HIPPOCAMPUS 17:898–908 (2007)

Memory, Perception, and the Ventral Visual-Perirhinal-Hippocampal Stream: Thinking Outside of the Boxes

T.J. Bussey[1,2]* and L.M. Saksida[1,2]

ABSTRACT: The prevailing paradigm in cognitive neuroscience assumes that the brain can be best understood as consisting of modules specialised for different psychological functions. Within the field of memory, we assume modules for different kinds of memory. The most influential version of this view posits a module called the ''medial temporal lobe memory system'' which operates in the service of ''declarative memory.'' This system can be contrasted with a separate ''perceptual representation system'' in the ventral visual stream, which is critical for perceptual learning and memory, an example of nondeclarative function. Here we question this modular memory systems view and suggest that a better way to understand the ventral visual-perirhinal-hippocampal stream is as a hierarchically organised representational continuum. We suggest that in general, rather than trying to map psychological functions onto brain modules, we could benefit by instead attempting to understand the functions of brain regions in terms of the representations they contain, and the computations they perform.

KEY WORDS: memory; perception; perirhinal cortex; object recognition; ventral visual stream; modularity; what pathway

INTRODUCTION

"The brain is modular"—who, these days, would disagree? The amygdala, for example, is for emotion, the hippocampus is for memory, and the visual cortex is for perception. In this way the brain is like a Swiss Army knife, with each anatomical area a 'tool' specialized for its own specific function (Cosmides and Tooby, 1994; Kanwisher, 2006). These tools are specified at the psychological level. We divide our textbooks up to conform to these divisions—an emotion chapter, a memory chapter, a perception chapter—and our University departments as well—an "Emotion Lab," a "Memory Lab," a "Perception Lab." The interpretation of our experiments also conforms: lesions produce impairments in emotion, memory and perception; imaging studies reveal blobs in "centers" for emotion, memory, and perception. Very simply, modularity of brain function is our current paradigm.

The "Multiple Memory Systems" view is a microcosm within this Swiss Army Knife universe. Thus we have modules for different kinds of memory (e.g., Schacter and Tulving, 1994). The most influential version of this view posits a module called the "medial temporal lobe (MTL) memory system" (Squire and Zola-Morgan, 1991), which is thought to include the hippocampus, entorhinal cortex, parahippocampal cortex, and perirhinal cortex and operates in the service of "declarative memory." This system can be contrasted with a separate "perceptual representation system" (Tulving and Schacter, 1990) in the ventral visual stream, which is critical for perceptual learning and memory, an example of nondeclarative function. Within the field of cognitive neuroscience of memory and perception, this Multiple Memory Systems view is our current paradigm.

But what if the current paradigm is wrong–or at least in need of some serious revision? Recently authors have argued just this (Gaffan, 2002; Bussey, 2004). In the present article, we outline some of the work that has led us to begin to question the utility of the modular view and suggest that rather than understanding the regions of the MTL and related structures as segregated into dedicated memory modules, it may be more useful to think in terms of the representations that they contain and the computations that they perform (Bussey and Saksida, 2005). Specifically we propose that structures within the MTL such as the perirhinal cortex may be best understood as an extension of the representational hierarchy within the ventral visual stream (Desimone and Ungerleider, 1989; Riesenhuber and Poggio, 1999). Furthermore, as perirhinal cortex sits at the interface between the assumed "memory" and "perceptual" systems of the Multiple Memory Systems paradigm, it is an ideal model structure on which to focus to test the idea that the brain is divided neatly into systems devoted to memory versus perception. If a structure such as perirhinal cortex can be thought of as having both a mnemonic and a perceptual role in cognition, then this can be taken as evidence against the modular view. As we will see, perirhinal cortex can indeed be viewed in this way, and moreover—and even more controversially—so can the hippocampus. We will consider the role of the perirhinal cortex in visual discrimination tasks, before turning to the issue of perirhinal cortex and object recognition. This will lead into a discussion of the place of the hippocampus in this scheme. As the first of these issues has been considered several times elsewhere (Bussey et al., 2002b,

[1] **Department of Experimental Psychology, University of Cambridge, Cambridge, United Kingdom;** [2] **The MRC and Wellcome Trust Behavioural and Clinical Neuroscience Institute, University of Cambridge, Cambridge, United Kingdom**
*Correspondence to: T.J. Bussey. E-mail: tjb1000@cam.ac.uk
Accepted for publication 1 May 2007
DOI 10.1002/hipo.20320
Published online 17 July 2007 in Wiley InterScience (www.interscience.wiley.com).

2005; Buckley, 2005; Bussey and Saksida, 2005; Lee et al., 2005a; Buckley and Gaffan, 2006; Murray et al., 2007), we will here give an abbreviated summary, and spend more time on the latter issues.

PERIRHINAL CORTEX AND VISUAL DISCRIMINATION TASKS

The canonical effect of perirhinal cortex damage is a delay-dependent impairment in object recognition, the ability to judge that one of two or more objects has not been previously encountered (i.e., is novel). This effect has been observed many times and is not controversial (Meunier et al., 1993; Eacott et al., 1994; Mumby and Pinel, 1994; Buffalo et al., 1998). Whereas object recognition involves one-trial learning and the discrimination of a familiar object from a novel object, it has also been found that perirhinal cortex lesions can impair visual discrimination tasks that are acquired more slowly over a number of trials, in which all stimuli are familiar (summarized below). Following such findings, researchers have broadened their conception of perirhinal cortex function beyond object recognition, and have begun to refer to the general role of perirhinal cortex as one of "object identification" (Buckley and Gaffan, 1998; Murray et al., 2000). Our work has been directed toward bringing together these findings and ideas in a unified framework.

Rather than taking the paradigm view of thinking about perirhinal cortex only as part of an MTL memory system involving the hippocampus, we thought it reasonable, given the anatomy, to think about perirhinal cortex as part of the ventral visual stream (Murray and Bussey, 1999; Bussey and Saksida, 2002). This system is thought to contain hierarchically organized representations of visual stimuli (Desimone and Ungerleider, 1989). We have instantiated a simplified version of this system (Fig. 1A) in a connectionist model (Fig. 1B) in which the "feature" layer (corresponding to regions caudal to perirhinal cortex) contains representations of simple features of objects, and the "feature conjunction" layer (corresponding to perirhinal cortex) contains representations of complex conjunctions of these visual features. This "perceptual-mnemonic/feature conjunction" (PMFC) model (Bussey and Saksida, 2002; Bussey et al., 2005) assumes that perirhinal cortex has both perceptual and mnemonic function. Details of the network are given in Bussey and Saksida (2002). Our first test of the model consisted of lesioning the component of the network corresponding to perirhinal cortex, and comparing the performance of lesioned networks and lesioned subjects on several tasks previously reported in the literature. Specifically, we investigated the findings that (1) perirhinal cortex lesions disrupt complex configural discrimination learning, in which an individual feature is rewarded when it is part of one object but not when it is part of another object, even when the stimulus set size is small; (2) perirhinal cortex lesions disrupt acquisition of concurrent visual discriminations when the size of the stimulus set is large, but not when it is small; and (3) perirhinal cortex lesions yield greater effects on retention of preoperatively-learned discrimination problems than on acquisition of new problems of the same type. The model was able successfully to account for these data, and even though the various impairments look to be quite different from each other on the surface, the mechanism by which the model accounted for them was the same in all cases: Lesioned networks did not have the conjunctive representations necessary effectively to cope with problems in which the individual features alone did not provide a reliable solution. We have referred to this property of cognitive tasks—in which simple features do not provide a reliable solution to a given problem—as "feature ambiguity," and

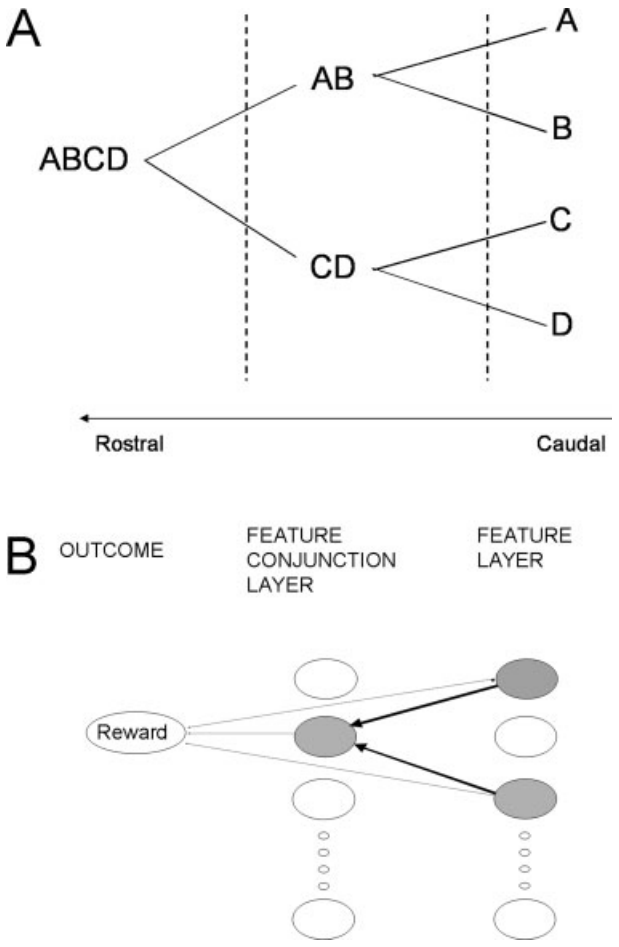


FIGURE 1. A: The proposed organization of visual representations in the ventral visual stream. A, B, C, and D represent simple visual features encoded in caudal regions of the ventral visual stream. More complex representations of the conjunctions of these features are stored in more rostral regions. B: Diagram of the connectionist model of Bussey and Saksida (2002). The network consists of two layers of units, the feature layer and the feature conjunction layer, as well as an outcome node representing a consequent event (e.g., reward). The feature conjunction layer represents perirhinal cortex and the feature layer represents more caudal regions of the ventral visual stream.

our hypothesis is that perirhinal cortex contains complex conjunctive representations that enable the system to resolve such feature ambiguity.

But the real test of a model is not to simulate extant data—although this is important—it is to allow the model to make novel predictions that can then be tested experimentally. The following section describes three experiments in which we combined modelling predictions with behavioural testing in rhesus monkeys with (or without) perirhinal cortex lesions.

Manipulating Feature Ambiguity in Concurrent Visual Discriminations

Buckley and Gaffan (1997), in one of the first studies to show that perirhinal cortex lesions can impair across-session acquisition of pair-wise discrimination tasks, showed that monkeys with perirhinal cortex lesions were impaired when learning a large, but not a small number of concurrent pair-wise visual discriminations. According to the PMFC model, however, it is not the number of objects that is the critical factor, but rather feature ambiguity. This hypothesis was investigated by testing monkeys with perirhinal cortex lesions on concurrent discriminations in which the number of problems (object pairs) was held constant, but the degree of feature ambiguity was varied (Bussey et al., 2002a). Monkeys were tested in three conditions, Maximum Feature Ambiguity, in which all four features were explicitly ambiguous (AB+, CD+, BC−, AD−; the biconditional problem); Minimum Feature Ambiguity, in which no features were explicitly ambiguous (AB+, CD+, EF−, GH−); and Intermediate Feature Ambiguity, in which two features were explicitly ambiguous (AB+, CD+, CE−, AF−) (Fig. 2A). The prediction was that perirhinal cortex lesions should have a greater effect on discrimination learning as the degree of feature ambiguity is increased, even though the number of problems to be discriminated was in each case held constant.

It was found that as the degree of feature ambiguity was increased, monkeys with lesions of perirhinal cortex became increasingly impaired (Fig. 2C). These data conform to the predictions of the PMFC model (2B), and have since been replicated in human subjects: subjects with MTL damage including perirhinal cortex lesions were impaired in the same way, whereas subjects with selective hippocampal damage, performed indistinguishably from controls (Barense et al., 2005). Additional evidence for the role of perirhinal cortex in configural discriminations comes from the observation that lesions of perirhinal cortex in monkeys severely impair the configural "transverse patterning" task (Saksida et al., 2007).

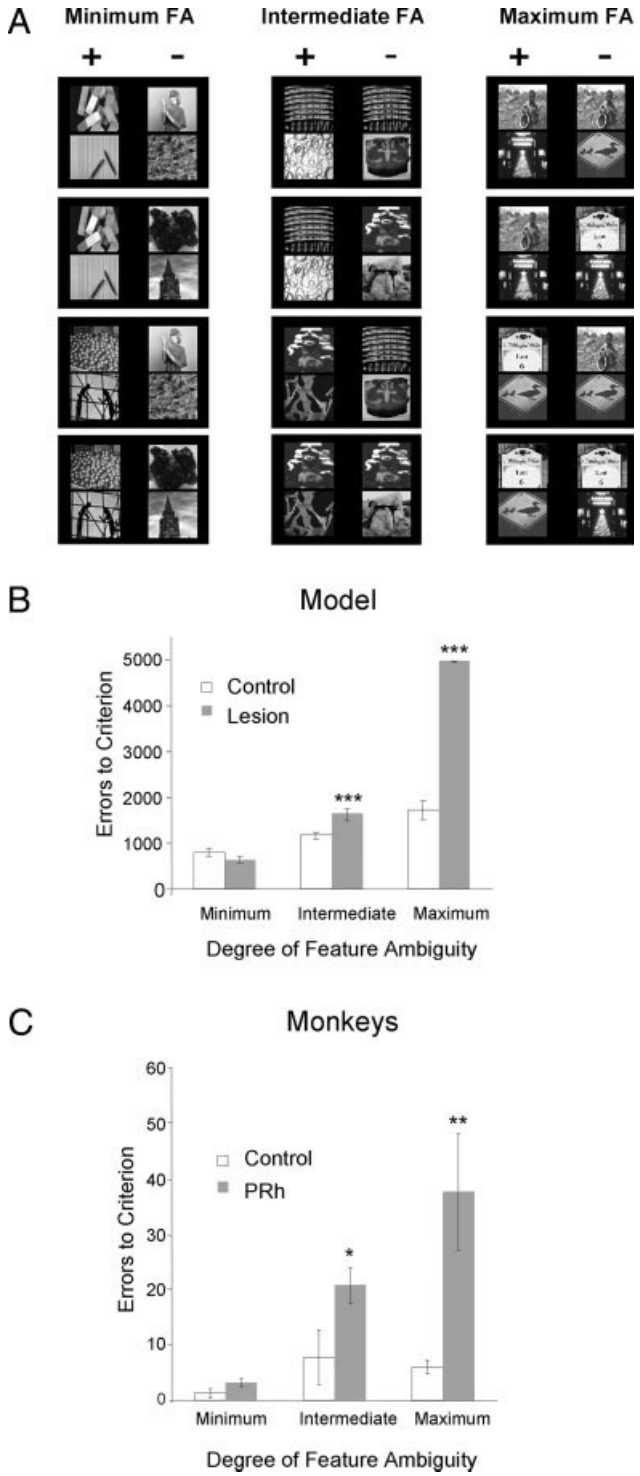
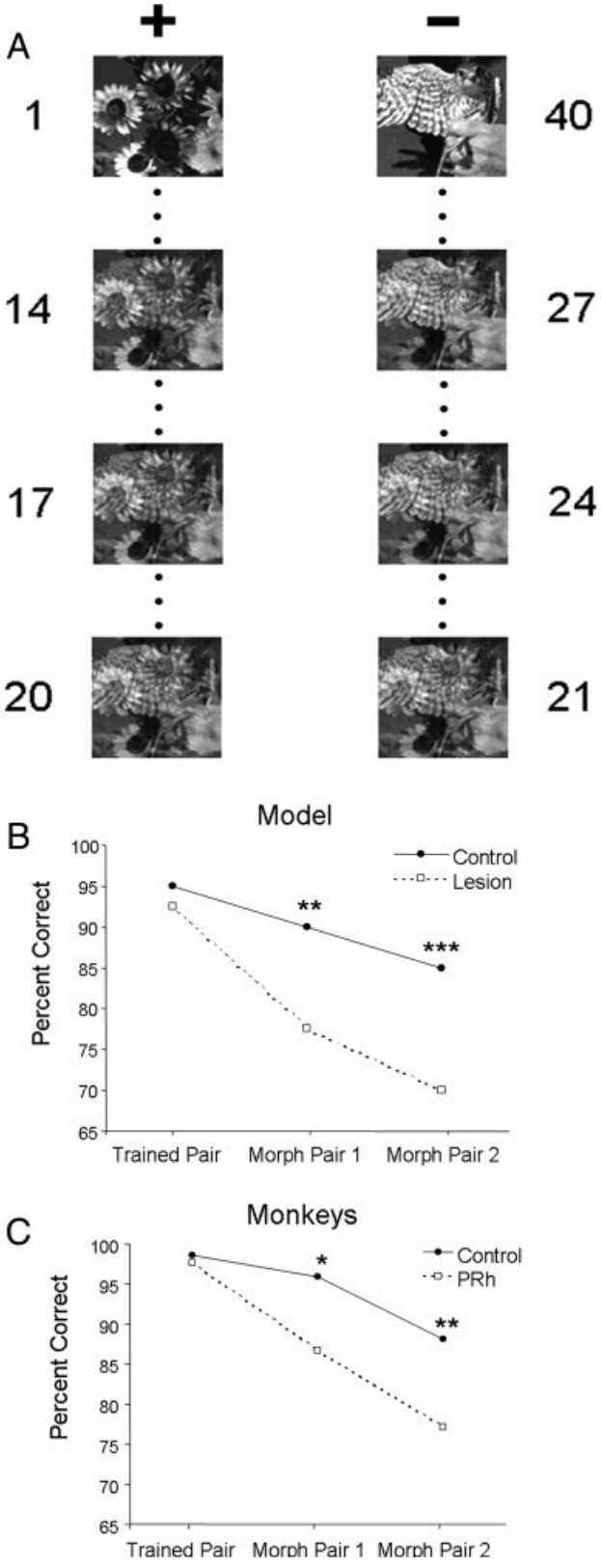


FIGURE 2. A: Example of stimulus pairs in the Minimum, Intermediate, and Maximum feature ambiguity conditions in the study by Bussey et al. (2002). In the Minimum condition, no features were explicitly ambiguous (i.e., each feature was consistently either rewarded or nonrewarded). In the Intermediate condition, two features were explicitly ambiguous; in the Maximum condition, all four features were explicitly ambiguous. B: Acquisition of intact networks and networks with the feature conjunction layer removed of four-pair concurrent discriminations in each of the Minimum, Intermediate, and Maximum Feature Ambiguity conditions. Lesioned networks were increasingly impaired as feature ambiguity was increased. C: Acquisition by control monkeys and monkeys with lesions of the perirhinal cortex of four-pair concurrent discriminations in each of the Minimum, Intermediate, and Maximum Feature Ambiguity conditions. Monkeys with perirhinal cortex lesions were increasingly impaired as feature ambiguity was increased. Data from Bussey et al. (2002).

Single-Pair Visual Discriminations

Whereas the previous experiment illustrates the concept of feature ambiguity, we now turn to an experiment that speaks most directly to the question of whether the current paradigm is correct in assuming separate and distinct memory and perceptual modules in brain. It is well established that perirhinal cortex is critical for memory; however is it important, as the PMFC model suggests, for high-level perceptual discriminations?

We tested this idea by using "morphed" greyscale picture stimuli (Bussey et al., 2003). Morphing creates pairs of stimuli with an increasing number of features shared in common, resulting in pairs that are relatively perceptually similar, and pairs that are relatively perceptually dissimilar (Fig. 3A). First, we found that monkeys with perirhinal cortex lesions were impaired on the acquisition of these discriminations, but only when the discriminations were perceptually demanding. Second, and most relevant to the question of perception, we examined the effect of increasing perceptual similarity in previously acquired, perceptually dissimilar discriminations. This was done by first training monkeys to criterion on a single-pair discrimination of unmorphed stimuli, and then in a single session testing performance on three pairs of stimuli: the Trained Pair, and two Morph Pairs created from the Trained Pair. The findings are shown in Figure 3C: Monkeys with perirhinal cortex lesions were again impaired when perceptual demands were high, but not when they were low. These data conform to the predictions of the PMFC model (Fig. 3B). Indeed, these findings, too, have been replicated in human subjects; subjects with MTL damage including perirhinal cortex were poor at discriminating morphed faces (whereas subjects with selective hippocampal lesions were not) (Lee et al., 2005c).



PERIRHINAL CORTEX AND OBJECT RECOGNITION

The previous section explains how the PMFC model accounts for impairments following perirhinal cortex lesions in visual discriminations. It does so, on our view, by assuming that perirhinal cortex contains complex conjunctive representations for the resolution of feature ambiguity. This function is particularly critical in tasks in which difficult high-level perceptual discriminations must be made, and in tasks which have configural properties. As mentioned above, however, the canonical impairment is in object recognition. Does perirhinal cortex have the same perceptual functions in object recognition?

FIGURE 3. A: Example of 'morphed' picture stimulus pairs used in Bussey et al. (2003). B: Performance of intact networks and networks with the feature conjunction layer removed on two-choice discriminations at three levels of perceptual similarity. Lesioned networks were increasingly impaired as perceptual similarity was increased. C: Performance of control monkeys and monkeys with lesions of perirhinal cortex on two-choice discriminations at three levels of perceptual similarity. Monkeys with lesions were increasingly impaired as perceptual similarity was increased. Data from Bussey et al. (2003).

To test this idea, Susan Bartko in our lab developed a method of adapting the spontaneous object recognition task (Ennaceur and Delacour, 1988), which allows the systematic manipulation of the perceptual demands of the task while minimising memory demands (Bartko et al., 2007). The task is carried out in a Y-apparatus designed to minimize spatial and other confounds (Winters et al., 2004; Forwood et al., 2005). Object recognition carried out in this apparatus is very sensitive to manipulations of perirhinal cortex (Winters et al., 2004, 2006; Winters and Bussey, 2005a,b,c; Bartko et al., 2007). A modification of this apparatus, shown in Figure 4A, allows sample and choice objects to be placed behind each other, separated by a barrier that can be rapidly removed, lifting out the sample objects as it is raised out of the apparatus. This method allows the testing of object recognition under conditions of "zero delay," which corresponds to the "immediate" delay condition in delayed matching- and nonmatching-to-sample studies with monkeys, and is regarded as requiring perceptual, rather than long-term mnemonic, function (Eacott et al., 1994; Buffalo et al., 2000). The zero-delay condition is achieved by first allowing the animal to explore the sample object for a predetermined amount of time. Immediately the animal has totalled up this amount of exploration, the barrier and sample objects are lifted out of the apparatus—the animal remaining in the apparatus—to reveal the choice objects behind.

We tested rats with combined perirhinal and postrhinal cortex lesions on object sets with two levels of perceptual similarity, shown in Figure 4B. Rats with perirhinal cortex lesions were impaired under conditions in which the discriminanda were perceptually similar, but not when they were perceptually dissimilar (Bartko et al., 2007) (Fig. 4C). This finding shows that the perceptual functions of perirhinal cortex come into play not only in a visual discrimination setting, but in an object recognition setting as well.

Although the impairment in this experiment was clearly related to perceptual difficulty, it might be argued that this was still a mnemonic impairment, because the sample was not present when the rat was making its choice, and so memory for the sample could come into play, albeit across a relatively short delay. Therefore, we tested rats with combined perirhinal and postrhinal cortex lesions, and also rats with selective perirhinal cortex lesions, on a spontaneous perceptual oddity discrimination task. In this task, carried out in the apparatus shown in Figure 5A, all objects were presented simultaneously (Bartko et al., 2007). Rats were presented with two copies of one object and one copy of another object; that is, three objects were presented, an odd object and two identical objects. We predicted that if the rat were able to determine that the two identical objects were perceptually identical and that the object was perceptually distinct from the repeating objects, then it would divide its exploration between the two identical objects, resulting in an overall "preference" for the odd object. We tested rats with four levels of perceptual difficulty (Fig. 5B).

The results of the oddity experiment are shown in Figure 5C, and are straightforward; again rats with perirhinal cortex lesions were impaired under conditions in which the discriminanda were perceptually similar, but not when they were perceptually dissimilar (Bartko et al., 2007). This finding replicates in rats a previous finding using oddity discriminations in monkeys (Buckley et al., 2001). These finding have also been replicated in human subjects: subjects with MTL damage including perirhinal cortex were impaired on difficult face dis-

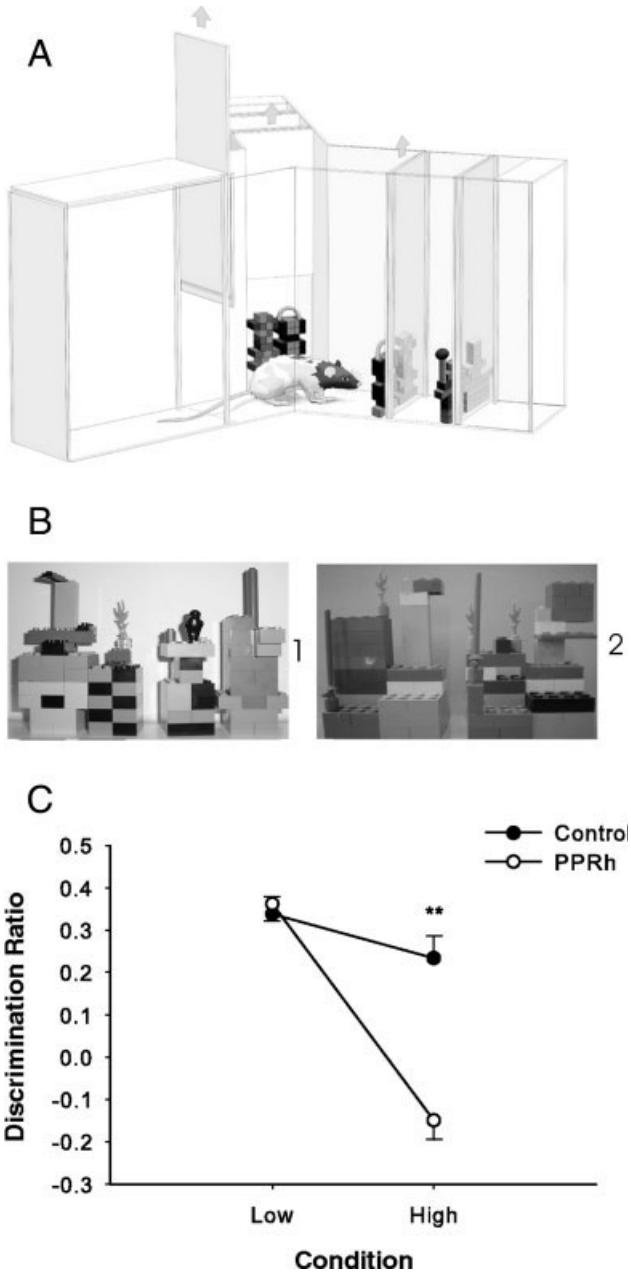


FIGURE 4. A: Illustration of the apparatus and representative stimuli used in the zero-delay object recognition task (Bartko et al., 2007). The figure illustrates examples of stimuli that could appear in the low perceptual similarity condition. B: Examples of stimuli in the low and high perceptual similarity conditions. C: Performance of control rats and rats with lesions of combined perirhinal and postrhinal cortex on the zero-delay object recognition task. Rats with lesions were impaired in the high, but not the low perceptual similarity condition. Data from Bartko et al. (2007).

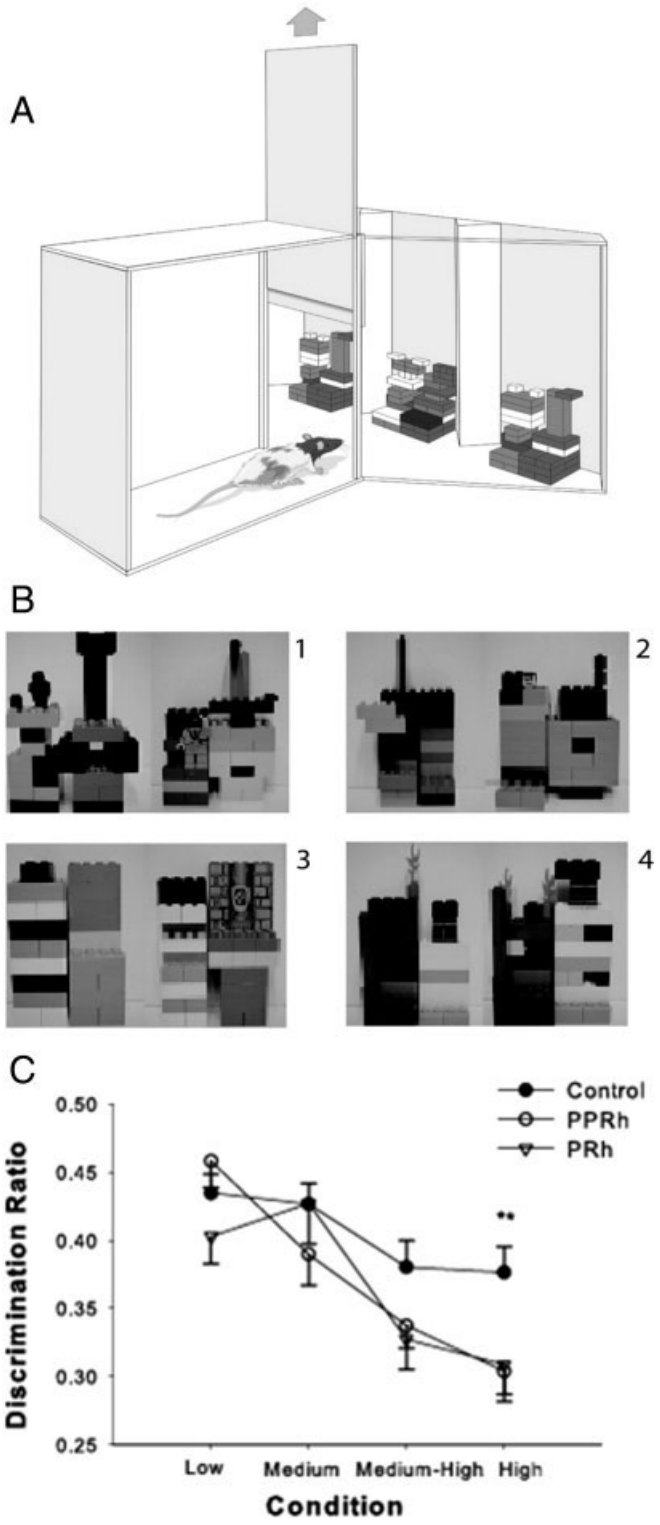


FIGURE 5. A: The spontaneous oddity apparatus (Bartko et al., 2007). B: examples of stimuli used in the spontaneous oddity task; 1, low; 2, medium; 3, medium-high; and 4, high similarity. C: Performance of control rats, rats with lesions of combined perirhinal and postrhinal cortex, and rats with selective perirhinal cortex lesions on the spontaneous oddity task. Rats with lesions were increasingly impaired as perceptual similarity was increased. Data from Bartko et al. (2007).

criminations, whereas subjects with selective hippocampal damage, performed indistinguishably from controls (Lee et al., 2005b,c).

Our experiments in rodents answer a number of criticisms that have been levelled at previous studies that have reported perceptual impairments following perirhinal cortex lesions. For example, the first experiment (to our knowledge) to suggest perceptual functions for perirhinal cortex (Eacott et al., 1994), which was essentially the same object recognition experiment outlined above but using matching-to-sample in monkeys, has been all but disregarded because of claims that the impairments could have been due to an impairment in the animals with perirhinal cortex lesions in the retention of the matching rule (Buffalo et al., 1999). In our object recognition experiment, however, rats perform the task spontaneously, and so there was no matching (or any other) rule to retain. Thus, we would suggest that the interpretation by Eacott et al. (1994), which the impairments were produced by perirhinal cortex lesions was due to a perceptual impairment, seems to have been correct.

The results from studies using oddity tasks in monkeys (Buckley et al., 2001) and humans (Lee et al., 2005b) have likewise been criticized because they have involved reward and/or repeated presentation of stimuli. It has been argued that learning across trials may occur in these paradigms, and therefore deficits on these tasks may be interpreted as impairments in learning (Levy et al., 2005; Shrager et al., 2006; Squire et al., 2006). However, because the spontaneous oddity task used in the present study is a nonrewarded, single-trial paradigm, deficits in learning cannot explain our data, as no across-trial learning can occur.

Thus, evidence for perceptual impairments following perirhinal cortex lesions has now been observed in monkey, human, and rodent subjects, in both visual discrimination and object recognition paradigms.

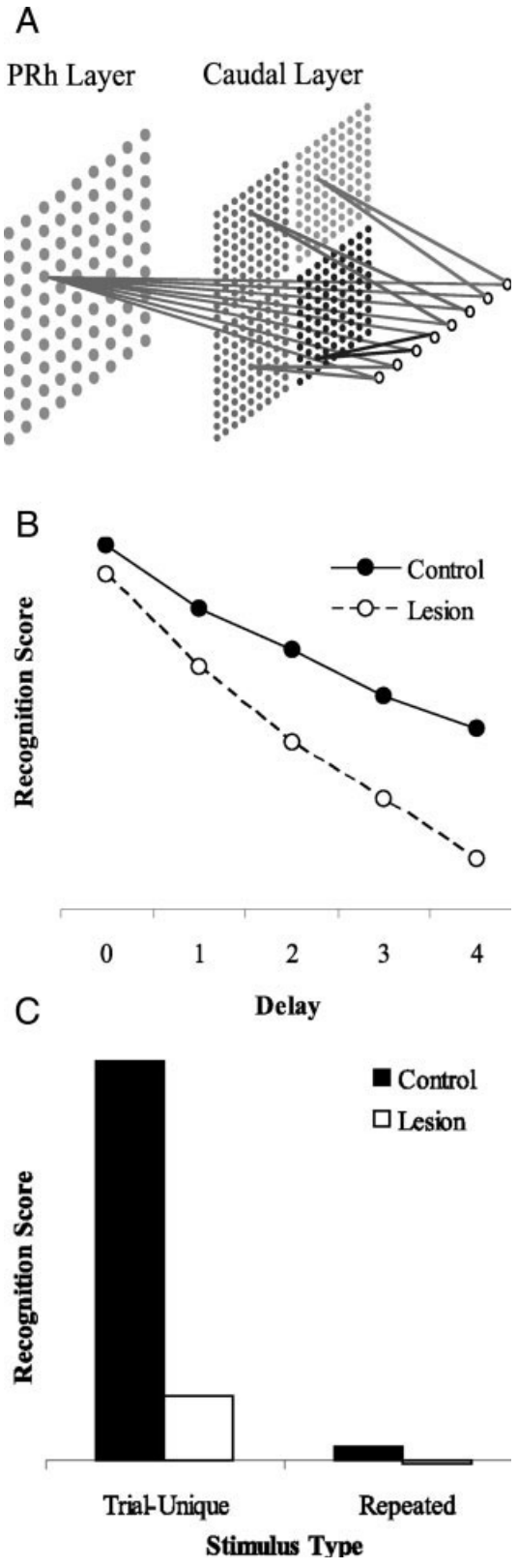
A CONNECTIONIST MODEL OF OBJECT RECOGNITION IN PERIRHINAL CORTEX

The simple computational model shown in Figure 1B is able to account for the effects of perirhinal cortex lesions on visual discrimination tasks. Yet as mentioned earlier, the canonical effect of perirhinal cortex lesions is a delay-dependent impairment in object recognition. Can the PMFC model account for delay-dependent and other impairments following perirhinal cortex lesions in object recognition?

Rosie Cowell in our lab has investigated whether the representational framework embodied in the PMFC model can explain impairments in object recognition memory following perirhinal cortex lesions. In the PMFC model, visual object representations are hard-wired and static: "A" is the same "A" no matter how much learning goes on in the network; the only learning that occurs is associative learning between representations and reward. In other words, the model does not include any facility for perceptual learning. In the model shown in

Figure 6A and described in much more detail in Cowell et al. (2006), the PMFC representational framework is maintained—with complex conjunctive representations in perirhinal cortex and simpler ("feature") representations in caudal regions of the ventral visual stream—but now the representations can become more efficient and tuned during exposure to stimuli. This is achieved using Kohonen grids, which are designed to model cortex including computational abstractions of cortical mechanisms such as lateral inhibition. The successive presentation of stimuli results in the sharpening of representations of these stimuli. A novel stimulus will elicit a moderate level of activity, broadly distributed across a large number of units in the grid; as that stimulus is presented repeatedly, the activation pattern it elicits becomes more selective until only a small area of the grid contains highly active units, producing a peak of activation. The development of sharply tuned representations thus can be used as the basis for familiarity judgments: as a stimulus representation becomes sharper, so it is judged to be more familiar. Other models use a similar index of familiarity (Norman and O'Reilly, 2003).

Using this model, Cowell et al. (2006) simulated the results from several empirical findings, including the finding that (1) impairments following damage to perirhinal cortex are exacerbated by lengthening the delay between presentation of to-be-remembered items and test (delay-dependent impairments), and (2) impairments are revealed only when stimuli are trial-unique, rather than repeatedly presented.



Delay-Dependent Impairments in Object Recognition Memory

As discussed earlier, the canonical impairment following perirhinal cortex lesions is a delay-dependent impairment in object recognition (Meunier et al., 1993; Eacott et al., 1994; Mumby and Pinel, 1994; Buffalo et al., 1998). As shown in Figure 6B, the model successfully simulates such impairments, and it does so as follows. During a delay between encoding a sample stimulus and being required to discriminate that stimulus from a novel item, we assume that the subject encounters numerous visual stimuli (real or imagined) containing simple features such as edges, line orientation, and color. These simple features are common to many visual objects and will be encountered repeatedly during the delay period. Moreover, they will appear in the objects used in the task. Because all of

FIGURE 6. A: Illustration of the connectionist model of Cowell et al. (2006). The input layer, containing eight nodes, is shown on the far right; the two Kohonen layers on which stimuli are represented are shown to the left of the input layer. On the perirhinal cortex layer, the four features are combined into a complex conjunctive representation, shown in gray. This representation is a conjunction of all features in the object stimulus. B: Performance of intact networks and networks with the perirhinal layer removed on object recognition at various delays. Lesioned networks were increasingly impaired as delay was increased. C: Performance of intact networks and networks with the perirhinal layer removed on object recognition with trial-unique versus repeating stimuli. Lesioned networks were impaired when trial-unique stimuli were used. Neither lesioned nor intact networks performed well when repeating stimuli were used; see text for discussion. Data from Cowell et al. (2006).

these features will be familiar, they will not be useful for discriminating the novel from the familiar object. In other words, a delay filled with such interfering information can lead to feature ambiguity.

However, the specific conjunction of visual features that comprises a given complex object is unique and is encountered during the delay with a far lower frequency, if at all. Thus, the complex conjunctive representations in perirhinal cortex resolve the feature ambiguity—the interference—caused by repeating features during the delay. As a result, an intact network, and an animal with an intact perirhinal cortex, has an advantage over a lesioned network or animal because it can represent unique conjunctions of stimulus features. In contrast the lesioned network, or animal, must rely on the spared representations of individual stimulus features to attempt to discriminate between the novel and familiar stimuli. This advantage of the control networks or animals increases as the delay increases.

The assumption that forgetting over a delay is caused by interference from events that interpose between encoding and retrieval is in line with the idea the human amnesia can be understood in terms of an increased susceptibility to interference (Warrington and Weiskrantz, 1974). The idea that amnesia can be thought of as an increased susceptibility to interference is these days rarely discussed. But all of the results discussed in the present article can be thought of in terms of interference; referred to here as feature ambiguity. Thus amnesia—at least "perirhinal amnesia"—can be thought of in the terms suggested by Warrington and Weiskrantz (1974).

Impairments are Revealed Only When Stimuli are Trial-Unique, Rather Than Repeatedly Presented

Object recognition as measured by the delayed nonmatching-to-sample (DNMS) or delayed matching-to-sample (DMS) tasks, is most often tested in monkeys and in humans using trial-unique stimuli. In this paradigm, the set of objects from which stimuli are drawn is so large that items are repeated either extremely infrequently or not at all. Alternatively, one can use a version in which items are drawn repeatedly from the set and viewed repeatedly by the subjects. Many studies have reported that damage to perirhinal cortex impairs object recognition memory with trial-unique stimuli (Meunier et al., 1993; Eacott et al., 1994; Mumby and Pinel, 1994; Buffalo et al., 1998). However, a study by Eacott et al. (1994) reported no effect of lesions of rhinal cortex (perirhinal and entorhinal cortex) on object recognition when stimuli were frequently repeated.

Cowell et al. (2006) simulated these findings; the results are shown in Figure 6C. In keeping with the monkey data, lesioned networks were impaired relative to control networks in recognition memory for trial-unique stimuli. In contrast, with recognition memory for repeated stimuli, neither control networks nor lesioned networks could perform the task. The explanation of the impairment in recognition of trial-unique stimuli following removal of the perirhinal cortex layer is the same as that for delay-dependent impairments, and the same as that for list length-dependent impairments (not shown here; see Cowell et al. 2006, Experiment 2): successive stimulus presentations lead to a build up of familiarity over individual stimulus features, but not over objects, as objects are unique. Thus, the features of both the sample and novel objects in each stimulus pair appear familiar according to the caudal layers of the network, but the conjunctive representations of the sample and novel objects on the perirhinal cortex layer remain discriminable on the basis of familiarity. Thus perirhinal cortex, which contains complex conjunctive representations specifying unique objects, protects the control subjects from this interfering feature ambiguity.

In repeating-items object recognition, neither the intact networks nor the lesioned networks were able to discriminate the novel from the familiar objects. This finding is consistent with the data from Eacott et al. (1994), which show that perirhinal cortex lesions in monkeys do not impair delayed matching-to-sample when repeated stimuli are used. The inability of either the feature-conjunction layer, or the feature layer of intact networks, to perform repeated-items recognition is important. In other simulations, such as those of the delay-dependent effects described above, successive stimulus presentations led to a build up of familiarity over individual stimulus features, but not over objects, as objects are unique. Thus perirhinal cortex, which contains complex conjunctive representations specifying unique objects, protects the control subjects from this interfering feature ambiguity. In the case of repeating items, however, not only are the features repeatedly presented, the objects are repeatedly presented. As a result, the representations in perirhinal cortex are not enough to protect the control subject from interference. One might say that an additional level of ambiguity—"object ambiguity"—has been created. Now, the resolution of ambiguity at this level would require an additional, more rostral layer, containing conjunctive representations of an even higher degree of complexity than those found in perirhinal cortex.

HIPPOCAMPUS IN THE HIERARCHY

We would like to suggest that such a higher-lever layer might be the hippocampus. Many authors have suggested that the hippocampus contains complex, multimodal representations of multiple objects, perhaps including the visuo-spatial relationships between them (Eichenbaum et al., 1994) or forming a "cognitive map" (O'Keefe and Nadel, 1978). Several researchers have suggested a hierarchical organization of brain structures with the hippocampus at the "top" of the hierarchy (Squire, 1992; Mishkin et al., 1997).

If the hippocampus is the "missing layer," then lesions of the hippocampus should impair repeating-items object recognition. Indeed, Rawlins et al. (1993) have reported that lesions of the hippocampus or fornix in rats impair performance of repeating-items delayed matching-to-sample. Addi-

tionally, Charles et al. (2004) found that monkeys with fornix transections were impaired on a recognition memory task in which they were required to judge the relative recency of stimuli. According to the present account, tasks such as these provide a higher level of ambiguity that must be resolved by even more complex conjunctive representations in a hierarchy that extends throughout the ventral visual stream through perirhinal cortex, and on into the hippocampus (Bussey and Saksida, 2005).

If the hippocampus is part of this perceptual-mnemonic system, then one might expect it to have perceptual functions. Indeed, experiments with patients with selective damage to the hippocampus provide evidence for this. Furthermore, these findings are consistent with expectations of the hierarchical model offered above in that the perceptual impairments are not at the level of objects, in the way that perirhinal cortex lesion-induced impairments are, but at a higher level—a level at which object representations combine to represent spatial "scenes." Thus, Lee et al. (2005c) found that patients with selective hippocampal damage were impaired in the visual discrimination of morphed scenes. These patients were not impaired, however, on morphed face discriminations. In another experiment, Lee et al. (2005b) found that these same hippocampal patients were impaired in a perceptual oddity task, but only when the stimuli were spatial (virtual reality rooms). Again, these patients were not impaired in perceptual oddity discriminations involving faces. These results suggest that the hippocampus has perceptual functions and contains representations at a higher level than perirhinal cortex.

CONCLUSION: GOING MODULE-FREE

And so we arrive at a point where we have been able to offer explanations for a number of phenomena, from impairments following perirhinal cortex lesions on visual discriminations with large numbers of objects, to those involving high-level perceptual discriminations, to those having configural properties, to classical impairments in object recognition, to perceptually demanding object recognition and oddity tasks. We have done so by appealing only to the simple idea—supported by electrophysiology and known properties of these cortical regions—of a self-organizing representational hierarchy, like that shown in Figure 1A, in which increasingly complex representations are built up as one proceeds though the ventral visual-perirhinal-hippocampal stream. At no point did we need to appeal to putative memory modules for say, declarative memory and nondeclarative memory, or a dedicated perceptual representation system distinct from the MTL. Indeed, such Multiple Memory System theories fail quite comprehensively to account for many of the findings described above.

It could be argued that our view is still, in a sense, modular. Thus although we view the ventral visual-perirhinal-hippocampal stream as a continuous hierarchy of increasingly complex representations, it is the case that different cortical areas within the hierarchy contain different representations. Thus one might say that our conception of perirhinal cortex is as "a module for representing conjunctions of a large number of features," and area TE is "a module for representing conjunctions of a fewer number of features than perirhinal cortex," and so on. That's fine with us, but we would ask: What is to be gained by describing the system in this way? It seems to us that more is to be gained by understanding the system more holistically, as a continuum, emphasising similarities between regions as well as differences.

And just as our scheme could be viewed in this way, as a "structural" model of cognition, so it could just as easily be viewed as a "processing" model: as one proceeds down the stream, information becomes more processed. Again, this is fine: the model has properties of both a structural model and a processing model, consistent with our emphasis on both representations and computations (Bussey and Saksida, 2005). One might even say that our approach resolves the classic conflict between structural and processing models of memory and cognition.

We should also emphasise that we are not saying that different brain regions don't do different things; that would be silly. What we do question is the assumption that the best way to try to understand the neural organisation of cognition is to attempt to map psychological (or folk-psychological) constructs onto different modules corresponding to different parts of the brain. The examples used above are memory, perception and emotion. But even concepts such as modules for "space" and "objects" may have limited utility. Is the perirhinal cortex a module for "object" cognition? Certainly we have shown above that rats, monkeys and humans with perirhinal cortex damage can be impaired on tasks requiring representations at the level of what we like to call "objects," and they are not impaired on tasks that do not involve such "objects." But objects are not represented just in perirhinal cortex; they are represented throughout the stream. What is present in perirhinal cortex, we think, is a conjunctive representation of roughly the complexity of everyday objects, but this does not mean that perirhinal cortex is a module for objects. Again, the best way to understand the functions of the regions in this stream—and perhaps the whole brain—is not to try to put a psychological label on them, but to try to understand what computations they perform, and what representations they contain.

We conclude, therefore, by appealing to our colleagues in this field to think the unthinkable: that our current paradigm—which assumes that the brain is organised into modules, the functions of which can be understood at the psychological level—may not, in fact, be the best way to understand the brain (Gaffan, 2002; Bussey, 2004). Perhaps it is time to think outside of the boxes.

REFERENCES

Barense MD, Bussey TJ, Lee ACH, Rogers TT, Davies RR, Saksida LM, Murray EA, Graham KS. 2005. Functional specialization in the human medial temporal lobe. J Neurosci 25:10239–10246.

Bartko SJ, Winters BD, Cowell RA, Saksida LM, Bussey TJ. 2007. Perceptual functions of perirhinal cortex in rats: Zero-delay object recognition and simultaneous oddity discriminations. J Neurosci 27:2548–2559.

Buckley MJ. 2005. The role of the medial temporal lobe in memory and perception: Evidence from rats, nonhuman primates and humans. Quart J Exp Psychol B 58:246–268.

Buckley MJ, Gaffan D. 1997. Impairment of visual object-discrimination learning after perirhinal cortex ablation. Behav Neurosc 111:467–475.

Buckley MJ, Gaffan D. 1998. Perirhinal cortex ablation impairs visual object identification. J Neurosci 18:2268–2275.

Buckley MJ, Gaffan D. 2006. Perirhinal cortical contributions to object perception. Trend Cogn Sci 10:100–107.

Buckley MJ, Booth MC, Rolls ET, Gaffan D. 2001. Selective perceptual impairments after perirhinal cortex ablation. J Neurosci 21: 9824–9836.

Buffalo EA, Reber PJ, Squire LR. 1998. The human perirhinal cortex and recognition memory. Hippocampus 8:330–339.

Buffalo EA, Ramus SJ, Clark RE, Teng E, Squire LR, Zola SM. 1999. Dissociation between the effects of damage to perirhinal cortex and area TE. Learn Mem 6:572–599.

Buffalo EA, Ramus SJ, Squire LR, Zola SM. 2000. Perception and recognition memory in monkeys following lesions of area TE and perirhinal cortex. Learn Mem 7:375–382.

Bussey TJ. 2004. Multiple memory systems: Fact or fiction? Quart J Exp Psychol 57:89–94.

Bussey TJ, Saksida LM. 2002. The organization of visual object representations: A connectionist model of effects of lesions in perirhinal cortex. Eur J Neurosci 15:355–364.

Bussey TJ, Saksida LM. 2005. Object memory and perception in the medial temporal lobe: An alternative approach. Curr Opin Neurobiol 15:730–737.

Bussey TJ, Saksida LM, Murray EA. 2002a. Perirhinal cortex resolves feature ambiguity in complex visual discriminations. Eur J Neurosci 15:365–374.

Bussey TJ, Saksida LM, Murray EA. 2002b. The role of perirhinal cortex in memory and perception: Conjunctive representations for object identification. In: Witter MP, Wouterlood FG, editors. The Parahippocampal Region: Organization and Role in Cognitive Functions. Oxford: Oxford University Press. pp 239–254.

Bussey TJ, Saksida LM, Murray EA. 2003. Impairments in visual discrimination after perirhinal cortex lesions: Testing "declarative" versus "perceptual-mnemonic" views of perirhinal cortex function. Eur J Neurosci 17:649–660.

Bussey TJ, Saksida LM, Murray EA. 2005. The PMFC model of perirhinal cortex function. Quart J Exp Psychol B 58:269–282.

Charles DP, Gaffan D, Buckley MJ. 2004. Impaired recency judgments and intact novelty judgments after fornix transection in monkeys. J Neurosci 24:2037–2044.

Cosmides L, Tooby J. 1994. Beyond intuition and instinct blindness: Toward an evolutionarily rigorous cognitive science. Cognition 50(1–3):41–77.

Cowell RA, Bussey TJ, Saksida LM. 2006. Why does brain damage impair memory? A connectionist model of object recognition memory in perirhinal cortex. J Neurosci 26:12186–12197.

Desimone R, Ungerleider LG. 1989. Neural mechanisms of visual processing in monkeys. In: Boller F, Grafman J, editors. Handbook of Neuropsychology. New York: Elsevier Science. pp 267–299.

Eacott MJ, Gaffan D, Murray EA. 1994. Preserved recognition memory for small sets, and impaired stimulus identification for large sets, following rhinal cortex ablations in monkeys. Eur J Neurosci 6:1466–1478.

Eichenbaum H, Otto T, Cohen NJ. 1994. Two functional components of the hippocampal memory system. Behav Brain Sci 17: 449–518.

Ennaceur A, Delacour J. 1988. A new one-trial test for neurobiological studies of memory in rats. I. Behavioral data. Behav Brain Res 31:49–57.

Forwood SE, Winters BD, Bussey TJ. 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. 2002. Against memory systems. Philos Trans Royal Soc, Lond B 357:1111–1121.

Kanwisher N. 2006. What's in a face? Science 311:617–618.

Lee AC, Barense MD, Graham KS. 2005a. The contribution of the human medial temporal lobe to perception: Bridging the gap between animal and human studies. Quart J Exp Psychol B 58:300–325.

Lee AC, Buckley MJ, Pegman SJ, Spiers H, Scahill VL, Gaffan D, Bussey TJ, Davies RR, Kapur N, Hodges JR and others. 2005b. Specialization in the medial temporal lobe for processing of objects and scenes. Hippocampus 15:782–797.

Lee AC, Bussey TJ, Murray EA, Saksida LM, Epstein RA, Kapur N, Hodges JR, Graham KS. 2005c. Perceptual deficits in amnesia: Challenging the medial temporal lobe 'mnemonic' view. Neuropsychologia 43:1–11.

Levy DA, Shrager Y, Squire LR. 2005. Intact visual discrimination of complex and feature-ambiguous stimuli in the absence of perirhinal cortex. Learn Mem 12:61–66.

Meunier M, Bachevalier J, Mishkin M, Murray EA. 1993. Effects on visual recognition of combined and separate ablations of the entorhinal and perirhinal cortex in rhesus monkeys. J Neurosci 13: 5418–5432.

Mishkin M, Suzuki WA, Gadian DG, Vargha-Khadem F. 1997. Hierarchical organization of cognitive memory. Philos Trans Royal Soc Lond B 352:1461–1467.

Mumby DG, Pinel JP. 1994. Rhinal cortex lesions and object recognition in rats. Behav Neurosci 108:11–18.

Murray EA, Bussey TJ. 1999. Perceptual-mnemonic functions of perirhinal cortex. Trend Cogn Sci 3:142–151.

Murray EA, Bussey TJ, Saksida LM, Hampton R. 2000. The parahippocamal region and object identification. Annal N Y Acad Sci 911: 166–174.

Murray EA, Bussey TJ, Saksida LM. 2007. Visual perception and memory: A new view of medial temporal lobe function in primates and rodents. Ann Rev Neurosci (in press).

Norman KA, O'Reilly RC. 2003. Modeling hippocampal and neocortical contributions to recognition memory: A complementary-learning-systems approach. Psychol Rev 110:611–646.

O'Keefe J, Nadel L. 1978. The hippocampus as a cognitive map. Oxford: Oxford University Press.

Rawlins JNP, Lyford GL, Seferiades A, Deacon RMJ, Cassaday HJ. 1993. Critical determinants of nonspatial working memory deficits in rats with conventional lesions of the hippocampus or fornix. Behav Neurosci 107:420–433.

Riesenhuber M, Poggio T. 1999. Hierarchical models of object recognition in cortex. Nat Neurosci 2:1019–1025.

Saksida LM, Bussey TJ, Buckmaster CA, Murray EA. 2007. Impairment and facilitation of transverse patterning after lesions of the perirhinal cortex and hippocampus, respectively. Cereb Cortex 17:108–115.

Schacter DL, Tulving E. 1994. Memory systems 1994. Cambridge, Massachusetts: MIT Press.

Shrager Y, Gold JJ, Hopkins RO, Squire LR. 2006. Intact visual perception in memory-impaired patients with medial temporal lobe lesions. J Neurosci 26:2235–2240.

Squire LR. 1992. Memory and the hippocampus: A synthesis from findings with rats, monkeys, and humans. Psychological Review 99:195–231.

Squire LR, Zola-Morgan S. 1991. The medial temporal lobe memory system. Science 253:1380–1386.

Squire LR, Shrager Y, Levy DA. 2006. Lack of evidence for a role of medial temporal lobe structures in visual perception. Learn Mem 13:106–107.

Tulving E, Schacter DL. 1990. Priming and human memory systems. Science 247:301–306.

Warrington EK, Weiskrantz L. 1974. The effect of prior learning on subsequent retention in amnesic patients. Neuropsychologia 12:419–428.

Winters BD, Bussey TJ. 2005a. Glutamate receptors in perirhinal cortex mediate encoding, retrieval, and consolidation of object recognition memory. J Neurosci 25:4243–4251.

Winters BD, Bussey TJ. 2005b. Removal of cholinergic input to perirhinal cortex disrupts object recognition but not spatial working memory in the rat. Eur J Neurosci 21:2263–2270.

Winters BD, Bussey TJ. 2005c. Transient inactivation of perirhinal cortex disrupts encoding, retrieval, and consolidation of object recognition memory. J Neurosci 25:52–61.

Winters BD, Forwood SE, Cowell RA, Saksida LM, Bussey TJ. 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. J Neurosci 24:5901–5908.

Winters BD, Saksida LM, Bussey TJ. 2006. Paradoxical facilitation of object recognition memory after infusion of scopolamine into perirhinal cortex: Implications for cholinergic system function. J Neurosci 26:9520–9529.