

Monkey perirhinal cortex is critical for visual memory, but not for visual perception: Reexamination of the behavioural evidence from monkeys

Robert R. Hampton

Emory University, Atlanta, GA, USA

Overdependence on discrimination learning paradigms to assess the function of perirhinal cortex has complicated understanding of the cognitive role of this structure. Impairments in discrimination learning can result from at least two distinct causes: (a) failure to accurately apprehend and represent the relevant stimuli, or (b) failure to form and remember associations between stimulus representations and reward. Thus, the results of discrimination learning experiments do not readily differentiate deficits in perception from deficits in learning and memory. Here I describe studies that do dissociate learning and memory from perception and show that perirhinal cortex damage impairs learning and/or memory, but not perception. Reanalysis and reconsideration of other published data call into further question the hypothesis that the monkey perirhinal cortex plays a critical role in visual perception.

The perirhinal cortex appears well placed in the brain to participate in both memory and perception. It is located at the downstream end of the ventral visual processing stream where it could contribute to the final stages of visual perceptual processing (Murray & Bussey, 1999). Alternatively, this access to highly processed visual input, combined with strong connections to the hippocampus via entorhinal cortex (Suzuki, 1996), could support a critical role in memory. Neurons in perirhinal cortex also have properties consistent with either role. They have large receptive fields (Jagadeesh, Chelazzi, Mishkin, & Desimone, 2001) and respond selectively to complex visual stimuli (Logothetis, 1998). Behavioural studies of monkeys with perirhinal cortex removed have been used to support both mnemonic and perceptual roles for perirhinal cortex. Delay-dependent deficits in recognition memory have

Correspondence should be addressed to Robert R. Hampton, Department of Psychology and Yerkes National Primate Research Center, Emory University, 532 Kilgo Circle, Atlanta, GA 30322, USA. Email: robert.hampton@emory.edu

The experimental work conducted by the author was supported by the National Institute of Mental Health Intramural Research Program. Preparation of the manuscript was supported by Yerkes National Primate Research Center Base Grant RR00165. Heather Kirby provided assistance with the figures and provided comments on earlier drafts.

been observed following removal of perirhinal cortex (e.g., Buffalo et al., 1999; Buffalo, Ramus, Squire, & Zola, 2000; Eacott, Gaffan, & Murray, 1994; Meunier, Bachevalier, Mishkin, & Murray, 1993; Zola-Morgan, Squire, Amaral, & Suzuki, 1989) and have generally been interpreted as reflecting amnesia. Other deficits following perirhinal cortex removal, although not inconsistent with a mnemonic role, have suggested contributions to perception. For example, the formation and maintenance of stimulus–stimulus associations between individual objects depend on the perirhinal cortex, and such associations may contribute to the ability to perceive whole objects (Buckley & Gaffan, 1998a; Eacott & Gaffan, this issue; Murray, 2000; Murray, Gaffan, & Mishkin, 1993). Based on the inference of interference between visual representations in discrimination learning, Buckley and Gaffan (1997, 1998b) argued that perirhinal cortex lesions cause impairments in perception or representation of stimuli. Thus, recent reports have posited a role for perirhinal cortex either exclusively in memory (Buffalo et al., 1999; Hampton & Murray, 2002) or in memory as well as in perception (Buckley, this issue; Buckley & Gaffan, 1997, 1998b; Bussey, Saksida, & Murray, this issue; Eacott & Heywood, 1995; Lee, Barense, & Graham, this issue; Murray, 2000; Murray & Bussey, 1999; Murray, Malkova, & Goulet, 1998).

In this paper I argue that there is strong evidence indicating that the perirhinal cortex is critical for learning and memory in monkeys, whereas support for the hypothesis that this structure contributes significantly to perceptual processes is comparatively weak. In making this argument I adopt specific definitions of perception and memory. While there is no a priori reason to presume that perception and memory do not share neural substrates, potentially including the perirhinal cortex (e.g., Murray & Bussey, 1999), the processes of perception and memory can be distinguished behaviourally. *Perception* involves the immediate apprehension and initial representation of stimuli currently impinging on a sensory surface. Complementing this role of perception in initially representing stimuli, *memory* involves the retention and retrieval of representations when stimuli are absent and therefore are not stimulating a sensory surface. For example, an otherwise normal subject that cannot detect the difference in colour between simultaneously presented squares is said to fail to perceive the colour difference. In contrast, a memory failure is inferred if the subject can correctly indicate that two squares differ in colour, but cannot indicate which one was recently seen and then withdrawn from view. Use of these definitions makes it straight forward to implement experiments that test the two processes independently. However, adopting these definitions does not commit one to the position that the neural substrates of memory and perception are distinct. Deficits in both perception and memory could be observed following selective brain damage to a given structure. Finally, it should be recognized that memory is not confined to retention of isolated representations, but can entail encoding of relationships such as lightning predicts thunder, and cardinals are birds that are red.

I apply these definitions of perception and memory to a review of the evidence regarding the function of the monkey perirhinal cortex, focusing exclusively on work with monkeys. In the first section I present a critique of some of the reports often cited in support of the hypothesis that perirhinal cortex is critical for visual perception and argue that reanalysis of the results indicates memory deficits rather than perceptual deficits. In the second section I summarize a series of experiments that demonstrate intact perception but impaired memory in monkeys lacking perirhinal cortex. In the third section, the significance of experiments testing the perceptual-mnemonic model of perirhinal cortex function in monkeys is considered.

What evidence indicates that perirhinal cortex contributes to perception?

The significance of the perirhinal cortex first became apparent through comparison with the function of the hippocampus, a structure widely believed to be critical for some types of memory. Much of the early work on the perirhinal cortex in monkeys was therefore motivated by interest in memory rather than perception. A series of studies conducted in the 1980s and 1990s showed that lesions of the perirhinal cortex produced recognition memory deficits (as measured by matching- and nonmatching-to-sample) nearly as severe as those resulting from large medial temporal lobe aspiration lesions that included the hippocampus (Meunier et al., 1993; Murray & Mishkin, 1986, 1998; Zola-Morgan et al., 1989). However, the observation of a set size effect (Eacott et al., 1994) in one early experiment directed thinking towards perceptual functions of perirhinal cortex. Using an automated matching-to-sample procedure, these authors found that the magnitude of the recognition memory impairment observed following perirhinal cortex removal was a function of the number of discriminanda employed in the memory tests. When stimuli were essentially trial unique, a large impairment was observed, whereas if a small set of highly familiar images was used, the deficit was relatively mild (and the task was very difficult for control and experimental animals alike). Because these results showed that the monkeys lacking perirhinal cortex were impaired on some but not other memory tests, they triggered a search for non mnemonic accounts of perirhinal cortex function.

Possibly stimulated by the set size effects observed in recognition memory by Eacott and colleagues, Buckley and Gaffan (1997) investigated the role of set size in discrimination learning. In discrimination learning, subjects learn over repeated presentations that one of two simultaneously presented images or objects is associated with food reward while the other is not. Successful performance requires both the ability to discriminate the items in each pair from one another and the ability to learn and remember the association of one of the items with food reward. In concurrent object discrimination learning, more than one discrimination problem is presented in each test session. Set size refers to the number of discrimination problems learned simultaneously, or concurrently. Buckley and Gaffan (1997) reported that monkeys with perirhinal cortex lesions were impaired in learning large, but not small, sets of object discrimination problems. This is probably the piece of evidence most often cited in support of the hypothesis that perirhinal cortex is critical for perception. Reanalysis of the original data demonstrates that there is in fact no set size effect.

Buckley and Gaffan (1997) proposed that stimuli in larger sets are more likely to be perceptually confused with one another than are stimuli in smaller sets. Due to the perceptual challenge inherent in learning a large set of discrimination problems simultaneously, they predicted that monkeys with perirhinal cortex removed would be especially impaired in learning large problem sets. The critical comparison in this study was of the number of errors made learning sets of 20, 40, or 80 object discriminations concurrently. While the results initially appear to demonstrate a perceptual impairment following perirhinal cortex removal, further examination shows this not to be the case. The following concrete example helps clarify the issue.

Two groups of monkeys make 5 and 10 errors, respectively, in learning a single discrimination problem. By a simple process of multiplication the groups would be expected to

make 50 and 100 errors, respectively, in learning a set of 10 problems of equal difficulty. Note that the magnitude of the difference between the groups is a function of the number of problems learned. The groups differ by 5 errors in learning a single problem, but differ by 50 errors in learning 10 problems (10 times as many problems, 10 times as many errors). However, in both cases the monkeys make 5 and 10 errors, respectively, *per problem*, and the ratio of errors made by the two groups is a constant 2 to 1. Analysis of variance (ANOVA) of the errors made learning 1 problem and learning the set of 10 problems would yield a significant Group \times Set Size interaction. Such a result could give the false impression that learning becomes more difficult as the number of problems learned increases. If it were actually more difficult for the slower group to learn discriminations as the set size is increased, a nonlinear increase in the difference in errors between the groups would be observed. That is, the slow group would commit more errors per problem in learning a larger set, and the number of errors made learning each problem by the two groups would change as set size increased. To assess the difficulty of learning each discrimination problem as a function of set size, performance should be measured as errors per problem (a ratio measure), rather than total errors.

In comparing the rate at which normal monkeys and monkeys lacking perirhinal cortex learned discrimination problems in different set sizes, Buckley and Gaffan (1997) failed to take into account the difference between errors per problem and total errors. The importance of this difference is highlighted graphically in Figure 1, which plots data from Buckley and Gaffan (1997; data for individual monkeys were provided in Table 1 of that paper). The left panel of Figure 1, which plots total errors, gives the impression of an interaction between group and set size. In contrast, the right panel indicates no such interaction. Rather, there is a consistent, marginally significant deficit in the monkeys lacking perirhinal cortex (mean errors/problem at each set size for monkeys lacking perirhinal cortex and control monkeys, respectively: Set Size 20, 6.07 vs. 3.34; Set Size 40, 7.26 vs. 3.44; Set Size 80, 7.44 vs. 3.5);

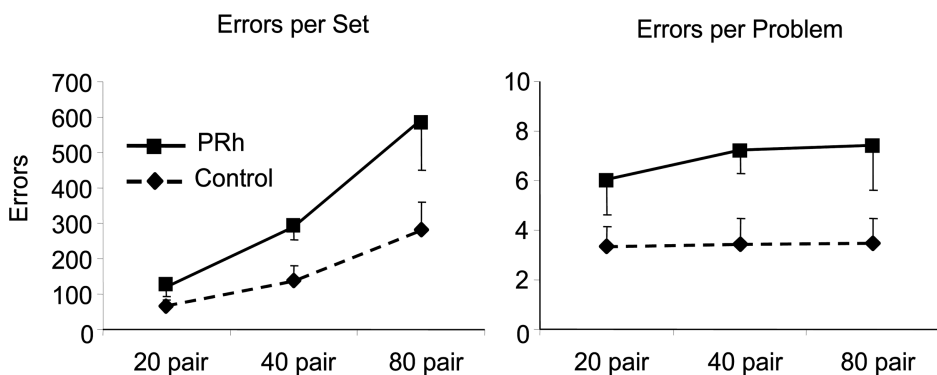


Figure 1. Graphs of data from Buckley and Gaffan (1997). Both the left and the right panels plot errors made learning three sets of discrimination problems by control monkeys and monkeys lacking perirhinal cortex. Total errors committed while learning the discrimination problem sets is plotted in the left panel. The more appropriate measure of errors per discrimination problem is plotted in the right panel. Note that the left panel gives the impression of an interaction between group and set size, while the right panel does not.

group, $F(1, 6) = 5.17$, $p = .06$; Set Size, $F(2,12) = 0.53$, $p = .60$; Group \times Set Size, $F(2, 12) = 0.66$, $p = .53$; log 10 transformed data. Statistically identical results are obtained with the untransformed data. This consistent difference in errors per problem is exactly the result predicted by a deficit in learning or memory rather than a deficit in perception. In evaluating the significance of this negative evidence, it should be noted that the perceptual account of perirhinal cortex might be interpreted to predict a huge increase in errors when monkeys learn the largest set because they have to learn this set after already learning many other discriminations earlier in the study.

In another set of influential studies, Buckley and Gaffan (1998b) presented monkeys with digitized images of objects taken from six different perspectives. After the discriminations had been learned from three of the six perspectives, the monkeys were tested for their ability to relearn discriminations of the same objects using the photographs taken from the remaining three perspectives. Because generalization to the new views is thought to be perceptually challenging, Buckley and Gaffan (1998b) predicted that monkeys with perirhinal cortex removed would be impaired relative to controls. Indeed, the perirhinal group was impaired in relearning the discriminations. But this result in isolation does not demonstrate that the deficit was due to a perceptual impairment. If tests with the new views taxed perception, and monkeys with perirhinal cortex removed were perceptually impaired, then the impairment in this group should be greater in relearning tests than in the initial learning of the discriminations. Otherwise the newly observed deficit simply recapitulates the deficit observed in initial learning. In initial learning of 40 discrimination problems, Buckley and Gaffan's (1998b) operated monkeys made, on average, nearly twice as many errors as did experimental animals (214 vs. 120 errors; inferential statistics were not reported). On the transfer test, controls made an average of 11 errors, while operated monkeys made an average of 41 errors (a significant difference by the one-tailed test reported). Given that one of the three operated monkeys made more than twice as many errors as did the other two, thus substantially biasing the mean, it seems unlikely that these scores represent a significant change from the 2:1 difference observed in initial learning. Monkeys lacking perirhinal cortex may have been impaired on the transfer test, not because of problems with generalization to the new views per se, but because of a general impairment in visual discrimination learning. This learning impairment could occur because in the experimental design used by Buckley and Gaffan (1998b) objects were photographed from different vantage points. As a result, new visual features appeared on the transfer tests (e.g., the back side of the objects). Because the transfer tests thereby required learning of new associations between visual features and reward, the observed impairment in monkeys lacking perirhinal cortex could be due to a learning or memory impairment (see Buckley, this issue, for further reanalysis of their data).

In a follow-up experiment the same monkeys were required to discriminate a subset of the familiar objects embedded in novel, cluttered scenes (Buckley & Gaffan, 1998b). Embedding the images in cluttered scenes was intended to tax perception. Monkeys with perirhinal cortex lesions were again impaired in relearning the discriminations to criterion, accruing double the errors made by controls (246 vs. 123 errors). Again, however, this manipulation of perceptual difficulty did not increase the magnitude of the deficit observed in operated animals over that found in initial learning (i.e., 2 to 1), so this result, too, is consistent with a general role for perirhinal cortex in visual discrimination learning rather than in perception.

Taken together, the foregoing reexaminations of published results cast doubt upon the idea that perirhinal cortex is critical for visual perception. Reanalysis of the discrimination set size experiments of Buckley and Gaffan (1997) shows that large set size does not exacerbate the deficit in discrimination learning observed in monkeys lacking perirhinal cortex. Rather, there is an invariant deficit in learning that is evident across set sizes. Failure to find such deficits in small sets is probably an issue of statistical power, which will increase with set size. While it is the case that monkeys lacking perirhinal cortex are impaired in learning to discriminate new views of familiar objects and familiar objects in new settings, these results do not demonstrate a role for perirhinal cortex in perception. As in the case of the set size manipulation, it appears that the deficits observed were invariant across variations in perceptual demand, a result that is inconsistent with the view that perirhinal cortex is especially important under conditions of perceptual difficulty.

Exhaustive review of the findings of Buckley and colleagues is beyond the scope of this paper. However, one more set of results deserves attention, as it is put forward as evidence contradictory to the foregoing analyses. Buckley, Booth, Rolls, and Gaffan (2001) presented normal monkeys and monkeys lacking perirhinal cortex with arrays of images in which all but one of the images were the same. The monkeys were required to identify the single image that differed from the others. In one type of problem, images deemed the same were exactly identical (image oddity). In the other type of problem, images deemed the same were views of the same stimulus from different vantage points, while the odd image was a view of a different stimulus (object oddity). Monkeys lacking perirhinal cortex were reported to be impaired in learning object oddity tasks but not impaired in learning image oddity tasks. In assessing these results it is critical to keep two points in mind. First, the dependent measures were again measures of *learning*, rather than perceptual generalization on a single trial, so perceptual and mnemonic processes were confounded. Second, because stimuli deemed to be the same in the object oddity task were different views of the same object, they necessarily contained different visual information, much as the front and back of an object can be visually distinct. It would appear that the only way these differing views could come to be treated as the same by monkeys is through learning. Therefore the impairment in acquiring object oddity problems is at least as likely to be due to a learning or memory impairment as to a perceptual impairment.

On a more technical note, the magnitude of the differences between the groups across the different tasks does not correlate with the statistical significance of the results in a sensible way (Buckley et al., 2001). For example, in the image oddity task employing human faces, monkeys lacking perirhinal cortex made about four times as many errors as did normal monkeys, but the difference was not significant. In the case of object oddity with human faces this ratio of errors is about 1.5, and the difference is significant. A similar inversion of the effect size and the statistical results occurs for these tests with monkey faces. In most of the remaining object oddity–image oddity contrasts, direct comparisons cannot be made because the data were treated differently, and different performance criteria were employed, for the two types of task (Buckley et al., 2001). In summary, these reanalyses and reexaminations of the data from Buckley and colleagues do not call into doubt the fact that monkeys lacking perirhinal cortex are impaired in various types of discrimination learning. However, the source of the impairment seems to be difficulty with learning or memory, not a difficulty in perceptual processing.

Evidence for intact perception and impaired retention

The reanalyses presented in the preceding section call into question the hypothesis that perirhinal cortex is critical for perception. To more directly distinguish between perceptual and mnemonic accounts of perirhinal cortex function, Hampton and Murray (2002) designed a series of experiments that independently assessed perceptual and mnemonic function. The first study in the series also assessed whether images that differed in visual complexity might be differentially difficult for monkeys lacking perirhinal cortex to learn to discriminate. If perirhinal cortex is responsible for the highest level of a hierarchical organization of perceptual processing in the ventral visual processing stream (Bussey et al., this issue; Murray & Bussey, 1999; Saksida & Bussey, 2002), then removal of this area might impair processing of complex images while leaving processing of simpler images intact.

Effect of stimulus complexity on learning

To test whether the complexity of the images to be remembered is a determinant of the involvement of perirhinal cortex in discrimination learning, Hampton and Murray (2002) examined acquisition of discrimination problems using different types of visual stimuli: (a) *Black-and-white* images were filled outline drawings of various objects resembling silhouettes; (b) *colour* images were similar to the black and white images in form, but included one or more colours and some internal details; (c) *detailed* images were perspective renderings approaching photographic quality (see Hampton & Murray, 2002, Figure 1, for examples of the stimuli). Monkeys were trained on each of the three types of image concurrently, receiving one trial with each discrimination problem each day. Monkeys with perirhinal cortex removed were impaired in learning all three types of discrimination, but were no more impaired in learning the more complex detailed images than they were in learning the simple images (Figure 2); Group, $F(1, 8) = 9.34, p < .05$; Image type, $F(2, 16) = 10.39, p < .01$; Group \times Image type, $F(2, 16) = 0.13$. While the discriminations involving the detailed images were learned more rapidly by both groups of monkeys, the operated group made roughly two errors to every one error made by the control group across the three types of problem. These results suggest that the perirhinal cortex is not especially critical for discriminating complex stimuli.

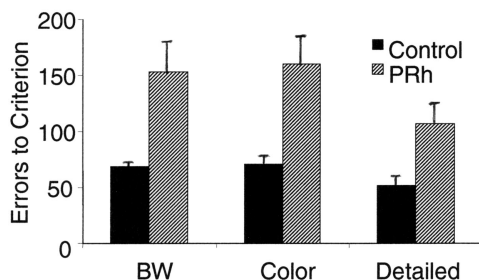


Figure 2. Average errors committed in learning object discrimination problems involving stimuli of three levels of complexity (Hampton & Murray, 2002, Exp. 1). Control monkeys, black bars; Monkeys lacking perirhinal cortex, striped bars. Vertical lines indicate standard errors. Monkeys lacking perirhinal cortex were impaired equally in learning all three types of discrimination problem.

Whereas these results do clearly show that monkeys with perirhinal cortex removed are impaired in learning new visual discriminations, they do not allow differentiation between impairment caused by deficits in visual perception and deficits in learning or memory. This is because the deficit in discrimination learning could be due either to a deficit in perception of the stimuli or to a deficit in learning or retention of the association between food reward and one of the images in each discrimination problem. In a series of subsequent experiments, Hampton and Murray (2002) therefore assessed visual perception free of the requirement for new learning. If the deficit in discrimination learning is due to problems in perception, then monkeys lacking perirhinal cortex should continue to be impaired in tests that isolate perceptual function.

Perceptual tests free from new learning

After both intact monkeys and monkeys lacking perirhinal cortex had learned a large set of discrimination problems to criterion, they were challenged with difficult discriminations consisting of altered versions of the now very familiar discriminanda. The discriminations were made difficult by altering both images in each discrimination problem in the following ways: shrinking, removing colour, rotating, exchanging colours between objects, and masking with an opaque screen (see Hampton & Murray, 2002, for examples of these manipulations). Critically, each altered pair of discriminanda was presented only once or twice, intermixed with normal trials, to preclude the occurrence of new learning. By this method performance on probe trials using the altered stimuli assessed perceptual generalization unconfounded with new learning.

Each of the manipulations of the stimuli had the intended effect of making the discriminations difficult, indicated by the fact that the performance of all monkeys decreased significantly. But monkeys with perirhinal cortex removed had no more difficulty with any of these perceptually difficult discriminations than did normal monkeys. In one example experiment, the discriminations were made difficult by placing a mask over the discriminanda (Hampton & Murray, 2002, Exp. 6). The masks always covered 50% of the area of the test image, and there were six types of mask, differing in the size of the blocks making up the mask. When masks made with the smallest size blocks were used, the effect was essentially to dim the images as if they were viewed through muslin. The largest size block completely obscured the left half of the images. Superposition of the masks on the discriminanda affected performance in both groups according to a U-shaped function. That is, the difficulty of the discriminations increased as the size of the blocks making up the mask increased until half of the image was occluded by a single block, and the discrimination then became easier (Figure 3). Despite a substantial effect on overall performance, superposition of the masks did not differentially affect the performance of monkeys lacking perirhinal cortex.

These findings show that in the absence of any requirement for new learning, and in the presence of a variety of perceptual challenges, perirhinal cortex is not required for perceptual generalization. Although these manipulations did make the discriminations substantially more difficult for both control and operated monkeys, none of the manipulations differentially affected the performance of monkeys with lesions of perirhinal cortex. Therefore, it would appear that the deficits observed in initial learning of the discrimination by monkeys lacking perirhinal cortex were due to a learning or memory impairment, rather

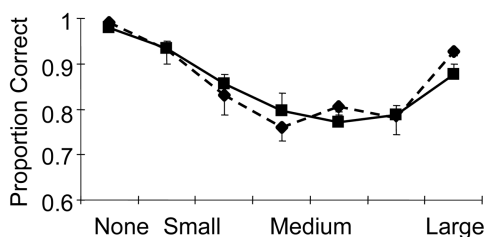


Figure 3. Accuracy on standard trials and on probe trials in which masks of six different mesh sizes were superimposed on the discriminanda (Hampton & Murray, 2002, Exp. 6). Control monkeys, solid lines; Monkeys lacking perirhinal cortex, dashed lines. Error bars are standard errors. While superposition of the masks made the discriminations difficult for both groups, there was no difference between the groups.

than an impairment in perception. This hypothesis was tested directly in a second series of experiments, described in the next section, in which new learning was required without any increase in perceptual demand.

Tests of learning free from new perceptual challenge

Monkeys with perirhinal cortex removed were impaired in learning new discrimination problems but were not impaired in generalizing this learning to altered views of the learned discriminations (Hampton & Murray, 2002). One interpretation of these findings is that monkeys with perirhinal cortex lesions are generally impaired in remembering stimulus–reward associations but have intact perception. If so, then they should be impaired under conditions of reversal learning. In reversal learning, the valence of each object discrimination problem is reversed such that the image that was previously unrewarded is now the correct image, while the previously correct image is now unrewarded. The value of reversal learning in the current context is that the monkeys have already demonstrated their ability to discriminate the two stimuli comprising each discrimination problem and thus have demonstrated perceptual mastery of the problems. The new demand placed on them by reversal learning is to learn and remember a new association between an image and food reward. That is, reversal learning provides a measure of learning that is relatively free of new demands on perceptual or representational mechanisms (e.g., Gaffan & Harrison, 1986, p. 7). A perceptual account of perirhinal cortex function predicts that monkeys lacking perirhinal cortex should be unimpaired in reversal learning, while a mnemonic account predicts an impairment. In three replications, monkeys with perirhinal cortex removed were impaired in reversal learning (Hampton & Murray, 2002, Exp. 7, 8, and 9). Reversal learning requires memory, but does not place new demands on perceptual processes. These results show that a memory impairment can be obtained in monkeys lacking perirhinal cortex without taxing perception.

Matching-to-sample

The preceding findings implicate perirhinal cortex in learning or memory, but not in perception. Matching- and nonmatching-to-sample are additional ways of assessing memory. In the primate literature these are generally referred to as recognition memory tests.

In recognition memory tests subjects are presented with a sample stimulus to which they make a study response, typically by touching the image or object. The object is then removed from view for a delay period during which the monkey must remember the stimulus in order to respond correctly at test. Following this delay, the sample stimulus is again presented, with one or more distractor stimuli. The monkeys must then either touch the previously viewed sample stimulus, or avoid this stimulus, depending on whether the rule is matching or nonmatching, respectively. Correct performance demonstrates that the monkey remembers or recognizes the sample stimulus. Manipulation of the delay interval over which monkeys must remember the sample stimulus provides a means of taxing memory—the longer the delay interval, the greater the demand on memory.

The performance of monkeys in recognition memory tests can be diagnostic of both memory impairments and perceptual impairments. When the delay between viewing the sample and presentation of the test is very short, the demand on memory is not great (although some demand does exist because there is a delay, however brief). Monkeys with memory impairments, but with intact perception, would be predicted to perform normally at very short delay intervals, but to perform increasingly poorly in comparison to normal monkeys as the delay interval is increased. Animals with perceptual impairments would be predicted to perform equally poorly relative to controls at all delays because they have difficulty in apprehending or representing the sample stimulus and in discriminating it from the distractor stimuli at test. The patterns of data predicted for animals with perceptual impairment and those with memory impairment are depicted in Figure 4.

A number of experiments have assessed recognition memory performance in monkeys with lesions that include the perirhinal cortex. In the majority of these studies monkeys lacking perirhinal cortex have shown delay-dependent impairments, such that performance compared to controls was worse at long delays than at short delays (Buffalo et al., 1999; Buffalo et al., 2000; Eacott et al., 1994; Meunier et al., 1993; Zola-Morgan et al., 1989; but

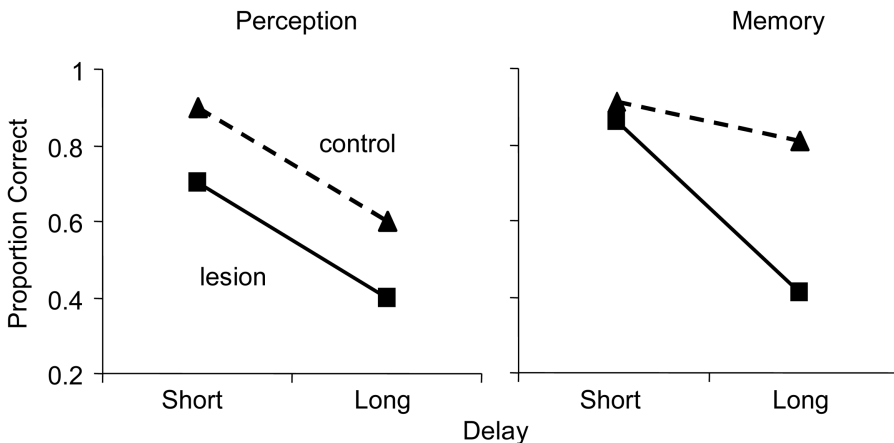


Figure 4. Patterns of deficit in recognition memory tests predicted by perceptual and mnemonic impairment. Accuracy is plotted on the vertical axis, while the duration of the delay between study and test is plotted on the horizontal axis. The left panel plots the pattern predicted by a perceptual deficit, while the right panel indicates the pattern expected in the case of a mnemonic deficit.

see Eacott et al., 1994, for an exception). Some of these studies also found deficits in performance at the shortest delay used, although often the shortest delay was still considerable. It has been a matter of debate whether or not the performance of normal monkeys and monkeys with perirhinal cortex removed can be equated at very short delays (e.g., Buffalo et al., 2000, pp. 379–380).

The same monkeys used in the experiments described previously (Hampton & Murray, 2002) have produced two relevant results in recognition memory experiments. First, the monkeys with perirhinal cortex removed were shown to have a dramatic delay-dependent memory impairment over the range of 2 to 32 seconds with no significant impairment at the shortest delay (Hampton & Murray, unpublished results). In a second recognition memory experiment, control monkeys were perceptually impaired by masking the sample stimulus with an opaque grid. Performance under these conditions was then compared to that under normal conditions, without the perceptually challenging mask. Masking the sample impaired performance at all delays, but the forgetting curve generated under the conditions of perceptual impairment was parallel to the normal forgetting curve, as in the hypothetical data in the left panel of Figure 4 (Hampton & Murray, unpublished results). The finding of a delay-dependent memory deficit reinforces the view that perirhinal cortex removal causes memory impairment. The second set of results suggests that even if monkeys with perirhinal cortex removed did have perceptual impairments, such impairments would not cause delay-dependent deficits in performance. Perceptually challenging normal monkeys by masking the sample images did not lead to more rapid forgetting than that which occurred under normal conditions. However, it remains for further work to test whether other perceptual manipulations have different effects on recognition memory.

In this section, I have reviewed data showing that monkeys lacking perirhinal cortex were unimpaired in a variety of difficult perceptual tests. The same monkeys were reliably impaired in reversal learning. Data from a variety of sources show that monkeys lacking perirhinal cortex show a delay-dependent impairment in recognition memory tests (e.g., Buffalo et al., 1999; Buffalo et al., 2000; Eacott et al., 1994; Meunier et al., 1993; Zola-Morgan et al., 1989). It has been argued that delay dependence is an indicator of memory impairment distinct from perceptual impairment. Taken together, these findings demonstrate a learning or memory impairment in the absence of a perceptual impairment. In the next section I present a critique of the influential perceptual-mnemonic model of perirhinal cortex.

What is perceptual-mnemonic?

The perceptual-mnemonic model of perirhinal cortex function posits that perihinal cortex plays a critical role in the binding of individual features making up whole objects (Bussey, Saksida, & Murray, 2002, 2003; Bussey et al., this issue; Lee et al., this issue; Murray & Bussey, 1999; Rolls, Franco, & Stringer, this issue; Saksida & Bussey, 2002). It is based on the observation that neurons located more rostrally in inferior temporal cortex have more complex response properties than do more caudally located neurons (e.g., Desimone & Ungerleider, 1989), suggesting that these rostral neurons represent complex conjunctions of features (Bright, Moss, Stamatakis, & Tyler, this issue). Applied to discrimination learning the perceptual-mnemonic theory is essentially a migration of configural learning theory out of the hippocampus and into subjacent cortex (Rudy & Sutherland, 1995).

The perceptual-mnemonic model presents the greatest challenge to the view put forward in this paper that the perirhinal cortex is involved in memory but not in perception.

I take up four criticisms of the perceptual-mnemonic model: (a) As currently stated, the model is almost invulnerable to direct falsification; (b) a central prediction of the model was shown not to obtain in the first section of this paper; (c) the model has not been evaluated with direct tests of perceptual function in monkeys, free of a requirement of learning; and (d) the model does not account for delay-dependent memory impairments following perirhinal cortex removal.

The perceptual-mnemonic model predicts that monkeys lacking perirhinal cortex will be impaired in discrimination learning only when the images being discriminated are similar such that some features are rewarded when part of one image, but not rewarded when part of another. This situation is referred to as feature overlap or feature ambiguity. When feature ambiguity is high, a configural representation of the discriminanda that binds together component features of an image is expected to greatly facilitate learning. The inability of monkeys lacking perirhinal cortex to form these configural representations would therefore lead to an impairment in discrimination learning only under conditions of feature ambiguity. This prediction has been evaluated in a creative set of experiments employing images that are blended with each other so that they are ambiguous and share many features (Bussey et al., 2002). All monkeys rapidly learned discriminations in which few or no features were shared between discriminanda, and monkeys with perirhinal cortex removed performed nearly as well as control monkeys. In contrast, when feature ambiguity was high, all monkeys learned comparatively slowly, and those lacking perirhinal cortex learned especially slowly (Bussey et al., 2002, 2003). These findings support the perceptual-mnemonic model.

When is feature ambiguity present?

The perceptual-mnemonic model predicts deficits only when feature ambiguity complicates the discrimination of stimuli (Bussey et al., 2002, 2003; Murray & Bussey, 1999; Saksida & Bussey, 2002). In their experiments testing the model, Bussey and colleagues have used novel and creative ways of creating feature ambiguity, most notably the use of software that allows blending of images such that they share many features (Bussey et al., 2003). By using these techniques they have been able to parametrically manipulate feature overlap in an objective manner. But it is difficult to apply the notion of feature ambiguity outside of the confines of these experiments. Further complicating the application of feature ambiguity is the fact that the model predicts that discrimination ability will depend on the perirhinal cortex only if the ambiguity is at a certain level in the hierarchy of visual representation proposed to exist in the ventral visual processing stream. Ambiguity at early stages in visual processing can be resolved at those early stages. It can therefore be argued post hoc whenever deficits in discrimination learning are observed that there must have been feature ambiguity, and when such deficits have not been observed there must have been no such ambiguity. It is difficult or impossible to independently assess the degree and level of feature ambiguity in a given set of stimuli.

Monkeys were trained on discrimination problems that minimized feature ambiguity in an effort to address the argument that feature ambiguity could explain the discrimination learning deficits observed in monkeys with perirhinal cortex removed (Hampton & Murray, 2002). This test limited feature ambiguity in two ways. First, the images used in each

discrimination problem were selected because they were extremely distinctive to human observers, subjectively more so than were the low ambiguity images used by Bussey et al. (2003). Second, the problems were presented one at a time (set size = 1), rather than concurrently, so that difficulty with feature overlap between problems would be minimized. Monkeys lacking perirhinal cortex were nonetheless found to be impaired in learning and in reversal of these discrimination problems (Hampton & Murray, 2002, Exp. 8). Given the finding presented in the first section of this paper that no set size effect occurs in discrimination learning, it is not surprising that a deficit was observed even when pairs were learned individually. But the impairment in learning despite a lack of obvious feature ambiguity presents a challenge to the perceptual-mnemonic model. Nonetheless, it can be argued that feature ambiguity was present but was not detected by the human observers. If this were the case, however, one would think that feature ambiguity must be a pervasive quality that would complicate learning of virtually all discrimination problems.

False prediction?

A connectionist model was developed by Saksida and Bussey (2002) in an effort to formalize the perceptual-mnemonic model of perirhinal cortex function. The model instantiates a hierarchical organization of the ventral visual processing stream, with a feature conjunction layer representing perirhinal cortex. The feature conjunction layer can be removed from the model to simulate the effects of removing the perirhinal cortex from a monkey. The validity of the connectionist model, and thus the perceptual-mnemonic model, was evaluated by comparing the performance of a complete system to one with the feature conjunction layer removed. Removing the feature conjunction layer was predicted to have similar effects to those following perirhinal cortex removal in monkeys.

Indeed, the connectionist model performed in a way that closely matched the behaviour hypothesized to occur in real monkeys. Most notably, the connectionist model lacking the feature conjunction layer was impaired in learning a large set of discrimination problems, but was not impaired in learning a small set (Saksida & Bussey, 2002, Exps. 1 and 3), replicating the result reported by Buckley and Gaffan (1997). But this set size effect was reexamined at length in the first section of this paper and was shown not to occur in monkeys! Thus, the model predicts a major result that does not occur in the real world.

Tests of perception confounded with learning

Evaluation of the hypothesis that perirhinal cortex makes a critical contribution to perception requires use of tests that measure perceptual performance free of a requirement for learning. Such tests have not been conducted with stimuli in which feature ambiguity has been systematically manipulated. The perceptual-mnemonic model is supported by the finding of a functional relationship between the degree of feature ambiguity and the magnitude of the impairment in discrimination learning in monkeys lacking perirhinal cortex. That is, Bussey et al. (2002, 2003) report that under conditions of low feature ambiguity monkeys lacking perirhinal cortex show little or no impairment in learning, whereas under conditions of high feature ambiguity the impairment is substantial. It is the apparent functional relationship between perceptual demand and degree of impairment that makes the case that the impairment is due to perceptual demand.

Interpretation of this functional relationship is made difficult by the confounding of learning and perception in discrimination learning. While feature ambiguity does appear to be a challenge to perception, it can also be interpreted as a challenge to learning. Discriminations involving feature ambiguity cannot be solved on the basis of single stimulus features (Saksida & Bussey, 2002). Thus to solve these problems monkeys must remember multiple features of the discriminanda. This means that in order to solve the discriminations, monkeys have to remember more about the stimuli than they would under conditions of low feature ambiguity. This knowledge must be acquired through learning. If indeed more learning is required to solve discriminations high in feature ambiguity, then the observed functional relationship between degree of feature ambiguity and rate of learning can be equally well predicted by mnemonic load as by perceptual load.

Fortunately, this issue can be easily resolved with the techniques described by Hampton and Murray (2002). The same types of blended stimuli used previously by Bussey et al. (2003), which provide an objective and elegant means for manipulating feature ambiguity, could again be used. Monkeys would be trained on a large set of object discriminations using low-ambiguity stimuli. Once monkeys have mastered these discriminations, they would be presented with a single trial involving each discrimination problem, but now the stimuli would be blended together to create feature ambiguity. Because only a single presentation of each pair would be provided, the monkeys could not relearn the altered discriminations. Thus, the tests would be a pure measure of perceptual generalization. The perceptual-mnemonic model predicts that monkeys lacking perirhinal cortex would be impaired on these perceptual generalization tests. A purely mnemonic account of perirhinal cortex predicts that there would be no such impairment, as was observed in the perceptual tests of Hampton and Murray (2002).

In their work with blended stimuli, Bussey and colleagues have come closest to a pure perceptual test in an experiment using performance tests (Bussey et al., 2003, Exp. 2). In this experiment, monkeys were trained on four discrimination problems with low feature ambiguity. In performance tests monkeys were given blocks of trials with the familiar discriminanda now blended together to create feature ambiguity. The problems were presented at two levels of feature ambiguity, and in the originally learned form, in three blocks of 32 test trials. A percentage correct measure was generated by averaging performance in the 32 trial blocks and was taken as a measure of perceptual generalization. Monkeys lacking perirhinal cortex were impaired relative to controls in the two ambiguity conditions. This would provide strong evidence for a perceptual impairment, except for that fact that monkeys had a combined total of 64 trials with the altered stimuli in each performance test. After the first test trial, the monkeys have the opportunity to relearn the discriminations, and any deficit observed could therefore be one in learning rather than in perception. Bussey et al. (2003) reported that no significant learning occurred during the performance test. Given the rate at which control monkeys learned high feature ambiguity discriminations in the first experiment in this series (Bussey et al., 2003, Exp. 1), this is a surprising result. In that experiment, normal monkeys mastered high feature ambiguity discriminations in 96 trials and showed considerable learning over any given block of 64 trials. The comparison performed by Bussey et al. may have lacked sufficient statistical power to detect the improvement in performance across trials within a block, but when all trials were averaged together, the overall difference may have been large enough to detect statistically. In any case, using many discrimination problems and only a

single perceptual generalization test for each problem would provide the most direct test of perceptual function in monkeys lacking perirhinal cortex.

Failure to account for amnesia

Delay-dependent recognition memory impairments have been repeatedly demonstrated in monkeys lacking perirhinal cortex (Buffalo et al., 1999; Buffalo et al., 2000; Eacott et al., 1994; Meunier et al., 1993; Zola-Morgan et al., 1989, but see Eacott et al., 1994, for an exception). The perceptual-mnemonic model does not readily offer an account for this pervasive finding. The challenge is to explain how an impairment in coping with feature ambiguity could produce a greater memory impairment at long delays than at short delays. Successful application of the perceptual-mnemonic model to the impairments in recognition memory would be an advance for the model.

GENERAL DISCUSSION

In this paper I have critically evaluated the evidence implicating perirhinal cortex in perceptual processes. Overuse of discrimination learning has complicated interpretation of the function of perirhinal cortex because discrimination learning necessarily confounds learning or memory with perceptual processes. Perceptual processes are best assessed using tests that require subjects to make judgements about stimuli that are presented in only a single test trial. After the first presentation, performance can be influenced by learning and memory.

In the first section of this paper, previously published findings were subjected to reanalysis and reconsideration. It was shown that the oft-cited set size effect that has been used to implicate perirhinal cortex in perception does not obtain. There is no functional relationship between discrimination problem set size and the degree of impairment in monkeys lacking perirhinal cortex, as has been reported (Buckley & Gaffan, 1997). Concomitantly, there is little evidence that impairment in relearning familiar discrimination problems under difficult conditions is exacerbated relative to initial learning. In fact, monkeys lacking perirhinal cortex make a remarkably consistent two errors for every one error made by normal monkeys across a variety of tests (Buckley & Gaffan, 1997, 1998b). There is general agreement that monkeys lacking perirhinal cortex are impaired in discrimination learning, under at least some conditions. But if monkeys lacking perirhinal cortex were perceptually impaired, then the magnitude of the learning deficits in this group would increase as perceptual demand is increased. This was not observed.

In the second section of this paper I reviewed a set of experiments in which perceptual function and learning were assessed independently in distinct tests (Hampton & Murray, 2002). Most significantly, the perceptual assessments involved just one or two presentations of each test. Monkeys lacking perirhinal cortex were unimpaired in the face of a variety of perceptual challenges, despite the fact that the tests were sufficiently difficult to cause significant drops in performance in both normal and operated monkeys. Conversely, when new learning was required that involved familiar and readily discriminated images, monkeys lacking perirhinal cortex were impaired, demonstrating a deficit in learning or memory in these monkeys. Finally, this set of experiments also showed that the impairment in acquisition of new discrimination problems was not affected by the complexity of the images used.

In the final section of this paper, I critically assessed the perceptual-mnemonic model of perirhinal cortex function. While this model and the data supporting it provide the greatest challenge to a purely mnemonic account of perirhinal cortex function, several questions were raised. First, in most situations feature ambiguity is difficult to quantify. This makes the perceptual-mnemonic model difficult to assess outside a narrow set of procedures developed by Bussey and colleagues (Bussey et al., 2002, 2003; Murray & Bussey, 1999; Saksida & Bussey, 2002). Second, the model predicts the set size effect. Buckley and Gaffan (1997) tested for this effect, but reanalysis shows that it did not occur. Third, the perceptual-mnemonic model has yet to be subjected to test by pure measures of perceptual function. The completion of such tests would be a major advance in the assessment of perirhinal cortex function. Finally, the perceptual-mnemonic model has yet to be applied to the most widely reported effect of perirhinal cortex removal—delay-dependent memory impairment.

Because of its location in the brain, it is reasonable to expect that perirhinal cortex is involved in memory, perception, or both. Resolving the functional contribution of this region can only be accomplished through behavioural studies in which perception and memory are clearly defined and operationalized. Here, I have raised the concern that what appears at first to be a body of converging evidence implicating monkey perirhinal cortex in perception may instead be nearly universally flawed by the confounding of perception and memory. Given the ambiguity of the evidence for a perceptual role, students of human neuropsychology might best regard with scepticism the idea that there is widespread agreement that monkey perirhinal cortex is critical for perception in monkeys. At present, the preponderance of evidence supports a role for perirhinal cortex in learning and memory, whereas the evidence for a role in perception is comparatively weak.

REFERENCES

- Bright, P. J., Moss, H. E., Stamatakis, E. A., & Tyler, L. K. (this issue). The anatomy of object processing: The role of anteromedial cortex. *Quarterly Journal of Experimental Psychology*, 58B, 361–377.
- Buckley, M. J. (this issue). The role of the perirhinal cortex and hippocampus in learning, memory and perception. *Quarterly Journal of Experimental Psychology*, 58B, 246–268.
- Buckley, M. J., Booth, M. C. A., Rolls, E. T., & Gaffan, D. (2001). Selective perceptual impairments after perirhinal cortex ablation. *Journal of Neuroscience*, 21(24), 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(6), 535–546.
- Buckley, M. J., & Gaffan, D. (1998b). Perirhinal cortex ablation impairs visual object identification. *Journal of Neuroscience*, 18(6), 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 & Memory*, 6, 572–599.
- Buffalo, E. A., Ramus, S. J., Squire, L. R., & Zola, S. M. (2000). Perception and recognition memory in monkeys following lesions of area TE and perirhinal cortex. *Learning & Memory*, 7(6), 375–382.
- Bussey, T. J., Saksida, L. M., & Murray, E. A. (2002). Perirhinal cortex resolves feature ambiguity in complex visual discriminations. *European Journal of Neuroscience*, 15(2), 365–374.
- 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(3), 649–660.
- Bussey, T. J., Saksida, L. M., & Murray, E. A. (this issue). The perceptual-mnemonic/feature conjugation model of perirhinal function. *Quarterly Journal of Experimental Psychology*, 58B, 269–282.

- Desimone, R., & Ungerleider, L. G. (1989). Neural mechanisms of visual processing in monkeys. In F. Boller & J. Grafman (Eds.), *Handbook of neuropsychology* (Vol. 2, pp. 267–299). Amsterdam: Elsevier.
- Eacott, M. J., & Gaffan, E. A. (this issue). The roles of the perirhinal cortex, postrhinal cortex, and the fornix in memory for objects, contexts, and events in the rat. *Quarterly Journal of Experimental Psychology*, *58B*, 202–217.
- 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*(9), 1466–1478.
- Eacott, M. J., & Heywood, C. A. (1995). Perception and memory: Action and interaction. *Critical Reviews in Neurobiology*, *9*, 311–320.
- Gaffan, D., & Harrison, S. (1986). Visual identification following inferotemporal ablation in the monkey. *The Quarterly Journal of Experimental Psychology*, *38B*, 5–30.
- Hampton, R. R., & Murray, E. A. (2002). Learning of discriminations is impaired, but generalization to altered views is intact, in monkeys (*Macaca mulatta*) with perirhinal cortex removal. *Behavioral Neuroscience*, *116*(3), 363–377.
- Jagadeesh, B., Chelazzi, L., Mishkin, M., & Desimone, R. (2001). Learning increases stimulus salience in anterior inferior temporal cortex of the macaque. *Journal of Neurophysiology*, *86*, 290–303.
- Lee, A. C. H., Barense, M. D., & Graham, K. S. (this issue). The contribution of the human medial temporal lobe to perception: Bridging the gap between animal and human studies. *Quarterly Journal of Experimental Psychology*, *58B*, 300–325.
- Logothetis, N. (1998). Object vision and visual awareness. *Current Opinion in Neurobiology*, *8*, 536–544.
- 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*(12), 5418–5432.
- Murray, E. A. (2000). Memory for objects in nonhuman primates. In M. S. Gazzaniga (Ed.), *The new cognitive neurosciences* (2nd ed., pp. 753–764). Cambridge, MA: MIT Press.
- Murray, E. A., & Bussey, T. J. (1999). Perceptual-mnemonic functions of the perirhinal cortex. *Trends in Cognitive Sciences*, *3*, 142–151.
- Murray, E. A., Gaffan, D., & Mishkin, M. (1993). Neural substrates of visual stimulus association in rhesus-monkeys. *Journal of Neuroscience*, *13*(10), 4549–4561.
- Murray, E. A., Malkova, L., & Goulet, S. (1998). Crossmodal associations, intramodal associations, and object identification in macaque monkeys. In A. Milner (Ed.), *Comparative neuropsychology* (pp. 51–69). Oxford, UK: Oxford University Press.
- Murray, E. A., & Mishkin, M. (1986). Visual recognition in monkeys following rhinal cortical ablations combined with either amygdalotomy or hippocampectomy. *Journal of Neuroscience*, *6*(7), 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*(16), 6568–6582.
- Rolls, E. T., Franco, L., & Stringer, S. M. (this issue). The perirhinal cortex and long-term familiarity memory. *Quarterly Journal of Experimental Psychology*, *58B*, 234–245.
- Rudy, J. W., & Sutherland, R. J. (1995). Configural association theory and the hippocampal formation: An appraisal and reconfiguration. *Hippocampus*, *5*, 375–389.
- Saksida, L. M., & Bussey, T. J. (2002). The organization of visual object representations: A connectionist model of effects of lesions in perirhinal cortex. *European Journal of Neuroscience*, *15*, 355–364.
- Suzuki, W. A. (1996). Neuroanatomy of the monkey entorhinal, perirhinal and parahippocampal cortices: Organization of cortical inputs and interconnections with amygdala and striatum. *Seminars in the Neurosciences*, *8*, 3–12.
- 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*(12), 4355–4370.