

Perspective

No consolidation without representation: Correspondence between neural and psychological representations in recent and remote memory

Asaf Gilboa^{1,2,3,*} and Morris Moscovitch^{1,2,3,*}

¹Rotman Research Institute, Baycrest Health Sciences, 3560 Bathurst Street, Toronto, ON M6A 2E1, Canada

²Department of Psychology, University of Toronto, 100 St. George Street, Toronto, ON M5S 3G3, Canada

³These authors contributed equally

*Correspondence: agilboa@research.baycrest.org (A.G.), momos@psych.utoronto.ca (M.M.)

<https://doi.org/10.1016/j.neuron.2021.04.025>

SUMMARY

Memory systems consolidation is often conceived as the linear, time-dependent, neurobiological shift of memory from hippocampal-cortical to cortico-cortical dependency. We argue that contrary to this unidirectional view of memory reorganization, information about events may be retained in multiple forms (e.g., event-specific sensory-near episodic memory, event-specific gist information, event-general schematic information, or abstract semantic memory). These representations can all form at the time of the event and may continue to coexist for long durations. Their relative strength, composition, and dominance of expression change with time and experience, with task demands, and through their dynamic interaction with one another. These different psychological mnemonic representations depend on distinct functional and structural neurobiological substrates such that there is a neural-psychological representation correspondence (NPRC) among them. We discuss how the dynamics of psychological memory representations are reflected in multiple levels of neurobiological markers and their interactions. By this view, there are only variations of synaptic consolidation and memory dynamics without assuming a distinct systems consolidation process.

INTRODUCTION

Consolidation is the process by which memories become more resistant to loss by psychological interference, neurobiological intervention, or neurological insult. Mindful of the temptation to consider consolidation in purely neurophysiological terms, Burnham (1903) warned that consolidation is also a psychological process by which new information is assimilated or integrated with existing knowledge and memories. Despite Burnham's warnings, investigations of the neurobiological basis of memory and its psychological aspects proceeded on separate tracks (Winocur and Moscovitch, 2011; Sekeres et al., 2018b). Picking up Burnham's banner, we review the recent evidence on how the nature of psychological representation goes hand in hand with the nature of neural representation, and by examining different levels of analysis, we argue that only by considering both will we have a full understanding of memory consolidation.

There are two putative forms of consolidation. Synaptic consolidation is a ubiquitous phenomenon that occurs within minutes to hours of learning (or reconsolidation) and entails protein synthesis and consequent changes to the strength and stability of connections between neurons. Systems consolidation, which is the focus of the present review, is thought to take longer (days to years) and involves reorganizational processes by which memory engrams that initially depend on the hippocampus (HPC) become independent of it and represented in neocortex (Dudai, 2012). Contrary to synaptic consolidation, whose underlying

cascade of neurobiological changes is described in great detail, a mechanistic understanding of systems consolidation has been elusive.

Here, we question the basic tenet of systems consolidation, namely that there is a linear process by which a single "memory engram" changes or transforms over time. Instead, we propose that (1) during and shortly after an event takes place, multiple psychological and neurobiological representations of the event are formed (Figure 1). These include detail-rich (episodic) representations, event-specific but detail-poor generic representations (gist), integrated schematic representation of commonalities across similar events (schemas), and abstracted (semantic) representation, not to mention representations that are inaccessible to consciousness. (2) The particular psychological and corresponding neurobiological characteristics of the different representations determine their initial potency and their dominance during memory expression (Hebscher et al., 2019b), with some remaining silent until the proper conditions arise (Joselyn and Tonegawa, 2020). (3) Over time and experience, and through interactions among them, memory representations undergo dynamic changes to their strength, stability, and composition. In response to these changes and changes in retrieval demands and goals, the likelihood of expression of one form of memory over its counterparts also changes. Thus, we place memory representation at the heart of understanding what transpires as memory expressions change with time and experience. In short, no consolidation without representation.

Neural-psychological representation correspondence (NPRC) : Parallel interactive memory representations of Aguiar's 10th birthday

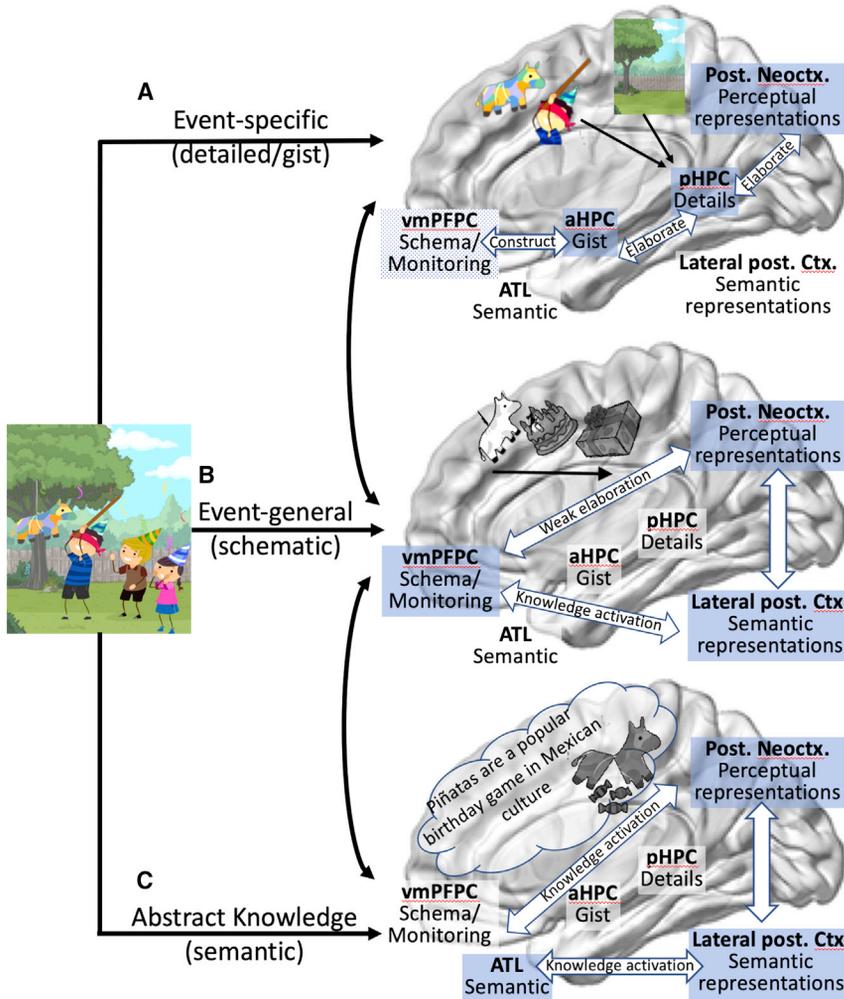


Figure 1. Schematic of the neural-psychological representation correspondence (NPRC) view

Multiple event representations can be formed in parallel at the time of encoding (black straight arrows). The different representations are all subject to the same principles of synaptic consolidation. Their dynamics of change over time and experience differ based on their respective representational attributes and corresponding systems-level neural substrates and processes (shaded, blue text boxes and white arrows). Which representation dominates at encoding or retrieval depends on conditions such as contextual relevance and attention, task demands, prior knowledge, type of retrieval cue, and time. Importantly, these different types of representations exist in dynamic interaction (black curved arrows) as memories are encoded, retrieved, and re-encoded. The arrows indicate how different structures interact with each other to mediate memory types and how different memory types interact and change each other. (A) Event-specific representations typically (but not always) dominate early on; posterior hippocampus (pHPC)-posterior cortical neural ensembles drive detailed contextual representations, while the anterior hippocampus (aHPC) and its interactions with schematic information mediate by ventromedial prefrontal cortex (vmPFC) lead to more coarse-level event-specific gist representations. (B) Statistical regularities can be stored and retrieved as schematic representations mediated by vmPFC in interaction with posterior cortical regions. These entail information about general event details, event structure, and action scripts. (C) Extraction and integration of decontextualized semantic information is mediated through interactions of anterior temporal lobe (ATL) and posterior cortical regions.

now be retained and retrieved directly from neocortex (and other structures) without hippocampal involvement. In other words, there is a change in neural representation without a corresponding change in psychological representation. This stage marks the end of the consolidation process, indicated by the asymptote of a temporally graded amnesia.

BRIEF HISTORY OF SYSTEMS CONSOLIDATION THEORIES

The early history of memory consolidation dates back over a century (Ribot, 1882). The modern, standard neuropsychological model of memory consolidation, however, was born with the publication of evidence that damage to the medial temporal lobes, particularly the hippocampus, leads to a severe and permanent anterograde amnesia for explicit declarative memories but a retrograde amnesia that seemed to have been limited to a short period before the neurological insult (Scoville and Milner, 1957; Penfield and Milner, 1958; Moscovitch 2012).

According to standard consolidation theories (SCTs), memories become reorganized with time via a process of systems consolidation, so that the very same memories that once were dependent on the hippocampus for retention and retrieval can

SCT paid little heed to the relation between memory changes at the neural level to those at the psychological level. Although some investigators noted the correspondence between psychological and neural representations (Penfield and Milner, 1958; Kinsbourne and Wood, 1975; Cermak, 1984), it was the publication of multiple trace theory (MTT) in 1997 that brought this issue to the fore (Nadel and Moscovitch, 1997). Reviewing the evidence, Nadel and Moscovitch emphasized the close correspondence between the nature of memory representation and the neural structures that mediate them, just as do theories of recently acquired memories. Episodic memories that preserve their detailed, perceptually rich representations over time remain perpetually dependent on the hippocampus, whereas remote semantic memories, assumed to arise primarily by extracting statistical regularities among events, are dependent on extra-hippocampal structures.

Building on MTT but taking a more dynamic perspective, trace transformation theory (TTT) (Winocur et al., 2010; Winocur and Moscovitch, 2011; Sekeres et al., 2018b) posited that though most event-specific memories are lost or inaccessible, some memories retain their episodic specificity over time, independent of influences of schemas and semantics (Alba and Hasher, 1983; Reyna and Brainerd, 1995; Goldsmith et al., 2005; Evans and Fisher, 2011; Bonnici and Maguire, 2018; Renoult et al., 2020), whereas others are transformed into more gist-like representations, retaining the central elements of the episode, but not the peripheral details (Sekeres et al., 2018b; Bartlett, 1932; Schacter et al., 2012). Still other memories may leave a schematic or semantic residue, retaining the overall structure of the event as part of a class of similar events, or the semantic information extracted from it, but no information specific to the event itself. The correspondence between psychological and anatomical representations has recently been highlighted for the medial prefrontal cortex (mPFC) and the anterior temporal cortex as crucial components of neural networks mediating schemas (Gilboa and Marlatte, 2017) and semantics (Ralph et al., 2017; but see Martin et al., 2014, and Martin, 2016), respectively, and the anterior and posterior hippocampus in mediating gist and details, respectively (Poppenk et al., 2013; Grady, 2020). These developments led Robin and Moscovitch (2017) to relate the different mnemonic transformations to the neural structures that are presumed to mediate them (see Figure 1 and Sekeres et al., 2018b). Following the principle of the structural functional isomorphism (Moscovitch et al., 2016), they proposed that the nature of the memory representations is aligned with the structures that mediate them and the networks of which they are a hub.

According to TTT, these different psychological representations related to episodic memories and their neural correlate can coexist from encoding to retrieval and can be in dynamic interactions or flux depending on a variety of factors, including attention, task demands, prior knowledge, and time. Thus, according to TTT, memories of events or experiences consist of multiple representations that include rich episodic details but also event-specific gist and general knowledge (schemas and semantic information) about the remembered event (Tulving, 1983). Episodic details refer to descriptions of a particular event, such as a birthday party (Figure 1A), including the people who were there, the shape and color of the room and cake, the sequence of events that took place, and so on, that together enable one to re-experience the event. “Gist” refers to a summary of a particular (specific) event that lacks such a rich description but retains the central elements of the event. Schemas refer to what happens at a typical event of its kind rather than to a specific event, such as what birthday parties are typically like (including rich generic contextual details). Semantics refers to the meaning of the event or the term “birthday party” without entailing a description of all that transpires there. Depending on prevailing conditions, one or the other aspect of the memory of the event dominates (Winocur and Moscovitch, 2011; Sekeres et al., 2018b). Thus, even shortly after the event occurs, one can draw on any of these representations to describe it. Even when a memory appears lost or silent, appropriate cues or reminders may revive the specific memory, even to the level of details, reinstating the dominance of a hippocam-

pal-dependent detailed memory over the ventromedial prefrontal cortex (vmPFC)-dependent schematic memory (Sekeres et al., 2018b; Winocur et al., 2007). Moreover, as episodic memories are retrieved or revived, they are re-encoded in relation to the context in which the recovery occurred, allowing for memories to become updated, altered, or distorted in the process (Nadel et al., 2000; Schacter et al., 2011; Nadel and Sederberg, 2020). Thus, according to MTT and TTT, the term “consolidation” as construed by some proponents of SCT is misleading, since it implies the end of a process of memory retention. MTT/TTT, on the other hand, captures the dynamic, open-ended, and ongoing nature of memory processes at both the psychological and neural levels (Dudai, 2012).

Here, we additionally highlight the little-noticed fact that the principles of neural-psychological representation correspondence (NPRC; see below) and representational dynamics that apply to different aspects of episodic memories also apply to schematic and semantic memories (Gilboa and Marlatte, 2017; Hebscher et al., 2019b). MTT/TTT emphasized these principles by demonstrating that in the few cases in which remote episodic memories retain their details, they also retain their hippocampal-dependent neurobiological characteristics, regardless of memory age. The other side of this principle is that event-specific, detail-poor, generic memories, as well as schematic and semantic memories, should display the same psychological characteristics early on as they do after weeks and years and should be supported by the same neurobiological substrates and mechanisms. This feature is most obvious at the psychological level; in the example provided in Figure 1, participants in Aguilar’s birthday can immediately access both event-specific rich perceptual details and gist, coarse-level representations of the event, depending on retrieval demands (Figure 1A). Schematic representations extracted from multiple previous similar birthday events (Figure 1B) help derive event-specific gist information at encoding and are themselves modified through integration of novel information (e.g., expansion of the types of games played in birthdays). Finally, modifications to decontextualized, abstract, semantic knowledge can also take place early after encoding (e.g., learning that quinceañera, celebrated at 15 years in Mexican culture, is akin to “sweet 16” in other cultures; Figure 1C). Hippocampal-based detail-rich memories typically dominate memory expression early on, making it difficult to observe the formation of new schematic and semantic cortical representations or their alteration in response to new information. However, experimental conditions that promote schematic and semantic memory formation and expression and curb the expression of episodic memories have begun lending support to this notion of coexisting and long-lasting multiple mnemonic representations. Similar ideas from the animal literature have been proposed, suggesting a dual-storage or distributed reinstatement dynamic model of memory consolidation (Sutherland et al., 2010, 2020).

In the remainder of the paper, we examine whether the correspondence between neural and psychological representations of memory (NPRC) holds at different levels of analysis as memory expression is transformed with retrieval demands, time, and experience. We focus on evidence from human research because animal research tends to be more limited in its

characterization of the psychological attributes of memory. Where possible, we draw on parallels between human and animal research because of the latter's greater precision and experimental control over the neural representational mechanisms of memory dynamics. We also provide a brief account of recent developments in animal studies that we think support our view and could help resolve some inconsistencies in the literature. To keep matters manageable for this short review, we will focus on the comparison of event-specific detailed memories to those that are event specific but gist-like and to schematic and semantic memories, since it is primarily these comparisons that have informed theories of memory consolidation and transformation.

LESIONS

From our reading of the literature on the effects of hippocampal/medial temporal lobe (MTL) damage, we believe the evidence is consistent with the representational views posited by MTT/TTT (Sekeres et al., 2018b; Grilli and Verfaellie, 2016; Sheldon et al., 2019; but see Lah and Miller, 2008), namely, that damage to the hippocampus leads to loss of detailed memories no matter how long ago they were acquired, whereas semantic or schematic aspects of those memories are relatively well preserved. Moreover, under some conditions, semantic and schematic memories can be acquired by people with hippocampal damage during development and in adulthood, consistent with the notion that these cortical memory traces are formed at the time of encoding with minimal hippocampal involvement (see below).

Conversely, because episodic, semantic, and schematic memories can coexist and interact with one another, detail-rich aspects of remote semantic and schematic memories are reduced following hippocampal damage, with only core semantic and schematic information remaining. This outcome has been observed in recall of specific details of semantic narratives (Rosenbaum et al., 2009; Verfaellie et al., 2014), public events (Petrican et al., 2010), famous personalities (Waidergoren et al., 2012), and familiar routes (Rosenbaum et al., 2000; Herdman et al., 2015) and even in generating exemplars on tests of free association (Sheldon et al., 2013). Because episodic aspects related to semantic memory, such as the personal significance of famous people, may be accessed rapidly and automatically (Moscovitch, 2008), performance on purely semantic tests, such as name recognition and reading (Westmacott and Moscovitch, 2003), lexical decision (Sheldon and Moscovitch, 2010), free association (Sheldon et al., 2013), and sense of self (Sawczak et al., 2019), is enhanced in neurologically intact people but absent or reduced in people with medial temporal lobe damage that includes the hippocampus (for review, see Renoult et al., 2012, 2019).

To our knowledge, there are no lesion studies in humans that have examined the differential effects of lesions to the anterior and posterior hippocampus, though it has been noted that the extent of damage to the hippocampus is not related to the severity and extent and retrograde amnesia (Winocur et al., 2010; Argyropoulos et al., 2020), consistent with evidence from rodent studies (Winocur et al., 2009; Sutherland et al., 2020). The integrity of thalamic and neocortical structures, however, is related to the temporal extent of retrograde amnesia (Argyro-

poulos et al., 2020; Kopelman, 1989; see Vetere et al., 2021 for rodents). With respect to hippocampal outputs via fornix (Gilboa et al., 2006) and subfields, such as CA1 (Bartsch et al., 2011) and CA3 (Miller et al., 2020), damage or dysfunction led to extended retrograde amnesia to episodic, but not semantic, aspects, with CA3 posited to be necessary for integrating information along the cortical default mode network (Miller et al., 2020). The persistence of autobiographical memory details is also related to the volume of the left pre- and para-subiculum, although evidence from lesion studies in humans about the role of the subiculum is lacking at the moment (Barry et al., 2021).

Although a case can be made to support the alternative that the effects of hippocampal damage on detailed and precise memory representations are time limited (Squire et al., 2015; Dede et al., 2016), attempts to identify the source of the discrepancy between the two views, whether attributed to the sensitivity of the memory tests or the location and extent of the lesion, have not been successful (readers are referred to the recent reviews listed above). Until that occurs, one must appeal to other sources of evidence to adjudicate between the two views.

NPRC also predicts that schematic and semantic knowledge can be acquired despite hippocampal damage; evidence for such learning is accumulating, although the notion is still controversial (Hebscher et al., 2019b). In developmental amnesia, semantic memory appears to be intact despite significant hippocampal agenesis and episodic memory impairment (Vargha-Khadem et al., 2001; Gadian et al., 2000; Guillery-Girard et al., 2004; Elward and Vargha-Khadem, 2018). Though developmental amnesia allows for normal knowledge of intrinsic features of concepts, it leads to abnormal semantic representations of extrinsic features of concepts (e.g., typical uses or locations of objects) (Blumenthal et al., 2017) similar to deficits described in remote semantic knowledge in adult-acquired amnesia (Waidergoren et al., 2012; Hilverman and Duff, 2021). Rapid acquisition of new knowledge has also been described in adult-acquired amnesia when it is tied to prior knowledge (Skotko et al., 2004; Ryan et al., 2013; Sharon et al., 2011; Merhav et al., 2014; Kopelman and Morton, 2015; Westmacott et al., 2004; Corkin, 2013), consistent with the notion that cortical memory traces can be formed rapidly at the time of encoding (Hebscher et al., 2019b). Interestingly, new cortical memories are highly susceptible to interference (Merhav et al., 2014) as predicted by models of cortical learning (McClelland et al., 1995) and in line with the principles of NPRC.

While evidence for acquisition of schematic and semantic memories despite hippocampal damage is just emerging, there are more robust indications that damage to the vmPFC and anterior temporal lobe (ATL) impairs schematic and semantic memories, respectively, leaving episodic memories relatively intact. Patients with vmPFC damage show moderately impaired knowledge of factual semantics (O'Connor and Lafleche, 2004; Kan et al., 2010; Hebscher et al., 2016) and more pronounced abnormalities in schematic processing (Ghosh et al., 2014; Stolk et al., 2015; Spalding et al., 2015; Warren et al., 2014; Melo et al., 1999). Conversely, severe impairments of semantic knowledge are well described following damage to the ATL (Patterson et al., 2007; Gainotti, 2017 for reviews). Patients with vmPFC damage do not typically display relatively preserved episodic

memory, though cases of it have been reported, indicating that this is possible in principle (see below). This concomitant episodic deficit may occur because of damage to neighboring basal forebrain structures that are crucial for cholinergic input to the hippocampus (Damasio et al., 1985; Gilboa and Moscovitch, 2002) or because access to episodic memories of remote events often depends on schemas and semantics and the interaction of hippocampus with vmPFC (Williams et al., 2020; McCormick et al., 2018a, 2018b). If, however, memories of the events can be accessed, people with vmPFC lesions can describe scenes from such events with normal detail (Kurczek et al., 2015; Thaiss and Petrides, 2008) but are deficient in incorporating self-schemas (Kurczek et al., 2015) or sequential aspects (Bertossi et al., 2016), consistent with our representational hypothesis.

Comparable studies have not been conducted in people with focal, lateral, or ATL lesions. Evidence from people with semantic dementia in whom those structures are compromised presents an inconsistent picture, with some studies showing preserved episodic details but impaired semantic memory and others showing impairment in both (Irish and Piguot, 2013).

fMRI

In contrast to evidence from lesion data, the evidence from fMRI studies in neurotypical people is overwhelmingly consistent with our representation hypothesis (Sekerkes et al., 2018b; Sheldon et al., 2019). The vast majority of studies have shown that there is equivalent hippocampal activation for both recent and remote episodic memory as long as the memories were specific, vivid, and perceptually detailed. Memories that were not vivid or detailed, however, showed a marked decrease or absence of hippocampal activation (Gilboa et al., 2004; Addis et al., 2004). The latter condition likely applies to the large proportion of remote memories leading to an expected overall pattern of a reduction of hippocampal activation with memory age when episodic detail and richness are not considered (Boccia et al., 2019; Gilboa et al., 2004).

To date, all the neuroimaging studies on autobiographical memory had participants either answer true/false questions or mentally relive the events while being scanned, followed by production of narratives offline that were scored for details. Capitalizing on advances in fMRI denoising, Gilmore et al. (2021) had participants narrate memories acquired on the day of scanning to those acquired months to years earlier while they were in the scanner. Compared to a control condition, they found a decline in posterior hippocampal activation over that period accompanied by a comparable decline in functional connectivity between the posterior hippocampus and neocortical regions implicated in memory. There was no change in anterior hippocampal activation. Although the authors conclude that this evidence supports SCT as the role of the hippocampus seems time limited, a closer examination of the data suggests that the findings are more in accord with MTT/TTT. Internal details also declined during that period, with the drop being most prominent in details pertaining to activity and object, which account for approximately half the total. Activity in anterior hippocampus, which codes for gist, remained stable across memory age. Thus, as predicted by MTT/

TTT, changes in posterior, but not anterior, hippocampal activation correspond to changes in memory representation for details.

The evidence for semantic memory, however, is more nuanced, as it was in the lesion studies. For the most part, semantic memory tasks do not engage the hippocampus and instead activate modality-specific regions and supra-modal cortical convergence zones (e.g., angular gyrus, ATL, inferior frontal, middle temporal gyri, posterior cingulate, and vmPFC) (Binder and Desai, 2011). NPRC predicts greater engagement of these structures under conditions that promote rapid semantic integration of new information into existing knowledge at encoding and short-delay retrieval (Hebscher et al., 2019b). For example, subsequent memory for associations encoded through fast-mapping was strongly predicted by multivoxel pattern analysis of activity in the ATL and less so by hippocampal activity, whereas hippocampal activity, but not ATL activity, predicted subsequent episodic memories that were intentionally encoded (Atir-Sharon et al., 2015; see also Chadwick et al., 2016). The extent of overlap between the prior knowledge activated at encoding and the learned novel information mediates anterior temporal and perirhinal engagement during successful encoding (Zaiser et al., 2019).

Rapid cortical integration of new semantic knowledge should be reflected not only by the establishment of new associations but also by changes to the existing knowledge structures into which these associations are embedded. At the psychological level, this prediction has been tested using lexical competition paradigms in which learning of novel word forms (e.g., cathedral) that share representations with existing ones (e.g., cathedral) lead to changes in the processing of the existing lexical knowledge, such as changes in performance on lexical decision tasks (Gaskell and Dumay, 2003). Rapidly emerging competition effects for existing word forms have been demonstrated in fast mapping compared with intentional episodic encoding, indicative of more rapid cortical integration (Coutanche and Thompson-Schill, 2014; Zaiser et al., 2021). As predicted, rapid emergence of lexical competition due to learning of novel similar word forms is associated with increased activity in posterior superior temporal gyrus and middle temporal gyrus, cortical regions known to be critical for lexical access processes and lexical-semantic interactions (Takashima et al., 2014).

As we noted earlier, semantic and episodic aspects of memory are not processed independently of each other. Some semantic memories of public events, habitual activities, or famous faces conjure both detailed, likely episodic information about the event, activity, or person in question and more abstract, semantic information (Westmacott and Moscovitch, 2003; Addis et al., 2004; Renoult et al., 2012, 2019). Consistent with NPRC, the extent to which one or the other is invoked will determine the degree of hippocampal activation, even for remotely acquired semantic information, with hippocampal activation modulated by detail. For example, in a word fluency task that requires listing the names of exemplars of a category, hippocampal activation is observed as less common exemplars are named (Sheldon et al., 2016). These findings on semantic memory, even more than those on episodic memory, underscore the importance of considering the nature of the underlying representations in interpreting the neural dynamics of memory transformation.

Of the cortical structures involved in remote memory retrieval (Svoboda et al., 2006; Cabeza and St Jacques, 2007; McDermott et al., 2009), the vmPFC is the primary structure to receive systematic investigation. Activation of the vmPFC typically increases with time since memory acquisition. In the most straightforward cases, increased vmPFC activation and a concomitant drop in hippocampal activation is associated with loss of detailed memories but retention of gist-like memories or schemas (Sekeres et al., 2018b). More interesting are those cases in which vmPFC activation and differentiation of one memory from another increases with time, even for memories that apparently remain detailed (Bonnici and Maguire, 2018; Takashima et al., 2006; Bonnici et al., 2013; Ezzyat et al., 2018) and continue to be associated with hippocampal activation even after 10 years (Bonnici and Maguire, 2018; Bonnici et al., 2013). Such findings suggest that as memories become older, their representations do not “transfer” from one location to another; rather, memories have multiple parallel and interactive neural representations that dynamically change over time. Even memories that remain detailed and associated with hippocampal activation also come express their more schematic representations mediated by the vmPFC. This is especially the case if memories are schema congruent and can benefit from schema-related cues for reconstruction by the hippocampus (Bonasia et al., 2018; van Kesteren et al., 2012). Schema-incongruent memories, however, show the same level of hippocampal activation immediately after acquisition and 7 days later (Bonasia et al., 2018).

Longitudinal investigations of newly formed memories over long durations are challenging and, therefore, rarer, but they provide an opportunity to examine the dynamics of memory representations. Using memory for video clips or univariate analyses examining changes in activation from minutes to weeks, investigators (Bonasia et al., 2018; Furman et al., 2012; Sekeres et al., 2018a) found that the pattern of results resembled those for autobiographical memory (see below). Hippocampal activation, particularly in the posterior portion, declined along with a reduction in memory for details and context but remained relatively stable if memory for details and context was retained, the extent of activation predicting memory for the videos (Furman et al., 2012). mPFC activation, however, was increased in both cases (Bonasia et al., 2018; Sekeres et al., 2018a), consistent with the notion that schemas mediated by the mPFC become increasingly important over time in retention and retrieval of all episodic memories.

Investigating the relation between memory for objects and their location in newly formed spatial schemas over 10 months, Sommer (2017) found that as recollection of object-location memory declined with delay and high-confidence familiarity judgements increased, there was a corresponding reduction in anterior hippocampal activation and an increase in vmPFC and ventrolateral PFC, structures implicated in schematic and semantic memory, respectively.

These studies show that changes in neural activation are confounded by the concomitant change in memory accuracy over time. It is difficult, therefore, to determine whether the decline in hippocampal activation results from a time-dependent consolidation process, as SCT predicts, or a decline in detailed representations, as MTT/TTT predicts. To address this problem,

Du et al. (2019) studied word-pair associations, a form of relational memory that is dependent on the hippocampus (Eichenbaum et al., 2007). By varying the number of repetitions at study, they equated associative memory as much as possible from 20 min to 1 month. In accord with NPRC, hippocampal activation remained relatively stable over time when memory representations remained similar. (See below for evidence on associations from single-unit recordings; De Falco et al., 2016.)

Neural similarity analyses afford the opportunity to relate time-dependent changes at the psychological level, with comparable changes at the neural level, as required by NPRC. In a paired associate learning procedure, Tomparry and Davachi (2017) found that it was only at a week’s delay that greater neural representational similarity emerged between items that were paired with a common picture (overlapping) as compared to those that were paired with different pictures. This similarity, evident primarily in mPFC and posterior hippocampus (but see Dandolo and Schwabe below), was inversely related to recognition accuracy. Because recognition emphasized detail specificity, this finding is indicative of greater dominance of gist memory coupled with less distinct neural representations. Focusing on the long axis of the hippocampus, Dandolo and Schwabe (2018) found that over the course of 1 month, as lures became increasingly mistaken for related targets, indicative of a shift from distinct to gist-like representations in memory, the neural similarity at retrieval, particularly in the anterior hippocampus, increased between related compared to unrelated items, consistent with our model (Figure 1).

Bonnici and Maguire (2018) compared autobiographical memories at 2 weeks with the same memories at 2 years and then compared those to 10-year-old memories while ensuring that all memories were equated for vividness (details) and along other dimensions. Using multivariate pattern analysis (MVPA), they found that the 2-year-old, compared to 2-week-old, memories were most clearly distinguishable from one another in the mPFC and hippocampus, particularly in its posterior portion, especially in the CA3/DG subfields, a pattern that was no different from that of memories that were 10 years older. Because each of the original memories was unique, differing from one another in both details and schemas, their distinguishing characteristics, represented in mPFC and posterior hippocampus (pHPC), respectively, coexisted as predicted by NPRC, and were accentuated with time.

FUNCTIONAL CONNECTIVITY

In addition to revealing structures that are activated during processing of different types of information, fMRI enables one to study the functional and effective connectivity among the nodes in the network. Functional network connectivity associated with memory transformation or consolidation has been studied through (1) post-encoding connectivity and representational similarity during rest to uncover memory-related reactivation that may predict memory retention (e.g., Tambini and Davachi, 2019). These studies typically involve short durations and for the most part do not consider possible changes in memory representations. Therefore, we review only (2) lab-based memory studies that examine rapid cortical integration as well as the

handful of longitudinal studies that examine memory dynamics over times that range from days to weeks and (3) several cross-sectional autobiographical memory studies that could speak to the relationship between changes in functional connectivity and changes in expression of memory representations over longer durations (up to years).

Longitudinal lab-based studies

Several studies have attempted to examine functional connectivity of lab-based acquisition of episodic memory and cortical knowledge integration typically over hours to a couple of days. A handful of other studies attempted to track trajectories of representations from days and up to several weeks later. The former likely tap synaptic consolidation and the latter, the initial phases of memory transformation or changes to memory expression in humans. In several of these studies, there was evidence for increased connectivity between mPFC and hippocampus that was predictive of memory retention (e.g., [Ezzyat et al., 2018](#); [Liu et al., 2017](#); [Berkers et al., 2018](#); [Thielen et al., 2015](#)), whereas in others (discussed below) cortico-cortical interactions better predict memory integration. We suggest that the prominence of mPFC-hippocampal connectivity in predicting memory acquisition and retention is related to the fact that most studies use recognition or cued recall of discrete, arbitrary, associative information. These designs also restrict conclusions about possible changes in memory quality, such as generalization or integration. As we will see, however, mPFC-hippocampal interactions at encoding or afterward influence the nature of subsequent representation, leading to fine resolution and detail-rich memory specificity ([Preston and Eichenbaum, 2013](#); [Guise and Shapiro, 2017](#); [Hebscher et al., 2019b](#)) at short or long delays that diminishes with time as hippocampal involvement decreases along with memory specificity.

Rodent research suggests that the trade-off between memory specificity and generalization is determined by mPFC control over hippocampal activation levels via the thalamic nucleus reuniens ([Xu and Südhof, 2013](#)). Increased hippocampal activation leads to more incorporation of contextual information and more memory specificity, countering cortico-cortical abstraction of gist information. With respect to specificity of arbitrary associations, increased mPFC-hippocampal connectivity predicts more distinctive representations. Importantly, these interactions can occur during, and shortly after, memory encoding but also at remote time points, via the anterodorsal nucleus of the thalamus ([Vetere et al., 2021](#)), as suggested by NPRC. Human neural connectivity findings are consistent with the animal data, though task designs often prevent conclusions about psychological representational dynamics. In tasks using arbitrary associations, increased mPFC-hippocampal connectivity predicted the distinctiveness of cortical representation in mPFC ([Ezzyat et al., 2018](#)). Moreover, thalamic midline nuclei were shown to mediate both hippocampal-mPFC and mPFC-posterior neocortex connectivity during the first 24 h after encoding, whereas at longer delays (up to 90 days), direct mPFC-parahippocampus connectivity became more prominent ([Thielen et al., 2015](#); [Sterpenich et al., 2009](#)). Because the tasks in all of these studies require item-specific or association-specific memory, the increase in mPFC-thalamic-hippocampal functional axis

connectivity could reflect regulation of memory-relevant cortical activity levels. Note that the tasks did not probe memory quality, but recognition memory at longer delays declined significantly, consistent with reduced memory specificity ([Takashima et al., 2006](#); [Thielen et al., 2015](#); [Vetere et al., 2021](#)).

These findings contrast with studies that report increased cortico-cortical connectivity but no interaction between cortex and hippocampus ([Sterpenich et al., 2009](#); [van Kesteren et al., 2010](#); [Merhav et al., 2015](#); [Takashima et al., 2014](#)). In these cases, the information learned is not arbitrary but instead is related to prior knowledge ([van Kesteren et al., 2010](#); [Merhav et al., 2015](#)), and we predict that appropriate tests would reveal that the memory is more generalized. One study reported interactions between mPFC and representational-relevant cortices such as somatosensory cortex for visuotactile learning of familiar object-fabric relations ([van Kesteren et al., 2010](#)). Another study demonstrated that learning new semantics in the context of old knowledge drove interactions between ATL and cortical regions that support semantic representations (lateral and inferior temporal cortices, temporo-parietal junction, and ventrolateral and dorsomedial prefrontal cortices), regardless of time since encoding ([Merhav et al., 2015](#)). Even when hippocampal-vmPFC connectivity is increased for information that is related to prior knowledge, there seems to be additional cortico-cortical connectivity contributing to memory facilitation effects of prior knowledge ([Liu et al., 2017](#)). Notably, vmPFC may be particularly involved when the relationship between new information and prior knowledge is conceptual. In a lexical integration study in which lexical competition was invoked with existing word forms ([Takashima et al., 2014](#)), but not with new conceptual learning, increased cortico-cortical functional connectivity was observed between auditory cortex and superior temporal gyrus, with no reported involvement of vmPFC, consistent with the representational demands of the task.

Although null effects of hippocampal connectivity are difficult to interpret, these imaging findings are consistent with models that suggest that prior cortical representations can support rapid integration of novel associations with little or no hippocampal involvement but may require support from supra-modal cortical hubs ([Hebscher et al., 2019b](#)). By this view, hippocampal-mPFC interactions are key when arbitrary or highly detail-specific memories are formed, but not when more generic knowledge is activated, or when new information is integrated into well-established knowledge networks ([Hebscher et al., 2019b](#); [Coutanche and Thompson-Schill, 2015](#)).

Recently, [Cowan et al. \(2020\)](#) showed that the type of detail retrieved could determine which long-axis hippocampal-cortical circuit would be engaged during synaptic consolidation, promoted by sleep spindles ([Peyrache and Seibt, 2020](#)). Overnight consolidation-related sleep spindles were related to anterior HPC-vmPFC connectivity for object-word paired associates and to posterior HPC-posteromedial cortex for scene-word pairs. This pattern of findings supports the idea that posterior hippocampus is more engaged for memories high in details, whereas objects that can be encoded more easily as conceptual representations engage anterior hippocampus networks ([Sheldon and Levine, 2018](#)). This interpretation is consistent with the observation of greater consolidation-related representational overlap in vmPFC for object-word memories that was mediated

by the degree of anterior hippocampal-vmPFC functional connectivity (Cowan et al., 2020).

Autobiographical memory studies

Most studies that explored connectivity patterns in the autobiographical domain have taken a cross-sectional approach. A typical finding from these studies is that hippocampal connectivity with cortical structures exists regardless of memory age, provided memories are roughly equated for qualities such as vividness, rehearsal, and personal significance (Gilboa et al., 2004; Addis et al., 2004). In people with unilateral left temporal lobe epilepsy with hippocampal atrophy, however, functional connectivity with the hippocampus was much reduced and was replaced by strong connectivity between the vmPFC and those structures (Addis et al., 2007). Consistent with NPRC, these patients have remote memories, but they tend to be more generic and impoverished in detail (St-Laurent et al., 2009). Differences sometimes are also reported in functional connectivity within neurotypical individuals with respect to the precise network of hippocampal-cortical interactions in recent versus remote memories that were collected longitudinally (Söderlund et al., 2012; Bonnici et al., 2012; Sheldon and Levine, 2013; Bonnici and McGuire, 2018). Such findings suggest that similar activity levels may reflect recruitment of distinct networks depending on memory quality.

Autobiographical memory retrieval unfolds over time, and some investigators have capitalized on this characteristic to understand the interaction between the nature of representation and the network that supports it (St Jacques et al., 2011). Examining detailed remote memories (typically older than 2 years), McCormick et al. (2015) observed that during an early construction phase, the greatest functional connectivity was between the anterior hippocampi with each other and with the vmPFC and anterior temporal pole. During a later elaboration phase, however, the pattern of functional connectivity shifted to the posterior hippocampi and posterior neocortex, although vmPFC activation could still be noted. When the same memory is retrieved multiple times within a session, anterior hippocampus and vmPFC activity only appears at the first retrieval, while posterior hippocampus and posterior cingulate activity does not change across retrievals (Gurguryan et al., 2021). Such shifts from anterior to posterior activation in memory retrieval, first noted by Conway et al. (2001), are consistent with the idea that schematic representations of an event coexist and interact with more detailed ones to support flexible memory expression. Schematic representations, mediated by vmPFC, first activate the anterior hippocampus to recover the gist, which, in turn, activates the posterior hippocampal-posterior neocortical ensembles to recover perceptually detailed representations of the event (see Figure 1). In a subsequent fMRI study with temporal lobe epilepsy patients who have impoverished detail memory, McCormick et al. (2018a) found that unlike the case for neurotypical people, there was no change between the two phases, with vmPFC-anterior hippocampal connectivity dominating both, consistent with the patients' poorly elaborated, gist-like memories.

The leading role played by mPFC in guiding retrieval (Moscovitch, 1992) in healthy adults is confirmed by a follow-up study

using magnetoencephalography (MEG) and broadband source analysis which showed mPFC activation precedes hippocampal activation by 65 ms for detailed autobiographical memories that range in age from 4 months to 5 years (McCormick et al., 2020). Using effective connectivity analysis, they showed that mPFC drove HPC activity throughout the entire retrieval phase, consistent with predictions from working-with-memory models (Moscovitch, 1992; Gilboa et al., 2004).

Connectivity analyses of prospectively collected everyday events, which addresses some of the inherent difficulty of biased retrospective selection of memories, demonstrated that when vividness is equated, the hippocampus was part of a network that included structures in posterior parts of the autobiographical memory network (Sheldon and Levine, 2013), similar to other studies equating vividness. Months-old memories that were beginning to change their nature and become less detailed activated a functional network that included the anterior cingulate, lateral prefrontal, and lateral temporal cortices, as well as the lateral and posterior regions of the thalamus, consistent with the anterior and lateral patterns that more gist-like memories evoke.

Together, findings from longitudinal lab-based memory studies and autobiographical memory studies suggest that functional connectivity patterns reflect the psychological representational characteristics of the memory from the time of encoding and may either change over time or remain stable as a function of the dynamics of memory expression. When highly specific associations and accuracy of arbitrary associations serve as a measure of memory, or when detail-rich autobiographical memories are accessed, hippocampal-cortical interactions dominate, regardless of memory age. Conversely, more direct mPFC-cortical connectivity is at play for integration of new information with prior knowledge and for schema-based memory representations (Hebscher et al., 2019b).

OSCILLATORY ACTIVITY AND MEMORY TYPES

Measures of neural firing rhythms, their possible anatomical distribution, and their interactions can reflect representational variations of different memory types and their evolution over time. Specifically, neural oscillations and cross-regional coupling of oscillatory activity may control or orchestrate the process of memory formation and specify memory representational dominance. Broadly speaking, synchrony/desynchrony between distant cortical cell assemblies is indexed by changes in phase coherence and phase-amplitude coupling, whereas local cell assembly synchrony/desynchrony is indexed by changes in amplitude (or power) and local phase-amplitude coupling. As we describe below, detail-rich episodic memories appear to entail changes in the theta (~4–7 Hz) and gamma (approximately >30 Hz) frequency ranges, whereas semantic and schematic representations and their influence on episodic memories are mediated more by cortical theta, alpha (~8–12 Hz), and beta (~12–30 Hz) frequency ranges.

There is an emerging literature of studies in rodents that directly track changes in oscillatory communication across time, neurofunctional networks, and memory kinds. For example, hippocampal-mPFC theta-phase coupling during retrieval of well-established context-specific memories reflects

hippocampal inputs about contextual information early in retrieval, followed by mPFC control over the hippocampus for retrieval of context-appropriate representations (Place et al., 2016; cf. Guise and Shapiro, 2017). The latter may occur through multiplexing hippocampal theta-gamma synchrony that supports successful learning (Tort et al., 2009). To our knowledge, there are no similar studies with this temporal resolution in humans, but clues from studies that examine well-established memories suggest that differential function of cortical and hippocampal oscillatory activity may be reflected in timing and directionality of cross-regional and cross-frequency coupling, similar to the findings in rodents.

Hippocampal-theta driving or “clocking” (Staresina and Wimber, 2019) cortical-gamma as a mechanism underlying recollection that retains details and vividness has been described in humans during context-rich retrieval of both recently acquired lab-based memories (Vaz et al., 2019; Köster et al., 2019) and remote autobiographical ones (Hebscher et al., 2019a; Fuente-milla et al., 2014). Inhibiting cortical function using Transcranial Magnetic Stimulation leads to altered network level connectivity of hippocampal-cortical phase-amplitude theta-gamma coupling (Hebscher et al., 2019a). This alteration, in turn, reduces the vividness of autobiographical memories that are recalled, suggesting a causal role (Hebscher et al., 2019a) possibly driven by altered timing of electrophysiological responses (Hebscher et al., 2020). In another study, statistical modeling of hippocampal-mPFC theta coupling was more consistent with mPFC driving hippocampal processing of mismatch signals (Garrido et al., 2015) similar to the findings from the Place et al. (2016) study mentioned above. These data are consistent with the idea that interactions between hippocampus and cortical modules support recollection of vivid memories, whether recent or remote. mPFC-HPC axis coupling appears to support online predictions and detection of prediction violations by hippocampal representations.

Theta/gamma multiplexing that supports binding and retrieval of episodic information has received much attention. Also commonly observed, however, are cortical alpha/beta synchrony and desynchrony. These appear to support multisensory information processing, including long-term knowledge representations whose activations may precede episodic encoding (Tulving, 2001). Intracranial recordings from humans performing an associative memory encoding/retrieval task demonstrate the expected precedence of cortical desynchrony during encoding and hippocampal gamma synchrony during retrieval (Griffiths et al., 2019). Together, such data are consistent with models that suggest that cortical time-frequency information aids the encoding of attributes in coordination with theta and gamma frequency bands in the hippocampus (Fell et al., 2001; Staresina et al., 2012; Halgren et al., 2015; Hanslmayr et al., 2016; Staresina and Wimber, 2019). Alpha and beta synchrony/desynchrony reflect activation of existing (semantic) cortical knowledge structures (Klimesch et al., 2010; Hanslmayr et al., 2016) that support the extraction of context-sensitive meaningful information for interpreting and encoding ongoing perceptual information (Klimesch et al., 2010; Gilboa and Marlatte, 2017).

It is not known, however, whether such hippocampal/cortical time-frequency modulations and coupling described in studies of recently acquired episodic memory support similar or different

memory traces as representations transform with time or as their expression is altered. A clue is provided by the cortico-cortical time-frequency phenomena described in studies on well-established semantic and schematic knowledge. Using representational similarity of time-frequency information, Clarke et al. (2018) found that during basic level naming, visual perceptual information represented in alpha activity feeds forward along the ventral visual pathway; correspondingly, abstracted semantic meaning was represented in theta and centered on ATL, reflecting both feed-forward and feed-backward connectivity. Theta effects for semantic category of words has also been shown in both anterior and posterior cortico-cortical connections in human intracranial recordings (Halgren et al., 2015). Causal evidence for the importance of cortico-cortical mPFC theta interactions during retrieval of schema-related information was described in a combined lesion-electrophysiological study (Gilboa and Moscovitch, 2017). Patients with vmPFC damage showed reduced schema-related pre-stimulus cross-regional theta desynchrony and smaller or absent markers of interactions between perceptual information and prior knowledge.

One study that examined changes to existing word representations following acquisition of new words (Bakker et al., 2015) found evidence consistent with NPRC’s prediction that changes to existing semantic knowledge can be rapid and be reflected by the same neural mechanisms as “old” semantic information. Specifically, recently acquired novel words showed the same desynchronization in the high beta range as existing words, and both differed from comparable non-words that were never trained. Interestingly, in the lower beta and theta ranges, novel words behaved like existing words only after a night’s consolidation period, consistent with the idea that semantic integration itself is a dynamic process that depends on synaptic consolidation and that different frequency bands may differentially drive these dynamics.

Based on the available cross-sectional data on differences in neural oscillations for episodic, semantic, and schematic information (Halgren et al., 2015; Gilboa and Moscovitch, 2017; Clarke et al., 2018), we propose that schematized/semantic representations are supported by cortico-cortical interregional interactions through theta, alpha, and beta desynchronization, while detail-rich episodic representations are mediated by hippocampal-cortical theta/gamma coupling. During schema-mediated memory formation, HPC-mPFC theta coupling is critical for the interactive, bi-directional, process by which mPFC provides context information to bias hippocampal function under conditions in which new information is inconsistent or only weakly related to prior knowledge (e.g., toward binding novel arbitrary associations or novel unexpected information). This functional axis allows the extraction of gist for ongoing events based on prior knowledge (Figure 1A), as well as the assimilation of new relevant information into existing schematic knowledge. This axis may be especially active when information is novel and needs to be integrated into existing knowledge. Note that although it is most commonly presumed that theta coupling drives theta/gamma phase-amplitude coupling during information processing of encoding and retrieval (e.g., Canolty et al., 2006; Hasselmo and Stern, 2014; Staresina and Wimber, 2019), it may also be the case the hippocampal gamma

oscillation drive theta (Nandi et al., 2019). The former pattern may reflect the influence of prior knowledge on encoding, whereas the latter may reflect processing of arbitrary associations.

Evidence for NPRC's prediction that multiple memory representations are formed during the initial experience has yet to be tested using oscillatory activity. There is evidence that cortical beta desynchrony emerges as soon as new semantic learning occurs. However, whether a form of cortical schematized memory is also created at the time of encoding, independent of the context-rich representation, has still to be determined. Human models of mPFC contributions to schema and decision-making emphasize the generalized context-sensitive application of knowledge in the service of action plans or scripts across time (Schoenbaum et al., 2011; Ghosh and Gilboa, 2014; Wilson et al., 2014; Yu et al., 2019; Hebscher et al., 2019b), but the oscillatory signature of these processes has yet to be investigated.

ECog AND SINGLE-UNIT RECORDINGS

Recordings from linear arrays of electrodes (ECog) provide more precise measures of neural activity than surface recordings of electromagnetic fields. ECog recordings lend support to some of our speculation regarding the neural correlates of the oscillations. Foster et al. (2013, 2015) reported that during retrieval of autobiographical, but not semantic, memory, there were transient increases in theta-phase synchronization between medial temporal lobes and retrosplenial cortex that preceded sustained theta activity in the latter, whose activity, in turn, was synchronized with inferior parietal cortex. Likewise, Steinorth et al. (2010) reported theta, delta, and gamma oscillations in left entorhinal cortex, particularly for retrieval of remote autobiographical memory. Whereas gamma was predominant in hippocampally projecting layers, prolonged theta, consistent with Foster's data, was evident in cortically projecting layers. Together, these data are consistent with our suggestion that hippocampal-posterior cortical communications, mediated through theta-phase coupling and theta/gamma phase-amplitude coupling, support retrieval of detailed episodic memories regardless of their age (Figure 1A).

Although not concerned with remote memory, evidence from studies examining sharp-wave ripples (SWRs) emanating from the hippocampus is consistent with the view that hippocampal activity at retrieval precedes activation in neocortex related to the retrieved information. Thus, in recognition memory of words, faces, and places, SWRs from the hippocampus precede word recognition (Vaz et al., 2019) and free recall of pictures of people and places (Norman et al., 2019) and the concomitant cortical reinstatement of patterns of activity observed at encoding.

Single-unit recordings from the hippocampus suggest that similar mechanisms are involved in retrieving remote episodic memories. Quiñones Quiroga (2019) and Rey et al., 2020 found that modality invariant activation of hippocampal "concept" cells by pictures of people and faces is related to personal autobiographical episodes and items associated with these stimuli (cf. Viskontas et al., 2009; Renoult et al., 2019). Likewise, De Falco et al. (2016) show that long-term coding of associations in human MTL neurons, apparent from the very first recording trials, reflect personal experiences rather than semantic categorization. Sup-

porting this interpretation, there is no topographic organization in the hippocampus, as occurs in neocortex. In neocortex, nearby neurons respond to similar items, supporting a hierarchical organization characteristic of semantic memory, whereas in the hippocampus, they responded to completely different items, an organizational structure that facilitates forming associations rapidly between any arbitrary items (Ison et al., 2015), as is required for episodic memory. These associations, however, may themselves be organized according to a hierarchical structure determined by hippocampal subfields and gradients along the hippocampal axis. Thus, the anterior hippocampus and the CA1 subfields, which are preferentially found there, may code for general context and statistical regularities among events and stimuli. By comparison, the posterior hippocampus and CA3 subfields code for details that distinguish similar events, or aspect of the same event, from one another (Poppenk et al., 2013; Brunec et al., 2018; Schapiro et al., 2017).

A NOTE ON STUDIES IN NON-HUMAN ANIMALS ON MEMORY CONSOLIDATION AND TRANSFORMATION

In previous reviews, we have noted a strong correspondence between human studies on memory consolidation and transformation and rodent studies conducted at the same level of analyses (Winocur et al., 2010; Dudai, 2012; Kandel et al., 2014; Sekeres et al., 2018a, 2018b, 2019). Here, we briefly review such findings in light of the different types of representations: detailed versus gist event-specific memory (Figure 1A), schematic event-general knowledge (Figure 1B), and what might be considered an animal analog to human abstract (semantic) knowledge (Figure 1C).

The main paradigm that has been used to investigate consolidation of event-specific memory in animals is contextual fear conditioning. Rodents receive shock in a particular context, and their memory for that context is measured by how much they freeze when reintroduced to it. By comparing performance when the organism is reintroduced to the identical context as at training to performance in a novel, yet similar, context, one can assess the specificity of the memory that serves as the rodent homolog of episodic memory. Recent studies on reactivation and suppression of engram cells by optogenetic and molecular biological intervention using that paradigm (Sekeres et al., 2018b; Moscovitch and Nadel, 2019; Josselyn and Tonegawa, 2020) are generally supportive of NPRC. The primary findings are that recovery or loss of precise, context-specific memories is related to reactivation or suppression, respectively, of hippocampal engram cells by natural or artificial means. Loss of context specificity over time, but development and maintenance of a generalized memory, as measured by increased freezing in the novel context, is related to hippocampally mediated formation of engram cells in the mPFC (Kitamura et al., 2017; Sekeres et al., 2018b; Moscovitch and Nadel, 2019; Josselyn and Tonegawa, 2020; Sekeres et al., 2019). Moreover, cortical memory engrams in mPFC are formed at the time of encoding and reflect a generalized, decontextualized form of the memory (de Sousa et al., 2019), the rodent analog of gist or schematic memory.

An often-overlooked characteristic of contextual fear conditioning is that it is disrupted by hippocampal damage in the retrograde direction, but not in the anterograde direction; contextual

fear conditioning can be acquired by animals with hippocampal damage (Ross and Eichenbaum, 2006; Maren et al., 1997; Sutherland et al., 2010; Wiltgen et al., 2006), as can a number of other tasks presumed to be dependent on the hippocampus (Sutherland et al., 2020). Such findings are difficult to reconcile with either SCT or MTT but can be accommodated within TTT when NPRC principles are considered. Specifically, such patterns are consistent with the idea that multiple memory representations for an event are formed at encoding but compete for expression dominance, which may shift over time and retrieval conditions. The formation of a dominant hippocampal trace at the time of encoding may render memory traces formed in other neural structures too weak to support behavior (Maren et al., 1997; Sutherland et al., 2010). Reaching the same level of a freezing response to a context despite extensive hippocampal damage can be achieved with some additional training (Wiltgen et al., 2006). Because usually single, prominent, contexts are used, however, it remains an open question whether in all cases extra-hippocampal memory representations can support fine detail discrimination or whether they only support coarse-level contextual discrimination (Jasnow et al., 2017), as predicted by TTT and in accord with NPRC.

Socially acquired food preference (Galef and Wigmore, 1983; Galef, 2012), in which an active social interaction leads to long-term changes in food choice behavior, is another single-event memory paradigm that is typically dependent on the hippocampus (Winocur et al., 2007; Pilarzyk et al., 2019). Using a similar rationale as the contextual fear experiments, investigators found that when the food choice is tested in a different context from the one in which the social interaction took place, rats with hippocampal damage show enhanced preference at 24 h, indicating that more generalized representations are operating (Winocur et al., 2007). Even with no context manipulation, there is evidence for parallel formation and consolidation of more than one memory trace in this paradigm, namely, a hippocampal trace dominating behavior after 1 day of consolidation and an independent cortical trace that dominates behavior after a week, even when the hippocampal trace is absent in the interim (Pilarzyk et al., 2019). This pattern hippocampal-independent single-event cortical learning is inconsistent with systems consolidation models which posit that the formation of remote extra-hippocampal traces always depend on a prolonged process of hippocampally guided modifications. Interestingly, the deficit in recent long-term memory was associated with reduced activation in ventral hippocampus (akin to aHPC in Figure 1A), whereas the cortical network supporting remote long-term food-preference memory included the mPFC (Pilarzyk et al., 2019; see also Cullen et al., 2015). We suspect, based on previous research, that these remote traces represented a more generalized (gist/schematic) form of event memory, though this was not tested.

Unlike event-specific memory paradigms, only a handful of studies have directly addressed the formation and long-term retention of schematic representations in animal models (Winocur et al., 2005; Tse et al., 2007; 2011; Hasan et al., 2019; Richards et al., 2014). These studies have demonstrated how dynamic interactions between well-established schemas and novel arbitrary associations accelerate the ability of cortical traces to

express memory independently of the hippocampus (Winocur et al., 2005; Tse et al., 2007, 2011; Hasan et al., 2019). Importantly, evidence from early gene expression (Tse et al., 2011) and lidocaine infusion (Hasan et al., 2019) indicates that assimilation of newly acquired memories into existing memory networks requires simultaneous encoding in hippocampus and mPFC and involves synaptic plasticity and myelination supported by peri-neuronal nets. The establishment of schematic memory itself over weeks of training is associated with increased myelination in mPFC and neurophysiological mechanisms such as increases in theta band power, spike-field coherence, and phase locking (Hasan et al., 2019) that have also been identified in the human literature (Gilboa and Moscovitch, 2017). In these studies (Tse et al., 2007; 2011; Hasan et al., 2019), prior knowledge involved specific patterns of well-learned odor-location paired associates, which may not capture the extraction of statistical regularities across multiple similar, but not identical, event types (Ghosh and Gilboa, 2014; Gilboa and Marlatte, 2017).

One study provided evidence for differences in the psychological representations associated with schematic representations extracted from statistical regularities versus event-specific memory representations (Richards et al., 2014). In a modified Morris water maze, mice learned platform locations that varied stochastically from a spatial distribution. Schematic knowledge, which depended on intact mPFC at encoding, only emerged after a delay of 30 days, after event-detail memory for specific locations “faded”. Learning of new schema-consistent locations was enhanced by schema knowledge, but when new locations conflicted with previously established knowledge, interference occurred.

Evidence of schema-like representations has been reported in the hippocampus of monkeys (Baraduc et al., 2019) and rats (McKenzie et al., 2014), which the authors interpreted to “...indicate that the hippocampus records common features of events within overlapping networks that link related memories” (p. 211). It is not clear, however, whether these representations, likely derived by extracting statistical regularities, resemble concept cells and gist more than schemas and whether and how they can be distinguished from related representations mediated by mPFC (Preston and Eichenbaum, 2013).

While most animal research has focused on detailed or gist event-specific memories, and a handful of studies have begun to emerge focusing on schema memory, the animal equivalent of abstract semantic knowledge (Figure 1C) has yet to be found. One potentially interesting representation learned by animals in many experiments is learning task principles and rules (Freedman and Miller, 2008; Miller and Wallis, 2010), but their influence on new event-specific memory (Hebscher et al., 2019b) and associations (Brincat and Miller, 2015; Cruzado et al., 2020) is just beginning. For example, animals that learned a variant of the classical Morris water maze could later learn event-specific information in another, similar task despite damage to CA1 subfield of the hippocampus (Ocampo et al., 2017). Moreover, even animals with total hippocampal damage demonstrated their generalized knowledge by completely altering their swim strategies, which also marginally improved performance on this highly hippocampal-dependent task.

CONCLUSION

In this review, we concentrated on only two major theories, MTT/TTT and SCT. Other theories, however, have been proposed in recent years that have elements in common with one or the other of these two but differ with respect to particulars (Dudai, 2012; Squire et al., 2015; Kandel et al., 2014; Sekeres et al., 2018b; Barry and Maguire, 2019; Quian Quiroga, 2019; Yonelinas et al., 2019; Josselyn and Tonegawa, 2020; Takehara-Nishiuchi, 2020; Jasnow et al., 2017; Hardt and Nadel, 2018; Sutherland et al., 2010; McClelland et al., 1995; McClelland, 2013; Goode et al., 2020; Yassa and Reagh, 2013). A systematic comparison of the theories with each other merits its own review (Moscovitch and Gilboa, 2021). Despite their differences, all are consistent with the main thesis advocated in this review that memory representations mediated by extra-hippocampal structures differ fundamentally from those mediated by the hippocampus. Here, we argue, in addition, that these different kinds of representations can all be formed at the time of the event, can coexist, and can be expressed as needed. Systems consolidation by this view may be a misnomer, as it suggests a uni-directional time-dependent neurobiological process that is merely influenced by conditions such as relatedness to prior knowledge or context specificity. Instead, in accord with the principle of NPRC, these different representations undergo interactive (bi-directional), dynamic changes in strength, composition, and dominance of expression influenced by task demands and time. This view does not negate the possibility that some neocortical representations can be modified by hippocampal input and are needed for remote memory formation and stabilization as systems consolidation posits. Instead, our view posits that (1) the neocortical representation that ensues is different from the hippocampal one, (2) neocortical representations are often laid down concurrently with hippocampal ones, (3) hippocampal memory trace formation is influenced by cortical representations of prior knowledge just as cortical traces are influenced by the hippocampus, and (4) neocortical and hippocampal representations continue interacting with one another and in the process can modify each other or their expression throughout the life of a memory. It remains to be determined whether the neurobiological mechanisms underlying these interactions are variations of synaptic consolidation that occurs at initial, hippocampal-dependent learning or are distinct from them, as some recent evidence suggests (Finnie et al., 2018).

Our understanding of the psychological processes and the neural mechanisms underlying the dynamics of memory formation, retention, and change not only challenges some models of systems consolidation but calls the very concept of systems consolidation into question (Sutherland et al., 2010, 2020). The present review suggests that many of the phenomena of memory dynamics are described best by the concept of “memory systems reorganization and expression.” Given our current state of knowledge, we believe that MTT/TTT and the guiding principle of NPRC provide the best account of this dynamic view of the varieties of memory representation and expression that are observed across time and experience.

ACKNOWLEDGMENTS

Preparation of this paper was supported by Natural Sciences and Engineering Research Council of Canada discovery grant 378291 to A.G. and by Canadian Institutes of Health Research (CIHR) grant MOP49566 to M.M. and grant PJT175159 to A.G.

DECLARATION OF INTERESTS

The authors declare no competing interests.

REFERENCES

- Addis, D.R., Moscovitch, M., Crawley, A.P., and McAndrews, M.P. (2004). Recollective qualities modulate hippocampal activation during autobiographical memory retrieval. *Hippocampus* 14, 752–762.
- Addis, D.R., Moscovitch, M., and McAndrews, M.P. (2007). Consequences of hippocampal damage across the autobiographical memory network in left temporal lobe epilepsy. *Brain* 130, 2327–2342.
- Alba, J.W., and Hasher, L. (1983). Is memory schematic? *Psychol. Bull.* 93, 203.
- Argyropoulos, G.P., Dell'Acqua, C., Butler, E., Loane, C., Roca-Fernandez, A., Almozal, A., Drummond, N., Lage-Martinez, C., Cooper, E., Henson, R.N., et al. (2020). Memory deficits following hippocampal versus parahippocampal damage double-dissociate according to both process and material type. *bioRxiv*. <https://doi.org/10.1101/2020.01.25.919423>.
- Atir-Sharon, T., Gilboa, A., Hazan, H., Koilis, E., and Manevitz, L.M. (2015). Decoding the formation of new semantics: MVPA investigation of rapid neocortical plasticity during associative encoding through fast mapping. *Neural Plast.* 2015, 804385.
- Bakker, I., Takashima, A., van Hell, J.G., Janzen, G., and McQueen, J.M. (2015). Changes in theta and beta oscillations as signatures of novel word consolidation. *J. Cogn. Neurosci.* 27, 1286–1297.
- Barry, D.N., and Maguire, E.A. (2019). Consolidating the case for transient hippocampal memory traces. *Trends Cogn. Sci.* 23, 635–636.
- Baraduc, P., Duhamel, J.R., and Wirth, S. (2019). Schema cells in the macaque hippocampus. *Science* 363, 635–639.
- Barry, D.N., Clark, I.A., and Maguire, E.A. (2021). The relationship between hippocampal subfield volumes and autobiographical memory persistence. *Hippocampus* 31, 362–374.
- Bartlett, F.C. (1932). *Remembering: A Study in Experimental and Social Psychology* (Cambridge University Press).
- Bartsch, T., Döhring, J., Rohr, A., Jansen, O., and Deuschl, G. (2011). CA1 neurons in the human hippocampus are critical for autobiographical memory, mental time travel, and autoegetic consciousness. *Proc. Natl. Acad. Sci. USA* 108, 17562–17567.
- Berkers, R.M.W.J., Ekman, M., van Dongen, E.V., Takashima, A., Barth, M., Paller, K.A., and Fernández, G. (2018). Cued reactivation during slow-wave sleep induces brain connectivity changes related to memory stabilization. *Sci. Rep.* 8, 16958.
- Bertossi, E., Tesini, C., Cappelli, A., and Ciaramelli, E. (2016). Ventromedial prefrontal damage causes a pervasive impairment of episodic memory and future thinking. *Neuropsychologia* 90, 12–24.
- Binder, J.R., and Desai, R.H. (2011). The neurobiology of semantic memory. *Trends Cogn. Sci.* 15, 527–536.
- Blumenthal, A., Duke, D., Bowles, B., Gilboa, A., Rosenbaum, R.S., Köhler, S., and McRae, K. (2017). Abnormal semantic knowledge in a case of developmental amnesia. *Neuropsychologia* 102, 237–247.
- Boccia, M., Teghil, A., and Guariglia, C. (2019). Looking into recent and remote past: Meta-analytic evidence for cortical re-organization of episodic autobiographical memories. *Neurosci. Biobehav. Rev.* 107, 84–95. <https://doi.org/10.1016/j.neubiorev.2019.09.003>.

Bonasia, K., Sekeres, M.J., Gilboa, A., Grady, C.L., Winocur, G., and Moscovitch, M. (2018). Prior knowledge modulates the neural substrates of encoding and retrieving naturalistic events at short and long delays. *Neurobiol. Learn. Mem.* *153* (Pt A), 26–39.

Bonnici, H.M., and Maguire, E.A. (2018). Two years later - Revisiting autobiographical memory representations in vmPFC and hippocampus. *Neuropsychologia* *110*, 159–169.

Bonnici, H.M., Chadwick, M.J., Lutti, A., Hassabis, D., Weiskopf, N., and Maguire, E.A. (2012). Detecting representations of recent and remote autobiographical memories in vmPFC and hippocampus. *J. Neurosci.* *32*, 16982–16991.

Bonnici, H.M., Chadwick, M.J., and Maguire, E.A. (2013). Representations of recent and remote autobiographical memories in hippocampal subfields. *Hippocampus* *23*, 849–854.

Brincat, S.L., and Miller, E.K. (2015). Frequency-specific hippocampal-prefrontal interactions during associative learning. *Nat. Neurosci.* *18*, 576–581. <https://doi.org/10.1038/nn.3954>.

Bruneck, I.K., Bellana, B., Ozubko, J.D., Man, V., Robin, J., Liu, Z.-X., Grady, C., Rosenbaum, R.S., Winocur, G., Barense, M.D., and Moscovitch, M. (2018). Multiple Scales of Representation along the Hippocampal Anteroposterior Axis in Humans. *Curr. Biol.* *28*, 2129–2135.

Burnham, W.H. (1903). Retroactive amnesia: Illustrative cases and a tentative explanation. *Am. J. Psychol.* *14*, 118–132.

Cabeza, R., and St Jacques, P. (2007). Functional neuroimaging of autobiographical memory. *Trends Cogn. Sci.* *11*, 219–227.

Canolty, R.T., Edwards, E., Dalal, S.S., Soltani, M., Nagarajan, S.S., Kirsch, H.E., Berger, M.S., Barbaro, N.M., and Knight, R.T. (2006). High gamma power is phase-locked to theta oscillations in human neocortex. *Science* *313*, 1626–1628.

Cermak, L.S. (1984). The episodic-semantic distinction in amnesia. In *Neuropsychology of Memory*, L.R. Squire and N. Butters, eds. (Guilford Press), pp. 55–62.

Chadwick, M.J., Anjum, R.S., Kumaran, D., Schacter, D.L., Spiers, H.J., and Hassabis, D. (2016). Semantic representations in the temporal pole predict false memories. *Proc. Natl. Acad. Sci. USA* *113*, 10180–10185.

Clarke, A., Devereux, B.J., and Tyler, L.K. (2018). Oscillatory dynamics of perceptual to conceptual transformations in the ventral visual pathway. *J. Cogn. Neurosci.* *30*, 1590–1605.

Conway, M.A., Pleydell-Pearce, C.W., and Whitecross, S.E. (2001). The neuroanatomy of autobiographical memory: A slow cortical potential study of autobiographical memory retrieval. *J. Mem. Lang.* *45*, 493–524.

Corkin, S. (2013). *Permanent Present Tense: The Unforgettable Life of the Amnesic Patient, HM* (Basic Books).

Coutanche, M.N., and Thompson-Schill, S.L. (2014). Fast mapping rapidly integrates information into existing memory networks. *J. Exp. Psychol. Gen.* *143*, 2296–2303.

Coutanche, M.N., and Thompson-Schill, S.L. (2015). Rapid consolidation of new knowledge in adulthood via fast mapping. *Trends Cogn. Sci.* *19*, 486–488.

Cowan, E., Liu, A., Henin, S., Kothare, S., Devinsky, O., and Davachi, L. (2020). Sleep spindles promote the restructuring of memory representations in ventromedial prefrontal cortex through enhanced hippocampal-cortical functional connectivity. *J. Neurosci.* *40*, 1909–1919.

Cruzado, N.A., Tiganj, Z., Brincat, S.L., Miller, E.K., and Howard, M.W. (2020). Conjunctive representation of what and when in monkey hippocampus and lateral prefrontal cortex during an associative memory task. *Hippocampus* *30*, 1332–1346.

Cullen, P.K., Gilman, T.L., Winiecki, P., Riccio, D.C., and Jasnow, A.M. (2015). Activity of the anterior cingulate cortex and ventral hippocampus underlie increases in contextual fear generalization. *Neurobiol. Learn. Mem.* *124*, 19–27.

Damasio, A.R., Graff-Radford, N.R., Eslinger, P.J., Damasio, H., and Kassell, N. (1985). Amnesia following basal forebrain lesions. *Arch. Neurol.* *42*, 263–271.

Dandolo, L.C., and Schwabe, L. (2018). Time-dependent memory transformation along the hippocampal anterior–posterior axis. *Nat. Commun.* *9*, 1–11.

De Falco, E., Ison, M.J., Fried, I., and Quian Quiroga, R. (2016). Long-term coding of personal and universal associations underlying the memory web in the human brain. *Nat. Commun.* *7*, 13408.

de Sousa, A.F., Cowansage, K.K., Zutshi, I., Cardozo, L.M., Yoo, E.J., Leutgeb, S., and Mayford, M. (2019). Optogenetic reactivation of memory ensembles in the retrosplenial cortex induces systems consolidation. *Proc. Natl. Acad. Sci. USA* *116*, 8576–8581.

Dede, A.J.O., Frascino, J.C., Wixted, J.T., and Squire, L.R. (2016). Learning and remembering real-world events after medial temporal lobe damage. *Proc. Natl. Acad. Sci. USA* *113*, 13480–13485.

Du, X., Zhan, L., Chen, G., Guo, D., Li, C., Moscovitch, M., and Yang, J. (2019). Differential activation of the medial temporal lobe during item and associative memory across time. *Neuropsychologia* *135*, 107252.

Dudai, Y. (2012). The restless engram: consolidations never end. *Annu. Rev. Neurosci.* *35*, 227–247.

Eichenbaum, H., Yonelinas, A.P., and Ranganath, C. (2007). The medial temporal lobe and recognition memory. *Ann. Rev. Neurosci.* *30*, 123–152.

Elward, R.L., and Vargha-Khadem, F. (2018). Semantic memory in developmental amnesia. *Neurosci. Lett.* *680*, 23–30.

Evans, J.R., and Fisher, R.P. (2011). Eyewitness memory: Balancing the accuracy, precision and quantity of information through metacognitive monitoring and control. *Appl. Cogn. Psychol.* *25*, 501–508.

Ezzyat, Y., Inhoff, M.C., and Davachi, L. (2018). Differentiation of human medial prefrontal cortex activity underlies long-term resistance to forgetting in memory. *J. Neurosci.* *38*, 10244–10254. Fell, J., Klaver, P., Lehnertz, K., Grunwald, T., Schaller, C., Elger, C.E., and Fernández, G. (2001). Human memory formation is accompanied by rhinal-hippocampal coupling and decoupling. *Nat. Neurosci.* *4*, 1259–1264.

Fell, J., Klaver, P., Lehnertz, K., Grunwald, T., Schaller, C., Elger, C.E., and Fernández, G. (2001). Human memory formation is accompanied by rhinal-hippocampal coupling and decoupling. *Nat. Neurosci.* *4*, 1259–1264.

Finnie, P.S.B., Gamache, K., Protopoulos, M., Sinclair, E., Baker, A.G., Wang, S.-H., and Nader, K. (2018). Cortico-hippocampal schemas enable NMDAR-independent fear conditioning in rats. *Curr. Biol.* *28*, 2900–2909.e5.

Foster, B.L., Kaveh, A., Dastjerdi, M., Miller, K.J., and Parvizi, J. (2013). Human retrosplenial cortex displays transient theta phase locking with medial temporal cortex prior to activation during autobiographical memory retrieval. *J. Neurosci.* *33*, 10439–10446.

Foster, B.L., Rangarajan, V., Shirer, W.R., and Parvizi, J. (2015). Intrinsic and task-dependent coupling of neuronal population activity in human parietal cortex. *Neuron* *86*, 578–590.

Freedman, D.J., and Miller, E.K. (2008). Neural mechanisms of visual categorization: insights from neurophysiology. *Neurosci. Biobehav. Rev.* *32*, 311–329.

Fuentemilla, L., Barnes, G.R., Düzel, E., and Levine, B. (2014). Theta oscillations orchestrate medial temporal lobe and neocortex in remembering autobiographical memories. *Neuroimage* *85*, 730–737.

Furman, O., Mendelsohn, A., and Dudai, Y. (2012). The episodic engram transformed: Time reduces retrieval-related brain activity but correlates it with memory accuracy. *Learn. Mem.* *19*, 575–587.

Gadian, D.G., Aicardi, J., Watkins, K.E., Porter, D.A., Mishkin, M., and Vargha-Khadem, F. (2000). Developmental amnesia associated with early hypoxic-ischaemic injury. *Brain* *123*, 499–507.

Gainotti, G. (2017). The differential contributions of conceptual representation format and language structure to levels of semantic abstraction capacity. *Neuropsychol. Rev.* *27*, 134–145.

Galef, B.G. (2012). A case study in behavioral analysis, synthesis and attention to detail: Social learning of food preferences. *Behav. Brain Res.* *231*, 266–271.

- Galef, B.G., Jr., and Wigmore, S.W. (1983). Transfer of information concerning distant foods: a laboratory investigation of the “information-centre” hypothesis. *Anim. Behav.* *31*, 748–758.
- Garrido, M.I., Barnes, G.R., Kumaran, D., Maguire, E.A., and Dolan, R.J. (2015). Ventromedial prefrontal cortex drives hippocampal theta oscillations induced by mismatch computations. *Neuroimage* *120*, 362–370.
- Gaskell, M.G., and Dumay, N. (2003). Lexical competition and the acquisition of novel words. *Cognition* *89*, 105–132.
- Ghosh, V.E., and Gilboa, A. (2014). What is a memory schema? A historical perspective on current neuroscience literature. *Neuropsychologia* *53*, 104–114.
- Ghosh, V.E., Moscovitch, M., Melo Colella, B., and Gilboa, A. (2014). Schema representation in patients with ventromedial PFC lesions. *J. Neurosci.* *34*, 12057–12070.
- Gilboa, A., and Marlatte, H. (2017). Neurobiology of schemas and schema-mediated memory. *Trends Cogn. Sci.* *21*, 618–631.
- Gilboa, A., and Moscovitch, M. (2002). The cognitive neuroscience of confabulation: A review and a model. *Handbook of memory disorders* *2*, 315–342.
- Gilboa, A., and Moscovitch, M. (2017). Ventromedial prefrontal cortex generates pre-stimulus theta coherence desynchronization: A schema instantiation hypothesis. *Cortex* *87*, 16–30.
- Gilboa, A., Winocur, G., Grady, C.L., Hevenor, S.J., and Moscovitch, M. (2004). Remembering our past: functional neuroanatomy of recollection of recent and very remote personal events. *Cereb. Cortex* *14*, 1214–1225.
- Gilboa, A., Winocur, G., Rosenbaum, R.S., Poreh, A., Gao, F., Black, S.E., Westmacott, R., and Moscovitch, M. (2006). Hippocampal contributions to recollection in retrograde and anterograde amnesia. *Hippocampus* *16*, 966–980.
- Gilmore, A.W., Quach, A., Kalinowski, S.E., González-Araya, E.I., Gotts, S.J., Schacter, D.L., and Martin, A. (2021). Evidence supporting a time-limited hippocampal role in retrieving autobiographical memories. *Proc. Natl. Acad. Sci. USA* *118*, e2023069118.
- Goldsmith, M., Koriati, A., and Pansky, A. (2005). Strategic regulation of grain size in memory reporting over time. *J. Mem. Lang.* *52*, 505–525.
- Goode, T.D., Tanaka, K.Z., Sahay, A., and McHugh, T.J. (2020). An integrated index: engrams, place cells, and hippocampal memory. *Neuron* *107*, 805–820.
- Grady, C.L. (2020). Meta-analytic and functional connectivity evidence from functional magnetic resonance imaging for an anterior to posterior gradient of function along the hippocampal axis. *Hippocampus* *30*, 456–471.
- Griffiths, B.J., Parish, G., Roux, F., Michelmann, S., van der Plas, M., Kolibius, L.D., Chelvarajah, R., Rollings, D.T., Sawlani, V., Hamer, H., et al. (2019). Directional coupling of slow and fast hippocampal gamma with neocortical alpha/beta oscillations in human episodic memory. *Proc. Natl. Acad. Sci. USA* *116*, 21834–21842.
- Grilli, M.D., and Verfaellie, M. (2016). Experience-near but not experience-far autobiographical facts depend on the medial temporal lobe for retrieval: Evidence from amnesia. *Neuropsychologia* *81*, 180–185.
- Guillery-Girard, B., Martins, S., Parisot-Carbuccia, D., and Eustache, F. (2004). Semantic acquisition in childhood amnesic syndrome: a prospective study. *Neuroreport* *15*, 377–381.
- Guire, K.G., and Shapiro, M.L. (2017). Medial prefrontal cortex reduces memory interference by modifying hippocampal encoding. *Neuron* *94*, 183–192.e8.
- Gurguryan, L., Rioux, M., and Sheldon, S. (2021). Reduced anterior hippocampal and ventromedial prefrontal activity when repeatedly retrieving autobiographical memories. *Hippocampus*.
- Halgren, E., Kaestner, E., Marinkovic, K., Cash, S.S., Wang, C., Schomer, D.L., Madsen, J.R., and Ulbert, I. (2015). Laminar profile of spontaneous and evoked theta: Rhythmic modulation of cortical processing during word integration. *Neuropsychologia* *76*, 108–124.
- Hanslmayr, S., Staresina, B.P., and Bowman, H. (2016). Oscillations and episodic memory: addressing the synchronization/desynchronization conundrum. *Trends Neurosci.* *39*, 16–25.
- Hardt, O., and Nadel, L. (2018). Systems consolidation revisited, but not revised: The promise and limits of optogenetics in the study of memory. *Neurosci. Lett.* *680*, 54–59.
- Hasan, M., Kanna, M.S., Jun, W., Ramkrishnan, A.S., Iqbal, Z., Lee, Y., and Li, Y. (2019). Schema-like learning and memory consolidation acting through myelination. *FASEB J.* *33*, 11758–11775.
- Hasselmo, M.E., and Stern, C.E. (2014). Theta rhythm and the encoding and retrieval of space and time. *Neuroimage* *82* (Pt 2), 656–666.
- Hebscher, M., Barkan-Abramski, M., Goldsmith, M., Aharon-Peretz, J., and Gilboa, A. (2016). Memory, decision-making, and the ventromedial prefrontal cortex (vmPFC): the roles of subcallosal and posterior orbitofrontal cortices in monitoring and control processes. *Cereb. Cortex* *26*, 4590–4601.
- Hebscher, M., Meltzer, J.A., and Gilboa, A. (2019a). A causal role for the precuneus in network-wide theta and gamma oscillatory activity during complex memory retrieval. *eLife* *11*, e43114.
- Hebscher, M., Wing, E., Ryan, J., and Gilboa, A. (2019b). Rapid cortical plasticity supports long-term memory formation. *Trends Cogn. Sci.* *23*, 989–1002.
- Hebscher, M., Ibrahim, C., and Gilboa, A. (2020). Precuneus stimulation alters the neural dynamics of autobiographical memory retrieval. *Neuroimage* *210*, 116575.
- Herdman, K.A., Calarco, N., Moscovitch, M., Hirshhorn, M., and Rosenbaum, R.S. (2015). Impoverished descriptions of familiar routes in three cases of hippocampal/medial temporal lobe amnesia. *Cortex* *71*, 248–263.
- Hilverman, C., and Duff, M.C. (2021). Evidence of impaired naming in patients with hippocampal amnesia. *Hippocampus*. Published online April 6, 2021. <https://doi.org/10.1002/hipo.23325>.
- Irish, M., and Piguet, O. (2013). The pivotal role of semantic memory in remembering the past and imagining the future. *Front. Behav. Neurosci.* *7*, 27.
- Ison, M.J., Quiñero, R., and Fried, I. (2015). Rapid encoding of new memories by individual neurons in the human brain. *Neuron* *87*, 220–230.
- Jasnow, A.M., Lynch, J.F., 3rd, Gilman, T.L., and Riccio, D.C. (2017). Perspectives on fear generalization and its implications for emotional disorders. *J. Neurosci. Res.* *95*, 821–835.
- Josselyn, S.A., and Tonegawa, S. (2020). Memory engrams: Recalling the past and imagining the future. *Science* *367*, eaaw4325.
- Kan, I.P., Larocque, K.F., Lafleche, G., Coslett, H.B., and Verfaellie, M. (2010). Memory monitoring failure in confabulation: evidence from the semantic illusion paradigm. *J. Int. Neuropsychol. Soc.* *16*, 1006–1017.
- Kandel, E.R., Dudai, Y., and Mayford, M.R. (2014). The molecular and systems biology of memory. *Cell* *157*, 163–186.
- Kinsbourne, M., and Wood, F. (1975). Short-term memory processes and the amnesic syndrome. In *Short-term Memory*, D.D. Deutsch and J.A. Deutsch, eds. (Academic Press), pp. 258–291.
- Kitamura, T., Ogawa, S.K., Roy, D.S., Okuyama, T., Morrissey, M.D., Smith, L.M., Redondo, R.L., and Tonegawa, S. (2017). Engrams and circuits crucial for systems consolidation of a memory. *Science* *356*, 73–78.
- Klimesch, W., Freunberger, R., and Sauseng, P. (2010). Oscillatory mechanisms of process binding in memory. *Neurosci. Biobehav. Rev.* *34*, 1002–1014.
- Kopelman, M.D. (1989). Remote and autobiographical memory, temporal context memory and frontal atrophy in Korsakoff and Alzheimer patients. *Neuropsychologia* *27*, 437–460.
- Kopelman, M.D., and Morton, J. (2015). Amnesia in an actor: Learning and re-learning of play passages despite severe autobiographical amnesia. *Cortex* *67*, 1–14.
- Köster, M., Martens, U., and Gruber, T. (2019). Memory entrainment by visually evoked theta-gamma coupling. *Neuroimage* *188*, 181–187.
- Kurczek, J., Wechsler, E., Ahuja, S., Jensen, U., Cohen, N.J., Tranel, D., and Duff, M. (2015). Differential contributions of hippocampus and medial prefrontal cortex to self-projection and self-referential processing. *Neuropsychologia* *73*, 116–126.

- Lah, S., and Miller, L. (2008). Effects of temporal lobe lesions on retrograde memory: a critical review. *Neuropsychol. Rev.* *18*, 24–52.
- Liu, Z.X., Grady, C., and Moscovitch, M. (2017). Effects of prior-knowledge on brain activation and connectivity during associative memory encoding. *Cereb. Cortex* *27*, 1991–2009.
- Maren, S., Aharonov, G., and Fanselow, M.S. (1997). Neurotoxic lesions of the dorsal hippocampus and Pavlovian fear conditioning in rats. *Behav. Brain Res.* *88*, 261–274.
- Martin, A. (2016). GRAPES—Grounding representations in action, perception, and emotion systems: How object properties and categories are represented in the human brain. *Psychon. Bull. Rev.* *23*, 979–990.
- Martin, A., Simmons, W.K., Beauchamp, M.S., and Gotts, S.J. (2014). Is a single ‘hub’, with lots of spokes, an accurate description of the neural architecture of action semantics? *Phys. Life Rev.* *11*, 261–262.
- McClelland, J.L. (2013). Incorporating rapid neocortical learning of new schema-consistent information into complementary learning systems theory. *J. Exp. Psychol. Gen.* *142*, 1190–1210.
- McClelland, J.L., McNaughton, B.L., and O’Reilly, R.C. (1995). Why there are complementary learning systems in the hippocampus and neocortex: insights from the successes and failures of connectionist models of learning and memory. *Psychol. Rev.* *102*, 419–457.
- McCormick, C., St-Laurent, M., Ty, A., Valiante, T.A., and McAndrews, M.P. (2015). Functional and effective hippocampal-neocortical connectivity during construction and elaboration of autobiographical memory retrieval. *Cereb. Cortex* *25*, 1297–1305.
- McCormick, C., Moscovitch, M., Valiante, T.A., Cohn, M., and McAndrews, M.P. (2018a). Different neural routes to autobiographical memory recall in healthy people and individuals with left medial temporal lobe epilepsy. *Neuropsychologia* *110*, 26–36.
- McCormick, C., Barry, D.N., Jafarian, A., Barnes, G.R., and Maguire, E.A. (2020). vmPFC Drives Hippocampal Processing during Autobiographical Memory Recall Regardless of Remoteness. *Cereb. Cortex* *30*, 5972–5987.
- McCormick, C., Ciaramelli, E., De Luca, F., and Maguire, E.A. (2018b). Comparing and contrasting the cognitive effects of hippocampal and ventromedial prefrontal cortex damage: A review of human lesion studies. *Neuroscience* *374*, 295–318.
- McDermott, K.B., Szpunar, K.K., and Christ, S.E. (2009). Laboratory-based and autobiographical retrieval tasks differ substantially in their neural substrates. *Neuropsychologia* *47*, 2290–2298.
- McKenzie, S., Frank, A.J., Kinsky, N.R., Porter, B., Riviere, P.D., and Eichenbaum, H. (2014). Hippocampal representation of related and opposing memories develop within distinct, hierarchically organized neural schemas. *Neuron* *83*, 202–215.
- Melo, B., Winocur, G., and Moscovitch, M. (1999). False recall and false recognition: An examination of the effects of selective and combined lesions to the medial temporal lobe/diencephalon and frontal lobe structures. *Cogn. Neuropsychol.* *16*, 343–359.
- Merhav, M., Karni, A., and Gilboa, A. (2014). Neocortical catastrophic interference in healthy and amnesic adults: a paradoxical matter of time. *Hippocampus* *24*, 1653–1662.
- Merhav, M., Karni, A., and Gilboa, A. (2015). Not all declarative memories are created equal: Fast Mapping as a direct route to cortical declarative representations. *Neuroimage* *117*, 80–92.
- Miller, T.D., Chong, T.T., Aimola Davies, A.M., Johnson, M.R., Irani, S.R., Husain, M., Ng, T.W., Jacob, S., Maddison, P., Kennard, C., et al. (2020). Human hippocampal CA3 damage disrupts both recent and remote episodic memories. *eLife* *9*, e41836.
- Miller, E.K., and Wallis, J.D. (2010). Executive function and higher-order cognition: Definition and neural substrates. *Encyclopedia of Neuroscience* (Elsevier), pp. 99–104.
- Moscovitch, M. (1992). Memory and working with memory: A component process model based on modules and central systems. *J. Cogn. Neurosci.* *4*, 257–267.
- Moscovitch, M. (2008). The hippocampus as a “stupid,” domain-specific module: Implications for theories of recent and remote memory, and of imagination. *Can. J. Exp. Psychol.* *62*, 62–79.
- Moscovitch, M. (2012). Memory before and after HM: An impressionistic historical perspective. In *Epilepsy and Memory*, A. Zeman, N. Kapur, and M. Jones-Gotman, eds. (Oxford University Press), pp. 19–50.
- Moscovitch, M., and Gilboa, A. (2021). Systems consolidation, transformation and reorganization: Multiple Trace Theory, Trace Transformation Theory and their competitors. In *The Oxford Handbook of Human Memory, Volume 1: Foundations*, M.J. Kahana and A.D. Wagner, eds. (Oxford University Press).
- Moscovitch, M., and Nadel, L. (2019). Sculpting remote memory: enduring hippocampal traces and vmPFC reconstructive processes. *Trends Cogn. Sci.* *23*, 634–635.
- Moscovitch, M., Cabeza, R., Winocur, G., and Nadel, L. (2016). Episodic memory and beyond: the hippocampus and neocortex in transformation. *Annu. Rev. Psychol.* *67*, 105–134.
- Nadel, L., and Moscovitch, M. (1997). Memory consolidation, retrograde amnesia and the hippocampal complex. *Curr. Opin. Neurobiol.* *7*, 217–227.
- Nadel, L., and Sederberg, P.B. (2020). Memory Reconsolidation: Making Predictions Better. In *Handbook of Human Memory*, M. Kahana and A. Wagner, eds. (Oxford University Press).
- Nadel, L., Samsonovich, A., Ryan, L., and Moscovitch, M. (2000). Multiple trace theory of human memory: computational, neuroimaging, and neuropsychological results. *Hippocampus* *10*, 352–368.
- Nandi, B., Swiatek, P., Kocsis, B., and Ding, M. (2019). Inferring the direction of rhythmic neural transmission via inter-regional phase-amplitude coupling (ir-PAC). *Sci. Rep.* *9*, 6933.
- Norman, Y., Yeagle, E.M., Khuvis, S., Harel, M., Mehta, A.D., and Malach, R. (2019). Hippocampal sharp-wave ripples linked to visual episodic recollection in humans. *Science* *365*, eaax1030.
- O’Connor, M.G., and Laffèche, G.M. (2004). Retrograde amnesia in patients with rupture and surgical repair of anterior communicating artery aneurysms. *J. Int. Neuropsychol. Soc.* *10*, 221–229.
- Ocampo, A.C., Squire, L.R., and Clark, R.E. (2017). Hippocampal area CA1 and remote memory in rats. *Learn. Mem.* *24*, 563–568.
- Patterson, K., Nestor, P.J., and Rogers, T.T. (2007). Where do you know what you know? The representation of semantic knowledge in the human brain. *Nat. Rev. Neurosci.* *8*, 976–987.
- Penfield, W., and Milner, B. (1958). Memory deficit produced by bilateral lesions in the hippocampal zone. *AMA Arch. Neurol. Psychiatry* *79*, 475–497.
- Petrican, R., Gopie, N., Leach, L., Chow, T.W., Richards, B., and Moscovitch, M. (2010). Recollection and familiarity for public events in neurologically intact older adults and two brain-damaged patients. *Neuropsychologia* *48*, 945–960.
- Peyrache, A., and Seibt, J. (2020). A mechanism for learning with sleep spindles. *Philos. Trans. R. Soc. B.* *375*, 20190230.
- Pilarzyk, K., Klett, J., Pena, E.A., Porcher, L., Smith, A.J., and Kelly, M.P. (2019). Loss of function of phosphodiesterase 11A4 shows that recent and remote long-term memories can be uncoupled. *Curr. Biol.* *29*, 2307–2321.e5.
- Place, R., Farovik, A., Brockmann, M., and Eichenbaum, H. (2016). Bidirectional prefrontal-hippocampal interactions support context-guided memory. *Nat. Neurosci.* *19*, 992–994.
- Poppenk, J., Evensmoen, H.R., Moscovitch, M., and Nadel, L. (2013). Long-axis specialization of the human hippocampus. *Trends Cogn. Sci.* *17*, 230–240.
- Preston, A.R., and Eichenbaum, H. (2013). Interplay of hippocampus and prefrontal cortex in memory. *Curr. Biol.* *23*, R764–R773.
- Quiñero, R. (2019). Plugging in to Human Memory: Advantages, Challenges, and Insights from Human Single-Neuron Recordings. *Cell* *179*, 1015–1032.

- Ralph, M.A., Jefferies, E., Patterson, K., and Rogers, T.T. (2017). The neural and computational bases of semantic cognition. *Nat. Rev. Neurosci.* *18*, 42–55.
- Renoult, L., Davidson, P.S., Palombo, D.J., Moscovitch, M., and Levine, B. (2012). Personal semantics: at the crossroads of semantic and episodic memory. *Trends Cogn. Sci.* *16*, 550–558.
- Renoult, L., Irish, M., Moscovitch, M., and Rugg, M.D. (2019). From Knowing to Remembering: The Semantic-Episodic Distinction. *Trends Cogn. Sci.* *23*, 1041–1057.
- Renoult, L., Armson, M.J., Diamond, N.B., Fan, C.L., Jeyakumar, N., Lev-
esque, L., Oliva, L., McKinnon, M., Papadopoulos, A., Selarka, D., et al. (2020). Classification of general and personal semantic details in the Autobiographical Interview. *Neuropsychologia* *144*, 107501.
- Rey, H.G., Gori, B., Chaure, F.J., Collavini, S., Blenkman, A.O., Seoane, P., Seoane, E., Kochen, S., and Quiñero, R. (2020). Single Neuron Coding of Identity in the Human Hippocampal Formation. *Curr. Biol.* *30*, 1152–1159.e3.
- Reyna, V.F., and Brainerd, C.J. (1995). Fuzzy-trace theory: An interim synthesis. *Learn. Individ. Differ.* *7*, 1–75.
- Ribot, T. (1882). *Diseases of Memory* (Appleton-Century-Crofts).
- Richards, B.A., Xia, F., Santoro, A., Husse, J., Woodin, M.A., Josselyn, S.A., and Frankland, P.W. (2014). Patterns across multiple memories are identified over time. *Nat. Neurosci.* *17*, 981–986.
- Robin, J., and 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.
- Rosenbaum, R.S., Gilboa, A., Levine, B., Winocur, G., and Moscovitch, M. (2009). Amnesia as an impairment of detail generation and binding: evidence from personal, fictional, and semantic narratives in K.C. *Neuropsychologia* *47*, 2181–2187.
- Rosenbaum, R.S., Priselac, S., Kohler, S., Black, S.E., Gao, F., Nadel, L., and Moscovitch, M. (2000). Remote spatial memory in an amnesic person with extensive bilateral hippocampal lesions. *Nat. Neurosci.* *3*, 1044–1048.
- Ross, R.S., and Eichenbaum, H. (2006). Dynamics of hippocampal and cortical activation during consolidation of a nonspatial memory. *J. Neurosci.* *26*, 4852–4859.
- Ryan, J.D., Moses, S.N., Barense, M., and Rosenbaum, R.S. (2013). Intact learning of new relations in amnesia as achieved through unitization. *J. Neurosci.* *33*, 9601–9613.
- Schacter, D.L., Guerin, S.A., and St Jacques, P.L. (2011). Memory distortion: an adaptive perspective. *Trends Cogn. Sci.* *15*, 467–474.
- Sawczak, C., McAndrews, M.P., Gaesser, B., and Moscovitch, M. (2019). Episodic simulation and empathy in older adults and patients with unilateral medial temporal lobe excisions. *Neuropsychologia* *135*, 107243.
- Schacter, D.L., Addis, D.R., Hassabis, D., Martin, V.C., Spreng, R.N., and Szpunar, K.K. (2012). The future of memory: remembering, imagining, and the brain. *Neuron* *76*, 677–694.
- Schapiro, A.C., Turk-Browne, N.B., Botvinick, M.M., and 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. Lond. B. Biol. Sci.* *372*, 20160049.
- Schoenbaum, G., Takahashi, Y., Liu, T.L., and McDannald, M.A. (2011). Does the orbitofrontal cortex signal value? *Ann. N Y Acad. Sci.* *1239*, 87–99.
- Scoville, W.B., and Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *J. Neurol. Neurosurg. Psychiatry* *20*, 11–21.
- Sekeres, M.J., Winocur, G., Moscovitch, M., Anderson, J.A.E., Pishdadian, S., Martin Wojtowicz, J., St-Laurent, M., McAndrews, M.P., and Grady, C.L. (2018a). Changes in patterns of neural activity underlie a time-dependent transformation of memory in rats and humans. *Hippocampus* *28*, 745–764.
- Sekeres, M.J., Winocur, G., and Moscovitch, M. (2018b). The hippocampus and related neocortical structures in memory transformation. *Neurosci. Lett.* *680*, 39–53.
- Sekeres, M.J., Moscovitch, M., Grady, C.L., Sullens, D.G., and Winocur, G. (2019). Reminders reinstate context-specificity to generalized remote memories in rats: relation to activity in the hippocampus and aCC. *Learn. Mem.* *27*, 1–5.
- Sharon, T., Moscovitch, M., and Gilboa, A. (2011). Rapid neocortical acquisition of long-term arbitrary associations independent of the hippocampus. *Proc. Natl. Acad. Sci. USA* *108*, 1146–1151.
- Sheldon, S., and Levine, B. (2013). Same as it ever was: vividness modulates the similarities and differences between the neural networks that support retrieving remote and recent autobiographical memories. *Neuroimage* *83*, 880–891.
- Sheldon, S., and Levine, B. (2018). The medial temporal lobe functional connectivity patterns associated with forming different mental representations. *Hippocampus* *28*, 269–280.
- Sheldon, S.A., and Moscovitch, M. (2010). Recollective performance advantages for implicit memory tasks. *Memory* *18*, 681–697.
- Sheldon, S., Romero, K., and Moscovitch, M. (2013). Medial temporal lobe amnesia impairs performance on a free association task. *Hippocampus* *23*, 405–412.
- Sheldon, S., McAndrews, M.P., Pruessner, J., and Moscovitch, M. (2016). Dissociating patterns of anterior and posterior hippocampal activity and connectivity during distinct forms of category fluency. *Neuropsychologia* *90*, 148–158.
- Sheldon, S., Fenerci, C., and Gurguryan, L. (2019). A Neurocognitive Perspective on the Forms and Functions of Autobiographical Memory Retrieval. *Front. Syst. Neurosci.* *13*, 4.
- Skotko, B.G., Kensinger, E.A., Locascio, J.J., Einstein, G., Rubin, D.C., Tupler, L.A., Krendl, A., and Corkin, S. (2004). Puzzling thoughts for H. M.: can new semantic information be anchored to old semantic memories? *Neuropsychology* *18*, 756–769.
- Söderlund, H., Moscovitch, M., Kumar, N., Mandic, M., and Levine, B. (2012). As time goes by: hippocampal connectivity changes with remoteness of autobiographical memory retrieval. *Hippocampus* *22*, 670–679.
- Sommer, T. (2017). The emergence of knowledge and how it supports the memory for novel related information. *Cereb. Cortex* *27*, 1906–1921.
- Spalding, K.N., Jones, S.H., Duff, M.C., Tranel, D., and Warren, D.E. (2015). Investigating the neural correlates of schemas: Ventromedial prefrontal cortex is necessary for normal schematic influence on memory. *J. Neurosci.* *35*, 15746–15751.
- Squire, L.R., Genzel, L., Wixted, J.T., and Morris, R.G. (2015). Memory consolidation. *Cold Spring Harb. Perspect. Biol.* *7*, a021766.
- St Jacques, P.L., Kragel, P.A., and Rubin, D.C. (2011). Dynamic neural networks supporting memory retrieval. *Neuroimage* *57*, 608–616.
- St-Laurent, M., Moscovitch, M., Levine, B., and McAndrews, M.P. (2009). Determinants of autobiographical memory in patients with unilateral temporal lobe epilepsy or excisions. *Neuropsychologia* *47*, 2211–2221.
- Staresina, B.P., and Wimber, M. (2019). A Neural Chronometry of Memory Recall. *Trends Cogn. Sci.* *23*, 1071–1085.
- Staresina, B.P., Fell, J., Do Lam, A.T., Axmacher, N., and Henson, R.N. (2012). Memory signals are temporally dissociated in and across human hippocampus and perirhinal cortex. *Nat. Neurosci.* *15*, 1167–1173.
- Steinvorth, S., Wang, C., Ulbert, I., Schomer, D., and Haigren, E. (2010). Human entorhinal gamma and theta oscillations selective for remote autobiographical memory. *Hippocampus* *20*, 166–173.
- Sterpenich, V., Albouy, G., Darsaud, A., Schmidt, C., Vandewalle, G., Dang Vu, T.T., Desseilles, M., Phillips, C., Degueldre, C., Balet, E., et al. (2009). Sleep promotes the neural reorganization of remote emotional memory. *J. Neurosci.* *29*, 5143–5152.
- Stolk, A., D’Imperio, D., di Pellegrino, G., and Toni, I. (2015). Altered communicative decisions following ventromedial prefrontal lesions. *Curr. Biol.* *25*, 1469–1474.

- Sutherland, R.J., Sparks, F.T., and Lehmann, H. (2010). Hippocampus and retrograde amnesia in the rat model: a modest proposal for the situation of systems consolidation. *Neuropsychologia* *48*, 2357–2369.
- Sutherland, R.J., Lee, J.Q., McDonald, R.J., and Lehmann, H. (2020). Has multiple trace theory been refuted? *Hippocampus* *30*, 842–850.
- Svoboda, E., McKinnon, M.C., and Levine, B. (2006). The functional neuroanatomy of autobiographical memory: a meta-analysis. *Neuropsychologia* *44*, 2189–2208.
- Takashima, A., Petersson, K.M., Rutters, F., Tendolkar, I., Jensen, O., Zwarts, M.J., McNaughton, B.L., and Fernández, G. (2006). Declarative memory consolidation in humans: a prospective functional magnetic resonance imaging study. *Proc. Natl. Acad. Sci. USA* *103*, 756–761.
- Takashima, A., Bakker, I., van Hell, J.G., Janzen, G., and McQueen, J.M. (2014). Richness of information about novel words influences how episodic and semantic memory networks interact during lexicalization. *Neuroimage* *84*, 265–278.
- Takehara-Nishiuchi, K. (2020). Prefrontal-hippocampal interaction during the encoding of new memories. *Brain Neurosci. Adv.* *4*, 2398212820925580.
- Tambini, A., and Davachi, L. (2019). Awake Reactivation of Prior Experiences Consolidates Memories and Biases Cognition. *Trends Cogn. Sci.* *23*, 876–890.
- Thaiss, L., and Petrides, M. (2008). Autobiographical memory of the recent past following frontal cortex or temporal lobe excisions. *Eur. J. Neurosci.* *28*, 829–840.
- Thielen, J.W., Takashima, A., Rutters, F., Tendolkar, I., and Fernández, G. (2015). Transient relay function of midline thalamic nuclei during long-term memory consolidation in humans. *Learn. Mem.* *22*, 527–531.
- Tompary, A., and Davachi, L. (2017). Consolidation promotes the emergence of representational overlap in the hippocampus and medial prefrontal cortex. *Neuron* *96*, 228–241.e5.
- Tort, A.B., Komorowski, R.W., Manns, J.R., Kopell, N.J., and Eichenbaum, H. (2009). Theta-gamma coupling increases during the learning of item-context associations. *Proc. Natl. Acad. Sci. USA* *106*, 20942–20947.
- Tse, D., Langston, R.F., Kakeyama, M., Bethus, I., Spooner, P.A., Wood, E.R., Witter, M.P., and Morris, R.G. (2007). Schemas and memory consolidation. *Science* *316*, 76–82.
- Tse, D., Takeuchi, T., Kakeyama, M., Kajii, Y., Okuno, H., Tohyama, C., Bito, H., and Morris, R.G. (2011). Schema-dependent gene activation and memory encoding in neocortex. *Science* *333*, 891–895.
- Tulving, E. (1983). *Elements of episodic memory* (Oxford University Press).
- Tulving, E. (2001). Episodic memory and common sense: how far apart? *Philos. Trans. R. Soc. Lond. B Biol. Sci.* *356*, 1505–1515.
- van Kesteren, M.T., Rijpkema, M., Ruiters, D.J., and Fernández, G. (2010). Retrieval of associative information congruent with prior knowledge is related to increased medial prefrontal activity and connectivity. *J. Neurosci.* *30*, 15888–15894.
- van Kesteren, M.T., Ruiters, D.J., Fernández, G., and Henson, R.N. (2012). How schema and novelty augment memory formation. *Trends Neurosci.* *35*, 211–219.
- Vargha-Khadem, F., Gadian, D.G., and Mishkin, M. (2001). Dissociations in cognitive memory: the syndrome of developmental amnesia. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* *356*, 1435–1440.
- Vaz, A.P., Inati, S.K., Brunel, N., and Zaghoul, K.A. (2019). Coupled ripple oscillations between the medial temporal lobe and neocortex retrieve human memory. *Science* *363*, 975–978.
- Verfaellie, M., Bousquet, K., and Keane, M.M. (2014). Medial temporal and neocortical contributions to remote memory for semantic narratives: evidence from amnesia. *Neuropsychologia* *61*, 105–112.
- Vetere, G., Xia, F., Ramsaran, A.I., Tran, L.M., Josselyn, S.A., and Frankland, P.W. (2021). An inhibitory hippocampal-thalamic pathway modulates remote memory retrieval. *Nat. Neurosci.* Published online March 29, 2021. <https://doi.org/10.1038/s41593-021-00819-3>.
- Viskontas, I.V., Quiroga, R.Q., and Fried, I. (2009). Human medial temporal lobe neurons respond preferentially to personally relevant images. *Proc. Natl. Acad. Sci. USA* *106*, 21329–21334.
- Waidergoren, S., Segalowitz, J., and Gilboa, A. (2012). Semantic memory recognition is supported by intrinsic recollection-like processes: “The butcher on the bus” revisited. *Neuropsychologia* *50*, 3573–3587.
- Warren, D.E., Jones, S.H., Duff, M.C., and Tranel, D. (2014). False recall is reduced by damage to the ventromedial prefrontal cortex: implications for understanding the neural correlates of schematic memory. *J. Neurosci.* *34*, 7677–7682.
- Westmacott, R., and Moscovitch, M. (2003). The contribution of autobiographical significance to semantic memory. *Mem. Cognit.* *31*, 761–774.
- Westmacott, R., Black, S.E., Freedman, M., and Moscovitch, M. (2004). The contribution of autobiographical significance to semantic memory: evidence from Alzheimer’s disease, semantic dementia, and amnesia. *Neuropsychologia* *42*, 25–48.
- Williams, A.N., Ridgeway, S., Postans, M., Graham, K.S., Lawrence, A.D., and Hodgetts, C.J. (2020). The role of the pre-commissural fornix in episodic autobiographical memory and simulation. *Neuropsychologia* *142*, 107457.
- Wilson, R.C., Takahashi, Y.K., Schoenbaum, G., and Niv, Y. (2014). Orbitofrontal cortex as a cognitive map of task space. *Neuron* *81*, 267–279.
- Wiltgen, B.J., Sanders, M.J., Anagnostaras, S.G., Sage, J.R., and Fanselow, M.S. (2006). Context fear learning in the absence of the hippocampus. *J. Neurosci.* *26*, 5484–5491.
- Winocur, G., and Moscovitch, M. (2011). Memory transformation and systems consolidation. *J. Int. Neuropsychol. Soc.* *17*, 766–780.
- Winocur, G., Moscovitch, M., Fogel, S., Rosenbaum, R.S., and Sekeres, M. (2005). Preserved spatial memory after hippocampal lesions: effects of extensive experience in a complex environment. *Nat. Neurosci.* *8*, 273–275.
- Winocur, G., Moscovitch, M., and Sekeres, M. (2007). Memory consolidation or transformation: context manipulation and hippocampal representations of memory. *Nat. Neurosci.* *10*, 555–557.
- Winocur, G., Frankland, P.W., Sekeres, M., Fogel, S., and Moscovitch, M. (2009). Changes in context-specificity during memory reconsolidation: selective effects of hippocampal lesions. *Learn. Mem.* *16*, 722–729.
- Winocur, G., Moscovitch, M., and Bontempi, B. (2010). Memory formation and long-term retention in humans and animals: convergence towards a transformation account of hippocampal-neocortical interactions. *Neuropsychologia* *48*, 2339–2356.
- Xu, W., and Südhof, T.C. (2013). A neural circuit for memory specificity and generalization. *Science* *339*, 1290–1295.
- Yassa, M.A., and Reagh, Z.M. (2013). Competitive Trace Theory: a role for the hippocampus in contextual interference during retrieval. *Front. Behav. Neurosci.* *7*, 107.
- Yonelinas, A.P., Ranganath, C., Ekstrom, A.D., and Wiltgen, B.J. (2019). A contextual binding theory of episodic memory: systems consolidation reconsidered. *Nat. Rev. Neurosci.* *20*, 364–375.
- Yu, L.Q., Kan, I.P., and Kable, J.W. (2019). Beyond a rod through the skull: A systematic review of lesion studies of the human ventromedial frontal lobe. *Cogn. Neuropsychol.* *79*, 1–45.
- Zaiser, A.K., Bader, R., and Meyer, P. (2019). Feature overlap modulates rapid semantic but not lexical integration of novel associations by means of fast mapping. *bioRxiv*. <https://doi.org/10.1101/594218>.
- Zaiser, A.-K., Meyer, P., and Bader, R. (2021). High feature overlap and incidental encoding drive rapid semantic integration in the fast mapping paradigm. *J. Exp. Psychol. Gen.* <https://doi.org/10.1037/xge0001070>.