decision Making. *Neuron*, *63*(6), 889–901. https://doi.org/10.1016/j.neuron.2009.07.030

Kwon, S., Richter, F. R., Siena, M. J., & Simons, J. S. (2022). Episodic Memory Precision and Reality Monitoring Following Stimulation of Angular Gyrus. *Journal of Cognitive Neuroscience*, 1–12. https://doi.org/10.1162/jocn_a_01814

Laux, L., Glanzmann, P., Schaffner, P., & Spielberger, C. D. (1981). *Laux, L., Glanzmann, P., Schaffner, P., & Spielberger, C. D. (1981). State-Trait Anxiety Inventory—Manual of the German version. Beltz: Weinheim, Germany.*

Lewis, G. A., Poeppel, D., & Murphy, G. L. (2019). Contrasting Semantic versus Inhibitory Processing in the Angular Gyrus: An fMRI Study. *Cerebral Cortex*, *29*(6), 2470–2481. https://doi.org/10.1093/cercor/bhy118

Li, Y., Umeno, K., Hori, E., Takakura, H., Urakawa, S., Ono, T., & Nishijo, H. (2009). Global synchronization in the theta band during mental imagery of navigation in humans. *Neuroscience Research*, *65*(1), 44–52. https://doi.org/10.1016/j.neures.2009.05.004

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Makris, N., Kennedy, D. N., McInerney, S., Sorensen, A. G., Wang, R., Caviness, V. S., Jr, & Pandya, D. N. (2005). Segmentation of Subcomponents within the Superior Longitudinal Fascicle in Humans: A Quantitative, In Vivo, DT-MRI Study. *Cerebral Cortex*, *15*(6), 854–869. https://doi.org/10.1093/cercor/bhh186

Makris, N., Papadimitriou, G. M., Sorg, S., Kennedy, D. N., Caviness, V. S., & Pandya, D. N. (2007). The occipitofrontal fascicle in humans: A quantitative, in vivo, DT-MRI study. *NeuroImage*, *37*(4), 1100–1111. https://doi.org/10.1016/j.neuroimage.2007.05.042

Maris, E., & Oostenveld, R. (2007). Nonparametric statistical testing of EEG- and MEG-data. *Journal of Neuroscience Methods*, *164*(1), 177–190. https://doi.org/10.1016/j.jneumeth.2007.03.024

Milivojevic, B., Vicente-Grabovetsky, A., & Doeller, C. F. (2015). Insight Reconfigures Hippocampal-Prefrontal Memories. *Current Biology*, *25*(7), 821–830. https://doi.org/10.1016/j.cub.2015.01.033

Nakazawa, K., Quirk, M. C., Chitwood, R. A., Watanabe, M., Yeckel, M. F., Sun, L. D., Kato, A., Carr, C. A., Johnston, D., Wilson, M. A., & Tonegawa, S. (2002). Requirement for Hippocampal CA3 NMDA Receptors in Associative Memory Recall. *Science*. https://doi.org/10.1126/science.1071795

Nicolás, B., Sala-Padró, J., Cucurell, D., Santurino, M., Falip, M., & Fuentemilla, L. (2021). Theta rhythm supports hippocampus-dependent integrative encoding in schematic/semantic memory networks. *NeuroImage*, *226*, 117558. https://doi.org/10.1016/j.neuroimage.2020.117558

Nolte, G., Bai, O., Wheaton, L., Mari, Z., Vorbach, S., & Hallett, M. (2004). Identifying true brain interaction from EEG data using the imaginary part of coherency. *Clinical Neurophysiology*, *115*(10), 2292–2307. https://doi.org/10.1016/j.clinph.2004.04.029

Oostenveld, R., Fries, P., Maris, E., & Schoffelen, J.-M. (2011). FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. *Computational Intelligence and Neuroscience*, *2011*, 1–9.

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Pacheco Estefan, D., Zucca, R., Arsiwalla, X., Principe, A., Zhang, H., Rocamora, R., Axmacher, N., & Verschure, P. F. M. J. (2021). Volitional learning promotes theta phase coding in the human hippocampus. *Proceedings of the National Academy of Sciences*, *118*(10), e2021238118. https://doi.org/10.1073/pnas.2021238118

Pehrs, C., Zaki, J., Taruffi, L., Kuchinke, L., & Koelsch, S. (2018). Hippocampal-Temporopolar Connectivity Contributes to Episodic Simulation During Social Cognition. *Scientific Reports*, *8*(1), Article 1. https://doi.org/10.1038/s41598-018-24557-y

Petit, L., Ali, K. M., Rheault, F., Boré, A., Cremona, S., Corsini, F., De Benedictis, A., Descoteaux, M., & Sarubbo, S. (2023). The structural connectivity of the human angular gyrus as revealed by microdissection and diffusion tractography. *Brain Structure and Function*, *228*(1), 103–120. https://doi.org/10.1007/s00429-022-02551-5

Pizem, D., Novakova, L., Gajdos, M., & Rektorova, I. (2022). Is the vertex a good control stimulation site? Theta burst stimulation in healthy controls. *Journal of Neural Transmission*, *129*(3), 319–329. https://doi.org/10.1007/s00702-022-02466-9

Ramanan, S., Piguet, O., & Irish, M. (2018). Rethinking the Role of the Angular Gyrus in Remembering the Past and Imagining the Future: The Contextual Integration Model. *The Neuroscientist*, *24*(4), 342–352. https://doi.org/10.1177/1073858417735514

Sarnthein, J., Petsche, H., Rappelsberger, P., Shaw, G. L., & von Stein, A. (1998). Synchronization between prefrontal and posterior association cortex during human working memory. *Proceedings of the National Academy of Sciences*, *95*(12), 7092–7096. https://doi.org/10.1073/pnas.95.12.7092

Schacter, D. L., Addis, D. R., & Buckner, R. L. (2008). Episodic Simulation of Future Events. *Annals of the New York Academy of Sciences*, *1124*(1), 39–60. https://doi.org/10.1196/annals.1440.001

Schlichting, M. L., & Preston, A. R. (2015). Memory integration: Neural mechanisms and implications for behavior. *Current Opinion in Behavioral Sciences*, *1*, 1–8. https://doi.org/10.1016/j.cobeha.2014.07.005

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Schulz, P., & Schlotz, W. (1999). Trierer Inventar zur Erfassung von chronischem Sre (TICS): Skalenkonstruktion, teststatistische Überprüfung und Validierung der Skala Arbeitsüberlastung. [The Trier Inventory for the Assessment of Chronic Stress (TICS). Scale construction, statistical testing, and validation of the scale work overload.]. *Diagnostica*, *45*(1), 8–19. https://doi.org/10.1026//0012-1924.45.1.8

Schurz, M., Radua, J., Aichhorn, M., Richlan, F., & Perner, J. (2014). Fractionating theory of mind: A meta-analysis of functional brain imaging studies. *Neuroscience & Biobehavioral Reviews*, *42*, 9–34. https://doi.org/10.1016/j.neubiorev.2014.01.009

Shohamy, D., & Daw, N. D. (2015). Integrating memories to guide decisions. *Current Opinion in Behavioral Sciences*, *5*, 85–90. https://doi.org/10.1016/j.cobeha.2015.08.010

Spalding, K. N., Schlichting, M. L., Zeithamova, D., Preston, A. R., Tranel, D., Duff, M. C., & Warren, D. E. (2018). Ventromedial Prefrontal Cortex Is Necessary for Normal Associative Inference and Memory Integration. *Journal of Neuroscience*, *38*(15), 3767–3775. https://doi.org/10.1523/JNEUROSCI.2501-17.2018

Steyer, R., Schwenkmezger, P., Notz, P., & Eid, M. (1997). *Der Mehrdimensionale Befindlichkeitsfragebogen*. Hogrefe.

Summerfield, C., & Mangels, J. A. (2005). Coherent theta-band EEG activity predicts item-context binding during encoding. *NeuroImage*, *24*(3), 692–703. https://doi.org/10.1016/j.neuroimage.2004.09.012

Thakral, P. P., Madore, K. P., Kalinowski, S. E., & Schacter, D. L. (2020). Modulation of hippocampal brain networks produces changes in episodic simulation and divergent thinking. *Proceedings of the National Academy of Sciences*, *117*(23), 12729–12740. https://doi.org/10.1073/pnas.2003535117

Thakral, P. P., Madore, K. P., & Schacter, D. L. (2017). A Role for the Left Angular Gyrus in Episodic Simulation and Memory. *Journal of Neuroscience*, *37*(34), 8142–8149. https://doi.org/10.1523/JNEUROSCI.1319-17.2017

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

Tulving, E. (1983). *Elements of Episodic Memory*. Oxford University Press.

Uddin, L. Q., Supekar, K., Amin, H., Rykhlevskaia, E., Nguyen, D. A., Greicius, M. D., & Menon, V. (2010). Dissociable Connectivity within Human Angular Gyrus and Intraparietal Sulcus: Evidence from Functional and Structural Connectivity. *Cerebral Cortex*, *20*(11), 2636–2646. https://doi.org/10.1093/cercor/bhq011

Wammes, J., Norman, K. A., & Turk-Browne, N. (2022). Increasing stimulus similarity drives nonmonotonic representational change in hippocampus. *ELife*, *11*, e68344. https://doi.org/10.7554/eLife.68344

Wang, J. X., Rogers, L. M., Gross, E. Z., Ryals, A. J., Dokucu, M. E., Brandstatt, K. L., Hermiller, M. S., & Voss, J. L. (2014). Targeted enhancement of cortical-hippocampal brain networks and associative memory. *Science*, *345*(6200), 1054–1057. https://doi.org/10.1126/science.1252900

Wang, Q., Bui, V.-K., & Song, Q. (2015). Narrative organisation at encoding facilitated children’s long-term episodic memory. *Memory*, *23*(4), 602–611. https://doi.org/10.1080/09658211.2014.914229

Wu, X., Chen, X., Li, Z., Han, S., & Zhang, D. (2007). Binding of verbal and spatial information in human working memory involves large-scale neural synchronization at theta frequency. *NeuroImage*, *35*(4), 1654–1662. https://doi.org/10.1016/j.neuroimage.2007.02.011

Zabelina, D. L., & Condon, D. M. (2019). The Four-Factor Imagination Scale (FFIS): A measure for assessing frequency, complexity, emotional valence, and directedness of imagination. *Psychological Research*. https://doi.org/10.1007/s00426-019-01227-w

Zeithamova, D., Dominick, A. L., & Preston, A. R. (2012). Hippocampal and Ventral Medial Prefrontal Activation during Retrieval-Mediated Learning Supports Novel Inference. *Neuron*, *75*(1), 168–179. https://doi.org/10.1016/j.neuron.2012.05.010

Zhang, B. B. B., Stöhrmann, P., Godbersen, G. M., Unterholzner, J., Kasper, S., Kranz, G. S., & Lanzenberger, R. (2022). Normal component of TMS-induced electric field is correlated with

bioRxiv preprint doi: https://doi.org/10.1101/2023.08.18.553803; this version posted August 18, 2023. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted bioRxiv a license to display the preprint in perpetuity. It is made available under aCC-BY-NC-ND 4.0 International license.

depressive symptom relief in treatment-resistant depression. *Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation*, *15*(5), 1318–1320. https://doi.org/10.1016/j.brs.2022.09.006

UHH Universität Hamburg
DER FORSCHUNG | DER LEHRE | DER BILDUNG

FAKULTÄT
FÜR PSYCHOLOGIE UND
BEWEGUNGSWISSENSCHAFT
Institut für Bewegungswissenschaft
Institut für Psychologie

Erklärung gemäß ***(bitte Zutreffendes ankreuzen)***

☐ **§ 4 (1c) der Promotionsordnung des Instituts für Bewegungswissenschaft der Universität Hamburg vom 18.08.2010**

☒ **§ 5 (4d) der Promotionsordnung des Instituts für Psychologie der Universität Hamburg vom 20.08.2003**

Hiermit erkläre ich,

Anna-Maria Grab (Vorname, Nachname),

dass ich mich an einer anderen Universität oder Fakultät noch keiner Doktorprüfung unterzogen oder mich um Zulassung zu einer Doktorprüfung bemüht habe.

Hamburg, den 30.10.23
Ort, Datum

Unterschrift

Universität Hamburg
DER FORSCHUNG | DER LEHRE | DER BILDUNG

FAKULTÄT
FÜR PSYCHOLOGIE UND
BEWEGUNGSWISSENSCHAFT
Institut für Bewegungswissenschaft
Institut für Psychologie

Eidesstattliche Erklärung nach ***(bitte Zutreffendes ankreuzen)***

☐ **§ 7 (4) der Promotionsordnung des Instituts für Bewegungswissenschaft der Universität Hamburg vom 18.08.2010**

☒ **§ 9 (1c und 1d) der Promotionsordnung des Instituts für Psychologie der Universität Hamburg vom 20.08.2003**

Hiermit erkläre ich an Eides statt,

1. dass die von mir vorgelegte Dissertation nicht Gegenstand eines anderen Prüfungsverfahrens gewesen oder in einem solchen Verfahren als ungenügend beurteilt worden ist.
2. dass ich die von mir vorgelegte Dissertation selbst verfasst, keine anderen als die angegebenen Quellen und Hilfsmittel benutzt und keine kommerzielle Promotionsberatung in Anspruch genommen habe. Die wörtlich oder inhaltlich übernommenen Stellen habe ich als solche kenntlich gemacht.

Hamburg, den 30.10.23
Ort, Datum

Unterschrift