Learning of Discriminations Is Impaired, but Generalization to Altered Views Is Intact, in Monkeys (Macaca mulatta) With Perirhinal Cortex Removal

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Rhesus monkeys (Macaca mulatta) were taught a large number of visual discriminations and then either received bilateral removal of the perirhinal cortex or were retained as unoperated controls. Operated monkeys were impaired in retention of the preoperatively learned problems. To test for generalization to novel views, the monkeys were required to discriminate, in probe trials, familiar pairs of images that were rotated, enlarged, shrunken, presented with color deleted, or degraded by masks. Although these manipulations reduced accuracy in both groups, the operated group was not differentially affected. In contrast, the same operated monkeys were impaired in reversal of familiar discriminations and in acquisition of new single-pair discriminations. These results indicate an important role for perirhinal cortex in visual learning, memory, or both, and show that under a variety of conditions, perirhinal cortex is not critical for the identification of stimuli.

Because of its position in the ventromedial aspect of the temporal lobe, at the extreme of the ventral visual processing stream, and its strong connections with the hippocampus via entorhinal cortex (Suzuki, 1996), perirhinal cortex appears positioned to play critical roles in both memory and perception (Murray & Bussey, 1999). Neurons in this region have large receptive fields (Jagadeesh, Chelazzi, Mishkin, & Desimone, 2001; C. Erickson, personal communication, August 28, 2001) and respond selectively to complex visual stimuli (Logothetis, 1998; N. Logothetis, personal communication, January, 1999), suggesting a role in representing whole visual objects. In addition, lesions limited to perirhinal cortex yield amnesia, as evidenced by impairments in stimulus recognition (Buffalo et al., 1999; Meunier, Bachevalier, Mishkin, & Murray, 1993). However, certain deficits observed after perirhinal cortex lesions suggest a role for this region beyond stimulus recognition. For example, perirhinal cortex appears to be important for the formation and maintenance of stimulus–stimulus associations about individual objects (Buckley & Gaffan, 1998a; Goulet & Murray, 2001; Murray, Gaffan, & Mishkin, 1993; for review, see Murray, 2000). Because perirhinal cortex participates in the association of different sensory qualities of individual objects in memory, it may aid in identifying objects given a tactile sensory input, or a partial visual sensory input (Murray, Bussey, Hampton, & Saksida, 2000). Thus, perirhinal cortex may play a general role in object identification, the ability to know that a particular object is one and the same across different instances in which it is experienced. Recent evidence implicates perirhinal cortex in object identification in yet another way. Based on findings from studies of visual discrimination learning, Buckley and Gaffan (1997, 1998a) argued that perirhinal cortex lesions led to an impairment in perception or representation of stimuli, which ultimately yielded a disruption in object identification. Other recent reports have posited a role for perirhinal cortex either exclusively in declarative memory (e.g., Buffalo et al., 1999), or in memory as well as the perceptual aspects of visual object identification (Buckley & Gaffan, 1997, 1998b; Eacott & Heywood, 1995; Murray, 2000; Murray & Bussey, 1999; Murray et al., 2000; Murray, Malkova, & Goulet, 1998).

One line of evidence suggesting a role for perirhinal cortex in perception or representation of visual information comes from experiments in which monkeys were trained to discriminate pairs of digitized pictures of objects (Buckley & Gaffan, 1998b). Each object was digitally photographed from six different vantage points. Animals were trained on a set of discrimination problems using three of these views, and, after reaching criterion, generalization to the remaining views was assessed. The extent of generalization was measured by recording errors to attain criterion with the new views. Monkeys with perirhinal cortex lesions made more errors in reaching criterion than did controls. Although Buckley and Gaffan (1998b) suggested that the impairment was one of “object identification,” the nature of the deficit remains unclear. This is because the trials to criterion measure confounds generalization, reflected in performance on the first exposure to a new view, and learning, reflected in the rate at which accuracy reaches the criterion level. Monkeys with perirhinal cortex lesions are impaired in learning discriminations, at least under some conditions (e.g., Buckley & Gaffan, 1997; Buffalo et al., 1999; Easton & Gaffan, 2000). Accordingly, it is possible that the monkeys with

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perirhinal cortex lesions studied by Buckley and Gaffan (1998b) had intact perceptual function and generalized to novel views as well as did the controls, immediately performing accurately with some, but not all, of the new views. However, any learning required to reach criterion with the novel views might be expected to proceed more slowly in monkeys with perirhinal cortex lesions, resulting in the reported group difference in errors to criterion. Alternatively, Buffalo, Stefanacci, Squire, and Zola (1998) accepted that those monkeys were perceptually impaired, but attributed the impairment to the small amount of Area TE damage sustained by these monkeys. To understand the nature of the perirhinal cortical contribution to object representations, we thought it important to assess generalization using measures not confounded with new learning.

In the present study, monkeys were trained on a large number of visual discrimination problems. Subsequently, two main types of test were administered. Generalization to new views, meant to tax perceptual aspects of object identification, was measured by presenting monkeys with only one or two probe tests, consisting of altered views of familiar stimuli, for each discrimination problem. Reversal learning, meant to tax mnemonic aspects of object identification relatively independently of perception, used stimuli that were already represented in memory and readily discriminated. If perirhinal cortex is critical specifically for the phenomenon of object invariance, as measured by generalization to novel views, animals with such lesions should be impaired on probe trials with altered views of familiar stimuli. In contrast, if perirhinal cortex is necessary for learning and memory, independent of perception, then reversal learning should be impaired.

Experiment 1

To confirm and extend previous findings of deficits in retention and acquisition of object discriminations resulting from damage to perirhinal and entorhinal cortex (Buckley & Gaffan, 1997; Buffalo et al., 1999; Gaffan & Murray, 1992; Thornton, Rothblat, & Murray, 1997) we trained two groups of monkeys preoperatively on a set of 48 object discriminations. Six monkeys then received bilateral aspiration lesions of the perirhinal cortex, whereas the remaining monkeys were retained as unoperated controls. We expected to confirm the previously reported deficits in retention of preoperatively acquired discrimination problems following lesions to perirhinal plus entorhinal cortex (e.g., Gaffan & Murray, 1992; Thornton et al., 1997) or to perirhinal alone (Buckley & Gaffan, 1997). Results concerning acquisition of discriminations following lesions including perirhinal cortex have been mixed, with some studies reporting deficits (e.g., Baxter, Hadfield, & Murray, 1999; Baxter & Murray, 2001; Buckley & Gaffan, 1997; Buffalo et al., 1999), but others not (Baxter & Murray, 2001; Buffalo et al., 1999; Buckley & Gaffan, 1997; Eacott, Gaffan, & Murray, 1994; Gaffan & Murray, 1992; Thornton et al., 1997). To test whether the nature of the images to be remembered is a determinant of the involvement of perirhinal cortex in memory, we examined acquisition of problems using different types of visual stimuli, from elementary shapes and colors to complex, highly detailed images.

Method

Subjects

Ten experimentally naive rhesus monkeys (Macaca mulatta; 8 males and 2 females) were used. The monkeys weighed 4.4 to 5.8 kg at the beginning of testing, were caged individually, and were fed daily an amount of biscuits and fruit adjusted for each animal to ensure sufficient motivation and nutrition. Water was always available in the home cage.

Apparatus and Materials

Monkeys were trained using an automated apparatus controlled by an IBM-compatible computer. During the test sessions, monkeys were seated in primate chairs (Crist Instruments, Damascus, MD) inside large, ventilated, sound-attenuating chambers, and positioned in front of 14-in. (35.56-cm) color video monitors fitted with touch-sensitive screens (3m Corp., Montreal, MA). To the left and right of the monitors were two small food cups for the automated delivery of peanuts and 190-mg primate pellets (P. J. Noyes, Lancaster, NH), respectively. The test chambers were illuminated by 15-W light bulbs. The discriminda consisted of two groups of 48 pairs of two-dimensional images (Corel Mega Gallery clip art, Corel Corp., Ottawa, Ontario, Canada). Images were sized to fill an area of 300 × 300 pixels (80 × 80 mm), and were presented on a black background on the rightmost and leftmost portions of the monitor screen, separated by 185 mm center to center. Each group of 48 stimuli consisted of 12 pairs of four different types of images: basic, B/W (black and white), color, and detailed. Basic stimuli consisted of gratings; bars of different orientations, sizes, and colors; and circles of different sizes and colors. B/W stimuli were filled outline drawings of various objects, resembling silhouettes. Color stimuli were similar to B/W images in form, but included one or more colors. Detailed stimuli were perspective renderings approaching photographic quality (see Figure 1).

Preoperative Testing

Pretraining. Over several days, each monkey was adapted to restraint in a primate chair and to the environment of the test chamber, until it would reliably eat rewards dispensed into the food cups. Monkeys were then shaped to touch stimuli presented centrally on the monitors. To familiarize monkeys with the test procedures, each animal was trained on a set of three object discrimination problems, presented concurrently in random order, for a total of 63 trials per daily session. Monkeys proceeded to the main experiment after attaining a mean of at least 90% correct responses over 3 consecutive days.

Visual discrimination learning. Monkeys were trained on the first group of 48 problems to a criterion of 10 or fewer errors in 10 days, simultaneously for each of the four types of problem. Each trial began with a 15-s intertrial interval (ITI), after which a randomly selected pair of stimuli was presented, one item of the pair on the left and one on the right side of the monitor. The left-right position of stimuli was randomized across trials, and the order of presentation of the pairs of images was randomized each day. Touching the correct stimulus (fixed-ratio 2) was followed by delivery of a peanut reward, an ITI, and the next trial. Touching the incorrect stimulus (fixed-ratio 2) had the same effects, but without the delivery of a reward. No correction procedure was used. A single trial with each image pair was presented daily, resulting in 48 trials per session. Thus, monkeys were trained on a 48-pair concurrent discrimination-learning task with 24-hr intertrial intervals (Malamut, Saunders, & Mishkin, 1984).

Discrimination of basic stimuli proved to be extremely difficult, so after the first 2 monkeys failed to learn these discriminations seven sessions after meeting criterion on all the other discriminations, mastery of this set of stimuli was dropped from the criterion. The remaining animals therefore

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completed preoperative training once they had met the criterion described previously, but for the B/W, color, and detailed stimulus sets only.

Two groups were formed, approximately matched for errors to criterion on the first set of 48 discriminations. Each group contained 1 female monkey and 1 of the 2 monkeys that had received the seven extra training sessions. The surgical group received bilateral aspiration lesions of the perirhinal cortex (Group PRh, n = 6). Control monkeys rested in the home cage for a period of time approximating the presurgical and recovery periods of experimental animals (Group Con, n = 4).

Surgery

Before surgery, monkeys were immobilized with Ketamine hydrochloride (10 mg/kg im), given atropine sulfate (.04 mg/kg im), and intubated. Surgical anesthesia was achieved with isoflurane gas (1.0–3.0% to effect), and vital signs were monitored throughout the procedure. Aseptic technique was used. A large bone flap was turned over each hemisphere, and the dura reflected in two locations to permit anterior and posterior access to perirhinal cortex. Mannitol (30% [wt/vol], 35 ml iv) was administered to improve access to the ventromedial aspect of the temporal lobe. With the aid of an operating microscope, the rhinal sulcus was identified, and then the tissue on the lateral bank of the sulcus was removed, together with 2–3 mm of cortex just lateral to the sulcus, by subpial aspiration through a small-gauge sucker. After the removal was completed, the opening was closed in anatomical layers. Dexamethasone sodium phosphate (0.5 mg/kg im) and cefazolin (23 mg/kg im, B.I.D.) were administered 1 day before surgery and for 1 week after surgery to reduce inflammation and to prevent infection, respectively. For 3 to 5 days after surgery, the monkeys received Banamine (1.0 mg/kg im, B.I.D.) and acetaminophen (10 mg/kg im, B.I.D.) as analgesics.

Assessment of Lesions By MRI

The subjects of these experiments are still being used in a series of studies of cognitive function. To reduce the number of monkeys required for our research, and to develop an integrated picture of the effects of perirhinal cortex lesions in a single set of subjects, we assessed the extent of the lesions in the operated subjects using in vivo MRI. Independent estimates of lesion size based on MRI and on Nissl-stained histological material from the same monkey suggest that the extent of perirhinal cortex lesions can be determined accurately from MRI (Liu, Murray, & Richmond, 2000). Although these observations are admittedly limited to a single subject, the excellent agreement between the two methods of evaluation in this case (within 1% of the volume of perirhinal cortex) and in two additional cases with other types of medial temporal lobe lesions (Bachevalier, Beauregard, & Alvarado, 1999; Bachevalier & Mishkin, 1994) suggests that MRI can provide reliable estimates of lesion volume. In addition, we also draw on our past experience; in earlier studies examining the behavioral effects of perirhinal cortex lesions (e.g., Baxter et al., 1999; Meunier et al., 1993) or entorhinal plus perirhinal cortex lesions (e.g., Liu et al., 2000; Meunier et al., 1993; Murray, Baxter, & Gaffan, 1998; Thornton et al., 1997) from this laboratory, the lesions were essentially as intended.

Monkeys were given a combination of ketamine hydrochloride and xylazine (0.1 ml/kg, 5:1 vol/vol), placed in a nonferrous stereotaxic frame (NIH Mechanical Design and Fabrication, Bethesda, MD) and scanned in a 1.5-Tesla magnetic resonance scanner (SPGR, number of excitations = 8, 256-square matrix, field of view 100 mm, 1-mm slices). The lesion in each monkey was evaluated on the coronal MR images and plotted at 1-mm intervals onto drawings of coronal sections of a standard rhesus monkey brain. The areas of perirhinal cortex, Area TE, Area TG, and entorhinal cortex were determined in each standard section using a digitizer and Scion Image software (Scion Corporation, 2001). Lesion volumes were then determined for each monkey, and the size of the lesion expressed as a proportion of the standard. The intended lesion, along with a representative MRI scan and plot of the lesion in Case PRh-E, are shown in Figure 2. Reconstructions of the lesions onto ventral surface views of the brain are shown in Figure 3. The percent damage observed in each of the 6 monkeys in Group PRh is reported in Table 1.

In all cases except PRh-C (discussed in the following), damage to perirhinal cortex approximated the intended lesion. Five of 6 monkeys had minor unintended damage to entorhinal cortex, ranging from near 0 to 10% (see Table 1). Area TG was damaged in every monkey, 13.1% on average. Each monkey sustained a small amount of damage to the laterally adjacent area TE, but for 5 of the 6 monkeys, this damage did not exceed 4% of the volume of TE, averaged across the two hemispheres. Case PRh-C was observed to have substantial inadvertent damage to area TE in the right
Figure 2. Location and extent of the perirhinal cortex (PRh) lesion in Monkey PRh-E. The intended lesion (shaded region) is shown on coronal sections from a standard rhesus monkey brain (left column). Postoperative magnetic resonance images (MRIs) from matching levels (middle column) and plots of the lesion (shaded region) onto sections (right column) show the extent of the lesion in PRh-E. Numerals indicate distance in millimeters from the interaural plane; white arrows in the MRIs show the boundaries of the lesion.
hemisphere, and slight hippocampal atrophy in the right hemisphere as well. During surgery, this monkey was noted to have tough, yellow tissue in the right temporal lobe, involving the perirhinal cortex, suggesting that the hippocampal atrophy, like the abnormal tissue, may have predated the surgery. Hippocampal damage was not evident in any other case.

Postoperative Training

A minimum of 2 weeks after surgery, or after a similar period of rest for the controls, postoperative testing was initiated. At first, monkeys were only required to touch the individual, centrally placed stimuli that had been used in initial training in order to receive rewards. When the monkeys reliably completed 63 rewarded trials per day, they were given a retention test for the discriminations learned preoperatively. This consisted of a single session in which each pair of discriminanda was presented for one trial only. Next, the monkeys were trained on a second set of discrimination problems, again using 48 pairs of images in the same four categories as during preoperative training. Finally, the monkeys were required to relearn the preoperatively acquired set of discriminations to criterion.

Statistics

To better equalize variance for analysis of variance (ANOVA), data were uniformly transformed following the recommendations of Kirk (1982). Whenever trials or errors to criterion was the dependent measure, the data were log_{10} transformed before analysis. Because these learning measures are bounded by a minimum score of 0 on the left side of the distribution, but can take on any positive value, they tend to show positive skew, which is corrected by the log_{10} transform. Whenever the dependent measure was proportion correct, the data were arcsine transformed before analysis. This transformation is almost universally recommended prior to the analysis of proportion-correct data by statisticians, and its utility was discussed by Ringo (1991). Results were considered significant at p < .05. Where no p value is given, the result was not significant.

Results

Learning Before and After Surgery

Before surgery, the two groups that were formed made similar numbers of errors in each image category before achieving criterion (see Figure 4, left side). In addition, the two groups did not differ in the number of days that intervened between the last day of preoperative testing and the single-session test of retention (Group Con, M = 36.0, range = 29–45 days; Group PRh, M = 34.3, range = 28–42 days).

Following surgery, Group PRh made substantially more errors than did Group Con in acquiring a new set of 48 concurrent discrimination problems (see Figure 4, right side). The emergence of a deficit following surgery is indicated by a significant Group × Surgery interaction: group, F(1, 8) = 1.83; surgery, F(1, 8) = 0.40; and Group × Surgery, F(1, 8) = 5.92, p < .05. Separate analyses of mean errors committed while learning all image types
Retention of Preoperatively Learned Discriminations

To assess retention of the preoperatively learned discriminations, accuracy during the last five sessions of testing given prior to surgery was compared with accuracy during the single critical test session following surgery. This comparison is a pure measure of retention, because the monkeys were presented with each discrimination problem only once, precluding new learning. Group PRh performed less accurately in the critical test session than did Group Con (see Figure 5), as evidenced by a Group PRh performed less accurately in the critical test session than did Group Con (see Figure 5), as evidenced by a Group PRh interaction: group, F(1, 8) = 2.18; surgery, F(1, 8) = 1.86; and Group × Surgery, F(1, 8) = 7.92, p < .05. Both groups of monkeys performed less well in discriminations involving the basic images because these were not learned to criterion, but image type did not interact significantly with any variables: image type, F(3, 24) = 17.91, p < .01; and Group × Image Type, F(3, 24) = 48.61, p < .01. Separate analyses of mean accuracy showed that the groups did not differ before surgery, t(8) = 2.94, p < .05.

Finally, we required monkeys to relearn the preoperatively acquired discrimination problems after they had already completed the critical one-session test for retention of these discriminations and had learned a second set of discrimination problems postoperatively. Despite the additional recovery time, and the intervening training on a new set of object discriminations, the monkeys with perirhinal cortex lesions were impaired, relative to controls, in relearning all image types equally (see Figure 6), and both groups again made most errors with the basic discriminations, which were never learned to criterion: group, F(1, 8) = 5.63, p < .05; image type, F(3, 24) = 37.09, p < .01; and Group × Image Type, F(3, 24) = 1.79.

In summary, perirhinal cortex lesions produced a significant impairment in retention of preoperatively learned discrimination problems as well as an impairment in acquisition of new problems of the same type. The type of images used in this study did not influence whether or not a deficit was found in animals with lesions, indicating that the perirhinal cortex is not especially critical for discriminating any of the particular types of stimulus material we used.

Experiment 2

Experiments 2–6 tested generalization, or image invariance, by presenting the now familiar discriminations from Experiment 1 in altered views. Within some tolerances, normal monkeys treat novel and familiar views of objects as equivalent (e.g., Buckley & Gaffan, 1998b; Holmes & Gross, 1984a, 1984b; Weiskrantz & Saunders, 1984). In Experiment 2 we presented monkeys with rotated, shrunken, and enlarged views of familiar picture pairs to assess generalization. Each variant of a given discrimination was presented once only to preclude the possibility of new learning.

Method

The same subjects and apparatus were used. Monkeys were tested with the combined set of preoperatively and postoperatively learned discriminations, excluding the basic stimuli. As in previous testing, each image pair was presented only once per session, resulting in 72 trials per session.
Consecutive trials were separated by a 15-s ITI. After achieving a criterion of better than 90% correct responses averaged over 10 consecutive sessions, monkeys began testing with altered views of the familiar stimuli. In each session, 10 trials were randomly designated as probe trials, in which subjects were presented with familiar discriminanda, both of which had been altered in one of the following ways: shrunken (from 300 × 300 pixels to 200 × 200 pixels), enlarged (400 × 400 pixels), or rotated in the plane of the computer monitor 30°, 60°, or 120°. Subjects were rewarded as usual for choosing the image in each pair that had been designated correct throughout testing to this point. Image pairs to be used in probe tests were randomly selected from the set, with the constraint that each picture pair be manipulated once before any given pair could be used again as a probe. Testing in this manner continued until each subject had experienced each discrimination in each of the five altered views. Completion of testing thus required 36 sessions.

Results

Group Con and Group PRh did not differ significantly in the number of errors required to achieve criterion with the combined set of 72 discriminations, nor was any image type significantly more difficult than the others: group, $F(1, 8) = 1.61; \text{image type}, F(2, 16) = 0.57; \text{and Group \times Image Type}, F(3, 24) = 0.54$. Both groups of monkeys generalized well to the discriminanda presented in rotated views, although performance dropped off gradually as the amount of rotation increased (see Figure 7). Perirhinal cortex lesions did not affect accuracy: group, $F(1, 8) = 0.001; \text{rotation}, F(3, 24) = 20.87, p < .01; \text{and Group \times Rotation}, F(3, 24) = 0.08$. Altering the size of the discriminanda also had a small but significant effect on accuracy (see Figure 7), but monkeys with perirhinal cortex lesions were not differentially affected: group, $F(1, 8) = 1.40; \text{size}, F(2, 16) = 4.07, p < .05; \text{and Group \times Size}, F(2, 16) = 0.79$.

Experiment 3

In Experiment 2, although our manipulations did produce moderate and significant decreases in performance by both groups of monkeys, Group PRh was not differentially affected. Nevertheless, it is possible that the information guiding the responses in the two groups was different. For example, perhaps monkeys with perirhinal cortex lesions attend to different features of the visual stimuli than do controls. In Experiment 3, we examined whether monkeys relied preferentially on color or shape information in making choices.

Method

The same subjects and apparatus were used. Monkeys were presented with two types of probe trials, using only the 12 images consisting of a single fill color. In the first type of trial, monkeys were presented with familiar shapes to discriminate, but the color filling the shapes had been switched between the discriminanda. Subjects were rewarded as usual for choosing the shape in each pair that had previously been designated correct. On other probe trials, two squares consisting of the colors that filled the shapes that would otherwise have been used on that trial were presented. The monkeys were rewarded for choosing the color corresponding to the object that was the reinforced stimulus (S+). Examples of the original stimuli plus the two probe types are shown in Figure 8. Each test session consisted of 40 trials, separated by 15-s ITIs. In each session, 8 trials were randomly designated as probe trials, 4 of each of the two types. Each variant of the 12 discriminations used was presented twice. Thus, completing these tests required six sessions.

Results

Exchanging the fill colors between discriminanda had a small effect on accuracy, whereas removing shape information resulted in chance levels of performance (see Figure 9). Neither manipulation revealed an impairment in Group PRh: group, $F(1, 8) = 0.59; \text{probe type}, F(2, 16) = 130.77, p < .01; \text{and Group \times Probe Type}, F(2, 16) = 2.23$. Thus, with this set of stimuli, both groups of monkeys relied heavily on shape information to guide their choices.

Experiment 4

In Experiment 3, exchanging color information between familiar discriminanda had a mild effect on overall performance and did not differentially affect monkeys in Group PRh. Because colors were not unique to particular stimuli, monkeys may have treated them as irrelevant to the discrimination tasks. The more complex fill patterns, in contrast, were much less likely to be shared by stimuli in the test set. Subjects might, therefore, use the fill information in making discriminations. Experiment 4 examined whether monkeys with perirhinal cortex lesions relied preferentially on pattern or shape information in making choices.

Method

The same subjects and apparatus were used. Only the 24 color and 24 detail image pairs were used. In each session 8 trials were randomly designated as probe trials. On probe trials, the discriminanda were presented with color fill patterns deleted. Subjects were rewarded for choosing the shape in each pair that corresponded to the shape of the S+. Three examples of original and fill-deleted test images are shown in Figure 10. Each test session consisted of 48 trials, separated by 15-s ITIs. Each image pair was presented as a probe two times. Thus, completing these tests required 12 sessions.

Results

Deleting the fill patterns from the discriminanda had a larger effect on accuracy than that found in Experiment 3 (see Figure 11). Again, however, the manipulation did not reveal an impairment in

![Figure 7](image-url)
Group PRh: group, $F(1, 8) = 0.19$; trial type, $F(1, 8) = 232.15$, $p < .01$; and Group × Trial Type, $F(1, 8) = 0.07$. These results show that even when fill information is relatively salient, and monkeys depend on it in making choices, monkeys with perirhinal cortex lesions do not differ from controls in the extent to which they use this information.

Experiment 5

Experiments 2 through 4 assessed the ability of monkeys to generalize previous learning to tests in which stimuli were presented in novel views. However, generalization should not be relied on as the sole measure of the quality or completeness of the representations of images possessed by monkeys with perirhinal cortex lesions. Indeed, poor discrimination can actually facilitate generalization. For example, subjects treat an altered view the same as an exemplar if the alteration is not detected. To test whether an inability to discriminate small changes in images might underlie the good generalization performance of monkeys with perirhinal cortex lesions, this experiment assessed the ability of monkeys to discriminate familiar views of images from views altered by rotations as in Experiment 2. The ability to discriminate a familiar, from a slightly altered, view of an image requires an accurate representation of the orientation of the familiar view. Thus, the manipulation used in the present experiment is the converse of that used in Experiment 2. Here we required monkeys to discriminate a familiar stimulus from that same stimulus rotated, whereas in Experiment 2 monkeys were required to treat rotated images the same as familiar images.

Method

The same subjects and apparatus were used. Each test session consisted of 72 trials, separated by a 15-s ITI. On each trial monkeys were presented with two images of the S+ from each of the 72 pairs of discriminanda. One of these images was in the orientation that had been used throughout training; the other image was rotated in the plane of the computer monitor either 30°, 60°, or 120°. Monkeys were rewarded for choosing the trained orientation over the altered orientation. Rotations were balanced within sessions such that after three sessions, each discrimination problem had been presented in each of the three rotations.
Results

All subjects spontaneously chose the trained orientation of the stimuli over the rotated views, but erred more often when the distracter was rotated only a small amount, making the discrimination most difficult (see Figure 12). Group PRh found the discriminations no more difficult than did Group Con: group, $F(1, 8) = 0.25$; rotation, $F(2, 16) = 199.64$, $p < .01$; and Group $\times$ Rotation, $F(2, 16) = 1.28$. The lack of a significant interaction indicates that even when discrimination was difficult, monkeys with lesions were as accurate as controls. These findings are consistent with previously reported failures of temporal lobe lesions to interrupt orientation discriminations (Holmes & Gross, 1984a, 1984b), and with demonstrations that parietal cortex is crucial in orientation discrimination (Eacott & Gaffan, 1991).

Experiment 6

In Experiment 6 we made familiar discriminations difficult by deleting half of the visual information available to monkeys by

![Figure 10](image1.png)

Examples of standard (trained) discriminanda (top row), and the same stimuli after deletion of the color fill (bottom row). In Experiment 4, both the reinforced and the nonreinforced stimuli in each discrimination problem were presented altered as in the bottom row.

![Figure 11](image2.png)

Figure 11. Mean ($\pm$ SEM) proportion correct on standard trials and on probe trials in which fill information was deleted from the discriminanda (Experiment 4). Solid bars represent the control group; gray bars represent the perirhinal cortex-lesioned group.

![Figure 12](image3.png)

Figure 12. Mean ($\pm$ SEM) proportion correct on tests in which the reinforced stimulus ($S^+$) of each object pair was presented with a duplicate, rotated either 30°, 60°, or 120° (Experiment 5). Monkeys were rewarded for choosing the orientation of the $S^+$ used in earlier training. Diamonds represent the control group; squares represent the perirhinal cortex-lesioned group.
placing a mask over the discriminanda. We used a method similar to that used by Buckley et al. (Buckley, Booth, Rolls, & Gaffan, 2001), who reported that occluding portions of test stimuli produced impairments in discrimination in an oddity task by monkeys with perirhinal cortex lesions.

Method

The same subjects and apparatus were used. Each session consisted of 72 trials, separated by 15-s ITIs. On half of the test trials, the discriminanda were not altered; on the other half of trials, a checkerboard mask was superimposed on both of the discriminanda. The mask always covered 50% of the area of the test images. There were six types of mask, differing in the size of the blocks making up the mask. Examples of the masked images with the smallest, intermediate, and largest sized blocks, are shown in Figure 13. 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. Both the image selected for a probe test, and the mask condition, were randomized with the constraint that each pair of images was used once before any were used again with a different mask. Completion of tests with all the discriminations and six different masks required 12 sessions.

Results

Superposition of the masks on the discriminanda affected performance in both groups according to a U-shaped function, where 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 (see Figure 14). Despite a substantial effect on overall performance, superposition of the masks did not differentially affect the performance of Group PRh: group, F(1, 8) = 0.03; mask, F(6, 48) = 35.81, p < .01; and Group × Mask, F(6, 48) = 0.84.

Experiment 7

In Experiment 1, Group PRh was mildly impaired in learning new visual discrimination problems. In Experiments 2–6, we found no impairments in Group PRh. In sum, although operated monkeys were impaired in learning, they showed no evidence of impaired performance once a discrimination had been acquired, even if the discrimination was made difficult. One interpretation of these findings is that monkeys with perirhinal cortex lesions are

Figure 13. Example of a standard (trained) pair of discriminanda (left) and the same stimuli with the smallest, intermediate, and largest masks superimposed (Experiment 6). S+ = reinforced stimulus; S– = nonreinforced stimulus.

Figure 14. Mean (± SEM) proportion correct on standard-trials and on probe trials in which masks of six different mesh sizes were superimposed on the discriminanda (Experiment 6). Diamonds represent the control group; squares represent the perirhinal cortex-lesioned group.
generally impaired in acquiring stimulus–reward associations, independently of any problem in stimulus identification. If so, they should be impaired even under conditions of reversal learning, in which the stimuli are already represented and stimulus pairs are readily discriminated. That is, reversal learning provides a measure of stimulus–reward association relatively free of new demands on perceptual or representational mechanisms (e.g., Gaffan, Harrison, & Gaffan, 1986, p. 7). To explore this possibility, we trained monkeys in reversals of familiar discriminations.

Method

The same subjects and apparatus were used. Six discrimination problems were chosen randomly for reversal, with the constraint that there were two from each category (B/W, color, detail). Each problem was first presented with the S+ and S− designated as in previous training, but now only one problem was given within a session. Animals had to achieve over 90% correct in a single session with this arrangement before proceeding to reversal. The day following acquisition of a given discrimination, the discrimination was reversed. The same criterion of 90% correct in a single session was used, and so on, until all six reversals had been administered, serially. Each test session consisted of 50 trials, separated by 10-s ITIs.

Results

Data were collapsed into two trial blocks, and averaged across the six discrimination reversals. In this and subsequent analyses of reversal learning, only the trials up to and including the block of trials in which controls achieve and maintain over 90% accuracy as a group are included. All monkeys learned the reversals quite rapidly on average (see Figure 15), but Group PRh was mildly impaired relative to Group Con as indicated by a significant Group × Trials interaction: group, $F(1, 8) = 1.85$; trials, $F(23, 184) = 47.13$, $p < .01$; and Group × Trials, $F(23, 184) = 2.65$, $p < .01$ (24 blocks of trials analyzed). To substantiate the impression given by Figure 15 that initially the two groups performed equally, whereas later in training they differed, we conducted post hoc $t$ tests. The groups did not differ in accuracy in the 1st block of 10 trials, $t(8) = 0.25$, but did differ significantly in the fourth block of 10 trials, $t(8) = 2.79$, $p < .05$. These results show that perirhinal cortex lesions disrupt stimulus–reward association, even under conditions in which stimuli are familiar and readily discriminated from one another.

Experiment 8

In Experiment 1 monkeys with perirhinal cortex lesions were impaired in the acquisition of a set of 48 concurrently learned discriminations. It has been suggested that set size is an important determinant of whether or not an impairment in discrimination learning is observed (Buckley & Gaffan, 1997). To test this idea, we trained monkeys on new single-pair visual discriminations. If stimulus set size is a critical factor in yielding a deficit after perirhinal cortex lesions, no deficit should be observed in the present experiment. The day following acquisition of a given discrimination, the discrimination was reversed. The same criterion of 90% correct in a single session was used.

Method

The same subjects and apparatus were used. Twelve pairs of novel discriminanda were used. These were images from the same clip art collection used in Experiment 1, and corresponded to the color and detailed categories used earlier. All other aspects of the experiment were the same as those in Experiment 7.

Results

Learning

Data were analyzed in two-trial blocks, collapsed across the 12 discrimination problems. Both groups of monkeys acquired the discriminations rapidly (see Figure 16), but Group PRh was mildly impaired relative to Group Con: group, $F(1, 8) = 15.33$, $p < .01$; trials, $F(2, 16) = 30.95$, $p < .01$; and Group × Trials, $F(2, 16) = 3.85$, $p < .05$ (three blocks of trials analyzed). Post hoc $t$ tests showed that the small difference between the groups in the first block of two trials was not significant, $t(8) = 1.51$, whereas the difference between the groups in both of the next two blocks of training was significant: $t(8) = 3.62$, $p < .01$, and $t(8) = 3.45$, $p < .01$, respectively.

Reversal

Monkeys with perirhinal cortex lesions were also impaired in reversal of the newly learned discriminations (see Figure 17): group, $F(1, 8) = 3.45$; trials, $F(3, 24) = 35.79$, $p < .01$; and Group × Trials, $F(2, 16) = 4.18$, $p < .05$ (four blocks of trials analyzed). To confirm that the two groups performed similarly at the beginning of reversal, but differed significantly later in training, post hoc $t$ tests were conducted. The groups did not differ in the first block of trials, $t(8) = 0.87$; the difference between the groups approached significance in the second block of trials, $t(8) = 1.88$, $p < .10$; and the groups differed significantly in the third block of trials, $t(8) = 2.59$, $p < .05$. These results, like those of Experiment 7, show that monkeys with perirhinal cortex lesions are impaired even when learning single-pair visual discriminations in which the demands placed on object identification are limited.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{Figure15.png}
\caption{Reversal of familiar discriminations (Experiment 7). Curves show group mean (± SEM) scores during acquisition of six different reversal problems, given serially. Diamonds represent the control group; squares represent the perirhinal cortex-lesioned group.}
\end{figure}
Experiment 9

Experiment 9 was conducted to determine whether the deficit in reversal learning is long lasting. Accordingly, as in Experiment 7, monkeys were tested on their ability to reverse additional problems from the originally learned set.

Method

The same subjects and apparatus were used. This experiment was conducted exactly as was Experiment 7, but six different familiar discriminations were used.

Results

Data were analyzed in two-trial blocks, collapsed across the six discrimination reversals. Group PRh was once again impaired relative to Group Con (see Figure 18): group, \( F(1, 8) = 4.72; \) trials, \( F(14, 112) = 15.70, p < .01; \) and Group \( \times \) Trials, \( F(14, 112) = 1.94, p < .05 \) (15 blocks of trials analyzed). Post hoc t tests showed that the two groups did not differ in the first block of trials, \( t(8) = 0.97; \) the difference between the groups approached significance in the second block of trials, \( t(8) = 2.01, p < .10; \) and the groups differed significantly in the third block of trials, \( t(8) = 2.70, p < .05. \) Monkeys with perirhinal cortex lesions, therefore, show a persistent impairment in reversal learning, even after extensive training in reversal learning with test stimuli that are familiar. Interestingly, both groups of animals learned these reversals considerably more rapidly than they did in Experiment 7, demonstrating that despite the persistent impairment in reversal learning, monkeys with perirhinal cortex lesions, like controls, developed a learning set: experiment, \( F(1, 8) = 49.73, p < .01; \) Experiment \( \times \) Trials, \( F(14, 112) = 3.58, p < .01; \) and Experiment \( \times \) Group, \( F(1, 8) = 1.88 \) (15 blocks of trials analyzed).

General Discussion

There were three main findings of the present study. First, we found that performance on a task taxing perceptual aspects of object identification, as measured by the ability to correctly select familiar stimuli presented in a variety of altered views, was normal in monkeys lacking perirhinal cortex. Second, we demonstrated the existence of persistent, mild deficits in both acquisition and in reversal of visual discrimination problems in monkeys with damage limited to perirhinal cortex. Third, we confirmed previously reported deficits in the retention of preoperatively learned discrimination problems following perirhinal cortex removals, either alone or in combination with entorhinal cortex removals. Taken together, these findings underscore the contribution of the perirhinal cortex to learning and memory, while placing constraints on the way in which this structure may be considered to promote object identification more generally.

Generalization to Altered Views

In Experiments 2–6 we evaluated object identification by challenging monkeys with difficult discriminations consisting of altered versions of familiar discriminaundata-driven model predictions and model robustness evaluation. To avoid confounding acquisition with performance, we used only one or two probe trials involving each manipulation of each discrimination problem, and

Figure 16. Learning of new, easy visual discrimination problems (Experiment 8). Curves show group mean (± SEM) scores during acquisition of 12 problems, given serially. Diamonds represent the control group; squares represent the perirhinal cortex-lesioned group.

Figure 17. Reversal of recently learned discrimination problems (Experiment 8). Curves show group mean (± SEM) scores for 12 problems, given serially. Diamonds represent the control group; squares represent the perirhinal cortex-lesioned group.

Figure 18. Reversal of a second set of familiar discrimination problems (Experiment 9). Curves show group mean (± SEM) scores for six problems, given serially. Diamonds represent the control group; squares represent the perirhinal cortex-lesioned group.
these were presented over several sessions that consisted mainly of trials with the original pair of images presented as in initial learning. 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. The absence of a deficit in generalization under challenging conditions conflicts with the results of Buckley and Gaffan (1998b), who reported deficits in generalization to new views in monkeys with perirhinal cortex lesions. As indicated in the introduction, Buckley and Gaffan (1998b) presented monkeys with pictures of objects that had been photographed from several different views. When those discriminations had been learned from one set of perspectives, the monkeys were tested for their ability to learn discriminations of the same objects photographed from a different set of perspectives. If these new discriminations were learned faster than the initial set, then this would indicate positive transfer and, therefore, accurate object identification. In initial learning of 40 discrimination problems, Buckley and Gaffan’s (1998b) operated monkeys made, on average, just under twice as many errors as did experimental monkeys (214 vs. 120 errors; inferential statistics were not reported). On the transfer test, controls made an average of 11 errors, whereas operated monkeys made an average of 41 errors (a significant difference by the one-tailed test reported). Given that 1 of the 3 operated monkeys made more than twice as many errors as did the other 2, thus substantially biasing the mean, it seems unlikely that these scores represent a significant change from the 2:1 difference observed in initial learning. Thus, monkeys with perirhinal cortex lesions 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 mild impairment in visual learning. This learning impairment could occur because in the experimental design used by Buckley and Gaffan (1998b), objects were rotated in three dimensions. As a result, new visual features appeared in objects on the transfer test. Thus, in their transfer test, unlike the probe trials in this study, new visual features presumably were associated with reward, thereby yielding the learning impairment in monkeys with perirhinal cortex lesions. An alternative possibility, suggested by Buffalo et al. (1999; Buffalo et al., 1998), is that the monkeys studied by Buckley and Gaffan (1998b) sustained sufficient damage to Area TE to produce deficits in visual perceptual processing.

In a follow-up experiment (Buckley & Gaffan, 1998b), the same monkeys were required to discriminate a subset of the familiar objects embedded in novel, cluttered scenes. 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, so this result, too, is consistent with a general role for perirhinal cortex in visual discrimination learning.

**Discrimination Learning and Reversal**

Despite intact performance on probe tests with altered views of familiar images, our monkeys with perirhinal cortex lesions were consistently mildly impaired in acquisition and reversal of discriminations. In contrast to Buckley and Gaffan (1997), but in agreement with Buffalo et al. (1999) and Baxter and Murray (2001), we found an impairment in object-discrimination learning even when single pairs of images were discriminated. Although Buckley and Gaffan (1997) reported that monkeys with perirhinal cortex lesions are impaired in learning large, but not small, sets of object-discrimination problems, reanalysis of their published data does not support that conclusion. A comparison of errors per discrimination problem, rather than total errors, across different stimulus set sizes shows no significant interaction between set size and group. There is, rather, a consistent, marginally significant deficit in the operated monkeys (mean errors/problem at each set size for Groups PRh and Con, 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): group, $F(1, 6) = 5.17, p < .06$; set size, $F(2, 12) = 0.53, p < .60$; and Group × Set Size, $F(2, 12) = 0.66, p < .53$ (log, transformed data; statistically identical results are obtained with the untransformed data). In light of the present finding of an impairment in learning single-pair object discriminations, replicating Buffalo et al. (1999) and Baxter and Murray (2001), combined with the reexamination of the data from Buckley and Gaffan (1997), we do not find empirical support for the hypothesis that large set size is important for obtaining deficits in monkeys with perirhinal cortex lesions. Instead, the available data indicate a consistent, relatively mild impairment in discrimination learning that is not affected by manipulations of set size.

**Retention of Preoperatively Learned Discriminations**

We have reconfirmed the previously reported findings of impaired retention of preoperatively learned object discriminations in monkeys with lesions that include perirhinal cortex (Buckley & Gaffan, 1997; Gaffan & Murray, 1992; Thornton et al., 1997). This result indicates that perirhinal cortex lesions either impair retrieval of representations of the objects being discriminated, or that perirhinal cortex is part of the neural substrate for storage of these representations, or both. Because both storage and retrieval are necessary for acquisition to occur and to be expressed, a deficit in either process alone, or the two together, could produce the pattern of discrimination learning, retention, and reversal deficits that we observed.

**How Does the Perirhinal Cortex Promote Object Identification?**

The present study investigated the role of the perirhinal cortex in object identification, the ability to know that a particular object is one and the same across different instances in which it is experienced. Successful object identification depends on both memory (i.e., the storage and retrieval of representations of objects) and perception (which provides representations for storage in memory, and permits apprehension of the stimuli before a monkey at a given time); thus, a deficit in either perception or memory might impair object identification. The generalization tests we used, by design, emphasized perceptual as opposed to mnemonic aspects of object identification. This was done by manipulating highly familiar stimuli that comprised well-learned discrimination problems. Once the monkeys identified an object, they had only to emit the associated response (to the $S^+$), which had already been learned. No new learning was required, and, in any event, the probe trial
format used here would have prevented any such learning. As we have seen, monkeys with perirhinal cortex lesions are as good as controls in identifying and selecting objects under a variety of perceptually challenging conditions. Consequently, these findings would seem to be at odds with the proposal, elaborated elsewhere (Murray & Bussey, 1999; Murray & Richmond, 2001), that perirhinal cortex is important for perceptual aspects of object identification. Indeed, these results, taken in isolation, are more compatible with the view that perirhinal cortex is important for memory but not for perception (Buffalo et al., 1999; Buffalo et al., 1998). However, although many studies, including this one, have emphasized a role for perirhinal cortex in memory, at least some evidence from recognition memory and discrimination-learning paradigms suggests a role for perirhinal cortex in perception as well (Bussey, Saksida, & Murray, 2002; Eacott et al., 1994; Murray & Bussey, 1999). Studies that assess perceptual function outside the context of learning or memory paradigms, such as tasks requiring same–different judgments, may help resolve this controversy.

In summary, we have dissociated acquisition of discriminations from performance with well-learned discriminations, showing that perirhinal cortex lesions impair learning or memory while leaving perceptual function intact under a variety of conditions. Although generalization to new views was intact in monkeys with perirhinal cortex lesions over all the conditions we tested, we emphasize that we may not have challenged perceptual processing in some crucial way, such as by increasing “feature overlap” (see Murray & Bussey, 1999). This aside, it is clear that perirhinal cortex does make mnemonic contributions to the general capacity for object identification, for example, by mediating recognition memory (Buffalo et al., 1999; Meunier et al., 1993), and supporting the formation of stimulus–stimulus associations (Buckley & Gaffan, 1998a; Goulet & Murray, 2001; Murray et al., 1993). Precisely how these memory processes work together in perirhinal cortex to promote object identification remains a topic for future study.

References


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