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Abstract	It is well established that the hippocampus and adjacent medial temporal lobe (MTL) cortical structures are necessary for long-term declarative (conscious) memory, but investigators continue to cast a wider net, suggesting a considerably broader reach for these structures than standard perspectives have proposed. The objective of this chapter is to explore possible contributions made by the hippocampus to perception, short-term or working memory, and expressions of memory in the absence of conscious awareness. Questions about whether and how the hippocampus supports processing in these domains have garnered a good deal of interest in recent years, and healthy debate about the viability of claims that have been made in	

the literature is ongoing (cf. Eichenbaum 2013; Squire and Dede 2015). In the sections that follow, background context for each of these domains is provided followed by select empirical findings that hint at possible hippocampal contributions to cognition beyond long-term declarative memory. Along the way, dissenting viewpoints and methodological hurdles are considered alongside alternative accounts for key findings. As will be seen, it is not always the case that we advocate for a particular perspective, but we do make efforts to be even-handed in our treatment of the literature. In the end, we conclude by attempting to identify questions that remain unresolved and offer some suggestions about how ongoing controversies might be reconciled in future work.

Beyond Long-Term Declarative Memory: Evaluating Hippocampal Contributions to Unconscious Memory Expression, Perception, and Short-Term Retention

Deborah E. Hannula, Jennifer D. Ryan, and David E. Warren

Abstract It is well established that the hippocampus and adjacent medial temporal lobe (MTL) cortical structures are necessary for long-term declarative (conscious) memory, but investigators continue to cast a wider net, suggesting a considerably broader reach for these structures than standard perspectives have proposed. The objective of this chapter is to explore possible contributions made by the hippocampus to perception, short-term or working memory, and expressions of memory in the absence of conscious awareness. Questions about whether and how the hippocampus supports processing in these domains have garnered a good deal of interest in recent years, and healthy debate about the viability of claims that have been made in the literature is ongoing (cf. Eichenbaum 2013; Squire and Dede 2015). In the sections that follow, background context for each of these domains is provided followed by select empirical findings that hint at possible hippocampal contributions to cognition beyond long-term declarative memory. Along the way, dissenting viewpoints and methodological hurdles are considered alongside alternative accounts for key findings. As will be seen, it is not always the case that we advocate for a particular perspective, but we do make efforts to be even-handed in our treatment of the literature. In the end, we conclude by attempting to identify questions that remain unresolved and offer some suggestions about how ongoing controversies might be reconciled in future work.

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It is well established that the hippocampus and adjacent medial temporal lobe (MTL) cortical structures are necessary for long-term declarative (conscious) memory, but investigators continue to cast a wider net, suggesting a considerably broader reach for these structures than standard perspectives have proposed. The objective of this chapter is to explore possible contributions made by the hippocampus to perception, short-term or working memory, and expressions of memory in the absence of conscious awareness. Questions about whether and how the hippocampus supports processing in these domains have garnered a good deal of interest in recent years, and healthy debate about the viability of claims that have been made in the literature is ongoing (cf. Eichenbaum 2013; Squire and Dede 2015). In the sections that follow, background context for each of these domains is provided followed by select empirical findings that hint at possible hippocampal contributions to cognition beyond long-term declarative memory. Along the way, dissenting viewpoints and methodological hurdles are considered alongside alternative accounts for key findings. As will be seen, it is not always the case that we advocate for a particular perspective, but we do make efforts to be even-handed in our treatment of the literature. In the end, we conclude by attempting to identify questions that remain unresolved and offer some suggestions about how ongoing controversies might be reconciled in future work.

Some Context: The Medial Temporal Lobe Memory System

As is often the case when MTL function is considered, it is appropriate to begin with a brief discussion of Henry Molaison (H.M.), who participated in research for decades following bilateral MTL surgical resection in 1953 (c.f. Corkin 2002; Eichenbaum 2013; Squire 2009). In early descriptions, and subsequent empirical work, it was immediately clear that H.M.'s long-term memory (LTM) was severely compromised—indeed, he was said to "forget the incidents of . . . daily life as fast as they occur[ed]" (p. 15, Scoville and Milner 1957). Nonetheless, as reported by Scoville and Milner (1957), he could retain three digit numbers and unrelated word pairs for several minutes in the absence of distraction, and his performance on a battery of tests that tapped perception, abstract thinking, and reasoning ability was preserved.

Subsequent studies of MTL function largely confirmed these initial observations and set the stage for decades of research that has been squarely focused on questions about how exactly structures in the MTL contribute to LTM. Most important for our purposes, this work has led to claims for the dissociation of declarative (consciously accessible, reportable) LTM, which arguably depends critically on MTL integrity, and non-declarative (consciously inaccessible) LTM, said to be independent of these structures. Once again, some of the earliest evidence in favor of this dissociation originated with HM. For example, severe impairments were evident on standardized tests of LTM, and it was noted that "once he had turned to a new task the nature of the preceding one could no longer be recalled, nor the test recognized if repeated" (Scoville and Milner 1957, p. 108). Nevertheless, H.M. did acquire new skills. For example, like healthy controls, his ability to trace within the outline of a star using only the reflection from a mirror improved with practice (Milner 1962; Milner et al. 1998; Gabrieli et al. 1993). What made this observation so striking was that his memories for the *experiences* associated with skill acquisition (e.g., the testing apparatus, task, and experimenter) were lost despite clear evidence for long-lasting gains in performance (for review, see Hannula and Greene 2012).

A major effort of contemporary research has been to determine whether the hippocampus contributes to LTM in a qualitatively different way than surrounding MTL cortical structures (i.e., perirhinal, parahippocampal, and entorhinal cortices). While general consensus has not yet been achieved, and perspectives continue to evolve (see chapter "Dynamic Cortico-Hippocampal Networks Underlying Memory and Cognition: The PMAT Framework" by Inhoff & Ranganath), many theories seem to share some version of the view that the hippocampus, which sits at the top of the MTL processing hierarchy, is ideally positioned to bind together converging inputs (e.g., Cohen and Eichenbaum 1993; Davachi 2006; Diana et al. 2007; Montaldi and Mayes 2010). As described in detail elsewhere, the resulting relational memory representations permit us to retrieve rich, multifaceted episodic memories of objects that co-occur in space and time (cf. Eichenbaum and Cohen 2014). It is in this context that questions have often been posed about whether or not the role of the hippocampus in cognition might go further than had originally been appreciated. Indeed, it was only in this context that we could begin to address these questions because tasks had to be developed that would tax the processing and representational affordances that are unique to the hippocampus. In so doing, it seems that the reach of the hippocampus is indeed broader than standard textbook descriptions would have us believe; research outcomes consistent with this claim are considered in the sections that follow, along with associated counterevidence that has been reported in the literature.

Unconscious or Implicit Memory

That the hippocampus contributes critically to consciously accessible, or declarative, memory is not subject to debate. Indeed, all previous and current memory systems theories acknowledge a connection between hippocampal function and conscious awareness—specifically, explicit memory. This position is based on indisputable evidence showing that amnesic individuals with hippocampal lesions have impaired conscious appreciation for prior learning episodes (Squire 1992; Cohen and Eichenbaum 1993; Moses and Ryan 2006; Henke 2010; Moscovitch 1992). These effects were first observed anecdotally in informal interaction with H.M. who was described by Scoville and Milner (1957) as being unable to remember where he had been, or what he had done, just hours after events had transpired. The same observations have been made in formal testing conducted with H.M. and other amnesic patients on tasks that require recall or recognition of materials presented during an encoding phase (Squire and Wixted 2011). However, it is important to note that even amnesic individuals who have severe memory impairments and widespread damage that goes beyond the hippocampus and surrounding MTL structures have conscious appreciation for the present moment (e.g., amnesic case K.C.—Rosenbaum et al. 2005; amnesic case E.P.—Insausti et al. 2013). That is, amnesic individuals can understand the current contextual setting, engage in conversation appropriately, follow instructions and perform tasks, etc. Therefore, the hippocampus does not appear to be critical for conscious experience, *per se*. Instead, it is conscious access to information experienced in the past minutes, hours, days, or years (i.e. prior learning episodes) that is severely compromised. Consequently, it is the position of declarative memory theory (and others) that the contents of hippocampus-mediated representations must be within conscious apprehension during encoding and that conscious awareness is part and parcel of the retrieval of such representations (e.g. Squire 2004; Graf and Schacter 1985; Moscovitch 1992). However, if conscious awareness were indeed a fundamental property of hippocampal processing and/or hippocampus-dependent representations, it would be difficult to imagine how amnesic individuals retain conscious appreciation for what is happening in the present moment (see also the Perception section).

In recent years, alternative theories of MTL function have emerged that suggest the primary role of the hippocampus in memory has less to do with conscious awareness than with the nature of the information that is retained in memory. In other words, it is the representational affordances and/or processing capabilities of MTL structures that set them apart from other brain regions. Specifically, relational memory theory posits that the hippocampus is critical for binding relations among distinct objects, and that these relational memory representations can be encoded, retrieved, and subsequently used in service of ongoing cognition. This is the case whether information is available to conscious access or not (Eichenbaum and Cohen 2001; Cohen and Eichenbaum 1993; Ryan et al. 2000). Similarly, the binding of items in context (BIC) model suggests that there may not be a one-to-one mapping of MTL structures and explicit memory; instead, the relationship between regions of the MTL and explicit memory processes may depend on task demands (Diana et al. 2007). Finally, this position has perhaps been articulated most strongly by Henke (2010), who indicates that "... hippocampal damage will impair the rapid associative encoding of compositional and flexible associations irrespective of consciousness of encoding and retrieval" (p. 530). In general, the prediction from these models is that the hippocampus is critical for fully-intact performance whenever the information processing demands of a task require representation of relational (or item-in-context) bindings whether or not that information is subject to conscious access. Consistent with this possibility, there are several reports in the literature of unconscious, implicit, memory that is indeed hippocampus-dependent. Many of these findings were reviewed in detail by Hannula and Greene (2012), and therefore, in this section of the chapter, we highlight just a few recent examples. Before turning to these studies, however, it is important to acknowledge that the number of examples is far fewer than reports linking the hippocampus to explicit memory; this is likely due, at least in part, to challenges associated with conducting studies that deal with conscious awareness—some of these pitfalls are referenced in the text below.

Neuropsychological Investigations of Implicit, Unconscious, Memory

Evidence that the hippocampus is critically involved in implicit, unconscious, memory began with two neuropsychological studies conducted with MTL amnesic patients. First, Chun and Phelps (1999) demonstrated that control participants were faster to search for and identify a target among distractors when search arrays were repeated (versus novel) across blocks, an outcome known as the contextual cuing effect. Effects of contextual cuing occurred even though participants could not explicitly identify or recognize the displays that had been repeated. Amnesic individuals whose damage included the hippocampus showed response time facilitation across blocks, demonstrating spared skill learning. However, compared to controls, these individuals were not differentially faster for repeated displays, suggesting that they were unable to create, and benefit from, the requisite memories in which the target could be located in reference to the relative positions of corresponding distractors.

The second study to provide evidence in favor of hippocampus-dependent memory expression absent awareness was reported by Ryan et al. (2000). Using eye tracking, these investigators demonstrated that both control participants and amnesic patients showed a decrease in the number of fixations that were made to repeated, as compared to novel, scenes. As above, this result suggests that basic reprocessing, or fluency, effects are intact in amnesia. However, only the control participants showed eye movements that were differentially attracted to changed regions within scenes. No evidence for this preferential viewing effect was evident in patient data, suggesting that the MTL, and the hippocampus specifically (see Ryan and Cohen 2004), was critical for binding the spatial relations among items that were embedded in previously studied pictures. Importantly, these eye-movement-based relational memory effects were absent from the viewing patterns of amnesic patients even though the same effects were observed in control data when concomitant awareness for what had been altered in the scenes was absent. In other words, eye movements were sensitive to relational memory even in the absence awareness, but not when individuals with hippocampal damage were tested. Whether or not viewing patterns index memory without awareness has been subject to some debate in the literature (Smith et al. 2006). However, the same investigators who have reported null outcomes in past work recently found that these effects are sensitive to instructional manipulations (Smith and Squire 2015). This is discussed in more detail below, but is mentioned here because it seems that discrepancies in the literature may come down to experiment-specific implementation details.

In the time since publication of these initial reports, Henke and colleagues have made great strides in this domain, reporting in several studies that the hippocampus contributes to unconscious encoding. In one of these studies (Duss et al. 2014), amnesic patients and matched controls were presented with pairs of unrelated words (e.g., rain-screw, coffee-tango) embedded in a visual masking sequence. Subsequently, pairs of words were presented supraliminally, and participants were asked to indicate whether the words in each pair were a good fit. Notably, all of these visible word pairs were novel (i.e. had not been presented subliminally), and were either semantically related to a previously encoded pair (intact pair: snow-nail), or not (broken pair: hail-waltz). Results indicated that intact pairs were endorsed more often by controls as a ‘fit’ than broken pairs. This outcome was said to reflect the influence of memory for the relations among subliminally presented word pairs on subsequent performance, and was reduced in the amnesic sample. Notably, some of the amnesic patients performed at levels comparable to the control group on the unconscious encoding/retrieval task, but were impaired when memory was tested directly. Neuroimaging data indicated that these individuals recruited spared tissue in the hippocampus during task performance. The authors conclude that the hippocampus has a role in both conscious and unconscious encoding/retrieval, and that based on functional connectivity results, a larger network of the hippocampal-anterior thalamic axis and neocortical connections may be required to support conscious access. Considered together, the above studies demonstrate that awareness is not an absolute requirement for hippocampus-supported memory.

Early Information Processing Is Modified Following Hippocampal Damage

While it is clear that amnesic patients have deficits in *conscious* access to remembered content, evidence also suggests that there are important changes in how information is processed by these individuals well before explicit memory decisions might be made. One possibility then is that these early processing abnormalities occur outside of conscious awareness. For example, in past work we have reported that eye movements index memory for learned scene-face relationships during a test trial within 500–750 ms of display onset, and as much as 1–1.5 s in advance of explicit recognition responses (Hannula et al. 2007); the same effect is completely absent from viewing patterns of amnesic patients with hippocampal damage. Based on this outcome, it was proposed that this eye-movement-based prioritization occurs in advance of, and may contribute to the development of conscious awareness for the associate (see also Hannula and Ranganath 2009). Studies outlined below suggest that in addition to the absence of changes in viewing that precede conscious reports, the manner by which hippocampal amnesic patients engage in basic processing is altered in the earliest moments of stimulus exploration (also see the Perception section).

This change in online processing is particularly well illustrated by an experiment that required amnesic patients and control participants to study an array of objects for a subsequent memory test (Voss et al. 2011). Critically, the objects used in this experiment were not revealed simultaneously; rather, the participant's eye movements were used to reveal the objects through a moving window. During exploration, control participants would occasionally revisit previously inspected objects/ locations, however, this "spontaneous revisitation" effect was nearly absent in the amnesic data. Further, results from control participants indicated that revisitation predicted subsequent memory and was associated with hippocampal activity as revealed with functional magnetic resonance imaging (fMRI). This study illustrates the utility of converging research methods (eye tracking with neuropsychological cases, functional neuroimaging of healthy individuals), and it provides initial evidence for the online influence of hippocampal processing on the manner by which information is extracted from the external world.

A recent study from Olsen et al. (2015) with the developmental amnesic patient H.C. echoes the findings described above (Voss et al. 2011) and provides yet another compelling example of changes in online information processing as a consequence of hippocampal damage. H.C. presents with hippocampal volume loss and abnormal development of the extended hippocampal system (Rosenbaum et al. 2014). However, the volume of H.C.'s MTL cortical structures are similar to those of controls. In this study, when faces were presented during an incidental encoding phase, H.C. directed significantly more viewing to the eyes, and less viewing to other face features, compared to the control participants (see Fig. 1). Furthermore, H.C. had a lower transition-to-fixation ratio than controls. Consistent with past reports (e.g., Bird and Burgess 2008; Mayes et al. 2002), H.C. showed relatively intact recognition for faces that were presented from the same viewpoint during study and test, but was impaired when the viewpoint at test was different from corresponding study exposures, or when faces had been presented from different viewpoints across individual study trials. These outcomes suggest that the manner in which the faces are studied and tested (i.e., same versus different viewpoint) can considerably impact recognition performance in amnesic patients, and that deficiencies in how materials are processed (as indexed by eye movement behavior) may contribute to this outcome. Consistent with descriptions in the STM section below, results from this experiment suggest a role for the hippocampus in intra-item feature binding when a high fidelity representation of encoded information is required for successful task performance. In other words, the focus of the hippocampus can be relatively wide, encompassing several objects embedded in an episodic context, or narrow (i.e., limited to relationships among item features), depending on task demands. Whether non-normative viewing patterns are responsible for compromised binding or vice-versa cannot be determined based on the outcomes of this work, but we suspect that the relationship is bi-directional (i.e., ongoing binding deficits change viewing patterns that are, in turn, non-optimal for binding; see Olsen et al. 2012).

Importantly, online processing, as indexed by eye movement behavior in studies described briefly above, is likely to be outside the domain of conscious experience.

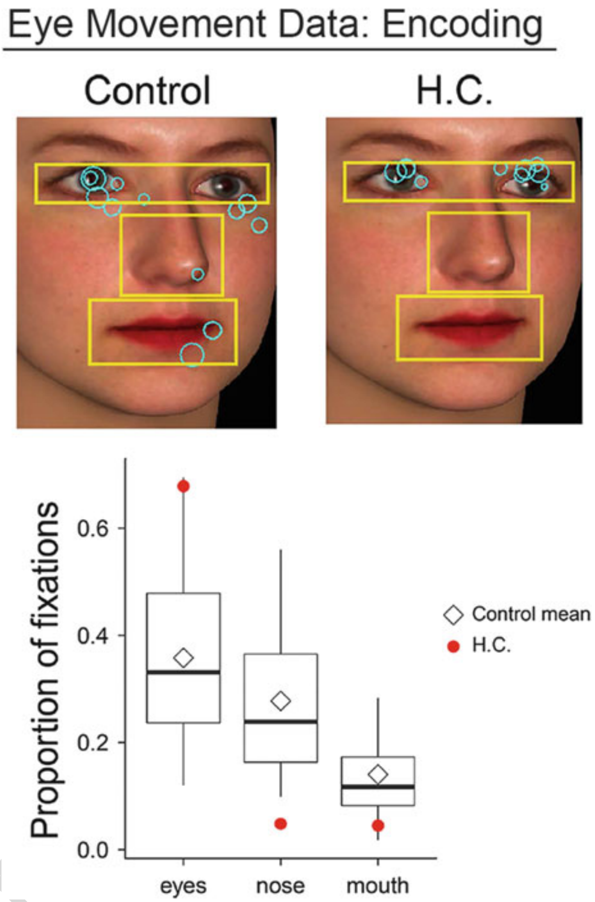

Fig. 1 This figure illustrates differences in the distribution of fixations to a face that was presented during encoding. Data from a representative control participant can be seen on the *left* and data from developmental amnesic patient H.C. can be seen on the *right* (*top*). The proportion of fixations directed to the nose and the mouth is reduced in H.C. relative to control participants; in contrast, more fixations were directed by H.C. to the eyes. Figure adapted from Olsen et al. (2015) and reproduced with permission according to the Creative Commons License agreement with the Journal of Neuroscience

For example, while the externally presented face in the study conducted with H.C. was certainly subject to conscious apprehension, it is unlikely that participants in this experiment were completely aware of their particular eye movement patterns, or the specifics of ongoing processing. Consistent with this possibility, participants perform poorly when they attempt to distinguish their own fixations patterns from those of other participants (Foulsham and Kingstone 2013). Furthermore, while participants can reasonably introspect about the placement of their own eye movements during a visual search task (Marti et al. 2015), introspection was not perfect. Indeed, reported gaze position was frequently inaccurate and false fixations were reported as well. More generally, there was an effect on eye movement placement that was related to the task of introspection itself, suggesting that asking people to report the position of their eye movements changes at least some aspects of eye movement behavior. Finally, while this was not tested directly, it may have been difficult for participants to distinguish instances of covert (attention in the absence of direct fixation) from overt attention (attention coincident with a direct fixation); evidence for this kind of misattribution error has been reported previously by Hollingworth et al. (2008). In sum, evidence suggests that participants have poor insight into their fixation patterns, and this may reflect a lack of insight into online processing. Questions about how exactly patterns of “free viewing” (absent search requirements or any other specific instruction) are related to conscious awareness (or introspection) have yet to be addressed.

One final bit of evidence that suggests eye movements and conscious experience can be dissociated comes from a study conducted by Spering et al. (2011). Specifically, these authors reported that the trajectory of eye movements can be separated from the conscious percept of a presented stimulus. Participants in this experiment were presented with two horizontally (90°) or vertically (0°) oriented sine-wave gratings that drifted orthogonally to their orientation. One of gratings was adapted to one eye, and then re-presented to the same eye as the other grating was presented to the other eye simultaneously. Whereas eye movement trajectories responded to the integrated motion of the two gratings (the diagonal), the conscious percept of the participants was typically in the direction of the un-adapted grating, or of two separate motions (one weak, one strong). Together with findings outlined above, this work indicates that the link between eye movements and continuous, accurate conscious apprehension is tenuous at best. Thus, what is observed in H.C., and other amnesic patients, is a change in behavior that is not likely to be fully within conscious apprehension. In short, the hippocampus may contribute information that supports conscious awareness of remembered content, but consciousness may not be bound up in the representation itself (Hannula and Greene 2012).

Neuroimaging Investigations of Implicit, Unconscious, Memory

Neuroimaging investigations have provided additional support for hippocampal contributions to memory in the absence of explicit knowledge for prior learning experiences. For instance, Reber et al. (2016) presented participants who were undergoing intracranial electroencephalography (iEEG) with sequences of word pairs, some of which contained a common associate (e.g., “winter-red”, “red-cat”), and asked participants to judge the goodness of fit of each pair. Although participants were not aware of the indirect relationships that linked distinct pairs (e.g., the word “red” in our example above), an ERP difference recorded from the hippocampus was observed 400 ms following the onset of the second word pair during encoding (e.g., “red-cat”) when the match was present. Subsequently, a test pair was presented that combined the words that were related indirectly by virtue of their shared associate (e.g., “winter-cat”), however there were no ERP differences that distinguished these pairs from others. Based on these outcomes, the authors proposed that relational learning occurred during encoding, even in the absence of awareness.

Work from Ryals et al. (2015) has indicated that hippocampal engagement during retrieval is sensitive to memory absent awareness as well. Their findings are similar to other recent reports, which show that hippocampus-dependent eye movement effects can be dissociated from explicit behavioral responses (e.g., Hannula and Ranganath 2009; Ryan et al. 2000; Nickel et al. 2015). Using eye movement monitoring and fMRI, Ryals et al. (2015) presented participants with scenes that were either new, or configurally similar to scenes that had been previously studied. Participants were asked to identify scenes that they felt were a configural match to (i.e. had the same global layout as) previously encoded exemplars. Results indicated that there was significant overlap in eye-movement-based exploration of configurally similar and previously studied scenes, and that this viewing effect was related to hippocampal activity. Furthermore, and especially important in the context of this section, eye-movement-based exploration effects were correlated with activity differences in the hippocampus even though performance (i.e., explicit identification of configurally similar scenes) was at chance.

Finally, a recent study that combined event-related potentials (ERPs) with patient testing indicated that a neural signature of recognition memory, evident in control data irrespective of awareness, was absent from patient data (Addante 2015). In this experiment, participants were presented with several words, and for each exemplar, made either an animacy or manmade judgment. In an unexpected, subsequent memory test, participants indicated whether individual words were old or new, and specified what kind of source judgment had been made earlier. Results indicated that both explicit item recognition and source memory decisions were impaired in amnesic patients. Additionally, amnesic individuals failed to show a neural signature in posterior regions that, in control participants, distinguished between previously studied and novel words, and was independent from explicit recognition reports. Once again, and much like studies described above, this outcome suggests that consciousness may be orthogonal to hippocampal function.

Early Information Processing Engages the Hippocampus

As indicated above, effects of memory on eye movement behavior are evident shortly after stimulus onset and precede explicit recognition responses (Hannula et al. 2007; see also Ryan et al. 2007); the same effects are absent from the viewing patterns of amnesic patients. One possibility suggested by this observation is that *early* recruitment of the hippocampus (not measured in the cited studies) indexes pattern completion processes and corresponding retrieval of memory representations that are then used in service of conscious awareness. That is, hippocampal representations may not be the seat of consciousness itself (Voss et al. 2012), but rather, may support the subsequent experience of conscious awareness (Hannula and Ranganath 2009; Ranganath 2010). This possibility is consistent with a two-stage model of conscious recollection (Moscovitch 2008; Sheldon and Moscovitch 2010), which states that the hippocampus supports automatic and obligatory retrieval of encoded content during stage one, and contributes to conscious appreciation of retrieved content (perhaps via interactions with the PFC), subsequently, in stage two.

Consistent with the two-stage model, it has been reported that activity differences in the hippocampus during presentation of a scene cue predicted eye-movement-based prioritization of a learned associate when a test display was presented (Hannula and Ranganath 2009). Because these activity differences were evident even when explicit recognition responses were incorrect, it was proposed that this outcome corresponds to stage one of the two-stage model (i.e. automatic, or obligatory retrieval of encoded content). Also consistent with the model, functional coupling of the hippocampus with PFC, identified in a connectivity analysis of data collected during test display presentation, was associated with successful explicit recognition memory performance. While these results suggest that the hippocampus contributes to obligatory retrieval of relational memory representations as indexed by early viewing patterns, nothing can be said about the time-course of hippocampal recruitment because fMRI methods were used. Only by using other neuroimaging approaches with much finer temporal resolution (e.g., iEEG, magnetoencephalography) can questions like these be addressed.

Consistent with the proposal that hippocampal engagement can occur early in processing, Riggs et al. (2009) reported that hippocampal theta responses, indexed with magnetoencephalography (MEG), distinguished old from new scenes during performance of a recognition task within just 250 ms of stimulus onset. This outcome suggests that the hippocampus may be obligatorily engaged during perceptual processing, well before explicit recognition would occur, when a task requires the comparison of external stimuli to internal representations of encoded content. Work from Olsen et al. (2013) complements this report by demonstrating that hippocampal theta responses index binding requirements when information must be integrated across time. In this experiment, objects were presented sequentially and participants were required to encode their relative visuospatial positions. Importantly, because items appeared one at a time, the amount of stimulus information visible from moment to moment remained the same over the course of the trial. Presumably, given that the participants were aware of the task demands (i.e. to integrate the objects), which remained constant as well, conscious experience was not appreciably different across time. Binding demands, however, did increase, as more elements had to be integrated into the existing memory representation as the trial progressed. Results indicated that hippocampal theta responses tracked binding demands, increasing with the introduction of each new item. As such, ongoing modulation of hippocampal responses seems to be especially sensitive to binding operations, rather than conscious experience per se. Of course, any strong claim in this regard would require evaluation of hippocampal theta oscillations absent awareness, perhaps by rendering materials invisible at encoding via masking, or by binning trials based on recognition accuracy.

Several additional studies provide converging evidence in favor of early hippocampal engagement. For example, hippocampal replay (i.e. reinstatement of neural activity patterns evident at encoding) has been reported within 500 ms of memory cue onset (Jafarpour et al. 2014). Additionally, Horner et al. (2012) recorded neural responses with MEG in a group of younger (predominantly developmental amnesic) patients of varying etiologies with a range of hippocampal volumes, as well as control participants. All of the participants were required to study words (items) superimposed on scenes (context). Patients' item memory did not differ from controls, but context memory (selection of a scene from a three alternative forced choice) was impaired and the magnitude of this impairment was correlated with hippocampal volume (Horner et al. 2012). Control participants showed a frontotemporal MEG effect between 350–400 ms following stimulus onset that reflected item memory and an effect 500–600 ms that distinguished context hits from misses; such effects were absent in the patient data suggesting they were hippocampus-dependent. These findings point to a role for the hippocampus in both item and context memory, but importantly for discussion here they showcase the early engagement of the hippocampus or brain regions that are connected to—i.e., depend upon information processing supported by—the hippocampus.

Perhaps most notable, was a report that provided specific information about the timing of hippocampal responses relative to explicit recognition decisions in a recent iEEG investigation (Staresina et al. 2012; See Fig. 2). In this experiment, recordings taken directly from the hippocampus in pre-surgical epilepsy patients indicated that there was a significant effect of successful source memory retrieval within 250–750 ms of stimulus onset during test. This source effect was followed by a sustained response sensitive to new (i.e. not studied) items. The late onset of this item-based response suggested that it might reflect the engagement in post-retrieval processing. Consistent with this possibility, a response-locked analysis of the data indicated that item-specific responses in the hippocampus were only evident after explicit recognition decisions had been made, and may therefore have reflected incidental encoding of new items into memory. Critically, source-specific responses were evident in hippocampal recordings before explicit recognition decisions were made. While the authors do not discuss this outcome in terms of conscious access, it aligns well with eye movement studies described above, and with the idea that the role of the hippocampus in conscious experience may be secondary to, and emerge from, its primary role in supporting a particular type of representation—here, bound representations of item and source.

AU2

Challenges for Evaluating Unconscious Memory

Any study that points to a role for the hippocampus in memory function outside of conscious awareness must consider whether there is potential contamination from explicit remembering. That is, a person may not explicitly report remembered content because they have adopted a strict response criterion, or because perceived task demands preclude them from disclosing awareness (for review, see Simons et al. 2007). However, counterarguments must be considered as well when linking hippocampal function to explicit memory. For instance, it is possible that responses that appear to index conscious knowledge of formed/stored information were

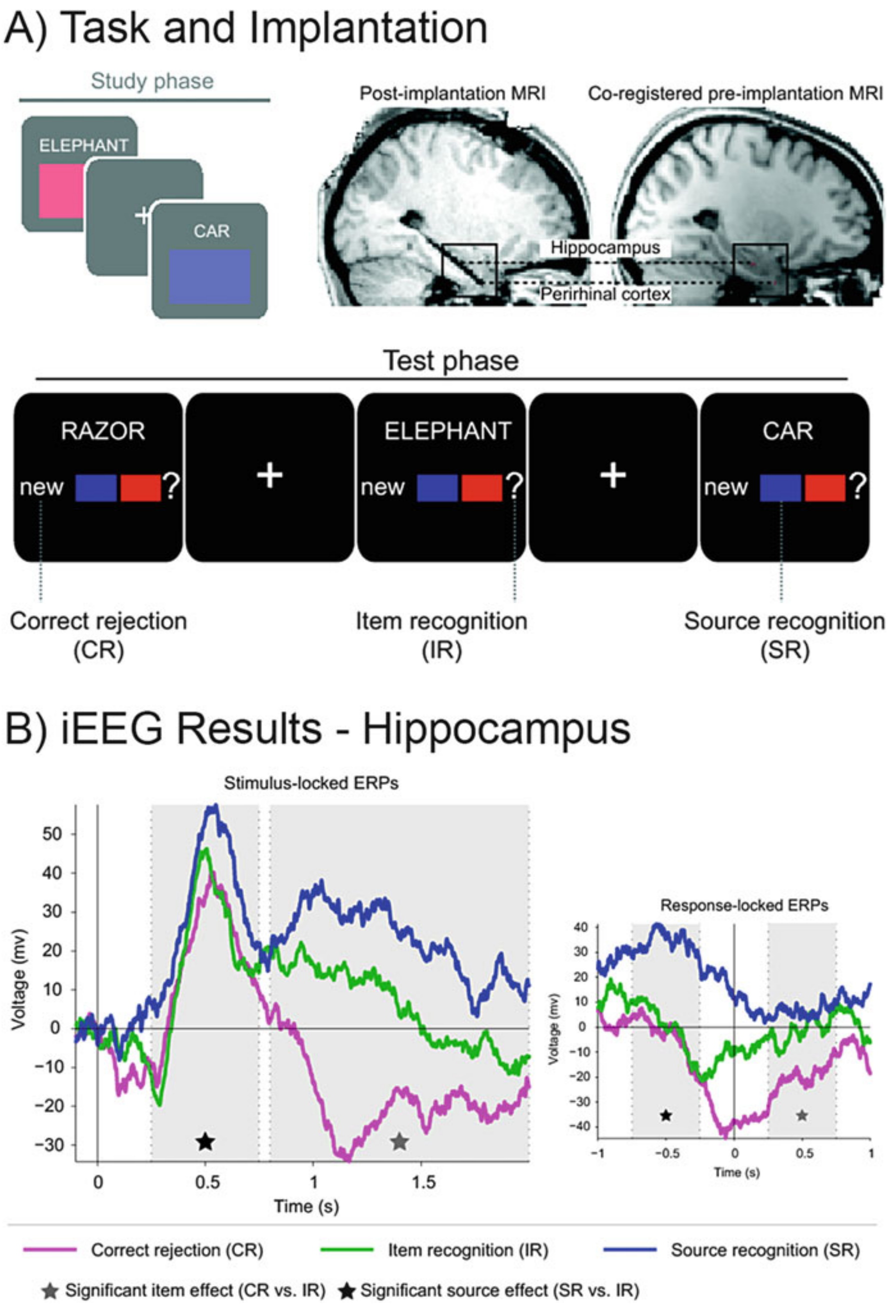

Fig. 2 Hippocampal iEEG recordings during performance of a source memory task. (**a**) Illustration of the experimental task and iEEG electrode placement. During the study phase, participants attempted to encode associations between concrete nouns and corresponding colors, indicating whether the combination was plausible. During the test phase, a concrete noun was presented at the *top* of the screen and participants indicated whether the word was "new", old and they remembered the source (indicated via color selection), or old but the source was forgotten ("?"). (**b**) iEEG

influenced by use of a liberal response criterion, or accurate guessing. Regardless, there are increasing numbers of studies that point to hippocampus-dependent memory effects outside of conscious awareness that have used careful methodological approaches in order to minimize contributions from explicit memory. Examples include subliminal masking procedures that, when effective, render a stimulus invisible as confirmed by strict forced-choice testing procedures (cf. Henke et al. 2003a; Nickel et al. 2015), and task designs that preclude the use of effortful retrieval strategies or strategic processing (Carlesimo et al. 2005). These methods should be considered in future studies that attempt to address questions about when and how the hippocampus contributes to unconscious expressions of memory.

AU3

Summary and Conclusion: Awareness

Evidence in support of the view that the hippocampus contributes to implicit, unconscious memory comes from four lines of work—namely, studies that report hippocampus-dependent encoding when materials are masked from view (e.g., Henke et al. 2003a, b), studies that indicate learning is impaired in the face of hippocampal damage, even when improvements in performance occur without awareness in controls (e.g., Chun and Phelps 1999; Smyth and Shanks 2008), studies that link hippocampal integrity or function to the expression of implicit eye-movement-based memory effects at retrieval (Hannula and Ranganath 2009; Ryan et al. 2000), and studies that document hippocampal responses in advance of explicit recognition decision (e.g., Staresina et al. 2012). Collectively, these outcomes make reasonable the proposition that the role of the hippocampus in memory is outside of, or orthogonal to, conscious awareness. With this in mind, questions about when and how hippocampus-dependent memories are formed and/or expressed outside of awareness can now be addressed. More generally, studies might attempt to pin down how exactly the hippocampus contributes to unconscious and conscious expressions of memory (Hannula et al. 2012).

AU4

Relevant to questions about when and how the hippocampus contributes to unconscious expressions of memory, Verfaellie et al. (2012) suggest that some forms of implicit relational memory are intact following hippocampal damage, while others are compromised. The authors used a category exemplar task in which participants read a word pair (e.g., mall-rain), heard a sentence that used the two words, and rated the plausibility of the sentence. In an indirect testing condition,

Fig. 2 (continued) results locked to stimulus onset (*left*) and to behavioral responses (*right*). iEEG responses were greater for correct source recognition responses than for correct rejections and item recognition shortly after the presentation of the test trial and in advance of button press responses. Figure adapted from Staresina et al. (2012) and reproduced with permission from the Nature Publishing Group and Copyright Clearance Center participants saw one word from the pair (e.g., the context word—mall) spelled backwards, and were asked to list the first four words that come to mind given a particular category descriptor (e.g., weather pattern). Amnesic patients with hippocampal damage generated the associates of context words at rates similar to controls when the context-category pairs from study were reinstated (vs. recombined) at test. However, when participants were asked to explicitly report the target words, in a direct test of memory, amnesic individuals failed to show this normative reinstatement benefit. The authors suggested that while direct expressions of memory required the hippocampus, indirect, and perhaps implicit, expressions of verbal relational memory were not compromised in hippocampal amnesia. It remains to be determined whether performance could have been supported by strategies that do not depend on the hippocampus (e.g., unitization), but the findings raise important questions about the role of the hippocampus in unconscious versus conscious memory.

Furthermore, and as indicated earlier, recent work suggests that task demands influence whether or not expressions of memory require conscious awareness (e.g., Smith and Squire, submitted). Specifically, it has been reported that whether or not the expression of eye-movement-based repetition effects (i.e., decreases in the number of fixations for previously viewed versus novel stimuli) depends on conscious awareness is influenced by task instructions. When participants were told that their memory would be tested, the repetition effect was only observed with concomitant conscious awareness of having previously viewed the scenes. However, when participants were simply instructed to view the scenes, the repetition effect was observed whether participants recognized the scenes as studied or not. Under free viewing conditions, the repetition (or reprocessing) effect was evident in viewing patterns of amnesic patients, as has been reported previously (Althoff and Cohen 1999; Ryan et al. 2000). These results indicate that changes in task instructions can dictate whether or not the same metric of memory is associated with conscious access.

Perception

Like unaware expressions of memory, perception is among the putative new roles that has been ascribed to the hippocampus (Bussey and Saksida 2007; Graham et al. 2010; Suzuki and Baxter 2009). In this section, we present empirical findings relevant to this topic, but first, we anchor our discussion by considering what constitutes perception and how it differs from other cognitive processes. With this information in mind, we briefly revisit a small subset of studies described above (Unconscious Memory section) in service of evaluating whether a hippocampal contribution to perception is feasible based on how quickly information is available for processing. Finally, we summarize the significant empirical literature from neuropsychological and neuroimaging studies that informs whether the human hippocampus contributes to perception, consider whether any such contributions are necessary, and present interim conclusions on this matter. To foreshadow that commentary, we will suggest that while the hippocampus contributes to ongoing cognition beyond long-term memory, it is not clear whether the term perception best describes those contributions.

Perception: Dissociations and Definitions

In the literature describing hippocampal function, the term perception has often been used without elaboration (e.g., Bussey and Saksida 2007; Graham et al. 2010; Suzuki and Baxter 2009), leaving interpretation to individual readers. Resulting differences in how this term is understood may therefore drive some of the debate over hippocampal involvement in perceptual processes. Differences of interpretation are not difficult to understand because perception interacts extensively with other cognitive processes, and these interactions are necessary for the integration and interpretation of information. For example, perception of external stimuli overlaps significantly with later stages of sensation, and a clear delineation between perceptual and sensory processes may be impossible (Lezak 2012).

Similarly, perception also interacts with memory in ways ranging from simple maintenance of current neural activity (STM), to processing of the contents of short-term memory (working memory, WM), and the ability to encode, store, and retrieve preexisting memories (LTM). Consider the example of a typical visual scene such as an office desk decorated with multiple complex objects arranged in a three-dimensional spatial configuration. Although a gist-level perceptual representation of this scene might be available with only a very brief exposure (Thorpe et al. 1996), elaboration and maintenance of the objects comprising the scene might require serial attention to multiple locations reflected in many fixations of the eyes spread across several seconds (Henderson and Hollingworth 1999). Furthermore, perception of the individual objects as such must rely to some extent on previous experience (i.e., memory). As with sensation, strict separation of perception from memory—especially short-term or working memory—may not be possible.

AU6

In addition to lying at the interface of other cognitive domains, perception is an ongoing process. That is, perception does not deliver a single, final product but instead provides a succession of interpretations that evolves over time in response to input from external sources and feedback from internal sources. An ambiguous part of a jigsaw puzzle may be resolved by finding an edge; motion may cause a roadside shrub to be re-evaluated as a half-seen deer; and extended viewing of a Necker cube will flip the observer's perspective. These scenarios illustrate the difficulty of deciding when perceptual processes have finished. Further, they illustrate the challenge of strictly distinguishing between perception and other cognitive processes, and they raise important questions about the nature of perception. In the example of the desk from earlier, at what moment has the desk scene been perceived? Is conscious awareness of the scene necessary for perception? At what instant should we expect a necessary contribution of memory processes for interpretation of information from the scene? To what extent does information have to be actively maintained to determine whether two percepts (e.g., of complex scenes) are exact copies or slightly different from one another?

In part, perception overlaps with other cognitive processes because our models of these processes are imperfect descriptions of complex, highly interactive systems that operate in parallel (Lezak 2012). Should concerns about whether perception is fundamentally dissociable from other cognitive processes influence our discussion? Or more simply, do these considerations obviate this section of the current chapter? We believe not. While perception clearly overlaps with other aspects of cognition, it has been established as a partially dissociable process that can be separately tested and uniquely impaired. In the spirit of decades of neuropsychological and cognitive neuroscience research studying brain-behavior relationships, we believe that it is perfectly appropriate to investigate whether the neural correlates of perception include the hippocampus. However, we hope that by noting the substantial interactivity between these different processes we might inform future discussions of whether the hippocampus could reasonably be said to contribute, for example, jointly to memory and perception rather than solely to memory. Isolating densely intertwined cognitive processes is difficult even in controlled laboratory tasks; conclusive dissociation of their neural correlates presents an even greater challenge.

To have any hope of distinguishing perception from other cognitive processes, careful definition of terms is important. For the purposes of this chapter, we will consider perception to be a set of cognitive processes representing the interaction of ongoing elementary sensory experience with top-down influences by other cognitive processes including memory, attention, and executive functions. For example, in the case of an external stimulus, perception is preceded by sensation, which involves the transduction of physical energy into neural signals, and can be succeeded by various other cognitive processes that may lead, for example, to encoding of stimulus information into lasting memory representations. A leading neuropsychological text describes perception as follows:

> Perception involves active processing of the continuous torrent of sensations …. This processing comprises many successive and interactive stages. The simplest physical or sensory characteristics, such as color, shape, or tone, come first . . . and serve as foundations for the more complex 'higher' levels of processing that integrate sensory stimuli with one another and with past experience (Lezak 2012, p. 26).

We will rely on this description and consider perception to be a process that supports interpretation of the most recent several seconds of sensory experience through the lens of existing knowledge and that has hierarchical as well as parallel aspects.

We note one further caveat here, which is that our consideration will focus almost exclusively on alleged hippocampal contributions to *visual* perception because that modality has received the most attention from researchers. Although we will speculate that hippocampal contributions generalize across many modalities, further research will be necessary to address this important issue.

The Timecourse of Hippocampal Involvement in Cognitive Processes

Perception is an active, ongoing cognitive process, which may place greater demands on speed than would be expected of cognitive processes historically associated with the hippocampus such as memory. Speed of processing is relevant to the current discussion because if the hippocampus is to contribute meaningfully to perception, it must be capable of receiving, processing, and transmitting information quickly. In this section, we briefly revisit a subset of the empirical findings that were described above (Unconscious Memory section) in service of evaluating whether the hippocampus might reasonably be expected to contribute to perception.

Results from studies that have examined the latency of hippocampal responses suggest that this structure can be engaged quickly, within a time window that begins as early as 250 ms following stimulus onset (e.g., Riggs et al. 2009; Staresina et al. 2012). Furthermore, response-locked analyses, based on iEEG recordings, indicate that hippocampal responses, sensitive to source memory, are evident before explicit recognition responses have been made by the participants (Staresina et al. 2012). Research studies have also indicated that individuals with hippocampal amnesia process visual stimulus information, as indexed by eye movement behavior, in qualitatively different ways than neurologically healthy controls (Voss et al. 2011; Olsen et al. 2015). They fail, for example, to distribute viewing among face features, which seems, in turn to affect recognition memory performance when faces are seen from different perspectives at study and test. Outcomes like these, particularly the latency data, indicate that the hippocampus does indeed respond quickly when stimuli are in view, although these activity differences were associated with memory rather than perception.

In short, the intervals in question are sufficiently brief that the hippocampus could reasonably be expected to respond to and influence activity in other brain regions within the scope of our working definition of perception (i.e., as a process that interprets the most recent several seconds of sensory experience). By comparison, other brain regions that have been less controversially associated with perception for complex stimuli such as faces are similarly situated in or near ventral temporal cortex and receive, process, and transmit information with similar latencies (Schmolesky et al. 1998). This prompts us to note that many brain regions would of course respond to visual stimuli at least as quickly as the hippocampus and therefore potentially contribute to perception. These non-hippocampal contributions to perception are no doubt critical, but they do not affect our main point, viz., the latency of hippocampal responses to external stimuli is not so long that the structure would be prevented from contributing to perception simply by virtue of its connectivity. In short, hippocampal processing is rapid enough to actively influence ongoing cognition rather than simply responding and recording. AU7

Empirical Findings

In the following sections, we discuss key empirical findings in the domain of perception and the human hippocampus. The dependence of perception on hippocampal function has perhaps most often been evaluated using an oddity task (e.g., Lee et al. 2005b; Behrmann et al. 2016). In this case, participants view an array of stimuli (e.g. colors, simple shapes, faces, scenes) and must select, from the alternatives that are present, the stimulus that is different from the remainders (i.e. the 'odd-one-out'). Other tasks require participants to select the exemplar from two or more alternatives that is most like a simultaneously presented sample stimulus (e.g., Sidman et al. 1968; Lee et al. 2005a; Hartley et al. 2007; Warren et al. 2010), to name/identify objects that are degraded or overlap in space (Warren et al. 2012), or to determine whether or not two pictures, presented simultaneously, are an exact match (e.g., Aly et al. 2013a). In the text that follows, neuropsychological studies that have provided critical insight regarding the necessity of hippocampus for perception are described and neuroimaging studies that have informed debate about how the hippocampus is functionally involved in putatively perceptual tasks are summarized. Notably, while there is also an extensive literature documenting MTL and hippocampal contributions to perception from animal models including rodents and non-human primates, a description of that work is beyond the scope of the current chapter (Graham and Gaffan 2005). Instead, we focus on the rich scholarship describing relevant work in human participants.

AU8

Neuropsychological Studies of Perception

AU9

was outlined briefly at the outset of this chapter, the hippocampus and surrounding MTL structures have been associated with LTM since the seminal report of Scoville and Milner (1957). Generally, damage to the medial temporal lobes or hippocampus has been reported to leave perception and STM intact (Cave and Squire 1992; Drachman and Arbit 1966; Warrington and Baddeley 1974; Wickelgren 1968). However, as described briefly below, the large literature based on work conducted with amnesic individuals has long included hints that the MTL and/or hippocampus might contribute to cognitive processes beyond LTM. The decades-long absence of research on this topic may seem odd in hindsight, but when interacting with individuals who have amnesia the severe memory deficit is obvious while any perceptual deficits are relatively subtle. Nevertheless, careful contemporary experimentation has revealed reliable performance deficits attributed to impaired perceptual processing among patients with broader MTL damage (e.g., Barense et al. 2007, 2012), as well as patients with more focal hippocampal damage (e.g., Lee et al. 2005a, b).

Without a doubt, the pattern of impaired declarative and spared non-declarative (or procedural) memory found in patient H.M. transformed theories of memory

(Scoville 1968; Scoville and Milner 1957; Cohen and Squire 1980), but deficits were also evident in his ability to maintain or perceive visual information. Although H.M.'s STM for many types of familiar, verbalizable stimuli was relatively normal, studies of the durability and quality of his non-verbal visual representations indicated impairment. In particular, Sidman et al. (1968) tested H.M.'s ability to perceive and maintain simple visual stimuli—ellipses of varying eccentricity—over intervals ranging from 0 to 32 s. With no delay, H.M. was as accurate as healthy control participants when choosing from a selection of related alternatives, but the accuracy of his responses decreased as a function of the maintenance interval until they were essentially at chance after 32 s; in contrast, the performance of control participants remained nearly unchanged even at the longest delay. This unexpected finding went largely unremarked when it was published, but suggested that either perception or maintenance processes were altered by H.M.'s MTL damage.

This early example of impairment in the representation of visual information at short intervals is important supporting evidence for more recent observations described below and we offer the speculative suggestion that results from additional non-published studies may have also pointed to a role for the hippocampus in short-lived representations but suffered from the "file drawer problem" (Rosenthal 1979). One piece of evidence potentially supporting this notion can be found in the doctoral dissertation work of Prisko (1963) which included findings similar to those reported by Sidman et al. (1968) but was never published in a peer-reviewed format. Formal analysis of this file-drawer suggestion is beyond the scope of this review, but the prospect is intriguing and may be worth further investigation.

AU10

Returning to results reported by Sidman et al. (1968), the impaired ability of patient H.M. to maintain hard-to-verbalize visual information for short periods of time was potentially attributable to deficits in at least two distinct abilities: visual perception or visual STM. From our perspective, evidence which supports the proposition that the hippocampus is involved in perception should rely on tasks that meet two key criteria: (1) very limited maintenance demands; and (2) relatively low memory load. Failure to meet either criterion would allow critics to suggest that LTM processes might have been recruited in service of task performance (Hales et al. 2015; Jeneson and Squire 2012; Jeneson et al. 2012; Squire and Wixted 2011).

Initial observations that may meet these criteria were reported by Lee et al. (2005a, b, 2006) who observed impairments of perception in patients with focal hippocampal damage when they were asked to perform visual discrimination tasks using complex, three-dimensional scene stimuli. In one such experiment (Lee et al. 2005b; see Fig. 3), participants were presented with a sample stimulus (e.g. a face, object, scene, art, or color swatch) at the top of the screen and had to choose the exemplar from two alternatives presented below that most resembled that item. The choice stimuli were blended exemplars of two baseline objects, one of which served as the sample. Use of this blending procedure meant that choice stimuli were more or less similar to each other and to the sample stimulus across trials. Consequently, selection of the closer match could not be achieved based on a single diagnostic feature, particularly when the level of blending was high. Results indicated that

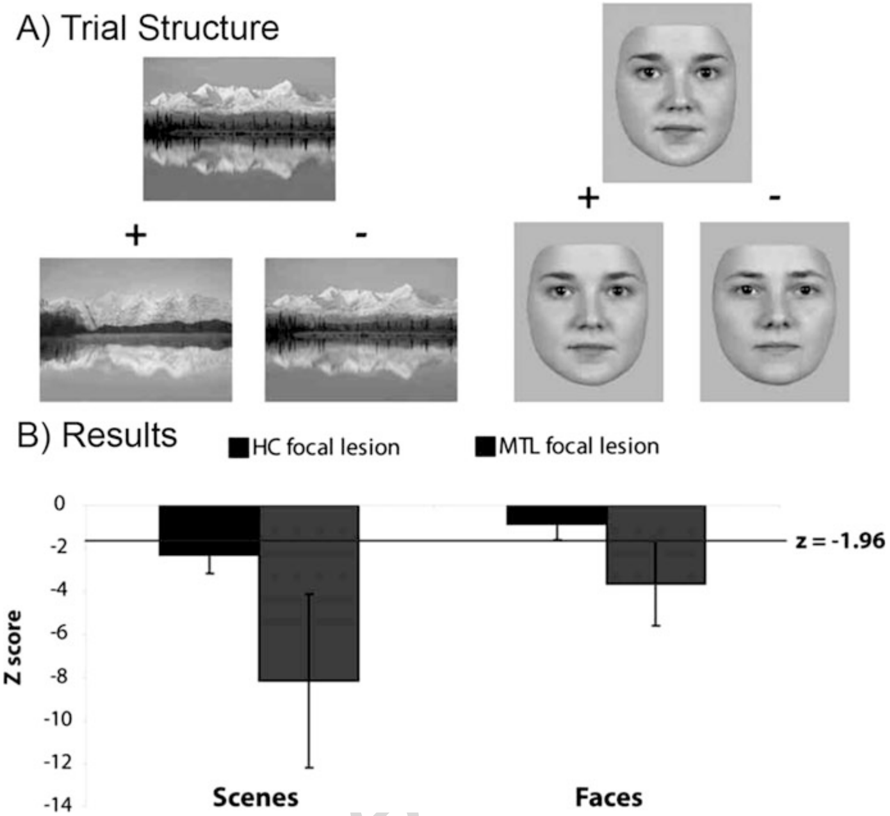

Fig. 3 Perceptual identification task. (**a**) Participants were to select the image from two alternatives that was the best match of a picture (scene or face, depending on the trial type) presented simultaneously at the *top* of the screen. (**b**) Patients with focal hippocampal lesions were impaired on the scene matching task, but performed within the normative range for faces. Figure adapted from Lee et al. (2012) and reproduced with permission according to the Creative Commons License agreement with Frontiers

patients with damage limited to the hippocampus (based on visual inspection of scans) had trouble distinguishing between alternatives when scenes were presented, but only when there was considerable feature overlap due to high levels of blending. Discrimination was intact for faces, objects, art, and color swatches.

Converging evidence for deficient scene perception among hippocampal amnesic patients has been reported using the oddity task (Lee et al. 2005a; Behrmann et al. 2016). In these experiments deficits in identification of the ‘odd-exemplar-out’ were only evident when scenes in a choice array were rendered from different, as compared to the same, viewpoints (see also Hartley et al. 2007). Much like the blending procedure, this manipulation places high demands on perceptual discrimination processes, as there is considerable ambiguity across array exemplars. This very specific outcome is consistent with a proposed role for the hippocampus in the processing and representation of arbitrary relationships among items embedded in scene contexts and taxes representational flexibility, a key property of hippocampal function (cf. Cohen and Eichenbaum 1993). Recent work also points to a potential role for the fornix, the main output pathway for the hippocampus, in perceptual disambiguation (Lech et al. 2016; Postans et al. 2014), but additional testing is required to determine how to best characterize these contributions.

While evidence consistent with a role for the hippocampus in perception has been reported with increasing frequency over the last decade, a significant volume of counter-evidence has also been published. Most frequently, this evidence has come in the form of failures to replicate relevant behavioral findings in samples of amnesic patients. In one early example, Stark and Squire (2000) adapted the methods employed in a study of non-human primates (Buckley et al. 2001). The original work suggested that perirhinal cortex played a role in object perception, but Stark and Squire did not observe behavioral impairments consistent with this account in a sample of patients with MTL damage (including hippocampus and perirhinal cortex). A potential explanation for this ambiguity was proposed by Aly et al. (2013a) who have found that perceptual discrimination of complex scenes can be supported by two distinct processes. According to this work, identification of specific details that permit disambiguation of perceptually similar inputs depends upon a *state-based process*, whereas a general sense of relational (mis)match used to the same end depends on a *strength-based process* (see Aly and Yonelinas (2012) for details). Critically, these processes were expected to show dissociable dependence on the hippocampus. Specifically, it was predicted that estimates of strength-based relational processing would be significantly reduced when hippocampal amnesics were tested, but that state-based processing, which might depend on the size or position of an individual scene feature, would be preserved. Indeed, this was the observed pattern when hippocampal amnesic patients were tested. Furthermore, converging evidence from an fMRI task, conducted with healthy young participants, confirmed that hippocampal activity differences were sensitive to the strength of the relational mismatch between scenes, as indexed by subjective confidence judgments. Based on these outcomes, the authors proposed that inconsistencies in the literature might reflect differences in the use of state- as compared to strength-based processing strategies when tasks require discrimination of perceptually similar complex pictures.

Other evidence fitting the criteria outlined above were reported by Warren et al. (2012) who found that patients with focal hippocampal damage were impaired on tasks requiring visual discrimination or recognition of complex objects based on partial information. These latter findings contrast to some extent with results from other labs which indicate that broader MTL damage (particularly to perirhinal cortex) may be necessary to impair object (as opposed to scene) discrimination performance (Barense et al. 2007, 2010; Lee et al. 2006). Critically though, this discrepancy does not diminish the most important implication of these findings which is that the hippocampus contributes to the representation of information even when stimuli are continuously present.

While the just-described findings seem to meet the minimum criteria that we established for excluding substantial contributions of LTM to performance (i.e., by limiting maintenance demands and memory load), labelling the underlying deficit as one of perception remains controversial (Hales et al. 2015; Shrager et al. 2006; Squire et al. 2006; Suzuki 2009). In our view, the ongoing debate over how to interpret these data reflects the complexity of disentangling cognitive abilities such as visual perception and visual STM. For example, while tasks such as visual discrimination or recognition based on partial information do not explicitly require maintenance (because all of the materials are presented simultaneously), there are still implicit demands on participants to maintain some amount of information while developing their response (cf. Olsen et al. 2012). When discriminating one complex scene from another, participants must examine the first scene (scene 1) and then maintain enough information about that scene to discriminate it from another (scene 2) (Barense et al. 2007, 2010; Lee et al. 2005a, b, 2006; Aly et al. 2013b). AU11 Even if the intervals between examining scenes 1 and 2 are very short (i.e., on the order of hundreds of milliseconds for attentional shifts and saccadic eye movements) there is still an implicit maintenance demand for visual or conceptual information sufficient to discriminate the two stimuli. Against this, it has been argued that the eye movements of amnesic patients do not differ from control participants during visual comparison or search tasks (e.g., Erez et al. 2013), but others have shown differences in eye-movement or related behaviors during search, comparison, or study tasks (Warren et al. 2011; Lee et al. 2010; Olsen et al. 2015; AU12 Voss et al. 2011).

Although delays of hundreds of milliseconds may seem trivial, there is evidence that damage to the MTL or hippocampus is sufficient to impair maintenance of very simple visual information (i.e., color or shape) over intervals as short as 1 s (Warren et al. 2014). Furthermore, it has been shown that amnesic patients (those with limited hippocampal damage and more extensive lesions) can successfully perform the oddity task when they are allowed to draw lines linking exact matches, which was "intended to reduce the burden on working memory" (Knutson et al. 2012, AU13 p. 609). In short, use of this memory aid meant that after identifying a match, that set of items could be completely disregarded. Collectively then, these findings suggest that the hippocampus is necessary for maintaining information over brief delays with the implication that even visual discrimination tasks that do not explicitly require LTM may still rely on hippocampus-dependent maintenance processes. This is consistent with the perspective that the hippocampus is necessary for normal visual experience. Whether the underlying deficit is best described as one of perception will be considered in more depth later.

Neuroimaging Studies of Perception

Studies using functional neuroimaging methods such as fMRI to investigate whether the hippocampus is involved in on-line cognition have found evidence which is consistent with that perspective. More specifically, fMRI studies testing perception have shown correlations between performance of perceptual tasks and hippocampal activity. Notably, many of the same caveats and concerns that were raised in the context of neuropsychological findings discussed above will also be relevant here.

Use of functional neuroimaging to investigate perception has motivated the adaptation of tasks previously used in neuropsychological studies (Lee et al. 2005a, 2006). In particular, scene discrimination tasks that are difficult for patients with hippocampal damage also evoke hippocampal activation in neurological healthy adults (Barense et al. 2010; Lech and Suchan 2014; Lee et al. 2013; Lee and Rudebeck 2010). These neuroimaging findings show a correlation between on-line scene discrimination performance and hippocampal activity which converges with neuropsychological findings (Lee et al. 2005a, 2006), and the originating authors suggest that the underlying deficit is perceptual. Additionally, one of the neuroimaging publications had the promising goal of—as suggested by the title—"Investigating the interaction between spatial perception and working memory in the human medial temporal lobe" (Lee and Rudebeck 2010) which is highly relevant to this chapter. The authors used 2 × 2 design to cross working memory load (1- or 2-back task) with item complexity (simple shapes vs. complex scenes) in a within-subjects design that required participants to perform these task conditions while fMRI data were collected. Analysis of this data revealed an interaction between working memory load and stimulus type in the right posterior hippocampus and parahippocampal cortex such that activation increased with working memory load in the complex-item condition but not the simple item condition. As such, this report is most consistent with a role for the hippocampus in perception and working memory rather than one or the other exclusively.

Notably, several of these studies have included measures intended to control for potentially confounding influences of incidental LTM or STM processes (Lee et al. 2013; Lee and Rudebeck 2010; Zeidman et al. 2015). In one typical example, Lee et al. (2013) asked participants to perform an oddity-detection task while fMRI data were collected, and later administered a surprise recognition task testing memory for the oddity task materials. They reported increased hippocampal activity associated with correct oddity responses irrespective of later recognition performance for the same items. These and similar findings are suggestive of a unique hippocampal contribution to scene discrimination or perception over and above activation related to LTM processes. Finally, one finding is intriguingly consistent with a perceptual role for the hippocampus but would extend that role beyond scenes to include faces and other complex but non-scenic stimuli (Barense et al. 2011) which would be consistent with other neuropsychological findings (Warren et al. 2012). Briefly, Barense et al. (2011) collected fMRI data from healthy participants while they performed a perceptual discrimination task that crossed two types of visual stimuli (faces and objects) with two levels of familiarity (familiar and unfamiliar). Object and face stimuli increased activity in the hippocampus and perirhinal cortex relative to a baseline condition, and a main effect for familiarity was evident in the same regions. These activity differences were orthogonal to subsequent memory,

AU14

suggesting that hippocampus (and perirhinal cortex) may contribute to object perception.

Recent developments in fMRI data analysis, which test the predictive accuracy derived from patterns of brain activity have also produced results that bear on a perceptual role for the hippocampus. Specifically, Lee et al. (2013) followed up their univariate analysis—described earlier—by applying multi-voxel pattern analysis (MVPA) to the same fMRI data collected from participants who were performing an oddity judgment task. The authors found that functional data from the regions of interest including the hippocampus or the parahippocampal cortex were sufficient to predict accurate performance of individual oddity judgment trials significantly better than chance (~57 % correct predictions) irrespective of later recognition memory performance for the test materials. A second MVPA analysis showed that the same functional data was also sufficient to predict subsequent recognition performance significantly better than chance (~53 %) irrespective of oddity judgment performance. Following on their findings from a univariate analysis in which hippocampal activation was more strongly related to oddity judgment than subsequent recognition, the authors produced new results consistent with their account that the hippocampus contributes to perception in addition to memory.

To summarize the neuroimaging findings, there is fMRI evidence that is consistent with the perspective that the hippocampus contributes to visual perception (Barense et al. 2010, 2011; Lech and Suchan 2014; Lee et al. 2013; Lee and Rudebeck 2010; Zeidman et al. 2015). However, as described in the section describing neuropsychological studies, the tasks used in neuroimaging studies cannot definitively be said to be process-pure; that is, these tasks cannot exclude the possibility that the observed associations between hippocampal activation and visual discrimination performance are due to other processes (e.g., maintenance). This concern is tempered to some extent by studies that control for subsequent memory effects (Barense et al. 2011; Lee et al. 2013; Zeidman et al. 2015), but that approach cannot entirely mitigate potential memory-related activity because subsequent memory is not perfectly related to hippocampal activity. Again, much like the neuropsychological evidence, neuroimaging data are suggestive of and consistent with a hippocampal role in perception, but not conclusive. AU15

Summary and Conclusions: Perception

As evidenced by studies discussed earlier in this section, the hippocampus appears to make necessary contributions to ongoing cognitive processes that may include perception. Although these findings have sometimes been critiqued on the grounds that hippocampal involvement may be related to coincident LTM processes (Hales et al. 2015; Jeneson et al. 2010, 2012; Jeneson and Squire 2012; Squire and Wixted 2011) several studies reviewed earlier addressed this issue in design and/or analysis have still found significant evidence of hippocampal contributions to cognitive processes over short intervals (Barense et al. 2012; Lee et al. 2013; Warren et al. 2012, 2014; Zeidman et al. 2015).

If—for the sake of discussion—we accept that the hippocampus makes necessary contributions to ongoing cognitive processes, a key question remains: does the hippocampus contribute to perception *per se*? To respond, we return to our working definition, which described perception as a "process that supports interpretation of the most recent several seconds of sensory experience through the lens of existing knowledge and that has hierarchical as well as parallel aspects". Considering these characteristics in turn, the findings reviewed here fall within the interval described in the definition, and existing knowledge appears to be exercised in support of task performance when available (e.g., real-world knowledge of spatial layouts). The critical remaining characteristic is "interpretation" and its meaning in this context. That is, "interpretation" could mean full appreciation of a stimulus in all its complexity simultaneously; "interpretation" could also mean understanding the broad nature of a stimulus without understanding it completely. For example, when the stimulus is a complex scene, the scene could be said to be perceived (i.e., interpreted) at any of the following stages: when its presence influences responses to other materials; when it is known to be a scene; when the type of scene is known; when objects in the scene have been identified; when the scene is recognized as previously viewed; etc. This nuance is important because—from our perspective—findings that could arbitrate questions of hippocampal necessity for perception hinge on exactly this issue. Therefore, we suggest that consensus on the theoretical issues at stake in this debate depend first on achieving consensus on what is meant by the "interpretation" of a stimulus during perception.

Other definitional issues related to a hippocampal role in perception also require further consideration. First, our understanding of perception as a separable cognitive construct may be an imperfect reflection of the underlying cognitive processes or neural representations. Second, it is not clear whether perception necessarily requires conscious awareness. Third, defining the timeline for an ongoing process such as perception is challenging; does failure to interpret a stimulus before a deadline constitute a perceptual failure? Fourth, defining the success or failure of perception is challenging because perception always yields a product whether accurate, normative, or otherwise. Finally, while the end result may be an adequate interpretation of the current environment and be sufficient for accurate performance of a perceptual test, the manner in which this outcome is achieved may be quite different across individuals or after brain injury. While these concerns are also important components of an expanded understanding of perception, we believe that a clear operational definition of perceptual "interpretation" remains most critical for understanding the role of the hippocampus in the prevailing ontology of cognition and for drawing strong conclusions about hippocampal contributions to perception.

Despite our inability to draw strong conclusions about whether hippocampus is necessary for normal perception based on empirical data, we suggest that an interim conclusion can be derived by drawing on the literature of neurology and neuropsychology for descriptions of alternative perceptual deficits. For example, remaining in the realm of visual perception, we can consider the examples of object agnosia, alexia, and prosopagnosia. In each of these three examples, relatively focal brain injury or dysfunction can produce a severe, selective cognitive deficit in the perception of objects, orthography, or faces, respectively. The severity of these deficits stands in stark contrast to the deficits in, for example, scene perception reported in patients with bilateral hippocampal damage or fornix disconnection (Lech et al. 2016; Lee et al. 2005a, 2006). In everyday life, patients with bilateral hippocampal damage are typically able to navigate through space relatively well, localize objects without noticeable difficulty, copy complicated shapes accurately, and describe complex scenes comprehensibly. In fact, these patients often perform less well than expected only when tested with challenging spatial tasks such as discrimination of very similar scenes (Lech et al. 2016; Lee et al. 2005a, 2006). Meanwhile, patients with object agnosia have famously mistaken their spouses for headgear (Sacks 1998), patients with pure alexia have gross deficits in the ability to perceive written language (Damasio and Damasio 1983), and patients with severe prosopagnosia are often unable to recognize individual faces with any success (Moscovitch et al. 1997; Newcombe et al. 1994). Returning to our earlier discussion, these perceptual deficits illustrate obvious failures of the ability to interpret sensory input normally.

The severity of these alternative examples of widely recognized visual perceptual deficits provide context for putative perceptual deficits in patients with hippocampal damage. While the latter findings are statistically significant, reported impairments in perception among patients with hippocampal damage present with much less urgency than the memory deficits of those patients, and with much less salience than the perceptual deficits experienced by patients with non-hippocampal brain injuries. Notably, impairments in scene discrimination performance are hardly unique in this regard—many non-LTM deficits reported in patients with hippocampal damage are statistically significant but modest relative to the patients' LTM deficits. Therefore, as an interim conclusion on this matter, we suggest that theories of hippocampal involvement in perception describe phenomena that are real and important, but that it is not clear whether perception is an appropriate descriptor. With that in mind, we consider, in a final section, whether the hippocampus might be reasonably said to contribute to short-term or working memory.

Short-Term or Working Memory

Short-term memory is a repository for information that is being kept active or in mind and, as is the case with perception, recent findings challenge claims that STM is completely independent of hippocampal function. The term STM is often used interchangeably with working memory in the literature, but the two are not synonymous. This is because working memory involves not only active retention, but also manipulation of content that is currently being represented. Here, we frequently refer to STM, as many investigations that have addressed questions about hippocampal contributions to these processes have required active retention, but not manipulation of stimulus information over the course of a brief delay. Furthermore, while early work evaluating the dependence of STM on hippocampal function emphasized active retention of verbal materials—e.g., unrelated word pairs, a string of digits (see Olsen and Ryan 2012)—contemporary studies have most often used visual stimuli and efforts have been made to minimize the influence or effectiveness of verbal rehearsal strategies. It is in this context that neuropsychological deficits in STM have most often been reported and hippocampal activity differences in neuroimaging investigations are evident.

A fundamental characteristic of STM is its limited capacity. While chunking can increase the capacity of STM tremendously (Miller 1956), the standard view has been that a small, fixed number of simple elements or items can be actively retained over the short term (Luck and Vogel 1997). This view has considerable appeal and a good deal of empirical support in the literature, but some researchers have recently come to endorse a different model of STM capacity that is based on a finite amount of available *resource* (Alvarez and Cavanagh 2004). In this case, there is not a fixed item-based STM capacity limit. Instead, capacity is determined by the complexity of to-be-retained information and the precision with which that information must be represented in order to meet task demands. In short, this perspective suggests that there is a tradeoff between the number of items that can be actively retained and the fidelity with which key features are represented. We revisit this important issue later in this section.

Much of the time, questions about the defining characteristics of STM are addressed using a *change detection task* (Luck 2008) though match- or non-match-to-sample protocols, n-back tasks, and delayed alternation tasks are also common. In a standard visual STM change detection task, participants attempt to actively retain information presented during a sample phase (e.g., a scene, a face, a set of simple objects) over the course of a short delay. At the end of the trial, when a test display appears, participants indicate yes or no, whether anything in the display has changed (e.g., the identity of a cued object). In some experiments, the number of items in the sample display is manipulated across trials or blocks so that investigators can evaluate changes in accuracy as a function of load and obtain STM capacity estimates based on participant performance (cf. Cowan 2001). Recent adaptations of the standard change detection task permit investigators to address more nuanced questions about the representational precision, or fidelity, of STM. In this case, participants are required to report specific information using a continuous scale about a characteristic feature of an item that was presented during the sample phase (e.g. color, orientation; Wilken and Ma 2004; Zhang and Luck 2008). This approach provides more precise insights into *why* forgotten information was not successfully retained—i.e., (1) because the representation is simply gone, or (2) because the representation became degraded and imprecise due to high memory loads or when longer delays were imposed. As described in more detail below, a handful of investigators have adapted this new testing procedure to address questions about the quality of visual STM in amnesic patients with hippocampal damage.

Finally, before describing relevant empirical findings, it is important to note that models of short-term or WM are currently in a state of flux (cf. Jonides et al. 2008). In contrast to the long-standing view that short- and long-term memory depend upon strictly dissociable systems, recent models propose that short-term retention is best characterized by states of representational accessibility that are mediated by interactions between attention and LTM. As summarized by LaRocque et al. (2014), state-based models conceptualize STM as activated (or currently relevant) representations from the long-term store. A small subset of information is prioritized and immediately accessible (e.g., in the "focus of attention") and additional information is either held in a "region of direct access", or remains in a heightened state ("activated LTM") by virtue of its recent prioritization (cf. Cowan 1993; Oberauer 2002). In short, there is a notable shift underway from systems- to state-based models in the STM literature, which is consistent with a broader movement in the cognitive neuroscience community pointing to association (rather than dissociation) of short- and long-term memory (cf. Ranganath and Blumenfeld 2005; Olsen et al. 2012). It is in this context that it becomes increasingly clear the time is ripe to re-evaluate claims for the complete independence of short-term retention from the hippocampus—we do so below based on recent empirical reports from the neuropsychological and neuroimaging literatures.

Neuropsychological Investigations of STM

As was outlined briefly in the section on perceptual processing, results from some of the earliest neuropsychological studies that evaluated whether, and to what extent, simple visual materials could be actively retained over the course of a short delay are difficult to reconcile with standard views of MTL function. For example, H.M.'s performance on a task that required identification of an ellipse that exactly matched the eccentricity of a sample stimulus was increasingly compromised as the retention interval between sample and test was lengthened. Indeed, performance was impaired even when the imposed delay was no more than 5 s long, suggesting that active maintenance was deficient (e.g., Sidman et al. (1968); see Ranganath and Blumenfeld (2005), Olsen and Ryan (2012) for more information about early work). However, reports of intact amnesic performance on STM tests (e.g. Cave and Squire 1992; Warrington and Baddeley 1974; Wickelgren 1968), combined with scores in the normative range on standardized neuropsychological tests (e.g., digit span; cf. Cave and Squire 1992; Rose et al. 2011) led to general consensus that STM does not depend on the integrity of MTL structures, including the hippocampus. Furthermore, as has been argued by some investigators, use of a short retention interval does not obviate instantiation of LTM processes (for review see Jeneson and Squire 2011). AU16 Whether these processes simply occur coincident with active retention or are necessary for fully intact performance on STM tests has been difficult to pin down.

Short-Term Retention of Inter-item and Item-Context Bindings

Doubts about a role for the hippocampus limited to LTM were raised in recent neuropsychological studies when deficits were documented using tasks that encouraged active retention of inter-item and item-context relationships (i.e., spatial positions of objects embedded in scenes, scene-face pairings, and object-location associations; Hannula et al. 2006; Olson et al. 2006b). For example, results reported by Olson et al. (2006b) indicated that amnesic patients, including a subset with damage limited to the hippocampus, were impaired on tests that required active retention of just three object-location associations over the course of 1 (experiment 2) or 8 (experiments 1 and 2) second delays. The deficits in these investigations were quite specific as the same hippocampal amnesic patients who performed poorly on tests of relational memory *could* successfully distinguish old from new scenes, old from new objects, and previously filled from empty locations (see also Cashdollar et al. 2009). A peculiarity, perhaps, of our work (Hannula et al. 2006) was the use of a lag-based design in which corresponding sample and test stimuli (i.e. rendered scenes) were not always presented in immediate succession. While this design choice meant that we could determine whether task performance did in fact depend critically on the hippocampus (i.e. chance performance at long lags), it also meant that we could not conclusively rule out potential contributions of LTM to performance when sample and test displays were presented consecutively. This is because participants may not have used an active retention strategy and because the interleaved lag-based trial structure meant that information about several scenes had to be stored simultaneously for upcoming test trials (see also Jeneson et al. 2011).

The above concerns were addressed recently in two new experiments that examined memory for the locations of items embedded in scenes (Yee et al. 2015; see Fig. 4). Several design changes were made, among them use of a standard delay-based change detection protocol. Replicating previous findings, results indicated that patients were impaired on the basic change detection decision, but perhaps more compelling was the finding that patients frequently failed to identify an object that had been displaced (via forced-choice response) despite having successfully indicated that a change was present. This result suggests that the memory representation was incomplete or degraded. Especially important for our purposes, marked deficits were documented despite performance among control participants that was near ceiling (experiment 2), and were evident even in a patient with confirmed volume reductions limited to the hippocampus, sparing adjacent MTL structures, parietal, frontal, and other temporal lobe regions.

Additional, complementary evidence for hippocampal contributions to active retention of relational memory representations has been reported recently in the literature. For example, impairments have been reported on tests that required short-term retention of inter-object bindings (van Geldorp et al. 2014), simple color-location associations (Finke et al. 2008, 2013; Braun et al. 2008, 2011), and color-shape associations (Parra et al. 2015). In this last example color patches and

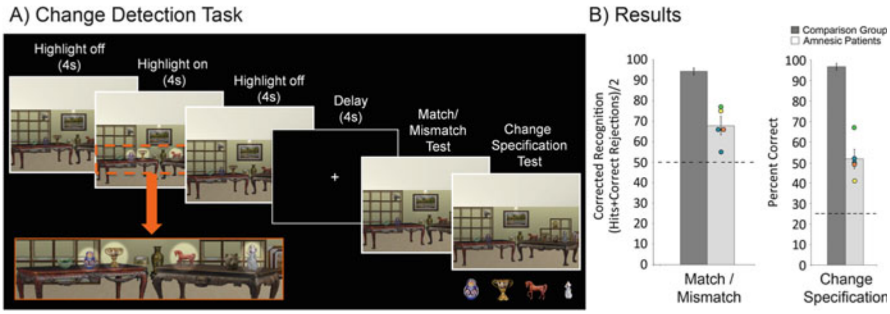

Fig. 4 Illustration of the change detection task and corresponding results from Yee et al. (2015). (**a**) Participants were presented with a scene during the sample phase of each trial. Four objects were highlighted briefly while the scene was in view and one might be displaced when the test picture was presented. Following a brief delay, participants indicated whether any of the objects had changed locations (match/mismatch test), and then attempted to identify the displaced item from four alternatives. (**b**) Results from amnesic patients and matched controls for the match/mismatch and change specification tests. Amnesic patients were significantly impaired on both tests, and frequently failed to specify the change correctly, even when a correct mismatch response had been made (shown here). Figure adapted from Yee et al. (2015) and reproduced with permission according to the Creative Commons License agreement with Frontiers

corresponding shapes were presented side by side to discourage unitization, and in each experiment, patients had lateralized MTL damage (e.g., due to stroke, tumor resection, or temporal lobe epilepsy). Impaired performance has also been reported on a test that required active retention of rendered topographical landscapes, but here participants were patients with damage limited to the hippocampus (Hartley et al. 2007). In this experiment, scenes in the choice array were shown from different perspectives than the sample, which meant that successful identification of the match (from four alternatives) required flexible representation of relative positions amongst key landscape features. Relevant to the Perception section, results indicated that two of four patients were impaired even when choice arrays were presented simultaneously with the sample, but all four patients were impaired when a delay was imposed. As above, short-term retention of other visual information in each of these studies—e.g., non-spatial components of the rendered landscapes (Hartley et al. 2007), individual colors or locations (e.g., Finke et al. 2008), object-color associations when color was a feature of the object, encouraging unitization (Parra et al. 2015; see also van Geldorp et al. 2014)—was intact. It seems then that one could conclude the hippocampus contributes to STM when participants must bind objects with context or with other objects (inter-item bindings; e.g., faces with scenes, objects with color patches), but not when single objects or fused/unitized associations (intra-item bindings; e.g. a green shoe) are to be maintained. Indeed, similar dissociations have been reported in the LTM literature (cf. Davachi 2006; Diana et al. 2007); however, as we shall see, findings summarized below suggest that this conclusion may require some modification.

Identification of impairments like those described above ultimately led investigators to question whether anything more specific could be said about the *kinds* of errors made by amnesic patients on STM tests. In one experiment (Watson et al. 2014), participants were presented with an array of two, three, four, or five objects. Subsequent to exposure, the objects were cleared to one side of the table, and after an eyes-closed delay of approximately 4 s, participants attempted to replace the objects in their previous locations. Several metrics were used to examine performance (e.g. misplacement distance, changes in overall configuration or shape, presence of swap errors) and amnesic patients were impaired on all of these measures relative to a healthy control group. Furthermore, with just one exception (i.e., the global configuration metric), the magnitude of reported impairment was unaffected by memory load. Critically, careful analysis revealed that patients made one kind of error far more often than others—namely, a "swap" error. This error was observed even during trials that required active retention of just two objects, and the same mistake was rarely made by control participants. Deficits on a similar task were also reported for some patients at low loads (i.e. 1–4 items) by Jeneson et al. (2010) when participants were required to minimize displacement errors to reach a criterion level of performance, but this modest low load impairment was deemphasized relative to a sharp discontinuity in displacement error among patients when four, five, or six objects had been presented. This sudden high-load performance change was not evident in results reported by Watson et al., and what drove the between-study differences is not clear. Procedural details, including the use of just four trials per condition and systematic increases in memory load across trials, may have rendered deficits at low loads less robust in the task reported by Jeneson, but because similar information was not reported by Watson, this is merely speculation. Nonetheless, results from these studies converge with findings described above, and implicate the hippocampus in short-term retention of memory representations; here, especially when mappings of objects to specific, previously filled, spatial locations had to be retained.

AU20

Precision of STM Representations

Efforts to better characterize STM deficits that have been reported in hippocampal amnesia continue to gain traction in the literature, and a handful of studies have approached this issue in terms of the representational precision or fidelity of information retained over the short term. In one early example (Warren et al. 2010; see also Ezzyat and Olson 2008), participants had to determine whether a target was present among foils created so that their resemblance to the corresponding sample stimulus varied parametrically. This manipulation meant that successful performance required retention of precise information about a tested feature (e.g. shape, luminance, line tilt, spatial frequency). The task was difficult for both patients and control participants, with performance near chance levels whether a delay was imposed or not and it was in this context that eye movements, which were recorded along with button press responses, proved particularly informative. Eye tracking results showed that when the sample stimulus was present simultaneously with the choice array, both groups of participants spent more time fixating foils that most resembled the sample. However, when a 6-s delay separated sample from test, the visual-similarity-based preferential viewing effect was attenuated in patient data; the basic effect persisted, but the correspondence between visual similarity and fixation time was reduced. This outcome suggests that representations were degraded, but had not been completely lost (see also Warren et al. 2011), and a potential mechanistic explanation for this pattern of performance is deficient hippocampus-supported pattern separation—a process that establishes orthogonalized representations of similar or confusable inputs (e.g., Yassa and Stark 2011).

Eye movement methods are notable because they provide researchers with a continuous index of cognitive processing while stimulus materials are being viewed (cf. Hannula et al. 2010). New behavioral testing procedures that use continuous rather than binary response metrics also permit investigators to address increasingly specific questions about the fidelity of STM representations, and recent neuropsychological studies have adapted these methods (Pertzov et al. 2013; Warren et al. 2014). In general, participants in these experiments attempt to identify a key feature (e.g., color, orientation) of one object from the sample array. This target object appears at test, stripped of critical information, and participants choose from a continuous range of options (e.g., on a color wheel, by manipulating the orientation of a colored bar) the feature value that provides the most precise fit (e.g. a specific shade of blue, a 45° angle). In two experiments, Pertzov et al. (2013) found that patients with amnesia secondary to a specific subtype of limbic encephalitis were impaired on STM tests that used continuous reporting metrics, but that their mistakes were due to swap errors. For example, when patients attempted to drag a fractal to its previously occupied location, they were just as likely as controls to get it near one of the locations occupied during the sample phase, but were more likely than controls to place it closest to a location previously filled by a different exemplar. Similarly, when patients attempted to specify the studied orientation of a colored bar, they oftentimes matched orientation to a different colored line presented prior to the delay, an effect that was evident even when the imposed load was just two object-orientation associations. In both of these examples, the fidelity or precision of memory for sample features (e.g., orientation) was intact, but the binding of objects to feature values or spatial location was compromised.

Much like Pertzov et al. (2013), Warren et al. (2014) reported that the fidelity of feature-based memory representations was comparably stable in amnesic patients and matched control participants across very short intervals (900 ms). In a task of color-location associations (Zhang and Luck 2008), responses made by selecting a remembered color from a color wheel were similarly accurate for healthy control participants and patients with hippocampal damage. In contrast to other studies though, the amnesic patients' memory representations were more likely to be completely lost than control participants' when the imposed memory load was three or six color values (see Fig. 5). Furthermore, follow-up analyses confirmed that this forgetting was not due to relational memory (or "swap") errors.

These outcomes are difficult to reconcile. While results from some studies suggest that STM representations in amnesia are degraded or lack fidelity (Warren et al. 2010, 2011; Yee et al. 2014), others suggest a very systematic pattern of

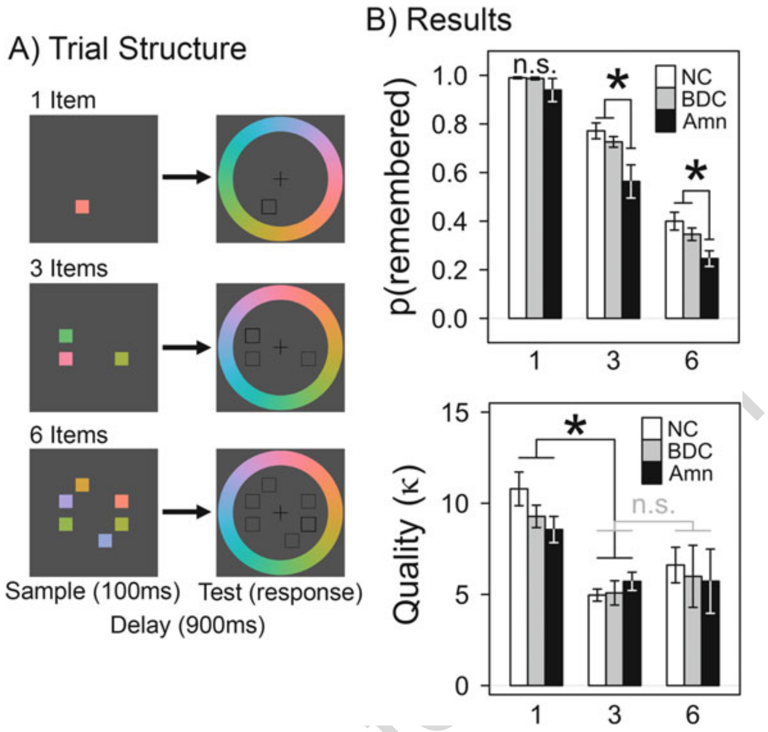

Fig. 5 Illustration of the color-wheel STM task and corresponding results from Warren et al. (2014). (**a**) Representative examples of 1, 3, and 6 item sample displays. On every trial, a sample stimulus was presented for 100 ms, followed by a brief delay (900 ms), and finally the appearance of the color wheel. One of the *squares* was marked as the target (thicker black outline) and participants attempted to specify the color of that exemplar. (**b**) Results indicated that the complete loss of information was more common among amnesic patients (amn) than normal controls (nc) and brain damaged controls (bdc) for sample sizes 3 and 6 (*top*). In contrast, the quality of retained color information was well-matched across groups (*bottom*). Figure adapted from Warren et al. (2014) and reproduced with permission according to the Creative Commons License agreement with Cold Spring Harbor Laboratory Press

mistakes—namely, swap errors (Pertzov et al. 2013; Watson et al. 2014). Furthermore, one study provides evidence for abnormally elevated levels of lost representations, even at low loads and in the context of a standard STM feature specification task (Warren et al. 2014). Notably, many of these studies have been conducted with the same group of well-characterized patients (e.g. Warren et al. 2010, 2011, 2014; Watson et al. 2014; Yee et al. 2014), which discounts the possibility that discrepant results are due to patient-specific qualities like differences in age, lesion location or extent, etc. across experiments. This suggests then, that properties of the tasks—e.g., the instructions, the duration of trial events, the materials—are driving reported differences. Consistent with this idea, event timing was considerably shorter in Warren et al. (2014) than other studies. As is standard (Zhang and Luck 2008), the sample array in this experiment, which consisted of one, three, or six colored squares was in view for just 100 ms, and was followed by a 900 ms delay. By comparison, sample arrays used by Pertzov et al. (2013), Watson et al. (2014), and others were in view for at least 1 s, and often several seconds more; furthermore, imposed delays were seconds, rather than milliseconds, long. With this in mind, one possibility is that amnesic patients require more time to establish (or vulcanize; Luck 2008) mental representations of the sample stimulus and that, even with more time, representational precision or relational mappings remain below normal levels. These possibilities could be tested in future work.

STM for Items

There are some exceptions to what have become fairly standard reports of impaired amnesic performance on tests that require retention of inter-item and item-context bindings across short delays. First, and perhaps most notable, there is some compelling evidence for deficits on tasks that seem not to have the same kinds of binding requirements as studies outlined above. For example, several reports indicate that active retention of a single face is deficient in amnesia (Ezzyat and Olson 2008; Nichols et al. 2006; Olson et al. 2006a; Race et al. 2013; Rose et al. 2011). These impairments have been documented at delays of just 1 s, although the faces in that case were artificial, rendered without hair, and morphed to obtain a range of foils for test that were more or less similar to the sample (Ezzyat and Olson 2008). To the extent that the hippocampus contributes to pattern separation, these relatively homogenous faces may have become nearly indistinguishable when presented in sequence. Nevertheless, amnesic patients could successfully indicate whether pairs of faces presented simultaneously were a match or not—that is, impairment was only evident when the delay was imposed.

Results like these seem to be at odds with claims that hippocampal contributions to STM are limited to situations that require inter-item or item-context binding, but are compatible with other observations in the literature. For example, as described above, deficits have been reported on tests that require short-term retention of complex novel objects (Warren et al. 2011), and are evident even when STM for simple features is tested provided that items in the choice array resemble the sample stimulus (Warren et al. 2010, 2014).

Second, two additional recent studies (Olson et al. 2006a; Piekema et al. 2007) have reported impairments on tests that require active retention of simple features (e.g., spatial locations, colors) absent high-fidelity testing protocols, but deficits may have been a consequence of more extensive MTL damage. In fact, it was proposed recently that even the reported deficits in active face retention are a consequence of broader MTL lesions. Race et al. (2013) tested two groups of patients—individuals with limited hippocampal damage and those with more extensive MTL lesions—and performance was only impaired when lesions went beyond the hippocampus. As indicated by the investigators, some caution is warranted in the interpretation of this outcome because patients with extensive damage also had greater volume reduction in the hippocampus itself; this is especially notable in light of neuroimaging findings summarized below. Collectively, however, these findings suggest that some reconsideration of our original conclusion about hippocampal contributions to STM might be needed. While there is good reason to expect hippocampal involvement when tasks require representation of inter-item or item-context bindings, there is also a growing body of evidence that points to hippocampal involvement when choice arrays require more precise representation of intra-item bindings. In other words, STM tasks that require high resolution bound representations of object features, object combinations, or objects and contexts may depend on processing that is supported by the hippocampus (Yonelinas 2013).

Evidence Against Hippocampus-Supported Short-Term Retention

The literature also contains evidence that runs counter to the observations summarized above (Allen et al. 2014; Baddeley et al. 2010, 2011; Jeneson et al. 2010, 2011, 2012; Shrager et al. 2008). It is possible that performance in some of these studies was intact because tasks required active retention of simple or unitized items/features and did not use testing protocols that would be expected to require representation of high-resolution bindings. We consider just one representative example. Jeneson et al. (2012) reported that estimates of STM capacity derived from performances of hippocampal amnesic patients on a standard STM change detection task were within normal limits at short delays. Critically though, the test displays in this experiment, which required short-term retention of a small collection of colored squares, did not tap memory for color-location bindings. When a change was present, the target object (specified with a bounding box), was always a new color that had not been presented in the sample array. Indeed, as reported by the authors, “the task was to decide whether a new color had been introduced, not whether a color that was present in the first array was now presented in a new location” (p. 3585). More generally, the colors themselves were perceptually distinctive (e.g., red, green, blue, yellow), effectively ruling out any requirement for high fidelity representation of the critical feature value. Another potential obstacle concerns the patients themselves. Recent work has indicated that the neural correlates of STM for object-location associations may be subject to considerable reorganization among patients treated surgically for epilepsy versus the presence of a tumor (Finke et al. 2013; see also Braun et al. 2008). Epilepsy patients often perform normally on object-location change detection tasks and show compensatory recruitment of contralesional hippocampus and STM network structures (e.g. DLPFC) relative to a healthy control group. Tumor patients, who have a much abbreviated disease history with very little time for neural reorganization are impaired on the same task, and do not show increased recruitment of these structures. In this context, it is notable that several of the published studies in which STM deficits have not been forthcoming were based on work conducted with Jon (Allen et al. 2014; Baddeley et al. 2010, 2011), a developmental amnesic patient in whom the possibility of neural reorganization seems not to have been explored.

Final Considerations from the Neuropsychological Literature

STM research has shown that there are documented tradeoffs between representational fidelity and stimulus complexity (Alvarez and Cavanagh 2004). If a stimulus is particularly complex and/or discrimination at test depends on high quality representation or differentiation of feature-specific minutiae, then the number of items stored in STM may go down. Results described above suggest that these reductions may be more pronounced following hippocampal damage. A particularly vexing problem, one that permeates the perception literature as well, concerns the potential impact of LTM on performance. While amnesic patients can effectively leverage preexisting knowledge (e.g. semantic information) to improve their performance on STM tasks (Race et al. 2015), they cannot encode durable LTM representations of new information. As such, it is possible that at least a subset of impairments reported in the literature reflect deficiencies in LTM, not STM. In light of these concerns, any resolution of questions about the boundary conditions and characteristics of STM deficits following hippocampal damage will require systematic consideration of these factors. This is particularly challenging because, in our opinion (as outlined below), definitive procedures for disambiguating the contributions of LTM and STM to performance have yet to be described.

The premise behind one such approach is as follows—if healthy control performance is disrupted by the introduction of interference during a STM delay period, active retention must have been required. In this case, the argument is that new information has displaced the active memory representation and because a more durable LTM trace was never established, response accuracy is reduced (Shrager et al. 2008). Consequently, one benchmark for concluding that the hippocampus does indeed contribute critically to short-term retention is impairment in an amnesic sample on the very same test where control performance drops in the face of interference. In principle, this seems like a reasonable suggestion, but in practice, there are problems that impact the viability and interpretation of reported outcomes. For example, as we have described in detail elsewhere (Yee et al. 2015), it is not clear to what extent control performance must drop for investigators to say conclusively that active retention was driving task performance. In the original work outlining this procedure, control performance was significantly reduced on a test of memory for six object-location bindings in the face of interference; amnesic patients were impaired on this test as well. It seems then, that this meets the definition of evidence for hippocampal contributions to STM. Instead, however, it was indicated that the drop in control performance, while significant, was insufficient for making these claims. More generally, as described in detail by Race et al. (2013), the kind of interference matters. In other words, failures to document interference effects in control performance may simply mean that representational requirements and/or processing demands of the interference task were orthogonal to task features or insufficiently taxing to displace represented content. Until these issues are addressed, any claims about disambiguation of short- from long-term memory contributions to task performance based on this method seem premature.

As we will see, questions about STM-LTM interactions have figured prominently in the neuroimaging literature as well, which is summarized next.

Neuroimaging Investigations of STM

Consistent with the neuropsychological literature, a great deal of effort has been made in the neuroimaging community to determine whether and under what circumstances the hippocampus (and adjacent MTL structures) might contribute to STM. This work provides important insights that are not afforded by work with amnesic individuals, including observations of sustained delay period activity, information about contributions of specific hippocampal subfields to active retention, and insights into STM/LTM interactions. Furthermore, recent advances in neuroimaging analyses permit investigators to decode the representational content of delay period activity. As is described elsewhere (cf. Norman et al. 2006) and below, these multivariate statistical approaches are sensitive when univariate outcomes are inconclusive, and therefore, promise to be informative in future work.

Three fMRI investigations reported some of the earliest evidence for hippocampal activity differences during the performance of STM tasks (Mitchell et al. 2000; Ranganath and D'Esposito 2001; Stern et al. 2001; see also Curtis et al. 2000). One of these experiments (Mitchell et al. 2000) was a procedural match to the neuropsychological study conducted by Olson et al. (2006b), described above. Participants, who were older and younger adults, were presented with three object-location associations and were either instructed to maintain information about the items, the filled locations, or the pairs in anticipation of a probe display. When this display was presented, participants indicated yes or no, whether the presented information had been seen during the sample phase. Most important for our purposes, activity was significantly greater in anterior hippocampus when young participants attempted to retain object-location bindings as compared to objects or locations alone; this activity pattern was absent from the fMRI data of older adults. This result is consistent with reported impairments of hippocampal amnesic patients on the same task, and with the claim that the hippocampus contributes to STM when relational memory representations are required for accurate performance. In contrast to subsequent investigations, individual trial components (i.e., sample, delay, and test) were not modeled separately here; instead, activity differences were modeled using timing parameters that collapsed across the sample phase and the early delay.

In two subsequent studies, the common denominator was hippocampal recruitment associated with active retention of novel, trial-unique materials (i.e., faces or scenes; see also Schon et al. 2013). In one of these experiments, activity differences were evaluated for subcomponents of the STM trial, and results indicated that short-term retention of novel but not familiar faces was correlated with sustained delay period activity in the hippocampus. A control experiment conducted with the same materials and timing parameters confirmed that this outcome could not be reproduced when participants engaged in intentional LTM encoding, and a subsequent report based on reanalysis of this data set indicated that there was significant functional coupling between an FFA seed region and the hippocampus (along with PFC, parietal, and occipital sites) during the delay period (Gazzaley et al. 2004). These observations provide compelling evidence in favor of the view that hippocampal contributions go beyond LTM, here, when active retention of object-locations associations, single faces, or a set of complex scenes was required.

Delay Period Activity in the Hippocampus Predicts Subsequent Memory

In the wake of these early studies, a number of investigators reported that hippocampal engagement during the delay period of a STM test predicted subsequent recognition memory performance (e.g., Axmacher et al. 2008; Nichols et al. 2006; Ranganath et al. 2005; Schon et al. 2004). Indeed, this was an outcome that had been anticipated early on, as Ranganath and D'Esposito (2001) had proposed that hippocampal delay period activity may serve two purposes—namely, active retention *and* incidental encoding. One example of evidence in favor of this dual-purpose role came from an experiment that required active retention of novel complex objects (Ranganath et al. 2005). In this experiment, hippocampal activity was evident early, but not late in the delay, and recruitment predicted performance on a surprise subsequent memory test. Corresponding results from a behavioral study indicated that LTM for actively retained objects was reduced when processing was disrupted via interference early, but not mid- or late-delay. Based on these observations, it was inferred that the hippocampus is a key site of STM-LTM interactions, and that incidental encoding operations supported by the hippocampus build a representation that is then reconstructed and retained late in the delay by specialized neocortical processing sites. Notably, despite robust effects of early distraction on LTM performance, active retention was not compromised. This may seem like evidence against hippocampal contributions to STM, but the authors point out that interference in the behavioral task was unlikely to affect retention of low-level features (e.g., a simple shape in the upper right corner of a complex object), and that this kind of detail could be used to rescue STM performance even when a bound high-resolution representation of the whole object had been lost. In contrast, because subsequent recognition required disambiguation of 120 complex, novel objects that were likely to share these elementary features, the same low-level information could not support accurate performance on the LTM test.

Consistent with the perspective outlined above, recent evidence suggests that delay period activity in the hippocampus may be particularly important for establishing and retaining orthogonalized representations of objects that are characterized by high levels of feature overlap (Newmark et al. 2013). In this high-resolution neuroimaging study, hippocampal subfields DG/CA3 and CA1 were engaged disproportionately when feature overlap was high (versus low) during the sample phase of the STM task. Furthermore, these activity differences were sustained in CA1 (and adjacent MTL cortical structures) over the course of the delay.[1] As above, these outcomes align well with recent results from neuropsychological studies that were described earlier.

The same group (Nauer et al. 2015) has also reproduced the finding that hippocampal activity is robust early in the delay, but decays with time. Here, however, use of high-resolution neuroimaging methods meant that the effects could be localized to specific hippocampal subfields (i.e. DG/CA3 and CA1). Skeptics might argue that it sounds suspiciously like delay period activity in these studies is merely a carryover effect associated with processing the sample stimulus, but Nauer et al. (2015) reported that a model based strictly on timing of the sample stimulus, excluding the ensuing delay period, was a poor fit to the raw fMRI data. Consistent with observations in the rodent literature (Knauer et al. 2013), it was suggested that activity differences early in the delay may be an indirect index of persistent neuronal spiking in hippocampal subfields (and elsewhere in the MTL). In sum then, results from both the neuroimaging and neuropsychological literatures coalesce by implicating the hippocampus in active retention of object representations when performance depends on the integrity of high-fidelity bound representations of intra-item features. Neuroimaging experiments go further though, as they permit investigators to evaluate correlations between delay period activity and subsequent LTM, and to examine hippocampal recruitment at the subfield level.

Activity Differences in Hippocampus Are Sensitive to STM Performance

Much of the time, STM task performance has been near ceiling in neuroimaging investigations, but there are a few reports in the literature that suggest activity differences and/or activity patterns in the hippocampus predict successful STM performance. In a difficult matching-to-sample task, for example, Olsen et al. (2009) had participants attempt to identify the face from two alternatives that had been presented during the sample phase. To make the task challenging, sample displays consisted of two faces and both faces had to be retained in anticipation of the test display. A small set of male faces, cropped to remove the hair, was used repeatedly across trials, and pre-exposure to the faces meant that, in contrast to studies above, the materials were not novel. Despite these changes in protocol, delay period activity differences were evident in anterior hippocampus (and other MTL structures); these activity differences distinguished high confidence correct STM responses from low confidence and incorrect responses, and persisted for the entire duration of the 30 s delay period. Much like results reported by Nauer et al. (2015), this outcome confirms that delay period activity was not a consequence of

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[1] For more information about hippocampal anatomy, including the designation of specific subfields, readers should consult chapter “The Nonhuman Primate Hippocampus: Neuroanatomy and Patterns of Cortical Connectivity” of this book.

carry-over effects from the sample stimulus. Furthermore, this work demonstrates that novel, trial-unique materials are not required to drive hippocampal activity up during the delay. Instead, activity differences were said to reflect requirements to bind specific, known face exemplars to the temporal context of a particular trial, insulating the representations from proactive interference.

Another approach that has been used to evaluate STM success effects incorporates a surprise LTM test (Bergmann et al. 2012, 2015, 2016). In these experiments, activity differences associated with successful (versus failed) short-term retention were identified for the subset of trials with incorrect long-term recognition responses. This meant that STM activity differences were unlikely to be a spurious consequence of LTM encoding and storage, although any absence of activity differences might reflect failed delay-period retrieval even if recognition (upon visual presentation of the test materials) was ultimately successful. Results across studies, two that required active retention of four face-house pairs and one that required active retention of the relative positions of objects embedded in scene contexts, varied. For example, it was found in the first study (face-house pairs) that hippocampal activity during the sample phase predicted subsequent long-term recognition, but not success on the test of STM; activity differences associated with delay and test could not be evaluated. The next study, a slightly modified version of the original, was run to permit separate analysis of STM trial components. In contrast to predictions, no suprathreshold activation in the MTL or anywhere else in the brain predicted STM accuracy during the delay period. The most recent experiment (Bergmann et al. 2016) required participants to retain information about the locations of four objects embedded in a rendered scene. Accuracy effects associated with "pure" STM contrasts (i.e. when LTM responses were incorrect) were evident in bilateral hippocampus during the test phase of STM trials (see also Hannula and Ranganath 2008), but there were no suprathreshold activations during the delay period. Furthermore, there were no activity differences anywhere in the brain that predicted LTM outcomes. Results from these experiments are surprising because amnesic patients with hippocampal damage are impaired on tasks like these when short delays are imposed (e.g., Hannula et al. 2006; Hartley et al. 2008; Yee et al. 2015), and because robust delay period activity in the hippocampus has been reported in several other experiments. One potential explanation for null outcomes, based on the report by Olsen et al. (2009) above, is that collapsing across correct STM responses without considering confidence obscured hippocampal activity differences. As a reminder, contrasts performed by Olsen et al. distinguished high confidence correct responses from low confidence and inaccurate responses. It seems worthwhile then for future studies to include subjective confidence ratings or remember/know judgments, and to subdivide STM trials on this basis. AU21

Finally, null delay period effects were also reported by Hannula and Ranganath (2008) on a test of spatial relational working memory. In this study, on every trial, participants were presented with four objects (from a set of nine), each in one of nine possible spatial locations in a 3 × 3 rendered grid. Over the course of the delay, participants attempted to mentally rotate the encoded sample stimulus so that they could detect, and discriminate among, changes in object-location bindings when the test display, which was presented from a different viewpoint, appeared on the screen. This was a very difficult test, and while univariate contrasts indicated that activity differences in the hippocampus were greater for correct than for incorrect WM responses during presentation of the sample and test displays, there was no evidence for above-threshold accuracy effects anywhere in the brain during the delay. As above, it is possible that incorporating a measure of memory strength would change reported outcomes, but here, because participants had to disambiguate test displays based not only on the presence (or absence) of a position change, but also the specific type of change that was in play, correct responses likely required precise memory representations. While we prefer not to place too much stock in null findings, alternative explanations for the lack of delay period activity are worth considering. First, the absence of differential recruitment could reflect efforts to retain and work with whatever had been encoded, whether those representations were complete or not. Second, it is possible that univariate BOLD signal contrasts were insufficiently sensitive to neural differences that are correlated with successful retention in this task. Consistent with this second possibility, recent re-evaluation of this data set using multivariate representational similarity analysis (RSA) showed that activity patterns during encoding and delay were correlated when participants successfully identified relational matches or manipulations on the WM test (Libby et al. 2014). A more compelling approach might have looked at delay period pattern similarity across trials with shared relational content (i.e. that required representations of the same bindings), but the experiment had been designed so that object-to-space and inter-object-to-space bindings were always trial unique. Therefore, decoding of specific relational representations could not be performed. Nevertheless, this outcome does suggest that representations of relational information persisted from encoding into the delay period when participants made correct responses, and more importantly, speaks to the sensitivity of multivariate approaches to fMRI data analysis. We are not aware of any other studies that have used multivariate (MVPA, RSA) techniques specifically to evaluate when and how the *hippocampus* supports active short-term retention (but see Lewis-Peacock et al. (2012) for an example of a promising paradigm that could be adapted for this purpose)—future studies could be performed with this in mind.

Effects of Memory Load and Task Demands on Hippocampal Recruitment

We end with a brief discussion of the potential impact of memory load and tasks demands on hippocampal recruitment during the performance of STM tasks. These issues are important to consider, as it is possible that STM capacity is exceeded when the imposed load is high or tasks become especially difficult. Consequently, any resulting activity differences in the hippocampus may reflect a shift to dependence on LTM mechanisms. Evidence that suggests this may be the case comes from a study that has shown a trade-off in functional connectivity with the fusiform face area (FFA) between the inferior frontal gyrus (IFG) and the hippocampus when the number of to-be-retained faces is systematically manipulated across trials (Rissman et al. 2008). Specifically, functional coupling between FFA and hippocampus increased linearly with sample size (i.e. 1–4 faces); IFG showed the opposite pattern. Much like this result, greater hippocampal recruitment for high (four symbols) versus low (one symbol) load working memory trials was also reported by Axmacher et al. (2009). However, in this experiment, participants were also required to encode a face that was presented during the delay period. Subsequent face recognition and hippocampal activity associated with face encoding were both down when the concurrent WM load was high. In contrast to the load-dependent proposal, but consistent with conclusions drawn in past work (e.g. Ranganath et al. 2004; see above), it was suggested that this outcome points to a dual-purpose role for the hippocampus in active retention *and* LTM encoding. When the hippocampus is recruited to support *active retention* of four symbols, it is less available for face *encoding* and subsequent recognition is compromised. The authors acknowledge that activity differences associated with high load WM trials may be a consequence of exceeding the capacity limits of STM (i.e. in the high load condition symbols may have been encoded into LTM and then subsequently retrieved), but raise several counterpoints against this interpretation of the data.

Finally, as proposed by Zanto et al. (2015), challenging tasks may elicit hippocampal recruitment because LTM is required. To test this possibility, they had participants attempt to retain a single face over the course of a delay, but in three experimental conditions, this basic task was made more difficult. Across conditions, a task-irrelevant distractor face was presented during the delay, the delay was lengthened, or foil faces at test were purposely selected based on their visual similarity to the sample. In each case, including a baseline condition (face retention absent the above challenges), participants knew what to expect (i.e. whether the task would be relatively easy or difficult). Relative to baseline, hippocampal engagement increased during the performance of “challenge” tasks when the sample face was in view and during the delay period there was increased functional coupling of hippocampus (and other structures in the parahippocampal gyrus) with FFA for the same contrast. Interestingly though, there were also significant activity differences in the hippocampus during the sample phase greater for baseline trials than for passive viewing trials. Delay period activity differences and connectivity patterns seem not to have been evaluated in a baseline/passive viewing contrast. Another key outcome of the study concerns the pattern of behavioral performance, which included assessment of face recognition on a surprise test of LTM. Specifically, there was a significant tradeoff between STM and LTM performance across tasks—short-term change detection was better in the baseline condition and LTM was better in the challenge conditions. This likely had to do with expectations participants had about task difficulty (based on instruction) and corresponding efforts to encode/retain the sample more effectively. Notably though, activity differences and connectivity patterns with the hippocampus during performance of “challenge” tasks were not correlated with subsequent LTM performance. While it was concluded that results provide strong evidence in favor of the standard view that dissociable brain systems support short- and long-term memory, the presence of hippocampal activity differences in the baseline condition and the lack of correspondence between hippocampal recruitment/connectivity and subsequent recognition performance leave room for alternative interpretation.

In sum, the results summarized above indicate that delay period hippocampal engagement is only present when load is high or tasks are especially challenging, but these outcomes do not jibe with reports of hippocampal recruitment during tasks that require active retention of just one item (e.g. a single face or object—Ranganath and D'Esposito 2001; Ranganath et al. 2004). More generally, there is important counterevidence to the LTM-based load argument that bears consideration. For instance, von Allmen et al. (2013) reported that set-size dependent hippocampal recruitment was evident within the capacity limits of visual STM when participants were required to retain color-location associations, and that these activity differences actually collapsed when capacity limits were exceeded. Furthermore, research that is based on recently proposed models of STM that distinguish between the "focus of attention", a "region of direct access", and the "activated part of LTM" (more accessible by virtue of its recent use) has consistently reported hippocampal recruitment (Nee and Jonides 2013, 2014; Öztekin et al. 2009, 2010). For example, Nee and Jonides (2013) have shown that hippocampal activity during presentation of a test stimulus is evident when decisions are being made about information that was held in the "region of direct access"; notably, and consistent with von Allmen et al. (2013), these activity differences were evident below the individual capacity limits of tested participants. It is difficult to reconcile these observations with the view that hippocampal engagement is only evident when LTM has to be engaged to support performance (i.e., because capacity limits were exceeded). In short, there is solid evidence in the literature consistent with a role for the hippocampus in short-term retention (see also Soto et al. 2012).

Summary and Conclusions: Short-Term Memory

There is a long-held tradition in cognitive neuroscience to view memory from a systems perspective. Especially notable here is what has been considered unambiguous dissociation of systems that support short- and long-term memory. The strongest evidence in favor of this perspective came from work with amnesic patients who had severely compromised LTM, but remained quite capable of retaining a limited amount of information in mind over the short term. Anecdotally, this divide is apparent in interactions with individuals who have hippocampal damage. While they can engage in basic conversation without difficulty, it soon becomes clear that their narrative is not anchored in the context of events that transpired even moments earlier. They can carry on though, as long as the topic of conversation stays on course. This is why, when short-term retention is tested, it has been so important to develop tasks that tap hippocampus-dependent representations. Only under these circumstances has it become clear that performance is not on par with healthy control participants, even when imposed delays are on the order of hundreds of milliseconds (e.g., Warren et al. 2014).

The neuroimaging literature has provided additional insights and converging evidence for a hippocampal stake in STM, and goes further than patient work, as specific questions about the delay period (e.g., whether activity differences persist) and STM-LTM interactions can be examined. While mechanism was not discussed here, human neuroimaging (particularly magnetoencephalography; Cashdollar et al. 2009; Olsen et al. 2013), and intracranial recording (e.g., Leszczynski et al. 2015) studies are a source of compelling evidence for *how* short-term retention may be achieved and/or mediated by the hippocampus. Based on these observations, it seems that some serious reconsideration of the memory systems perspective is required. AU23

That said, there remains much to do in this domain. For example, it is increasingly apparent that brain injury may give rise to significant reorganization of the neural correlates of STM depending on the time-course of the underlying disease process (e.g., Finke et al. 2013). Studies that combine functional neuroimaging and patient work have great potential to provide new insights into how and when brain function is reorganized subsequent to damage, and whether reorganization affects performance on STM tasks. Work is also needed in the neuropsychological literature that makes inroads with contemporary STM models. For example, as proposed by LaRocque et al. (2014) and consistent with fMRI outcomes (Nee and Jonides 2013, 2014), one might expect that amnesic patients would be impaired on simple short-term memory tasks when information is being held in the “region of direct access”, but not the “focus of attention”. Alternatively, impairments might even be evident for information in the focus of attention depending on the representational demands of the task. In turn, fMRI studies that take advantage of multivariate analysis techniques might provide important new insights into what exactly is represented by the hippocampus over the course of a delay period. This kind of work could serve to test claims made here, and elsewhere (Yonelinas 2013), that the hippocampus is likely to support or contribute to STM when tasks require active retention of inter-item and item-context bindings, or when the testing procedure requires representation of high-resolution object details that distinguish the target on the current trial, from one seen several trials earlier, or from similar foils in the test array. In short, it seems reasonable to conclude that the hippocampus contributes to STM. Consistent with conclusions drawn elsewhere (e.g., Ranganath and Blumenfeld 2005), this is important because intact performance on STM tasks following hippocampal damage was considered linchpin evidence for separate short- and long-term memory systems.

General Conclusions

In this chapter, we reviewed three current topics related to hippocampal function, each of which is addressed by a distinct portion of the literature. However, perception, short-term retention, and conscious awareness are linked by a common, historical exclusion: according to long-held views of hippocampal function (cf. Squire and Dede 2015), none depends on the hippocampus. Recent work has prompted our field to reconsider this widely-held perspective by suggesting that perception, short-term retention, and memory expression absent awareness may in fact require and recruit the hippocampus. The field's acknowledgement of broader hippocampal contributions is evident in the proliferation of new theories (or refocusing of existing theories) to describe a synthesis between recent findings and the established role of the hippocampus in LTM processes. We close by (re-) considering a few theoretical accounts related to the topics we reviewed.

Relational memory theory (Eichenbaum and Cohen 2001, 2014) and related proposals (Davachi and Dobbins 2008; Ranganath 2010) have indicated that the hippocampus supports the binding together of arbitrarily related stimuli at encoding, and supports part-cued retrieval of associated content during a temporally-extended consolidation process. Empirical support for the predictions of relational memory theory in LTM is considerable, but a key theoretical question for this chapter has been to what extent the hippocampus contributes this kind of relational processing to other cognitive operations. For example, when binding is required by tests that do not tap long-term declarative memories, is a hippocampal contribution required? Much of the evidence that we have reviewed here is consistent with this possibility. As such, the relational memory theory continues to make important and accurate predictions more than two decades after its debut.

Despite the continued success of relational memory theory, findings that imply a hippocampal role in perception could constitute something of a challenge. As implied by its name, the perceptual-mnemonic theory (PMT) of MTL and hippocampal function suggests that these structures contribute to (at least) two distinct cognitive domains, namely perception and memory (Bussey and Saksida 2007; Graham et al. 2010; Graham and Gaffan 2005; Lee et al. 2012). A key concept in PMT is that the hierarchical organization of the dorsal stream (Mishkin et al. 2000) is preserved and extended in the MTL (Bussey and Saksida 2007). PMT is appealing because it tackles recent findings for hippocampal involvement in cognitive processes over short intervals head on, and because it extends an established model of hierarchical visual representation in the brain (Mishkin et al. 2000). Befitting the apical position of the hippocampus in the ventral visual stream, PMT suggests that this structure is uniquely capable of contributing to the perception of complex scenes (Bussey and Saksida 2007; Graham et al. 2010; Graham and Gaffan 2005; Lee et al. 2012). Some findings described in this chapter support this claim (reviewed by Douglas and Lee 2015; Lee et al. 2012), but it is not yet clear whether the scope of PMT is sufficient to encompass the entire breadth of hippocampal contributions to cognition. Despite this uncertainty, the originators deserve great credit for proposing a theory with solid empirical foundations that is capable of generating empirically testable hypotheses.

Another recent account that explicitly attempts to address a potential dual role for the hippocampus in perception and memory is the high-resolution binding theory (HRBT) (Yonelinas 2013). HBRT suggests that the hippocampus supports "… the generalization and utilization of complex high-resolution bindings that link together the qualitative aspects that make up an event" (p. 34). HRBT incorporates key components of the declarative and relational memory theories to address hippocampal contributions to memory as well as portions of perceptual-mnemonic theory to account for recent perception-oriented findings. The claims of HRBT are broadly consistent with contemporary data although certain findings of hippocampal involvement in the maintenance of relatively simple stimuli over short intervals or specific relational failures may not be addressed (Race et al. 2013; Warren et al. 2010, 2014; Watson et al. 2013). A more thorough evaluation of HRBT may require the accumulation of new data to test whether its impressive explanatory power will be matched by the quality of its novel predictions (e.g., evidence of high-resolution bindings operating in recollection, language, and other cognitive processes).

Finally, a model proposed recently by Henke (2010) takes an aggressive stance on the consciousness issue. This model shares a number of key tenets with the relational memory theory (Cohen and Eid 1993) and related proposals that have made increasingly specific claims about the role of MTL cortical structures (particularly perirhinal and parahippocampal cortices) in memory (e.g., Davachi 2006; Eicehenbaum et al. 2007; Diana et al. 2007). This model holds tight to proposed divisions between long-term memory systems (e.g., episodic, semantic, procedural), but suggests that the differences among them come down to processing speed and flexibility of the resulting memory representations, rather than consciousness. There is a good deal of existing empirical support for this model, and it suggests a number of hypotheses that can be tested to further evaluate the viability of claims that have been made. It does not seem, however, to directly consider hippocampal contributions to cognitive function outside the domain of LTM (e.g., perception and short-term retention), though it seems possible that the same basic principles would apply.

In conclusion, our summary finds the literature describing hippocampal contributions to cognition at a moment of significant change that prompts fundamental questions about the nature of conscious memory access, perception, and representation of information over the short-term. For example, an important constraint on hippocampal involvement in cognitive processes beyond LTM may be the representational and/or processing demands of a particular task. Much recent work was initiated in the context of theories that have proposed a role for the hippocampus in relational binding and representation. As indicated above, this view implicates the hippocampus in the encoding, subsequent retrieval, and flexible use of representations that contain information about items bound together in space and time. In turn, this new work, including several of the studies that were summarized here, has led to important observations that compel reconsideration of some key tenets of established theories. For example, in each of the three domains that were examined, it seems to be the case that the hippocampus contributes not only to binding of items and context or inter-item binding, but also to feature binding when task demands require detailed intra-item information for successful performance. As we have suggested, it may be the case that the lens of the hippocampus can be dynamically adjusted, so that the "focus" of this structure targets items in broader contextual settings, or is optimized to process features within an item, depending on task demands. For example, when face recognition depends critically on high-fidelity representation of the component parts, because it has been viewed from several different perspectives during encoding, flexible representation of the relationships among face features may be required to support successful performance. Similarly, when an ellipse, tilted 45° from vertical, has to be distinguished from similar exemplars in a test display, or insulated from other similar exemplars across trials, a bound representation of *that* item (i.e. its features) to specific temporal context might be required for successful performance. In sum, it seems that the reach of the hippocampus does indeed go beyond long-term declarative memory; now, investigators must begin to address questions about the specific characteristics of these contributions.

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AU25

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