Neuropsychologia 48 (2010) 2251–2261

Contents lists available at ScienceDirect

Neuropsychologia

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

Implications of animal object memory research for human amnesia

Boyer D. Winters[a,*], Lisa M. Saksida[b,c], Timothy J. Bussey[b,c]

[a] Department of Psychology, University of Guelph, Guelph, Ontario N1G 2W1, Canada
[b] Department of Experimental Psychology, University of Cambridge, Downing Street, Cambridge CB2 3EB, UK
[c] The MRC and Wellcome Trust Behavioural and Clinical Neuroscience Institute, University of Cambridge, Downing Street, Cambridge CB2 3EB, UK

ARTICLE INFO

Article history:
Received 13 August 2009
Received in revised form 25 January 2010
Accepted 27 January 2010
Available online 2 February 2010

Keywords:
Amnesia
Animal models
Declarative memory
Rats
Monkeys
Object recognition
Medial temporal lobe
Perirhinal cortex
Hippocampus

ABSTRACT

Damage to structures in the human medial temporal lobe causes severe memory impairment. Animal object recognition tests gained prominence from attempts to model 'global' human medial temporal lobe amnesia, such as that observed in patient HM. These tasks, such as delayed nonmatching-to-sample and spontaneous object recognition, for assessing object memory in non-human primates and rodents have proved invaluable as animal models of specific aspects of human declarative memory processes. This paper reviews research in non-human primates and rats using object recognition memory tasks to assess the neurobiological bases of amnesia. A survey of this research reveals several important implications for our understanding of the anatomical basis of memory and the medial temporal lobe amnesic syndrome. First, research with monkeys and rats reveals that the contributions of medial temporal lobe structures such as the hippocampus and perirhinal cortex to memory processes are dissociable, with particular structures contributing to specific tasks on the basis of the specific type of information that a structure is optimized to process. Second, the literature suggests that cognitive tasks requiring integration of different types of information, such as in the case of complex, multimodal declarative memory, will recruit structures of the medial temporal lobe in an interactive manner. The heterogeneity of function within the medial temporal lobe, as well as the multimodal and complex nature of human declarative memory, implies that animal tests of object recognition memory, once believed to be comprehensive models for the study of human global amnesia, model just one important facet of human declarative memory. Finally, in light of the research reviewed here, it is apparent that the specific nature of amnesia observed in an individual with medial temporal lobe damage will depend on the particular medial temporal lobe regions affected and their specific representational capacities.

1. Introduction

Systematic analysis of the mnemonic impairment of the recently deceased neurological patient H.M. has been integral to the emergence of our current understanding of the organization of human memory (Corkin, 1984; Milner, Corkin, & Teuber, 1968; Scoville & Milner, 1957; Squire, 2009). The pattern of spared and impaired memory ability displayed by H.M. and other patients with similar brain damage has strongly influenced our thinking about mnemonic function and has led, in part, to the proposal that there exist multiple forms of memory (Squire & Zola-Morgan, 1988; Squire & Zola, 1996). Findings from such patients have specifically implicated a collection of brain structures in the human medial temporal lobe (MTL) in the conscious memory for facts and events—what is often referred to as declarative memory (Squire & Zola-Morgan, 1988). These MTL structures include the hippocampus (HPC), perirhinal cortex (PRh), entorhinal cortex, and parahippocampal cortex, and have been hypothesized to form a unitary "memory system" specifically subserving declarative memory function (Squire & Zola-Morgan, 1991). This proposal is related to reports that H.M., whose brain damage included parts of several MTL structures (Corkin, Amaral, Gonzalez, Johnson, & Hyman, 1997), displayed enduring amnesia for episodic memory while many of his "nondeclarative" memory abilities and general intellectual and perceptual functions remained intact (Corkin, 1968, 1984; Milner et al., 1968; Scoville & Milner, 1957). Indeed, the concept of a memory taxonomy grew directly from such dissociations. It should, however, be noted that the idea of MTL involvement in declarative memory has sometimes been taken to the extreme, leading to the common circular reasoning that any task which is sensitive to MTL damage should be classified as a test of "declarative memory". Indeed, the object recognition tasks that are the focus of this review are generally soluble on the basis of familiarity judgements and may not normally even tax advanced conscious recollective processes. Despite this consideration, several past findings implicated the hippocampus in object recognition task performance, and

* Corresponding author. Tel.: +1 519 824 4120; fax: +1 519 837 8629.
E-mail address: bwinters@uoguelph.ca (B.D. Winters).

0028-3932/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.neuropsychologia.2010.01.023

for this reason alone, object recognition tasks have commonly been presented as accurate means for assessing declarative memory in animals. Much of the research discussed in the following review indicates that the relationship between MTL structures and memory processes is more complicated than was once believed, and that such circular logic, as always, should be avoided.

Early results from patients with MTL amnesia prompted a great proliferation of studies investigating the role of the MTL in learning and memory in humans and non-humans. This has resulted in a vast literature further implicating the MTL in memory processes. Although animal research has struggled to define the extent to which information is consciously recalled in non-humans (Eichenbaum, Yonelinas, & Ranganath, 2007; Squire, Wixted, & Clark, 2007), this work has nonetheless proved highly valuable in enabling us to make inferences regarding the building blocks of conscious declarative memory in humans. Moreover, the systematic analyses afforded by the use of non-human animal subjects has provided detailed evidence to suggest dissociable, but possibly overlapping, contributions of certain MTL structures to aspects of declarative memory function. Indeed, while it is clear that various MTL structures contribute to declarative memory, the extent to which they perform homogeneous or dissociable mnemonic functions remains controversial. Much evidence, however, now seems to indicate that anatomically distinct MTL regions have specific representational roles that could be sufficient for the performance of certain behavioural tasks. Tasks, however, that require the integration of different types of information (e.g., visual and spatial) may require interaction between various MTL regions for their successful performance. One major implication of this 'representational' account of MTL function is that structures such as the HPC and PRh may not be limited to purely declarative memory processes, but may also perform perceptual functions and that these perceptual and mnemonic functions may, in fact, not be as readily separable as prevailing theories of brain function, such as the idea of a unitary MTL memory system, would seem to suggest (Bussey & Saksida, 2007; Gaffan, 2002) [see Bussey and Saksida review, in this issue].

This review will focus on non-human primate and rodent models of human declarative memory. Specifically, we will review literature that grew out of researchers' early attempts to model human MTL amnesia in monkeys. Arguably, the most historically influential tasks for modelling MTL amnesia are those that test object recognition abilities. Accordingly, the emphasis of this review will be on animal models of object recognition memory. Research using object recognition tasks in non-human primates and rodents has revealed much about the neurobiological bases of this type of memory and has clarified the specific roles of certain MTL structures in object memory. These findings have important implications for our understanding of human memory and the nature of dysfunction associated with human amnesia.

2. Non-human primate research with delayed nonmatching-to-sample: studying the role of MTL structures in object recognition memory

The ability to recognize that an object has been previously encountered is thought to be an important aspect of human declarative memory, and deficits in object recognition memory are commonly displayed by patients with MTL brain damage (Buffalo, Reber, & Squire, 1998; Hajilou & Done, 2007; Holdstock, 2005; Irle, Kessler, Markowitsch, & Hofmann, 1987; Laatu, Revonsuo, Jaykka, Portin, & Rinne, 2003; Lee, Rahman, Hodges, Sahakian, & Graham, 2003; Manns & Squire, 1999; Purdy, McMullen, & Freedman, 2002; Reed & Squire, 1997). In general, non-declarative memory such as procedural memory for habits or skills is thought to be acquired incrementally, whereas many forms of declarative memory are thought to be acquired after only a single exposure to the to-be-remembered material. This one-trial nature of information acquisition is a common feature of the most widely used tests of object recognition memory in animals and, as such, these tests provide some of our best animal models for the study of amnesia.

Following the first reports of H.M.'s impairment, researchers began trying to develop methods to better understand the functions of the structures damaged during H.M.'s surgery. An effective animal model would allow for the conduction of controlled experiments to assess the neurobiological bases of human memory dysfunction. Specifically, localised lesions could be made to study which aspects of H.M.'s MTL damage were responsible for his memory disruption. In the mid-1970s two separate laboratories published reports of non-human primates performing in a test of object recognition memory (Gaffan, 1974; Mishkin & Delacour, 1975) that would subsequently be revealed to be sensitive to MTL damage (Bachevalier, Parkinson, & Mishkin, 1985; Bachevalier, Saunders, & Mishkin, 1985; Gaffan, 1974; Mahut, Zola-Morgan, & Moss, 1982; Mishkin, 1978; Mishkin & Delacour, 1975; Saunders, Murray, & Mishkin, 1984; Zola-Morgan & Squire, 1985). This task is referred to as delayed nonmatching-to-sample (DNMS) and, along with the delayed matching-to-sample (DMS) version, remains one of the most common tests of animal memory in use today.

DNMS and DMS are tested according to the same general procedure, which consists of three main stages: the sample phase, the retention delay, and the choice phase. In the sample phase, the subject is presented with a sample stimulus, either a 'junk' object presented over a central baited food well of the Wisconsin General Testing Apparatus (Gaffan, 1974; Mishkin & Delacour, 1975) or a visual stimulus presented on a touchscreen monitor (e.g., Ogura & Aigner, 1993; Parker, Eacott, & Gaffan, 1997; Parker & Gaffan, 1998). The subject must displace the object or touch the visual stimulus for a small reward, after which the stimulus is removed and the retention delay begins. The length of the retention delay can be varied by the experimenter from just a few seconds to several minutes or hours in order to assess the effects of increasing the mnemonic demands of the task. After the retention delay, the sample stimulus is presented in conjunction with a novel stimulus in the choice phase. Depending on the specific task being used, the subject must displace or touch either the novel stimulus (DNMS) or the sample stimulus (DMS) for reward. Thus, the successful performance of the task is likely based on multiple cognitive processes, for example the proper execution of the matching or nonmatching rule and the animal's ability to recognize the stimulus presented in the sample phase and guide responding accordingly in the choice phase. Several such trials typically occur in each testing session, and different object pairs are often used for each trial. In addition to the introduction of variable retention delays and/or sample list lengths (i.e., the number of to-be-remembered sample objects presented to the subject prior to the choice phase), two manipulations that can be used to increase memory demands, a key difference between the versions of D(N)MS that emerged in the mid-1970s and earlier versions (e.g., Correll & Scoville, 1965; Weinstein, 1941) was the use of trial-unique or pseudo-trial-unique stimuli. Whereas earlier D(N)MS tasks used small (e.g., two objects) stimulus sets that were presented to the subjects repeatedly over several trials, the more recent versions of the task employed larger stimulus sets to eliminate or substantially reduce the number of object repetitions across trials and sessions. This method discourages the use of alternative strategies for performing the task, such as the formation of stimulus-reward associations or the use of relative recency rather than familiarity judgements (Charles, Gaffan, & Buckley, 2004). Moreover, the use of trial-unique or pseudo-trial-unique objects reduces the impact of proactive interference on task performance, which can be an important consideration when studying the effects of brain damage on object recognition memory (Owen & Butler, 1984).

In a seminal paper on MTL involvement in object memory, Mishkin (1978) reported that combined but not separate removal of the amygdala and hippocampus in monkeys severely disrupted object recognition memory in the trial-unique DNMS task. The monkeys with combined lesions performed similarly to controls when short retention delays (approximately 10 s) were interposed between the sample and choice phases, but their performance plummeted when delays of 60 s or longer were used. This was in contrast to the relatively intact performance of monkeys with separate removals of either the amygdala or HPC alone. This finding was exciting because of the resemblance of the monkeys' amnesia to the delay-dependent nature of memory impairment seen in patients with MTL damage: while explicit memory is generally disrupted in such patients when they are asked to remember information over extended periods or with distraction occurring between learning and retrieval, patients with even rather large MTL lesions tend to demonstrate normal short-term memory (Drachman & Arbit, 1966; Scoville & Milner, 1957). Mishkin (1978) therefore suggested that either the amygdala or HPC was sufficient to mediate object recognition memory and that the combined removal of these medial temporal lobe structures was responsible for the delay-dependent deficit observed in this experiment, as well as the anterograde amnesia displayed by patient H.M and others like him. Subsequent studies seemed to confirm the requirement of combined amygdala and HPC removal for object recognition impairment (Murray & Mishkin, 1984; Saunders et al., 1984; Zola-Morgan & Squire, 1985; Zola-Morgan, Squire, & Mishkin, 1982), consistent with the suggestion that either structure could mediate object recognition memory.

The MTL damage sustained by patient H.M. included the hippocampal formation (HPC, dentate gyrus, subiculum, and entorhinal cortex), the amygdala, and the surrounding perirhinal and parahippocampal cortices (Corkin et al., 1997), and the combined aspiration of the HPC and amygdala in the Mishkin (1978) study damaged many of the same regions. The damage to subjacent MTL cortical structures produced by these surgeries was not originally given much consideration, but later studies have indicated that regions other than the HPC and amygdala contribute greatly to the performance of object recognition memory tasks. Early attempts to assess the behavioural effects of extensive MTL damage in monkeys yielded results in the DNMS task that were consistent with the suggestion that combined amygdala and hippocampal removal disrupted object recognition memory. These lesions, however, included damage to surrounding cortical regions in addition to the amygdala and HPC and were termed H+A+ lesions by Zola-Morgan, Squire and colleagues (Squire & Zola-Morgan, 1988), where H refers to the HPC, A refers to the amygdala, and + refers to the adjacent underlying cortical areas. The same authors also reported that amygdala-sparing lesions of the HPC and surrounding cortex (the H+ lesion) were sufficient to impair DNMS performance (Mahut et al., 1982; Zola-Morgan & Squire, 1986; Zola-Morgan, Squire, & Amaral, 1989b). Although the memory impairment was less severe than the deficit caused by H+A+ lesions, this result indicated that damage to the amygdala was not required to disrupt object recognition memory. Further supporting this assertion was the finding that selective lesions of the amygdaloid complex (the A lesion), sparing the cortex adjacent to the amygdala, did not impair DNMS performance (Zola-Morgan, Squire, & Amaral, 1989), nor were monkeys with combined hippocampal formation and selective amygdala lesions (the H+A lesion) more impaired than those with H+ lesions. Thus, damage limited to the amygdala did not disrupt object recognition memory or worsen the impairment caused by lesions of the HPC and surrounding cortex. This pattern of results also suggests that the memory impairment caused by H+A+ lesions was worse than that following H+ lesions because of the additional damage to adjacent cortex in the former, which may have included perirhinal, periamygdaloid, and anterior entorhinal cortices.

Evidence that damage to adjacent MTL cortical areas contributed to the object recognition deficits reported earlier was provided by Murray and Mishkin (1986), who studied the effects of combined perirhinal and entorhinal cortex lesions. Monkeys with rhinal cortex lesions combined with either amygdala or HPC lesions were severely impaired in the DNMS task, indicating that combined amygdala and HPC damage was not necessary for object recognition memory impairment. Consistent with these findings, Zola-Morgan, Squire and colleagues found that amygdala-sparing lesions of the HPC, anterior entorhinal cortex, and perirhinal cortex (the H++ lesion) disrupted DNMS performance to the same degree as H+A+ lesions (Zola-Morgan, Squire, Clower, & Rempel, 1993). Furthermore, these authors later reported that lesions restricted to the perirhinal and parahippocampal cortices were sufficient to cause DNMS deficits as large as those observed following H+A+ lesions (Zola-Morgan, Squire, Amaral, & Suzuki, 1989). Importantly, this result, along with the findings of Murray and Mishkin (1986), indicates that damage to the perirhinal and related cortex is a crucial factor in the severe DNMS impairment caused by the H+A+ lesion and that serious object recognition memory deficits can result from damage to this region even when the HPC is fully intact. Moreover, Murray and Mishkin (1998) reported that monkeys with excitotoxic lesions limited to the HPC and amygdala that spared adjacent cortex were unimpaired on the DNMS task.

These findings, taken together, suggest that damage to the rhinal cortex is necessary and sufficient to produce object recognition memory impairments in monkeys. Conflicting findings, however, were reported by two separate groups who showed that monkeys with excitotoxic damage restricted to the hippocampal formation were impaired on tests of recognition memory, including DNMS (Beason-Held, Rosene, Killiany, & Moss, 1999; Zola et al., 2000). One notable difference between these studies is that the monkeys in Murray and Mishkin (1998) received extensive pre-surgical training on the recognition task, whereas subjects in the two studies reporting deficits following HPC lesions received postoperative training only. This is a substantial procedural difference that could explain the inconsistent results reported by these authors. For example, animals might learn to perform the tasks using very different strategies depending on the MTL structures that are intact during acquisition. Regardless of the exact explanation for the conflicting results, it should be noted that, in cases where HPC lesions are reported to cause recognition memory impairments, these deficits tend to be much milder than those produced by damage to surrounding cortical regions. Furthermore, a consistent finding is the absence of a positive correlation between the extent of HPC damage and severity of impairment (Baxter & Murray, 2001). This latter phenomenon is consistent with the idea that incomplete HPC damage might cause indirect disruption of information processing in other brain areas, leading to direct impairment in object recognition tasks (Mishkin & Murray, 1994; Murray, Bussey, Hampton, & Saksida, 2000).

Although controversy remains regarding the relative contributions of the HPC and other MTL cortical regions, recent work in this area in monkeys and rats (see below) has strongly implicated the PRh specifically in object recognition memory. Indeed, monkeys with combined PRh and entorhinal cortical damage show significant delay-dependent deficits in DNMS and DMS (Eacott, Gaffan, & Murray, 1994; Meunier, Bachevalier, Mishkin, & Murray, 1993), and studies using even more selective lesions have revealed that damage to PRh alone is sufficient to cause severe object recognition disruption in monkeys (Buffalo et al., 1999; Horel, Pytko-Joiner, Voytko, & Salsbury, 1987; Meunier et al., 1993). Moreover, testing in a different object recognition task, visual paired comparison (VPC), has yielded results consistent with the literature discussed above.

In the VPC task, like the DNMS task, there is a familiarization phase, followed after a delay by a choice phase in which the previously viewed object is presented along with a novel object. Unlike DNMS, however, in VPC animals passively view visual stimuli, and recognition of the familiar object is inferred when animals spend more time looking at the new object in the choice phase. Although the DNMS and VPC tasks probably involve different cognitive processes related to their distinct response requirements, previous studies have demonstrated that PRh damage causes robust impairments in both of these object recognition tasks (Bachevalier, Nemanic, & Alvarado, 2002; Nemanic, Alvarado, & Bachevalier, 2004). Moreover, HPC damage tends to produce more reliable impairments in VPC compared to DNMS performance (Bachevalier et al., 2002), but the deficit caused by HPC lesions in VPC are still milder than those produced by PRh damage (Nemanic et al., 2004). These findings further emphasize the crucial role for PRh and the apparently secondary involvement of the HPC in object memory processing.

Thus, the data from non-human primate research are highly suggestive of heterogeneity of function within the MTL, whereby specific information processing functions are mediated relatively independently by certain MTL regions. Specifically, whereas the HPC and other MTL areas are clearly important for other aspects of mnemonic function (Squire, Stark, & Clark, 2004), damage to PRh consistently produces robust object recognition memory deficits. Indeed, it is very likely that these structures interact in the service of cognitive tasks requiring the integration of specific information types (Bussey & Aggleton, 2002). This view implies that the qualitative nature of amnesia produced by MTL damage in humans will depend on the specific MTL structures affected. The rodent studies reviewed below further support the idea of functional specialization and cooperation between distinct MTL regions.

3. Rodent object recognition studies support and extend the findings from non-human primates

While the introduction of the DNMS paradigm for non-human primates was an important development for the study of the neural bases of memory, perhaps equally important was the adaptation of this task for use with rats. The development of several rodent versions of the DNMS task (Aggleton, 1985; Kesner, Bolland, & Dakis, 1993; Mumby, Pinel, & Wood, 1990; Rothblat & Hayes, 1987) made it possible for many more researchers to study the neurobiological bases of object memory because of the relative availability of rats as experimental subjects. Thus, analogous studies can be run with much larger numbers of subjects than is typically possible when using non-human primates.

Several variations of rodent DNMS have appeared in the literature, but the version most closely resembling non-human primate DNMS was developed by Mumby and colleagues (Mumby et al., 1990). This task is run in a specially designed runway apparatus, which contains two goal areas separated from the central start area by guillotine doors. Rats are released from the start area into one of the goal areas, where they must displace the sample object to retrieve a food reward from a recessed well. The sample object is then removed for the duration of the variable retention interval (typically 15–600 s), at the end of which the rat is given access to the other goal area where the sample object and a novel object are now located. Rats must displace the novel object to receive food reward. The rat can then return to the central start area for the commencement of the next trial. This rat DNMS task is typically run with several daily sessions consisting of many discrete trials per session. The object stimuli are similar in nature to the 'junk' objects used in the standard monkey version of the task and, as with the monkey version, stimuli are usually presented in a pseudo-trial-unique manner. Thus, large sets of objects are used, and individual objects are not repeated within a session, although they can recur in later sessions. It is assumed that this procedure involves similar recognition processes as those required by truly trial-unique methods (Mumby, 2001), but it must be noted that responses on trials in which objects are repeated may be mediated by recency judgements rather than absolute familiarity.

Consistent with results from non-human primates, rats with combined entorhinal and PRh cortex damage or inactivation were impaired in a delay-dependent manner on the DNMS task (Barnes, Floresco, Kornecook, & Pinel, 2000; Mumby & Pinel, 1994). Moreover, adding amygdala damage to rhinal cortex lesions did not exacerbate the DNMS deficit (Mumby & Pinel, 1994), consistent with the findings reviewed above that suggest minimal involvement of the amygdala in object recognition memory. Bilateral HPC damage or combined bilateral lesions of the HPC and amygdala have been found to produce DNMS deficits in rats (Mumby, Pinel, Kornecook, & Redila, 1995; Mumby et al., 1996; Mumby, Wood, & Pinel, 1992), but these effects are considerably milder than those seen following rhinal cortex damage, and in some cases this impairment may be related to extrahippocampal brain dysfunction (Mumby, 2001).

An alternative to the DNMS paradigm for rodents is the simpler spontaneous object recognition (SOR) task, which is based on the fact that normal rats will preferentially explore novel rather than familiar objects (Ennaceur & Delacour, 1988), and which is a rodent analogue of the primate VPC task introduced above. The SOR task is commonly carried out in an open field arena, although recent studies have employed a Y-shaped apparatus in attempts to study object recognition memory while minimising the influence of spatial or contextual factors (Forwood, Winters, & Bussey, 2005; Winters, Forwood, Cowell, Saksida, & Bussey, 2004). Regardless of the testing apparatus, the general procedure resembles the following in most studies. Rats are commonly run in several SOR trials, each of which consists of sample and choice phases separated by a variable retention interval. The number and length of the sample phases varies across studies, but each of these generally involves the introduction of the rat into the testing apparatus, which contains two identical junk objects. The rat is allowed to explore the sample objects for a limited amount of time before being removed from the apparatus. At the end of the retention interval, the rat is reintroduced to the apparatus, which now contains a triplicate copy of the sample object and a novel object, which the rat has never explored. Normal rats typically explore the novel object significantly more than the sample object in the choice phase, and this behaviour is assumed to indicate that the sample object is familiar to the rat.

The SOR task has become a preferred test for object recognition assessment in rodents because of the relative ease with which data can be collected. This task requires no extensive training time because rats perform 'spontaneously' on the basis of natural preference behaviour, whereas the DNMS task requires many sessions of pretraining for the animals to learn the nonmatching rule. Thus, any effects of neurobiological manipulations on SOR performance can generally be interpreted in terms of effects on object memory rather than some aspect of rule application or reference memory. Researchers must be aware, however, of the possibility that certain manipulations might affect rats' natural tendency to explore novel objects rather than their memory for the sample object. Under such conditions, a reduction in novel object preference might be interpreted as a memory deficit when the animals merely no longer display the typical novelty bias. Thus, the use of multiple retention delays to demonstrate, for example, that the detrimental effects of a lesion are delay-dependent, or transient inactivation techniques to disrupt 'offline' processes are important considerations in the assessment of the role of a brain region or system in SOR task performance.

Research using the SOR task in rats has greatly increased our knowledge about the neural underpinnings of object recognition memory. Indeed, lesion studies with the SOR task have supported and extended the findings from monkey and rat DNMS reports, particularly those suggesting functional heterogeneity within the MTL. Rats with excitotoxic lesions of PRh or PRh plus postrhinal cortex show delay-dependent deficits in the SOR task, but perform normally on allocentric spatial memory tasks such as delayed non-matching to position, delayed spatial alternation in the t-maze, and spatial navigation in the Morris water maze (Bussey, Duck, Muir, & Aggleton, 2000; Bussey, Muir, & Aggleton, 1999; Ennaceur, Neave, & Aggleton, 1996). Prompted by findings indicating intact object recognition abilities in animals with HPC damage and the well-established role of HPC in spatial memory, Winters et al. (2004) predicted that a functional double dissociation could be demonstrated between the HPC and PRh if the SOR task were run in such a manner that minimized the contribution of spatial or contextual factors. Indeed, earlier findings had hinted at such a double dissociation, but these studies had looked at the effects of fornix lesions rather than direct damage to the HPC (Bussey et al., 2000; Ennaceur et al., 1996). Nonetheless, in general the results of these studies had indicated that PRh lesions disrupted SOR performance with no effects on spatial memory, whereas fornix lesions, which would be expected to disrupt HPC functioning, produced the opposite pattern of effects.

This functional double dissociation between MTL structures was confirmed by Winters et al. (2004), who compared the effects of excitotoxic lesions of the HPC and PRh plus postrhinal cortex (PPRh) on object recognition memory in the SOR task and allocentric spatial memory in the radial arm maze. Critically, the SOR task was run in a Y-shaped apparatus with high opaque white walls and a ceiling; this apparatus was designed to prevent the influence of spatial or contextual information on SOR task performance and thereby minimize the possibility that the HPC would be involved in object encoding or retrieval. It had previously been suggested that the HPC might be recruited when spatial factors become relevant to task performance (Aggleton & Brown, 1999; Bussey & Aggleton, 2002; Cassaday & Rawlins, 1997; Gaffan, 1994; Nadel, 1995; Zola et al., 2000), and we hypothesized that this could explain why hippocampal system damage sometimes caused memory deficits in DNMS or SOR tasks. The results supported this view and demonstrated a clear functional double dissociation between MTL regions, as rats with PPRh damage displayed a delay-dependent impairment in the SOR task and intact spatial memory, whereas the HPC-lesioned animals were severely impaired in the radial arm maze but performed as well as control rats in the SOR task with retention intervals as long as 24 h.

Previous reports of spared object recognition function following HPC lesions in monkeys (e.g. Murray & Mishkin, 1998) have been criticized on the basis that these studies involved extensive pretraining that might mask any impairment in the DNMS task (Zola et al., 2000). Although it could be argued that, if anything, more extensive pretraining would only serve to minimize task confounds such as performance of the rule or resilience to changing task conditions, the Winters et al. (2004) study escapes this completely because of the absence of pretraining involved in the SOR task. Moreover, subsequent studies have gone on to show further instances of intact object recognition memory following HPC damage with longer retention intervals between the sample and choice phases (Forwood et al., 2005), with one recent report demonstrating intact performance of HPC-lesioned rats following a 3-week retention interval (Mumby, Tremblay, Lecluse, & Lehmann, 2005). In a separate study, the same group reported that PRh lesions significantly disrupted SOR performance with a 3-week retention interval using the same testing procedure (Mumby, Piterkin, Lecluse, & Lehmann, 2007). Thus, the collective findings from rats and non-human primates imply a critical role for PRh, but not the HPC, in object recognition memory. This pattern of results strongly suggests that the structures comprising the putative MTL memory system do not perform identical functions and are not even necessarily required for all aspects of object memory processing.

Consistent with such suggestions, there is a growing body of literature implicating MTL structures such as the PRh and HPC in dissociable aspects of human recognition processes. This work has focused primarily on the apparently distinctive roles of MTL subregions in memory recollection and familiarity-based processes. Specifically, functional imaging and neuropsychological studies have implicated PRh and other temporal lobe cortical areas in familiarity-based recognition processes (Bowles et al., 2007; Montaldi, Spencer, Roberts, & Mayes, 2006; Ranganath et al., 2004), which are thought to be relatively automatic and lacking in contextual detail (Eichenbaum et al., 2007; Yonelinas, 2001). Conversely, HPC and posterior parahippocampal cortex appear to be more sensitive to processing involved in contextually rich recollective aspects of recognition memory (Montaldi et al., 2006; Ranganath et al., 2004). Such dissociations from the human literature have been put forth to support dual-process accounts of MTL involvement in recognition memory (Brown & Aggleton, 2001; Eichenbaum et al., 2007), and recent elegant studies in rats have yielded findings consistent with a selective role for the HPC in recollection, but not familiarity (Fortin, Wright, & Eichenbaum, 2004; Sauvage, Fortin, Owens, Yonelinas, & Eichenbaum, 2008). An alternative account has, however, been proposed, which suggests that recollection and familiarity signals are found in both the HPC and PRh and that methods commonly used to differentiate between recollection and familiarity actually distinguish between strong and weak memories (Squire et al., 2007). While a detailed assessment of this issue is beyond the scope of this review, the fact that data exist from human subjects to suggest such functional dissociations between MTL structures further highlights the complexity and multifaceted nature of human memory as something that must be borne in mind when considering the results of studies attempting to model aspects of human memory in non-human animals. Moreover, the suggestion by some findings of a specific role for the HPC in recollective processes is highly consistent with findings from non-human research implicating the HPC in spatial and contextual aspects of object information processing, a topic addressed more directly in the following section.

4. What contributions does the HPC make to object recognition processes?

As the foregoing discussion illustrates, there is now ample evidence to support an important role for PRh in object recognition memory. Moreover, although the HPC may be involved in some object recognition tasks, the weight of the evidence suggests that this involvement may be related to something other than the memory for objects *per se*. Despite many findings suggesting a role for the HPC in object recognition processes (Alvarez, Zola-Morgan, & Squire, 1995; Baker & Kim, 2002; Beason-Held et al., 1999; Broadbent, Squire, & Clark, 2004; Clark, West, Zola, & Squire, 2001; Clark, Zola, & Squire, 2000; de Lima, Luft, Roesler, & Schroder, 2006; Gaskin, Tremblay, & Mumby, 2003; Hammond, Tull, & Stackman, 2004; McKee & Squire, 1993; Mumby, Pinel, et al., 1995; Mumby et al., 1992; Nemanic et al., 2004; Pascalis, Hunkin, Holdstock, Isaac, & Mayes, 2004; Prusky, Douglas, Nelson, Shabanpoor, & Sutherland, 2004; Rampon et al., 2000; Rossato et al., 2007; Squire, Zola-Morgan, & Chen, 1988; Zola-Morgan, Squire, & Amaral, 1986; Zola-Morgan, Squire, Rempel, Clower, & Amaral, 1992; Zola et al., 2000), there have been several reports that clearly show no lasting or major object recognition impairments in subjects with HPC

damage (Aggleton, Hunt, & Rawlins, 1986; Bachevalier, Saunders, et al., 1985; Bussey et al., 2000; Cassaday & Rawlins, 1995; Duva et al., 1997; Forwood et al., 2005; Gaffan, 1994; Jackson-Smith, Kesner, & Chiba, 1993; Kesner et al., 1993; Mumby, 2001; Mumby, Gaskin, Glenn, Schramek, & Lehmann, 2002; Mumby, Kornecook, Wood, & Pinel, 1995; Mumby et al., 2005, 1996, 1992; Murray & Mishkin, 1998; Rawlins, Lyford, Seferiades, Deacon, & Cassaday, 1993; Rothblat & Kromer, 1991; Shaw & Aggleton, 1993; Steele & Rawlins, 1993; Winters et al., 2004; Yee & Rawlins, 1994) (for a more extensive review of this literature, see Mumby, 2001). The equivocal nature of the literature, combined with more specific recent analyses (Forwood et al., 2005; Mumby, Gaskin, et al., 2002; O'Brien, Lehmann, Lecluse, & Mumby, 2006; Piterkin, Cole, Cossette, Gaskin, & Mumby, 2008; Winters et al., 2004), suggests that the HPC contributes to the performance of certain object recognition tasks when spatial or contextual information becomes important (Aggleton & Brown, 1999; Bussey & Aggleton, 2002; Eacott & Gaffan, 2005).

The preceding discussion strongly supports the suggestion of functional heterogeneity within the MTL. Nonetheless, as previously noted, there is much reason to believe that the interconnected anatomical regions of the MTL normally interact in the service of complex memory functions. Indeed, it has been previously suggested that one example of such interaction might be in cases requiring integration of object and spatial information (Bussey & Aggleton, 2002). Bussey and colleagues reported evidence in support of this suggestion from a study using a variation on the SOR task that requires recognizing objects in novel spatial locations. In this task, rats explored four objects in an open field. After the sample phase, the rats were removed from the apparatus for a retention delay, followed by a test phase in which the same four objects were presented, but two of the objects were now in different locations. Normal rats preferentially explored the relocated objects compared with the objects that had not been moved, and rats with either peri-plus postrhinal cortex lesions or HPC-disrupting fornix lesions failed to show this discriminative response (Bussey et al., 2000). Similar results have been reported for rats performing in other variants of the SOR task that assess recognition of visuo-spatial combinations (Eacott & Gaffan, 2005; Eacott & Norman, 2004; Norman & Eacott, 2005). Specifically, rats with fornix lesions have been found to be impaired on a putative test of episodic-like memory that taxes recognition of particular objects in specific spatial locations within a given context (Eacott & Norman, 2004). Such findings are consistent with reports from rats and monkeys performing conditional tasks requiring similar integration of object and place information (Bussey, Dias, Amin, Muir, & Aggleton, 2001; Gaffan & Harrison, 1989). Moreover, Gaffan and Parker (1996) reported that lesions producing a putative disconnection between the PRh and fornix in monkeys severely disrupted object-in-place memory. These findings, taken with the vast literature implicating PRh in object information processing and HPC in spatial memory functions, suggest that PRh provides object information, whereas the HPC mediates spatial aspects of such tasks.

Further recent evidence in support of a role for the HPC specifically in spatial or contextual aspects of object processing come from the work of Mumby and colleagues. In one recent study, Mumby et al. (2002a) assessed the role of the HPC in SOR and two analogous tests of spatial and contextual memory. All three tests were based on spontaneous preference for novel stimulus conditions with the only difference being the nature of the stimuli being changed from the sample to the choice phase. Rats with HPC lesions showed normal preference for novel objects compared to familiar objects, but failed to show similar responses when familiar objects were presented in novel locations or different contexts. These findings indicate that the HPC, although not important for object-specific memory, plays a role in memory for the spatial or contextual aspects of a learning episode, including where an object was previously encountered (Mumby, Gaskin, et al., 2002; O'Brien et al., 2006). A subsequent study replicated and extended this finding by showing that HPC-lesioned rats selectively failed to recognize familiar objects in changed contexts when distal contextual features were altered from sample to test phase, but not when the contextual change involved only proximal, 'local' cues (Piterkin et al., 2008). These results suggest that the HPC lesion-induced impairment was not one of context representation *per se*, nor a general inability to recognize familiar objects, but rather a deficit in recognizing familiar objects when they are presented in different contexts (O'Brien et al., 2006). Although further research is required, these findings imply a subtle, but possibly important role for the HPC in object information processing.

The foregoing results highlight the fact that laboratory-based memory tasks vary in the extent to which spatial and object information are required for their solution. Well-controlled studies of object recognition memory have devised methods to minimize the contribution of spatial or contextual factors to task performance, thereby revealing the fact that the HPC is not necessary for all aspects of object memory. Nonetheless, normal everyday episodic memories are generally more complex than this, requiring the integration of multimodal information. It is the interaction between MTL structures, such as that between HPC and PRh highlighted here, which likely underlies our ability to store and recall such complex memories. These findings together strongly support the suggestion made earlier that MTL structures, although capable of functioning independently, necessarily interact in the mediation of certain types of information processing [see Warburton and Brown, this issue, for a comprehensive consideration of this topic]. This pattern of independence and interaction within the MTL implies that the nature of amnesia resulting from MTL damage in a given patient will depend on the specific MTL structures affected and the normal information processing roles of these structures.

5. The utility of transient manipulations in animal object recognition research: memory acquisition, consolidation, or retrieval?

Medial temporal lobe amnesia typically results from permanent damage to structures such as the HPC and PRh. Studies of patients with such damage have revealed much about the anatomical basis of human memory, and animal models such as those discussed above echo and extend these findings. The animal models of MTL amnesia discussed thus far have primarily examined the effects of permanent MTL damage in tests of object recognition memory. In addition to the enhanced control over the localization of brain damage afforded by animal research, studies with monkeys and, particularly, rats can also be done in ways that provide greatly increased temporal resolution. Transient intracranial manipulations can be employed to study the specific phases of memory storage that could be affected by MTL dysfunction. Indeed, a continuing debate concerns the specific nature of the amnesic syndrome and whether MTL damage causes deficits primarily in memory storage or retrieval (Kopelman, 2002). Recent studies with rats have provided insight into this issue by showing that transient disruption of PRh function can interfere with the acquisition, consolidation, and retrieval of memory for objects.

In one recent study, temporary inactivation of PRh was induced by intracranial infusion of the sodium channel blocker lidocaine during the sample phase, the retention interval, or the choice phase to assess the role of this MTL region in object memory acquisition, consolidation/storage, and retrieval, respectively (Winters & Bussey, 2005b). Intra-PRh infusions of lidocaine immediately before the sample phase significantly impaired object recognition

memory, a result consistent with a role for PRh in acquisition of the object memory. It remains unclear, however, whether this effect should be interpreted as an impairment in memory acquisition or consolidation because the action of lidocaine would be expected to last anywhere from 10 to 20 min (Boeijinga, Mulder, Pennartz, Manshanden, & Lopes da Silva, 1993; Seamans & Phillips, 1994); thus, PRh neuronal activity would likely be affected during the early part of the retention delay even in the pre-sample infusion condition. Similar results implicating PRh in object memory acquisition, however, have been reported following more selective temporary blockade of glutamatergic receptors in PRh during the sample phase of the SOR task (Barker et al., 2006; Winters & Bussey, 2005a), and the apparent involvement of PRh in object memory acquisition is consistent with a growing body of literature implicating PRh in object identification and perceptual representation (Bartko, Winters, Cowell, Saksida, & Bussey, 2007a; Buckley, Booth, Rolls, & Gaffan, 2001; Buckley & Gaffan, 1997; Bussey & Saksida, 2002; Bussey, Saksida, & Murray, 2002a, 2002b, 2003; Eacott, Machin, & Gaffan, 2001; Murray & Bussey, 1999; Murray, Bussey, & Saksida, 2007; Saksida, Bussey, Buckmaster, & Murray, 2007) [see Bussey and Saksida review in this issue]. The possible involvement of PRh in object memory acquisition suggests that at least part of the mnemonic deficit observed in cases of MTL amnesia may be related to dysfunctional memory storage processes.

Consistent with this suggestion, a second finding from the Winters and Bussey (2005b) study showed that PRh inactivation within the retention delay also disrupted object recognition memory. Specifically, intra-PRh lidocaine administered immediately or up to 20 min following the end of the sample phase disrupted object recognition memory, whereas inactivation at 40, 60, or 80 min after the sample phase did not cause impairments. This result is further supported by other subsequent studies showing that blockade of AMPA or NMDA glutamate receptors immediately following the sample phase also caused severe object recognition deficits (Abe, Ishida, & Iwasaki, 2004; Winters & Bussey, 2005a). These findings suggest that PRh function is required for maintenance and consolidation of the object memory for long-term storage. These studies provide further evidence for a memory storage capacity of MTL structures. In this case, there is evidence for MTL involvement in storage processes that continue after the stimulus material is no longer present.

Finally, Winters and Bussey (2005b) showed that PRh inactivation during the choice phase also disrupted object recognition memory performance in the SOR task, indicating a role for this MTL structure in memory retrieval. Other studies have likewise indicated a role for PRh in object memory retrieval processes (Hannesson, Howland, & Phillips, 2004; Mumby, Glenn, Nesbitt, & Kyriazis, 2002b; Winters & Bussey, 2005a). This is perhaps not surprising if, as the foregoing data suggest, the sample object representation is stored in PRh for long-term maintenance.

In all, this pattern of results suggests that certain MTL structures, such as PRh, are involved in multiple aspects of memory processing. These results have important implications for human MTL amnesia as they suggest that the question may not be a matter of whether storage or retrieval processes are impaired, but rather the extent to which all of these processes are affected by the particular pattern of brain damage and the resultant combined effect on information processing.

6. Representational hierarchy in the MTL: findings with animal models and implications for human amnesia

The research just reviewed indicates that PRh is involved in object memory encoding, consolidation, and retrieval. This pattern of findings mirrors those implicating the HPC in multiple stages of learning and memory tasks involving spatial information processing (Day, Langston, & Morris, 2003; Riedel et al., 1999). Consistent with such results, several researchers have recently posited that MTL structures such as the HPC and PRh contribute to particular cognitive functions on the basis of the types of information these regions are specialized to represent (Bussey & Saksida, 2007; Gaffan, 2002; Murray & Bussey, 1999; Murray et al., 2007; Winters et al., 2004). So, for example, the HPC receives a great deal of highly processed multimodal information, and this anatomical characteristic may render it more capable of representing information about the spatial relationships between stimuli (Eichenbaum, Otto, & Cohen, 1994; O'Keefe & Nadel, 1978). This would help to explain the role of HPC in spatial aspects of various memory tasks as reviewed above. Furthermore, PRh has been conceptualized as an anatomical extension of the ventral visual object processing stream (Bussey & Saksida, 2007; Murray & Bussey, 1999; Murray et al., 2007), which consists of several cortical regions that contain hierarchically organized visual representations (Ungerleider & Mishkin, 1982). In this view, PRh, which is located at the most rostral extent of the ventral visual stream, stores representations of complex conjunctions of features the likes of which make up 'real world' objects. Thus, PRh could be expected to contribute importantly not only to object memory, but object perception functions as well (Murray & Bussey, 1999; Murray et al., 2007). This hierarchical-representational view is consistent with the findings reviewed above indicating that disruption of PRh function impairs object recognition memory in rats when carried out during any of the encoding, consolidation, or storage stages of the SOR task (Winters & Bussey, 2005b). Moreover, recent human research has implicated PRh in the processing of multimodal object information (Holdstock, Hocking, Notley, Devlin, & Price, 2009; Taylor, Moss, Stamatakis, & Tyler, 2006), and several recent findings from rats, non-human primates, and humans implicate PRh and HPC in perceptual processing of object and spatial information, respectively (Barense et al., 2005; Barense, Gaffan, & Graham, 2007; Bartko et al., 2007a; Bartko, Winters, Cowell, Saksida, & Bussey, 2007b; Buckley et al., 2001; Buckley & Gaffan, 1997; Bussey et al., 2002a, 2003; Eacott et al., 2001; Lee, Buckley, et al., 2005; Lee, Bussey, et al., 2005; Saksida et al., 2007) [see Bussey and Saksida review in this issue]. These results provide still more support for the view that PRh is specifically involved in aspects of object representation, whereas the HPC is important for mediating spatial cognition.

The hierarchical-representational account of MTL function has potentially important implications for human amnesia. Specifically, this view, and data in support of its suggestion that certain MTL regions may have important roles in perception and memory by virtue of their representational capacities, may help to elucidate the specific nature of cognitive deficits in cases of MTL amnesia. Indeed, a longstanding focus in amnesia research concerns the possibility that brain damage can cause increased susceptibility to interference and that this enhanced interference can account for observed memory deficits (Kopelman, 2002; Warrington & Weiskrantz, 1970). This theoretical issue is closely linked to the use of interference procedures in research addressing another related question: is the principal deficit in amnesia one of memory storage or memory retrieval? The hierarchical-representational account, however, suggests that these two explanations need not be mutually exclusive. For example, the perceptual-mnemonic feature conjunction (PMFC) model (Bussey & Saksida, 2002), which is a connectionist model formalization of the hierarchical-representational view, accounts for object memory deficits in terms of compromised conjunctive object representations resulting from PRh damage. According to the model, PRh damage leaves only lower level ('feature') representations intact, and these features alone are often insufficient to overcome interference from similar, incidentally encountered visual stimuli (Cowell, Bussey, & Saksida, 2006). Thus,

in the case of PRh damage, delay-dependent object memory deficits could be explained in terms of compromised storage *and* retrieval mechanisms resulting from incomplete or absent object-level conjunctive representations and interference from stimuli that are perceptually similar to the task-relevant objects.

A recent study tested this hypothesis explicitly (S.J. Bartko, R.A. Cowell, B.D. Winters, L.M. Saksida, T.J. Bussey, unpublished observations). Rats with PRh damage were assessed for their sensitivity to object interference in the SOR task. Animals were exposed to a task-irrelevant object either before or after the regular sample phase in the SOR task. The nature of the interpolated object was also manipulated such that on some trials the object was very similar to the sample object, whereas on other trials there was very little perceptual similarity. Rats with PRh damage showed enhanced susceptibility to interference, both proactively and retroactively, only when the interpolated object was perceptually similar to the to-be-remembered sample object. This finding suggests that susceptibility to interference is likely an important aspect of MTL amnesia, and this is probably closely related to the hierarchical nature of stimulus representation throughout the ventral visual–perirhinal–hippocampal stream (Bussey & Saksida, 2007).

According to the hierarchical–representational view, the representation of an object is distributed throughout this object processing stream, with object features stored caudally and object representations consisting of conjunctions of these features stored rostrally in PRh. Thus, damage to an area such as PRh affects only part of the representation of an object. Furthermore, because only part of the object representation is disrupted following PRh damage, the hierarchical–representational approach provides an explanation of increased interference in amnesia in terms of combined storage and retrieval deficits. That is, damage to PRh disrupts the encoding and storage of a conjunctive object representation that could normally be used to resolve feature ambiguity and interference from other similar information. The absence of this complex representation leads to a retrieval deficit because the animal has access only to simple feature-based information stored in more caudal regions, and these features are highly likely to be shared between task-relevant and interfering object stimuli. This explanation is also consistent with data discussed above that show object recognition impairments caused by PRh disruption during encoding, consolidation, or retrieval stages of the SOR task. Systematic studies in animals and humans will be required to determine if similar principles apply to other MTL regions such as the HPC, but recent findings suggest that this may well be the case (Lee, Buckley, et al., 2005; Lee, Bussey, et al., 2005) [see Bussey and Saksida review in this issue].

7. Conclusion

Animal object recognition tests emerged from attempts to model 'global' human amnesia. Beginning with the introduction in the 1970s of trial-unique versions of monkey DNMS tasks up to the continued use of these and similar tasks in non-human primates and rodents in the present day, animal models of object amnesia have provided great insight into the neural bases of human memory and amnesia. Over time, however, systematic analyses have indicated that object recognition impairments caused by damage to specific regions of the MTL comprise only a portion of the amnesic syndrome often observed in brain-damaged humans. Indeed, animal research on object recognition is no longer viewed as an accurate means to study 'global' human amnesia, but rather a specific aspect of the amnesic syndrome. The literature reviewed in the current article strongly supports this conceptual shift. Research using animal object recognition tasks such as DNMS and SOR, while unable to provide a comprehensive understanding of the human amnesic syndrome, nonetheless is highly valuable in providing animal models for the study of specific facets of human memory. Object recognition memory comprises just one aspect of the complex and multimodal cognitive function that is human declarative memory, but the ability to study such a complex process in piecemeal fashion is one of the strengths of such animal models. Indeed, animal research with object recognition tasks has revealed much about the anatomical, cellular, and molecular bases of object recognition memory (Winters, Saksida, & Bussey, 2008), and these mechanisms likely generalize to other aspects of declarative memory processes. Perhaps one of the most important implications of the literature reviewed herein is that the structures of the MTL contribute to memory processes heterogeneously. Animal object memory research has revealed that PRh plays a critical role in object memory acquisition, storage, and retrieval, whereas the HPC is involved in very different aspects of object processing, primarily in terms of how objects relate to contextual and spatial information. Such findings from animal object memory research indicate that different aspects of the complex cognitive function of declarative memory may be disrupted depending on the locus of brain damage. This may, in fact, be the most important contribution to date of animal research with regard to our understanding of human amnesia: revealing functional independence and interactivity between MTL structures and shining a light on the possibility that these (and other) brain regions participate in specific aspects of memory processing not because they belong to memory-specific modules, but rather because of the types of information they optimally represent [see Bussey and Saksida review in this issue].

References

Abe, H., Ishida, Y., & Iwasaki, T. (2004). Perirhinal N-methyl-D-aspartate and muscarinic systems participate in object recognition in rats. *Neuroscience Letters*, *356*, 191–194.

Aggleton, J. P. (1985). One-trial object recognition by rats. *Quarterly Journal of Experimental Psychology*, *37B*, 279–294.

Aggleton, J. P., & Brown, M. W. (1999). Episodic memory, amnesia, and the hippocampal-anterior thalamic axis. *Behavioral and Brain Sciences*, *22*, 425–444.

Aggleton, J. P., Hunt, P. R., & Rawlins, J. N. (1986). The effects of hippocampal lesions upon spatial and non-spatial tests of working memory. *Behavioural Brain Research*, *19*, 133–146.

Alvarez, P., Zola-Morgan, S., & Squire, L. R. (1995). Damage limited to the hippocampal region produces long-lasting memory impairment in monkeys. *Journal of Neuroscience*, *15*, 3796–3807.

Bachevalier, J., Nemanic, S., & Alvarado, M. C. (2002). The medial temporal lobe structures and object recognition memory in nonhuman primates. In L. R. Squire, & D. L. Schacter (Eds.), *Neuropsychology of memory* (pp. 326–338). New York: Guilford.

Bachevalier, J., Parkinson, J. K., & Mishkin, M. (1985). Visual recognition in monkeys: effects of separate vs. combined transection of fornix and amygdalofugal pathways. *Experimental Brain Research*, *57*, 554–561.

Bachevalier, J., Saunders, R. C., & Mishkin, M. (1985). Visual recognition in monkeys: effects of transection of fornix. *Experimental Brain Research*, *57*, 547–553.

Baker, K. B., & Kim, J. J. (2002). Effects of stress and hippocampal NMDA receptor antagonism on recognition memory in rats. *Learning and Memory*, *9*, 58–65.

Barense, M. D., Bussey, T. J., Lee, A. C., Rogers, T. T., Davies, R. R., Saksida, L. M., Murray, E. A., & Graham, K. S. (2005). Functional specialization in the human medial temporal lobe. *Journal of Neuroscience*, *25*, 10239–10246.

Barense, M. D., Gaffan, D., & Graham, K. S. (2007). The human medial temporal lobe processes online representations of complex objects. *Neuropsychologia*, *45*, 2963–2974.

Barker, G. R., Warburton, E. C., Koder, T., Dolman, N. P., More, J. C., Aggleton, J. P., Bashir, Z. I., Auberson, Y. P., Jane, D. E., & Brown, M. W. (2006). The different effects on recognition memory of perirhinal kainate and NMDA glutamate receptor antagonism: implications for underlying plasticity mechanisms. *Journal of Neuroscience*, *26*, 3561–3566.

Barnes, S. J., Floresco, S. B., Kornecook, T. J., & Pinel, J. P. (2000). Reversible lesions of the rhinal cortex produce delayed non-matching-to-sample deficits in rats. *Neuroreport*, *11*, 351–354.

Bartko, S. J., Winters, B. D., Cowell, R. A., Saksida, L. M., & Bussey, T. J. (2007a). Perceptual functions of perirhinal cortex in rats: zero-delay object recognition and simultaneous oddity discriminations. *Journal of Neuroscience*, *27*, 2548–2559.

Bartko, S. J., Winters, B. D., Cowell, R. A., Saksida, L. M., & Bussey, T. J. (2007b). Perirhinal cortex resolves feature ambiguity in configural object recognition and perceptual oddity tasks. *Learning and Memory*, *14*, 821–832.

Baxter, M. G., & Murray, E. A. (2001). Opposite relationship of hippocampal and rhinal cortex damage to delayed nonmatching-to-sample deficits in monkeys. *Hippocampus*, *11*, 61–71.

Beason-Held, L. L., Rosene, D. L., Killiany, R. J., & Moss, M. B. (1999). Hippocampal formation lesions produce memory impairment in the rhesus monkey. *Hippocampus*, *9*, 562–574.

Boeijinga, P. H., Mulder, A. B., Pennartz, C. M., Manshanden, I., & Lopes da Silva, F. H. (1993). Responses of the nucleus accumbens following fornix/fimbria stimulation in the rat. Identification and long-term potentiation of mono- and polysynaptic pathways. *Neuroscience*, *53*, 1049–1058.

Bowles, B., Crupi, C., Mirsattari, S. M., Pigott, S. E., Parrent, A. G., Pruessner, J. C., Yonelinas, A. P., & Kohler, S. (2007). Impaired familiarity with preserved recollection after anterior temporal-lobe resection that spares the hippocampus. *Proceedings of the National Academy of Sciences of the United States of America*, *104*, 16382–16387.

Broadbent, N. J., Squire, L. R., & Clark, R. E. (2004). Spatial memory, recognition memory, and the hippocampus. *Proceedings of the National Academy of Sciences of the United States of America*, *101*, 14515–14520.

Brown, M. W., & Aggleton, J. P. (2001). Recognition memory: what are the roles of the perirhinal cortex and hippocampus? *Nature Review Neuroscience*, *2*, 51–61.

Buckley, M. J., Booth, M. C., Rolls, E. T., & Gaffan, D. (2001). Selective perceptual impairments after perirhinal cortex ablation. *Journal of Neuroscience*, *21*, 9824–9836.

Buckley, M. J., & Gaffan, D. (1997). Impairment of visual object-discrimination learning after perirhinal cortex ablation. *Behavioral Neuroscience*, *111*, 467–475.

Buckley, M. J., & Gaffan, D. (1998a). Perirhinal cortex ablation impairs configural learning and paired-associate learning equally. *Neuropsychologia*, *36*, 535–546.

Buckley, M. J., & Gaffan, D. (1998b). Perirhinal cortex ablation impairs visual object identification. *Journal of Neuroscience*, *18*, 2268–2275.

Buffalo, E. A., Ramus, S. J., Clark, R. E., Teng, E., Squire, L. R., & Zola, S. M. (1999). Dissociation between the effects of damage to perirhinal cortex and area TE. *Learning and Memory*, *6*, 572–599.

Buffalo, E. A., Reber, P. J., & Squire, L. R. (1998). The human perirhinal cortex and recognition memory. *Hippocampus*, *8*, 330–339.

Bussey, T. J., & Aggleton, J. P. (2002). The "what" and "where" of event memory: independence and interactivity within the medial temporal lobe. In A. Parker, E. Wilding, & T. J. Bussey (Eds.), *The Cognitive Neuroscience of Memory: Encoding and Retrieval* (pp. 217–233). London: Psychology Press.

Bussey, T. J., Dias, R., Amin, E., Muir, J. L., & Aggleton, J. P. (2001). Perirhinal cortex and place-object conditional learning in the rat. *Behavioral Neuroscience*, *115*, 776–785.

Bussey, T. J., Duck, J., Muir, J. L., & Aggleton, J. P. (2000). Distinct patterns of behavioural impairments resulting from fornix transection or neurotoxic lesions of the perirhinal and postrhinal cortices in the rat. *Behavioural Brain Research*, *111*, 187–202.

Bussey, T. J., Muir, J. L., & Aggleton, J. P. (1999). Functionally dissociating aspects of event memory: the effects of combined perirhinal and postrhinal cortex lesions on object and place memory in the rat. *Journal of Neuroscience*, *19*, 495–502.

Bussey, T. J., & Saksida, L. M. (2002). The organization of visual object representations: a connectionist model of effects of lesions in perirhinal cortex. *European Journal of Neuroscience*, *15*, 355–364.

Bussey, T. J., & Saksida, L. M. (2007). Memory, perception, and the ventral visual-perirhinal-hippocampal stream: thinking outside of the boxes. *Hippocampus*, *17*, 898–908.

Bussey, T. J., Saksida, L. M., & Murray, E. A. (2002a). Perirhinal cortex resolves feature ambiguity in complex visual discriminations. *European Journal of Neuroscience*, *15*, 365–374.

Bussey, T. J., Saksida, L. M., & Murray, E. A. (2002b). The role of perirhinal cortex in memory and perception: conjunctive representations for object identification. In M. P. Witter, & F. G. Wouterlood (Eds.), *The Parahippocampal Region: Organization and Role in Cognitive Functions* (pp. 239–254). Oxford University Press: Oxford.

Bussey, T. J., Saksida, L. M., & Murray, E. A. (2003). Impairments in visual discrimination after perirhinal cortex lesions: testing 'declarative' vs. 'perceptual-mnemonic' views of perirhinal cortex function. *European Journal of Neuroscience*, *17*, 649–660.

Cassaday, H. J., & Rawlins, J. N. (1995). Fornix-fimbria section and working memory deficits in rats: stimulus complexity and stimulus size. *Behavioral Neuroscience*, *109*, 594–606.

Cassaday, H. J., & Rawlins, J. N. (1997). The hippocampus, objects, and their contexts. *Behavioral Neuroscience*, *111*, 1228–1244.

Charles, D. P., Gaffan, D., & Buckley, M. J. (2004). Impaired recency judgments and intact novelty judgments after fornix transection in monkeys. *Journal of Neuroscience*, *24*, 2037–2044.

Clark, R. E., West, A. N., Zola, S. M., & Squire, L. R. (2001). Rats with lesions of the hippocampus are impaired on the delayed nonmatching-to-sample task. *Hippocampus*, *11*, 176–186.

Clark, R. E., Zola, S. M., & Squire, L. R. (2000). Impaired recognition memory in rats after damage to the hippocampus. *Journal of Neuroscience*, *20*, 8853–8860.

Corkin, S. (1968). Acquisition of motor skill after bilateral medial temporal-lobe lesion. *Neuropsychologia*, *6*, 255–265.

Corkin, S. (1984). Lasting consequences of bilateral medial temporal lobectomy: clinical course and experimental findings in H.M. *Journal of Neuroscience*, *2*, 1214–1229.

Corkin, S., Amaral, D. G., Gonzalez, R. G., Johnson, K. A., & Hyman, B. T. (1997). H.M.'s medial temporal lobe lesion: findings from magnetic resonance imaging. *Journal of Neuroscience*, *17*, 3964–3979.

Correll, R. E., & Scoville, W. B. (1965). Performance on delayed match following lesions of medial temporal lobe structures. *Journal of Comparative and Physiological Psychology*, *60*, 360–367.

Cowell, R. A., Bussey, T. J., & Saksida, L. M. (2006). Why does brain damage impair memory? A connectionist model of object recognition memory in perirhinal cortex. *Journal of Neuroscience*, *26*, 12186–12197.

Day, M., Langston, R., & Morris, R. G. (2003). Glutamate-receptor-mediated encoding and retrieval of paired-associate learning. *Nature*, *424*, 205–209.

de Lima, M. N., Luft, T., Roesler, R., & Schroder, N. (2006). Temporary inactivation reveals an essential role of the dorsal hippocampus in consolidation of object recognition memory. *Neuroscience Letters*, *405*, 142–146.

Drachman, D. A., & Arbit, J. (1966). Memory and the hippocampal complex. II: Is memory a multiple process? *Archives of Neurology*, *15*, 52–61.

Duva, C. A., Floresco, S. B., Wunderlich, G. R., Lao, T. L., Pinel, J. P., & Phillips, A. G. (1997). Disruption of spatial but not object-recognition memory by neurotoxic lesions of the dorsal hippocampus in rats. *Behavioral Neuroscience*, *111*, 1184–1196.

Eacott, M. J., Gaffan, D., & Murray, E. A. (1994). Preserved recognition memory for small sets, and impaired stimulus identification for large sets, following rhinal cortex ablations in monkeys. *European Journal of Neuroscience*, *6*, 1466–1478.

Eacott, M. J., & Gaffan, E. A. (2005). The roles of perirhinal cortex, postrhinal cortex, and the fornix in memory for objects, contexts, and events in the rat. *Quarterly Journal of Experimental Psychology B*, *58*, 202–217.

Eacott, M. J., Machin, P. E., & Gaffan, E. A. (2001). Elemental and configural visual discrimination learning following lesions to perirhinal cortex in the rat. *Behavioural Brain Research*, *124*, 55–70.

Eacott, M. J., & Norman, G. (2004). Integrated memory for object, place, and context in rats: a possible model of episodic-like memory? *Journal of Neuroscience*, *24*, 1948–1953.

Eichenbaum, H., Otto, T., & Cohen, N. J. (1994). Two functional components of the hippocampal memory system. *Behavioral Brain Science*, *17*, 449–518.

Eichenbaum, H., Yonelinas, A. P., & Ranganath, C. (2007). The medial temporal lobe and recognition memory. *Annual Review of Neuroscience*, *30*, 123–152.

Ennaceur, A., & Delacour, J. (1988). A new one-trial test for neurobiological studies of memory in rats. 1: Behavioral data. *Behavioural Brain Research*, *31*, 47–59.

Ennaceur, A., Neave, N., & Aggleton, J. P. (1996). Neurotoxic lesions of the perirhinal cortex do not mimic the behavioural effects of fornix transection in the rat. *Behavioural Brain Research*, *80*, 9–25.

Fortin, N. J., Wright, S. P., & Eichenbaum, H. (2004). Recollection-like memory retrieval in rats is dependent on the hippocampus. *Nature*, *431*, 188–191.

Forwood, S. E., Winters, B. D., & Bussey, T. J. (2005). Hippocampal lesions that abolish spatial maze performance spare object recognition memory at delays of up to 48 hours. *Hippocampus*, *15*, 347–355.

Gaffan, D. (1974). Recognition impaired and association intact in the memory of monkeys after transection of the fornix. *Journal of Comparative and Physiological Psychology*, *86*, 1100–1109.

Gaffan, D. (1994). Dissociated effects of perirhinal cortex ablation, fornix transection and amygdalectomy: evidence for multiple memory systems in the primate temporal lobe. *Experimental Brain Research*, *99*, 411–422.

Gaffan, D. (2002). Against memory systems. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences*, *357*, 1111–1121.

Gaffan, D., & Harrison, S. (1989). Place memory and scene memory: Effects of fornix transection in the monkey. *Experimental Brain Research*, *74*, 202–212.

Gaffan, D., & Parker, A. (1996). Interaction of perirhinal cortex with the fornix-fimbria: memory for objects and "object-in-place" memory. *Journal of Neuroscience*, *16*, 5864–5869.

Gaskin, S., Tremblay, A., & Mumby, D. G. (2003). Retrograde and anterograde object recognition in rats with hippocampal lesions. *Hippocampus*, *13*, 962–969.

Hajilou, B. B., & Done, D. J. (2007). Evidence for a dissociation of structural and semantic knowledge in dementia of the Alzheimer type (DAT). *Neuropsychologia*, *45*, 810–816.

Hammond, R. S., Tull, L. E., & Stackman, R. W. (2004). On the delay-dependent involvement of the hippocampus in object recognition memory. *Neurobiology of Learning and Memory*, *82*, 26–34.

Hannesson, D. K., Howland, J. G., & Phillips, A. G. (2004). Interaction between perirhinal and medial prefrontal cortex is required for temporal order but not recognition memory for objects in rats. *Journal of Neuroscience*, *24*, 4596–4604.

Holdstock, J. S. (2005). The role of the human medial temporal lobe in object recognition and object discrimination. *Quarterly Journal of Experimental Psychology B*, *58*, 326–339.

Holdstock, J. S., Hocking, J., Notley, P., Devlin, J. T., & Price, C. J. (2009). Integrating visual and tactile information in the perirhinal cortex. *Cerebral Cortex*, *19*, 2993–3000.

Horel, J. A., Pytko-Joiner, D. E., Voytko, M. L., & Salsbury, K. (1987). The performance of visual tasks while segments of the inferotemporal cortex are suppressed by cold. *Behavioural Brain Research*, *23*, 29–42.

Irle, E., Kessler, J., Markowitsch, H. J., & Hofmann, W. (1987). Primate learning tasks reveal strong impairments in patients with presenile or senile dementia of the Alzheimer type. *Brain and Cognition*, *6*, 429–449.

Jackson-Smith, P., Kesner, R. P., & Chiba, A. A. (1993). Continuous recognition of spatial and nonspatial stimuli in hippocampal-lesioned rats. *Behavioral and Neural Biology*, *59*, 107–119.

Kesner, R. P., Bolland, B. L., & Dakis, M. (1993). Memory for spatial locations, motor responses, and objects: triple dissociation among the hippocampus, caudate nucleus, and extrastriate visual cortex. *Experimental Brain Research*, *93*, 462–470.

Kopelman, M. D. (2002). Disorders of memory. *Brain*, *125*, 2152–2190.

Laatu, S., Revonsuo, A., Jaykka, H., Portin, R., & Rinne, J. O. (2003). Visual object recognition in early Alzheimer's disease: Deficits in semantic processing. *Acta Neurologica Scandinavica*, *108*, 82–89.

Lee, A. C., Buckley, M. J., Pegman, S. J., Spiers, H., Scahill, V. L., Gaffan, D., Bussey, T. J., Davies, R. R., Kapur, N., Hodges, J. R., & Graham, K. S. (2005). Specialization in the medial temporal lobe for processing of objects and scenes. *Hippocampus*, *15*, 782–797.

Lee, A. C., Bussey, T. J., Murray, E. A., Saksida, L. M., Epstein, R. A., Kapur, N., Hodges, J. R., & Graham, K. S. (2005). Perceptual deficits in amnesia: challenging the medial temporal lobe 'mnemonic' view. *Neuropsychologia*, *43*, 1–11.

Lee, A. C., Rahman, S., Hodges, J. R., Sahakian, B. J., & Graham, K. S. (2003). Associative and recognition memory for novel objects in dementia: implications for diagnosis. *European Journal of Neuroscience*, *18*, 1660–1670.

Mahut, H., Zola-Morgan, S., & Moss, M. (1982). Hippocampal resections impair associative learning and recognition memory in the monkey. *Journal of Neuroscience*, *2*, 1214–1220.

Manns, J. R., & Squire, L. R. (1999). Impaired recognition memory on the Doors and People Test after damage limited to the hippocampal region. *Hippocampus*, *9*, 495–499.

McKee, R. D., & Squire, L. R. (1993). On the development of declarative memory. *Journal of Experimental Psychology. Learning, Memory, and Cognition*, *19*, 397–404.

Meunier, M., Bachevalier, J., Mishkin, M., & Murray, E. A. (1993). Effects on visual recognition of combined and separate ablations of the entorhinal and perirhinal cortex in rhesus monkeys. *Journal of Neuroscience*, *13*, 5418–5432.

Milner, B., Corkin, S., & Teuber, H.-L. (1968). Further analysis of the hippocampal amnesic syndrome: 14-year follow-up study of H.M. *Neuropsychologia*, *6*, 215–234.

Mishkin, M. (1978). Memory in monkeys severely impaired by combined but not by separate removal of amygdala and hippocampus. *Nature*, *273*, 297–298.

Mishkin, M., & Delacour, J. (1975). An analysis of short-term visual memory in the monkey. *Journal of Experimental Psychology: Animal Behavior Processes*, *1*, 326–334.

Mishkin, M., & Murray, E. A. (1994). Stimulus recognition. *Current Opinion on Neurobiology*, *4*, 200–206.

Montaldi, D., Spencer, T. J., Roberts, N., & Mayes, A. R. (2006). The neural system that mediates familiarity memory. *Hippocampus*, *16*, 504–520.

Mumby, D. G. (2001). Perspectives on object-recognition memory following hippocampal damage: lessons from studies in rats. *Behavioural Brain Research*, *127*, 159–181.

Mumby, D. G., Gaskin, S., Glenn, M. J., Schramek, T. E., & Lehmann, H. (2002). Hippocampal damage and exploratory preferences in rats: memory for objects, places, and contexts. *Learning and Memory*, *9*, 49–57.

Mumby, D. G., Glenn, M. J., Nesbitt, C., & Kyriazis, D. A. (2002). Dissociation in retrograde memory for object discriminations and object recognition in rats with perirhinal cortex damage. *Behavioural Brain Research*, *132*, 215–226.

Mumby, D. G., Kornecook, T. J., Wood, E. R., & Pinel, J. P. J. (1995). The role of experimenter-odor cues in the performance of object-memory tasks by rats. *Animal Learning and Behavior*, *23*, 447–453.

Mumby, D. G., & Pinel, J. P. (1994). Rhinal cortex lesions and object recognition in rats. *Behavioral Neuroscience*, *108*, 11–18.

Mumby, D. G., Pinel, J. P., & Wood, E. R. (1990). Nonrecurring-items delayed nonmatching-to-sample in rats: a new paradigm for testing non-spatial working memory. *Psychobiology*, *18*, 321–326.

Mumby, D. G., Pinel, J. P. J., Kornecook, T. J. M. J. S., & Redila, V. A. (1995). Memory deficits following lesions of hippocampus or amygdala in rat: assessment by an object-memory test battery. *Psychobiology*, *23*, 26–36.

Mumby, D. G., Piterkin, P., Lecluse, V., & Lehmann, H. (2007). Perirhinal cortex damage and anterograde object-recognition in rats after long retention intervals. *Behavioural Brain Research*, *185*, 82–87.

Mumby, D. G., Tremblay, A., Lecluse, V., & Lehmann, H. (2005). Hippocampal damage and anterograde object-recognition in rats after long retention intervals. *Hippocampus*, *15*, 1050–1056.

Mumby, D. G., Wood, E. R., Duva, C. A., Kornecook, T. J., Pinel, J. P., & Phillips, A. G. (1996). Ischemia-induced object-recognition deficits in rats are attenuated by hippocampal ablation before or soon after ischemia. *Behavioral Neuroscience*, *110*, 266–281.

Mumby, D. G., Wood, E. R., & Pinel, J. P. J. (1992). Object recognition memory is only mildly impaired in rats with lesions of the hippocampus and amygdala. *Psychobiology*, *20*, 18–27.

Murray, E. A., & Bussey, T. J. (1999). Perceptual-mnemonic functions of the perirhinal cortex. *Trends in Cognitive Science*, *3*, 142–151.

Murray, E. A., Bussey, T. J., Hampton, R. R., & Saksida, L. M. (2000). The parahippocampal region and object identification. *Annals of the New York Academy of Sciences*, *911*, 166–174.

Murray, E. A., Bussey, T. J., & Saksida, L. M. (2007). Visual perception and memory: A new view of medial temporal lobe function in primates and rodents. *Annual Review of Neuroscience*, *30*, 99–122.

Murray, E. A., & Mishkin, M. (1984). Severe tactual as well as visual memory deficits follow combined removal of the amygdala and hippocampus in monkeys. *Journal of Neuroscience*, *4*, 2565–2580.

Murray, E. A., & Mishkin, M. (1986). Visual recognition in monkeys following rhinal cortical ablations combined with either amygdalectomy or hippocampectomy. *Journal of Neuroscience*, *6*, 1991–2003.

Murray, E. A., & Mishkin, M. (1998). Object recognition and location memory in monkeys with excitotoxic lesions of the amygdala and hippocampus. *Journal of Neuroscience*, *18*, 6568–6582.

Nadel, L. (1995). The role of the hippocampus in declarative memory: a comment on Zola-Morgan, Squire, and Ramus (1994). *Hippocampus*, *5*, 232–239.

Nemanic, S., Alvarado, M. C., & Bachevalier, J. (2004). The hippocampal/parahippocampal regions and recognition memory: insights from visual paired comparison versus object-delayed nonmatching in monkeys. *Journal of Neuroscience*, *24*, 2013–2026.

Norman, G., & Eacott, M. J. (2005). Dissociable effects of lesions to the perirhinal cortex and the postrhinal cortex on memory for context and objects in rats. *Behavioral Neuroscience*, *119*, 557–566.

O'Brien, N., Lehmann, H., Lecluse, V., & Mumby, D. G. (2006). Enhanced context-dependency of object recognition in rats with hippocampal lesions. *Behavioural Brain Research*, *170*, 156–162.

O'Keefe, J., & Nadel, L. (1978). *The Hippocampus as a Cognitive Map*. Oxford: Oxford University Press.

Ogura, H., & Aigner, T. G. (1993). MK-801 impairs recognition memory in rhesus monkeys: comparison with cholinergic drugs. *Journal of Pharmacology and Experimental Therapeutics*, *266*, 60–64.

Owen, M. J., & Butler, S. R. (1984). Does amnesia after transection of the fornix in monkeys reflect abnormal sensitivity to proactive interference? *Behavioural Brain Research*, *14*, 183–192.

Parker, A., Eacott, M. J., & Gaffan, D. (1997). The recognition memory deficit caused by mediodorsal thalamic lesion in non-human primates: a comparison with rhinal cortex lesion. *European Journal of Neuroscience*, *9*, 2423–2431.

Parker, A., & Gaffan, D. (1998). Interaction of frontal and perirhinal cortices in visual object recognition memory in monkeys. *European Journal of Neuroscience*, *10*, 3044–3057.

Pascalis, O., Hunkin, N. M., Holdstock, J. S., Isaac, C. L., & Mayes, A. R. (2004). Visual paired comparison performance is impaired in a patient with selective hippocampal lesions and relatively intact item recognition. *Neuropsychologia*, *42*, 1293–1300.

Piterkin, P., Cole, E., Cossette, M. P., Gaskin, S., & Mumby, D. G. (2008). A limited role for the hippocampus in the modulation of novel-object preference by contextual cues. *Learning and Memory*, *15*, 785–791.

Prusky, G. T., Douglas, R. M., Nelson, L., Shabanpoor, A., & Sutherland, R. J. (2004). Visual memory task for rats reveals an essential role for hippocampus and perirhinal cortex. *Proceedings of the National Academy of Sciences of the United States of America*, *101*, 5064–5068.

Purdy, K. S., McMullen, P. A., & Freedman, M. (2002). Changes to the object recognition system in patients with dementia of the Alzheimer's type. *Brain and Cognition*, *49*, 213–216.

Rampon, C., Tang, Y. P., Goodhouse, J., Shimizu, E., Kyin, M., & Tsien, J. Z. (2000). Enrichment induces structural changes and recovery from nonspatial memory deficits in CA1 NMDAR1-knockout mice. *Nature Neuroscience*, *3*, 238–244.

Ranganath, C., Yonelinas, A. P., Cohen, M. X., Dy, C. J., Tom, S. M., & D'Esposito, M. (2004). Dissociable correlates of recollection and familiarity within the medial temporal lobes. *Neuropsychologia*, *42*, 2–13.

Rawlins, J. N., Lyford, G. L., Seferiades, A., Deacon, R. M., & Cassaday, H. J. (1993). Critical determinants of nonspatial working memory deficits in rats with conventional lesions of the hippocampus or fornix. *Behavioral Neuroscience*, *107*, 420–433.

Reed, J. M., & Squire, L. R. (1997). Impaired recognition memory in patients with lesions limited to the hippocampal formation. *Behavioral Neuroscience*, *111*, 667–675.

Riedel, G., Micheau, J., Lam, A. G., Roloff, E., Martin, S. J., Bridge, H., Hoz, L., Poeschel, B., McCulloch, J., & Morris, R. G. M. (1999). Reversible neural inactivation reveals hippocampal participation in several memory processes. *Nature Neuroscience*, *2*, 898–905.

Rossato, J. I., Bevilaqua, L. R., Myskiw, J. C., Medina, J. H., Izquierdo, I., & Cammarota, M. (2007). On the role of hippocampal protein synthesis in the consolidation and reconsolidation of object recognition memory. *Learning and Memory*, *14*, 36–46.

Rothblat, L. A., & Hayes, L. L. (1987). Short-term object recognition memory in the rat: nonmatching with trial-unique junk stimuli. *Behavioral Neuroscience*, *101*, 587–590.

Rothblat, L. A., & Kromer, L. F. (1991). Object recognition memory in the rat: the role of the hippocampus. *Behavioural Brain Research*, *42*, 25–32.

Saksida, L. M., Bussey, T. J., Buckmaster, C. A., & Murray, E. A. (2007). Impairment and facilitation of transverse patterning after lesions of the perirhinal cortex and hippocampus, respectively. *Cerebral Cortex*, *17*, 108–115.

Saunders, R. C., Murray, E. A., & Mishkin, M. (1984). Further evidence that amygdala and hippocampus contribute equally to recognition memory. *Neuropsychologia*, *22*, 785–796.

Sauvage, M. M., Fortin, N. J., Owens, C. B., Yonelinas, A. P., & Eichenbaum, H. (2008). Recognition memory: opposite effects of hippocampal damage on recollection and familiarity. *Nature Neuroscience*, *11*, 16–18.

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

Seamans, J. K., & Phillips, A. G. (1994). Selective memory impairments produced by transient lidocaine-induced lesions of the nucleus accumbens in rats. *Behavioral Neuroscience*, *108*, 456–468.

Shaw, C., & Aggleton, J. P. (1993). The effects of fornix and medial prefrontal lesions on delayed non-matching-to-sample by rats. *Behavioural Brain Research*, *54*, 91–102.

Squire, L. R. (2009). The legacy of patient H.M. for neuroscience. *Neuron*, *61*, 6–9.

Squire, L. R., Stark, C. E., & Clark, R. E. (2004). The medial temporal lobe. *Annual Review of Neuroscience*, *27*, 279–306.

Squire, L. R., Wixted, J. T., & Clark, R. E. (2007). Recognition memory and the medial temporal lobe: a new perspective. *Nature Review Neuroscience*, *8*, 872–883.
Squire, L. R., & Zola-Morgan, S. (1988). Memory: brain systems and behavior. *Trends in Neurosciences*, *11*, 170–175.
Squire, L. R., & Zola-Morgan, S. (1991). The medial temporal lobe memory system. *Science*, *253*, 1380–1386.
Squire, L. R., Zola-Morgan, S., & Chen, K. S. (1988). Human amnesia and animal models of amnesia: performance of amnesic patients on tests designed for the monkey. *Behavioral Neuroscience*, *102*, 210–221.
Squire, L. R., & Zola, S. M. (1996). Structure and function of declarative and non-declarative memory systems. *Proceedings of the National Academy of Sciences of the United States of America*, *93*, 13515–13522.
Steele, K., & Rawlins, J. N. (1993). The effects of hippocampectomy on performance by rats of a running recognition task using long lists of non-spatial items. *Behavioural Brain Research*, *54*, 1–10.
Taylor, K. I., Moss, H. E., Stamatakis, E. A., & Tyler, L. K. (2006). Binding crossmodal object features in perirhinal cortex. *Proceedings of the National Academy of Sciences of the United States of America*, *103*, 8239–8244.
Ungerleider, L. G., & Mishkin, M. (1982). Two cortical visual systems. In D. J. Ingle, M. A. Goodale, & R. J. W. Mansfield (Eds.), *Analysis of visual behavior* (pp. 549–586). Cambridge, MA: MIT Press.
Warrington, E. K., & Weiskrantz, L. (1970). Amnesic syndrome: consolidation or retrieval? *Nature*, *228*, 628–630.
Weinstein, B. (1941). Matching-from-sample by rhesus monkeys and by children. *Journal of Comparative Psychology*, *31*, 195–213.
Winters, B. D., & Bussey, T. J. (2005a). Glutamate receptors in perirhinal cortex mediate encoding, retrieval, and consolidation of object recognition memory. *Journal of Neuroscience*, *25*, 4243–4251.
Winters, B. D., & Bussey, T. J. (2005b). Transient inactivation of perirhinal cortex disrupts encoding, retrieval, and consolidation of object recognition memory. *Journal of Neuroscience*, *25*, 52–61.
Winters, B. D., Forwood, S. E., Cowell, R. A., Saksida, L. M., & Bussey, T. J. (2004). Double dissociation between the effects of peri-postrhinal cortex and hippocampal lesions on tests of object recognition and spatial memory: heterogeneity of function within the temporal lobe. *Journal of Neuroscience*, *24*, 5901–5908.
Winters, B. D., Saksida, L. M., & Bussey, T. J. (2008). Object recognition memory: neurobiological mechanisms of encoding, consolidation and retrieval. *Neuroscience and Biobehavioral Reviews*, *32*, 1055–1070.
Yee, B. K., & Rawlins, J. N. (1994). The effects of hippocampal formation ablation or fimbria-fornix section on performance of a nonspatial radial arm maze task by rats. *Journal of Neuroscience*, *14*, 3766–3774.
Yonelinas, A. P. (2001). Components of episodic memory: the contribution of recollection and familiarity. *Philosophical Transactions of the Royal Society of London Series B: Biological Sciences*, *356*, 1363–1374.
Zola-Morgan, S., & Squire, L. R. (1985). Medial temporal lesions in monkeys impair memory on a variety of tasks sensitive to human amnesia. *Behavioral Neuroscience*, *99*, 22–34.
Zola-Morgan, S., & Squire, L. R. (1986). Memory impairment in monkeys following lesions limited to the hippocampus. *Behavioral Neuroscience*, *100*, 155–160.
Zola-Morgan, S., Squire, L. R., & Amaral, D. G. (1986). Human amnesia and the medial temporal region: enduring memory impairment following a bilateral lesion limited to field CA1 of the hippocampus. *Journal of Neuroscience*, *6*, 2950–2967.
Zola-Morgan, S., Squire, L. R., & Amaral, D. G. (1989a). Lesions of the amygdala that spare adjacent cortical regions do not impair memory or exacerbate the impairment following lesions of the hippocampal formation. *Journal of Neuroscience*, *9*, 1922–1936.
Zola-Morgan, S., Squire, L. R., & Amaral, D. G. (1989b). Lesions of the hippocampal formation but not lesions of the fornix or the mammillary nuclei produce long-lasting memory impairment in monkeys. *Journal of Neuroscience*, *9*, 898–913.
Zola-Morgan, S., Squire, L. R., Amaral, D. G., & Suzuki, W. A. (1989). Lesions of perirhinal and parahippocampal cortex that spare the amygdala and hippocampal formation produce severe memory impairment. *Journal of Neuroscience*, *9*, 4355–4370.
Zola-Morgan, S., Squire, L. R., Clower, R. P., & Rempel, N. L. (1993). Damage to the perirhinal cortex exacerbates memory impairment following lesions to the hippocampal formation. *Journal of Neuroscience*, *13*, 251–265.
Zola-Morgan, S., Squire, L. R., & Mishkin, M. (1982). The neuroanatomy of amnesia: amygdala-hippocampus versus temporal stem. *Science*, *218*, 1337–1339.
Zola-Morgan, S., Squire, L. R., Rempel, N. L., Clower, R. P., & Amaral, D. G. (1992). Enduring memory impairment in monkeys after ischemic damage to the hippocampus. *Journal of Neuroscience*, *12*, 2582–2596.
Zola, S. M., Squire, L. R., Teng, E., Stefanacci, L., Buffalo, E. A., & Clark, R. E. (2000). Impaired recognition memory in monkeys after damage limited to the hippocampal region. *Journal of Neuroscience*, *20*, 451–463.