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Research report

Distinct patterns of behavioural impairments resulting from fornix transection or neurotoxic lesions of the perirhinal and postrhinal cortices in the rat

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Abstract

The present study provides evidence that lesions of the fornix (FNX) and of the perirhinal/postrhinal cortex (PPRH), which both disconnect the hippocampus from other brain regions, can lead to distinct patterns of behavioural impairments on tests of spatial memory and spontaneous object recognition. For example, whereas FNX lesions impaired allocentric spatial delayed alternation in a T-maze but generally spared a test of spontaneous object recognition, PPRH lesions produced the opposite pattern of results. Indeed, on the T-maze task PPRH animals significantly outperformed controls when the retention delay was increased to 60 s. In addition, some evidence was found that contributions from both the fornix and perirhinal/postrhinal cortex may be required when object and spatial information must be integrated. In an object-in-place test, for example, PPRH animals failed according to two measures, and FNX animals failed according to one measure, to discriminate objects that had remained in fixed locations from those that had exchanged locations with other objects. Neither lesion, however, affected performance of a visuospatial conditional task, a Pavlovian autoshaping task, or a one-pair pattern discrimination task. It is suggested that the perirhinal/postrhinal cortex, rather than being specialised for a particular type of associative learning, is important for processing complex visual stimuli.

Keywords: Episodic memory; Spatial memory; Object recognition; Visual discrimination; Temporal lobe

1. Introduction

The hippocampus — a region known to have a critical role in certain types of learning and memory — communicates with other brain regions via two major pathways: (i) connections via the fornix and (ii) connections via parahippocampal regions such as the perirhinal and postrhinal cortices. The former pathway not only contains subcortical and cortical projections from the hippocampus, but also conveys afferents to the hippocampus, including those from the septum [25,39]. The parahippocampal pathway is thought to be a major source of afferent sensory information [6], which is conveyed to the hippocampus from the perirhinal/postrhinal cortex via the entorhinal cortex [6,38]. In addition to this indirect route via the entorhinal cortex, there may also be direct projections from the perirhinal/postrhinal cortex to the hippocampus [45]. This tight interconnectivity has provided the foundation for theories that emphasize a unitary memory system comprising these various regions [14,37].

It is perhaps surprising, then, that lesions of the fornix or of parahippocampal cortical regions do not always have equivalent effects, and do not always mimic the effects of hippocampal lesions. Indeed, in one study that compared directly the effects of fornix lesions and perirhinal cortex lesions in rats, a double dissociation was obtained [17]. While fornix lesions

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severely disrupted performance on two spatial tasks that are also sensitive to hippocampal damage (T-maze alternation and delayed nonmatching-to-position in an operant chamber), the same fornix lesions had no effect on a spontaneous test of object recognition. In contrast, perirhinal cortex lesions resulted in a recognition deficit but had no effect on the spatial tasks.

All other comparisons between the effects of such lesions in rats have been indirect, as only one or the other of the two sites has been examined in a given study. While a comparison of these studies does support this dissociation on tests of object recognition [3,8,31], the results from spatial tasks have been less consistent, as some studies have reported deficits after perirhinal cortex damage [3,8,15,23,26–29,42,43].

In view of the inherent limitations of such indirect comparisons and the potential importance of these dissociations for understanding the functions of the hippocampus and related structures, the present study sought to compare directly the effects of these different hippocampal disconnections on object recognition and spatial memory tasks. Unlike the study of Ennaceur et al. [17], we extended the perirhinal cortex lesions caudally to include the postrhinal cortex and dorsally to include area TE. This was for two reasons. First, by sparing the postrhinal cortex the study of Ennaceur et al. [17] had left a route by which spatial information could reach the hippocampus and this might explain the lack of any apparent effect on tests of spatial memory. Second, by extending the cortical lesion dorsally it might be expected that a more robust recognition deficit would emerge, so further testing the reported dissociation.

Although our prediction was that the effects of fornix and perirhinal/postrhinal cortex lesions would be dissociable, such a finding would not rule out the possibility that these lesions could have similar effects under certain conditions in which, for example, the hippocampus and perirhinal/postrhinal cortex interact, i.e. in situations where object and spatial information must be integrated. This was tested using two very different paradigms having both 'object' and 'spatial' characteristics. The first was an 'object-in-place' test, carried out in the same apparatus and with the same stimulus material as the object recognition test. Unlike the object recognition test, however, in the object-in-place test rats recognise not that a specific object has been seen before, but that a specific object has exchanged position with another specific object. We also tested these animals on an 'object location' test in which rats recognise that an object is in a place that had not previously been occupied by any object; thus this task requires the use of spatial information only.

The second object/place task we examined was a visuospatial conditional learning task, carried out in a computerised touchscreen apparatus [11], in which rats must learn a rule of the type: 'If stimulus A go left; if B go right'. Both fornix and hippocampal lesions have been reported to disrupt visuospatial conditional discrimination [34,36,40], and it has been suggested that impairments on such tasks may result from inadvertant damage to perirhinal cortex [34]. Furthermore both the hippocampus and the perihinal/postrhinal cortex are connected with the posterior cingulate cortex, which has been shown to be necessary for normal acquisition of visuospatial conditional tasks [9,10]. In order to ensure that lesioned rats could discriminate nonspatial and spatial computer graphic stimuli in this apparatus, we first tested the rats on two additional touchscreen tasks: stimulus–reward learning in a discriminative Pavlovian autoshaping paradigm [7], and a pattern discrimination learning task using equiluminant shape stimuli. An additional motivation for using these particular tasks is that the results could help to clarify whether the perirhinal/postrhinal region is important for any particular class of learning and memory task, or whether it is specialised for the processing of particular stimulus material.

2. General methods

2.1. Subjects

The study involved 36 naive, male rats of the pigmented DA strain (Bantin and Kingman, Hull, UK). Throughout the period of the experiment the rats were housed in pairs under diurnal conditions (14 h light/10 h dark). At the time of surgery they were aged around four months and weighed between 210 and 270 g. All animals were given a minimum of 2 weeks to recover from surgery before the first test (object recognition) began. For some of the postoperative test period the animals were placed on a restricted diet, but they were weighed regularly and their food adjusted to ensure that they did not fall below 85% of normal body weight. Throughout the study all animals had unrestricted access to water.

2.2. Surgical and histological procedures

The rats were divided into three groups; perirhinal plus postrhinal cortex lesions (PPRH, $n = 12$), fornix lesions (FNX, $n = 11$) and surgical controls (CONT, $n = 13$). Prior to surgery all animals were deeply anaesthetised by intraperitoneal injection (60 mg/kg) of pentobarbitone sodium (Sagatal, Rhône Mérieux, UK) and then placed in a stereotaxic headholder (David Kopf Instruments, Tujunga, CA) with the nose bar at $+5.0$. The scalp was then cut and retracted to expose the skull. Craniotomies were then made directly above the target regions, and the dura cut to expose the cortex.

For the cortical lesions (PPRH), injections of 0.2 μl of 0.09 M *N*-methyl-D-aspartic acid (NMDA; Sigma Chemical Company Ltd., Poole) dissolved in phosphate buffer (pH 7.2) were made through a 1 μl Hamilton syringe into five sites in each hemisphere. Each injection was made gradually over a 5 min period and the needle was left in situ for a further 4 min before being withdrawn. The stereotaxic co-ordinates relative to ear-bar zero were: AP + 3.9, LAT ± 5.9, HT 2.0; AP + 2.4, LAT ± 6.1, HT + 1.6; AP + 0.6, LAT ± 6.2, HT + 2.5; AP − 0.8, LAT ± 6.2, HT + 2,7; and AP − 0.8, LAT ± 6.2, HT + 4.3.

The fornix lesions (FNX) were made using a Radionics TCZ (Radionics Inc., Burlington) electrode (0.3 mm tip length, 0.25 mm diameter) equipped with a thermister. The probe was lowered vertically into the appropriate site and the tip temperature raised to 75°C for 60 s using an RFG4-A Lesion Maker (Radionics Inc., Burlington). Two lesions were made in each hemisphere, the coordinates of the lesions relative to ear-bar zero were AP + 5.3, LAT ± 0.7, and AP + 5.3, LAT ± 1.8. The medial lesion was placed 3.7 mm below the top of the cortex, and the lateral lesion was placed 0.1 mm deeper.

The control animals (CONT) received sham surgeries (eight fornix; five perirhinal/posthinal cortex) in which exactly the same initial surgery was performed (including craniotomy) but no injections were made. At the completion of all surgeries the skin was sutured and an antibiotic powder ('Acramide', Dales Pharmaceuticals, Skipton) applied. The animals then received 5 ml glucose saline (s.c.) containing etamiphylline ('Millophylline', Arnold's, Romford; 35 mg/kg, s.c.), a cardiac stimulator. Post-operative care also included systemic analgesia (temgesic, Reckett and Colman, UK).

On completion of the experiment all animals were killed with an overdose of Euthatal (Rhône Mérieux) and perfused intracardially with saline followed by 10% formol-saline. The brains were then removed and placed in 10% formol-saline for a minimum of 2 hours. Following fixation the brain was transferred to 20% sucrose in 0.2 M phosphate buffer and left overnight. The brain was cut on a freezing microtome into 60 μm coronal sections, and sections were mounted and then stained with cresyl violet, a Nissl stain.

3. Experiment 1

Experiment 1 compared the effects of fornix transection and excitotoxic lesions of the perirhinal/postrhinal cortex on object recognition and spatial memory tasks. The object recognition task was the same as that used previously [16,17], in which rats recognise that an object has been encountered previously. Spatial memory was examined in a delayed alternation task carried out in a T-maze.

4. Materials and methods

4.1. Spontaneous object recognition test

4.1.1. Apparatus

The apparatus consisted of an open arena (100 × 100 × 46 cm) made of wood, the inside of which was painted grey. The floor was covered with sawdust. The arena was situated in a room containing features such as a door, light fixtures and a video camera, and a large dark screen which served to conceal the experimenter. Triplicate copies were obtained of the objects to be discriminated, which were made either of glass, plastic or metal. For any given test the pairs of objects to be discriminated were typically composed of the same material so that they could not readily be distinguished by olfactory cues. The height of the objects ranged from 6.3 to 22.0 cm, while their weight ensured that they could not be displaced by the rats. As far as could be ascertained the objects had no natural significance for the rats and they had never been associated with a reinforcer.

4.1.2. General procedure

All rats were given a minimum of four habituation sessions prior to the first test. For each of these habituation sessions the rat was placed in the empty arena for 10 min. Forty-eight hours later, testing began. Rats were given a series of test sessions, with a minimum interval of 48 h between each session. During these tests the experimenter did not know the group membership of the animals. The time spent exploring objects during the various tests was assessed from video recordings of the sample and test phases. Throughout these tests the rats were on ad libitum food and water.

4.1.3. Object recognition test

Each test session consisted of two phases (see Fig. 1A). In the initial sample phase two identical objects (A1 and A2) were placed in the far corners of the arena, each 10 cm from the side wall. A rat was then placed in the middle of the arena and the total time spent exploring the two objects was determined from video taped recordings. Exploration of an object was defined as directing the nose to the object at a distance of less than 2 cm and/or touching it with the nose. Turning around or sitting on the object was not considered as exploratory behaviour. This 'sample phase' ended when the rat had explored the two identical objects for a total of 25 s.

After a delay of 15 min the rat was reintroduced to the arena ('choice phase'). The arena now contained a third identical copy of the familiar object (A3) and a new object (B). These were placed in the same locations as the sample stimuli. The location of the two choice objects was counterbalanced between rats and across

sessions. All rats were tested with two sets of objects, and received a total of four tests. Thus on test 1, object A was the sample and object B was the novel alternative. For test 2 (48 h later) their roles were reversed, i.e. object B was the sample and object A was the 'novel' alternative. This 48 h interval was thought to be sufficient as previous studies have shown that under these conditions rats fail to treat the sample stimulus as familiar if the delay between sample exposure and test is longer than 24 h [16]. For tests 3 and 4 new pairs of objects were used (C and D) in a similar, counterbalanced order. Objects C and D were both constructed from 'Duplo' (Lego Limited) and hence were visually distinct but could not be distinguished by olfactory or tactile cues.

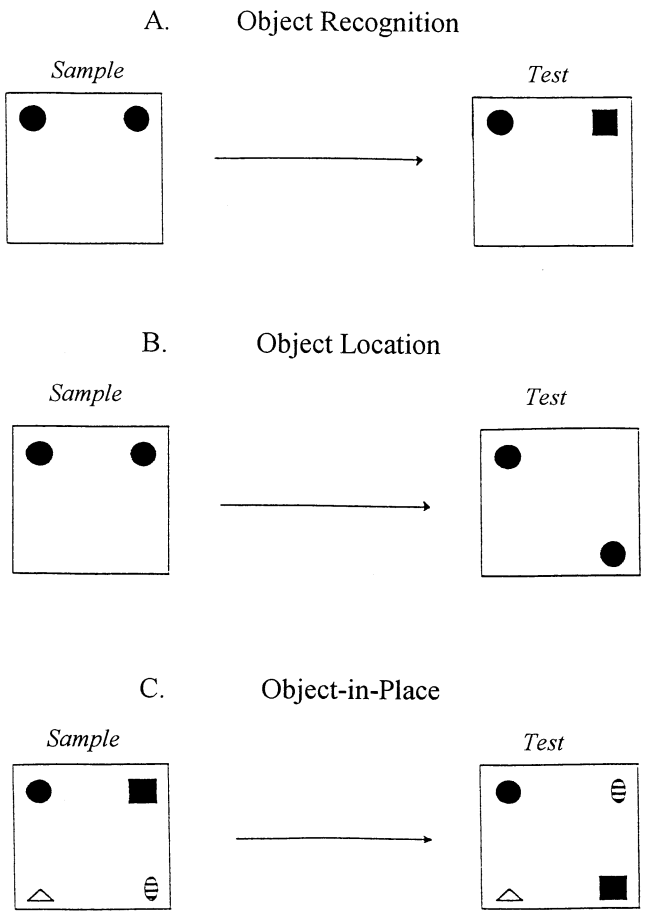

Fig. 1. Schematic diagram of the three spontaneous recognition tests used in experiments 1 and 2. (A) Object recognition test. Two identical objects are presented, and following a delay a novel object and a copy of the now-familiar object are placed in the arena. Normal rats spend more time exploring the novel object. (B) Object location test. This test is similar to the object recognition test with the exception that normal discrimination requires that the rat recognise that an object has changed location. Normal rats spend more time exploring the displaced object. (C) Object-in-place test. After the delay the positions of two adjacent objects were exchanged. Normal rats explore the objects that have been exchanged. Thus discrimination requires the use of information about both object identity and place.

4.2. T-maze alternation

4.2.1. Apparatus

The animals were tested in a standard T-maze. The floors of the T-maze were 10 cm wide and made of wood painted white. The stem was 70 cm long with a guillotine door located 25 cm from the distal end. When this door was closed a start box was created. The cross piece was 140 cm long and at each end there was a food well 2 cm in diameter and 0.75 cm deep. The walls of the maze were 17 cm high and made of clear Perspex. The maze was supported on two stands 94 cm high. Lighting was provided by a fluorescent light suspended 164 cm above the apparatus.

4.2.2. Procedure

Each animal was given a minimum of four 5 min pretraining sessions. By the end of these sessions the rats would run down the stem of the maze to find food pellets in the food wells in both arms. Following this the experiment proper began. At the start of each trial, which consisted of two stages, three food pellets (45 mg Campden Instruments, Loughborough) were placed in each food well and a metal barrier was placed at the neck of the T-maze so closing off one arm. As a consequence, the animal was forced to enter a pre-selected arm on each 'sample run' and then allowed to eat the food there. The animal was then picked up and confined in the start box for a delay of 15 s, during which the metal barrier was removed. The door to the start box was then opened and the animal allowed a free choice between the two arms of the T-maze. On this 'choice run' the criteria for selecting an arm consisted of the rat placing a back foot in one of the arms. No retracing was permitted. If the rat had alternated, i.e. had entered the arm not previously visited on the sample run, it was allowed to eat the food reward before being returned to its cage. If the other arm was chosen, i.e. the same arm as visited on the sample run, the rat was confined to that arm for approximately 10 s, and then returned to its cage. The rats were tested in groups of three or four with each rat having one trial in turn, so that the intertrial interval was about 4 min. The animals received six trials a day, for a total of six sessions.

4.2.3. Mixed delays

Immediately following the acquisition session the rats received a further six sessions, each of six trials. For half of the trials within each session there was a delay of 15 s between the choice run and the test run, and for the other half there was a delay of 60 s. The delay on a given trial was determined pseudorandomly. During the delay period the animal remained in the start box at the base of the stem. The rest of the procedure remained unchanged. Throughout the test period the

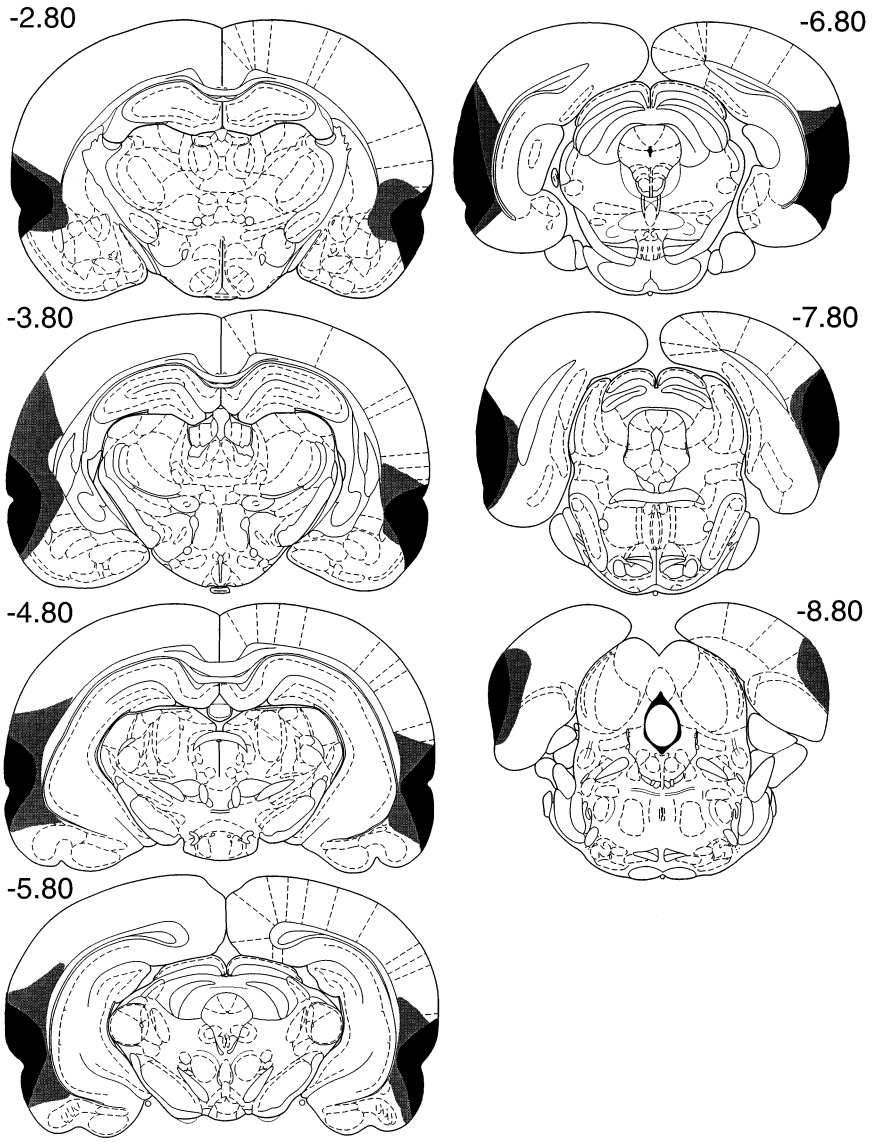

Fig. 2. Coronal sections illustrating the extent of the largest (gray) and smallest (black) lesions of the perirhinal/postrhinal cortex. The numbers correspond to the approximate position from bregma [35].

animals were food deprived, but their body weight did not fall below 85% of free feeding weight.

5. Results

5.1. Histological analysis

The PPRH lesions consistently removed almost all of the perirhinal and postrhinal cortex. The rostral limit of the lesions was level with the rostral third of the amygdala while caudally the lesions often extended to the most posterior portions of the postrhinal cortex (Fig. 2). Within the extent of the lesion there was essentially no evidence of neuronal sparing, although in two cases there was some unilateral sparing of deeper cortical layers at the junction of the postrhinal and perirhinal cortices. At the more rostral levels the lesions consistently encroached ventrally to include the most lateral parts of the piriform cortex, and in seven cases there was partial damage to the lateral nucleus of the amygdala (bilateral in two cases). More caudally the lesions consistently involved the lateral portions of the lateral entorhinal cortex, but spared the medial entorhinal cortex. The lesions were more variable in their dorsal extent. Area TE was involved in all PPRH animals, and in nine cases the lesions also included parts of the auditory association cortex immediately dorsal to TE (unilateral in six cases, bilateral in three cases). Although the neurotoxic damage extended to the depths the rhinal sulcus, the hippocampus was almost completely spared. In six cases there was no

evidence of any neuronal loss in the hippocampus, while in five of the remaining cases the only cell loss was in a very restricted portion of the CA1 hippocampal field immediately adjacent to the most caudal part of area TE. In one case there was very restricted bilateral damage to this same portion of CA1.

Two FNX animals in which there was considerable sparing of the fimbria/fornix were rejected and their data discarded. In the remaining nine animals the fornix lesions produced extensive bilateral damage to the tract (Fig. 3). The median extent of damage involved 80% of the tract, with the largest lesions severing the fimbria/fornix completely and the smallest sparing the most lateral 30% of the fimbria (Fig. 3). In one case the tract lesion extended caudally to involve the head of the hippocampus. In all cases the lesions spared the corpus callosum but the very dorsal margin of the anterior thalamic nuclei was involved in four cases. The cingulum bundle was always spared and there was no direct damage to the cingulate cortex.

Following histological analysis the three groups comprised: CONT, $n = 13$; FNX, $n = 9$; PPRH, $n = 12$. One of the PPRH animals suddenly fell ill after completion of the object recognition test (experiment 1) and was removed from the remainder of the study.

5.2. Spontaneous object recognition test

5.2.1. Exploration during sample period

We first considered the duration of the sample period (the total time spent in the arena in order to accumulate 25 s of object exploration) as a group difference in this phase might be related to subsequent recognition performance. An analysis of variance revealed a highly significant group effect, $F(2,31) = 23.5$, $P < 0.0001$. Newman–Keuls post-hoc analysis revealed that this difference reflected the shorter sample period of the FNX group which differed from both of the other two groups (mean of all four sample periods in seconds, FNX = 76.4, PPRH = 140.0, CONT = 123.3; both $P <$ 0.01). There were no other differences. If the shorter sample periods of the FNX group were to have a systematic effect on recognition performance it would only be to diminish subsequent discriminations between novel and familiar objects.

5.2.2. Recognition during test period

Total exploration times were calculated for the novel and familiar objects summed across the two matching pairs of test trials. From these pairs of sessions, exploration times were calculated both for the entire 3 min session and for the first minute of each test session. The latter was included as the initial period of exploration could logically be regarded as the most sensitive measure of discrimination, i.e. when the familiarity difference is the greatest. Consistent with this is evidence showing that normal animals often do not discriminate during the second or third minute of the object recognition test [13]. From these results we calculated d_1, the absolute difference in time spent exploring the novel and familiar objects for each of the two sets of objects and d_2, the proportion of total exploration time spent exploring the novel objects for each pair of objects (i.e. the difference in exploration times for the novel and familiar object, d_1, divided by the total time spent exploring the objects). This discrimination ratio (d_2) is informative as it takes into account individual differences in the total amount of exploration time. Finally, 95% confidence limits of the mean were calculated to determine if the group d_1 and d_2 scores were above zero ($P < 0.05$), and so demonstrate whether the individual groups displayed a significant preference for the novel stimuli.

Analysis of variance using the difference scores (d_1) for all 3 min of the object recognition test sessions (Fig. 4B) revealed evidence of a group effect, $F(2,31) = 3.56$, $P = 0.041$. A similar analysis using the discrimination index scores (d_2) for all 3 min (Fig. 4D) also revealed a significant group effect, $F(2,31) = 4.35$, $P = 0.022$. Post hoc analyses using the Newman–Keuls test showed that both of these differences reflected the poor performance of the PPRH group, which differed significantly from the CONT group ($P < 0.05$). Similar analyses for the first minute of the object recognition test sessions (Fig. 4A and C) revealed even clearer evidence of group differences: d_1, $F(2,31) = 3.72$, $P = 0.036$; d_2, $F(2,31) =$

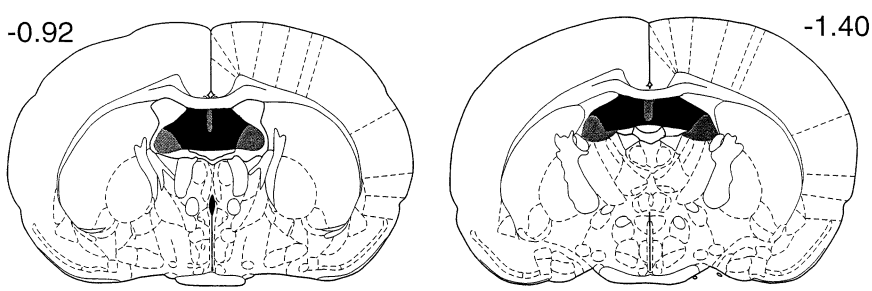

Fig. 3. Coronal sections illustrating the extent of the largest (gray) and smallest (black) lesions of the fornix. The numbers correspond to the approximate position from bregma [35].

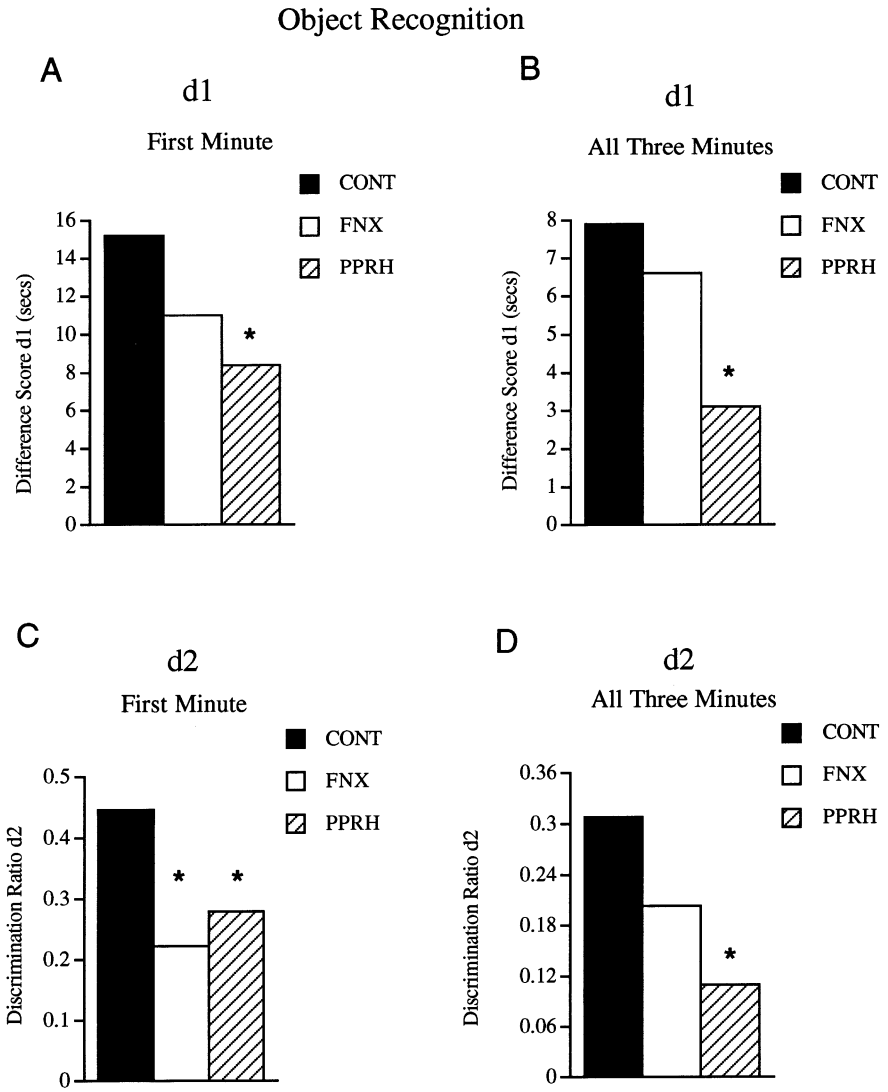

Fig. 4. Performance of PPRH, FNX, and CONT animals on the spontaneous object recognition test. Panel A shows the difference in time spent exploring the novel and familiar objects (d_1) for the first minute of exploration during the test period. Panel B shows the difference in time spent exploring the novel and familiar objects (d_1) for all 3 min of exploration during the test period. Panel C shows the ratio of time spent exploring the novel object (d_2) for the first minute of exploration during the test period. Panel D shows the ratio of time spent exploring the novel object (d_2) for all 3 min of exploration during the test period. Asterisks indicate significantly poorer performance of lesioned animals relative to controls; * $P < 0.05$.

6.78, $P = 0.0036$. Post hoc analyses using the Newman–Keuls test showed that for d_1 the differences reflected the poor performance of the PPRH group, which differed significantly from the CONT group ($P < 0.05$), while for d_2 both the PPRH and FNX groups discriminated significantly more poorly than the CONT group ($P < 0.05$).

Analysis of confidence limits (95%) of the mean d_1 and d_2 indices from all 3 min and from all object sets showed that for both d_1 and d_2 all three groups were able to discriminate the novel from the familiar object (see Table 1).

Table 1
Discrimination by CONT, FNX, and PPRH animals based on 95% confidence limits of the mean[a]

	CONT		FNX		PPRH	
	d_1	d_2	d_1	d_2	d_1	d_2
Object recognition	✓	✓	✓	✓	✓	✓
Object location	✓	✓	X	X	✓	✓
Object-in-place	✓	✓	✓	X	X	X

[a] ✓, significant discrimination; x, failed to discriminate.

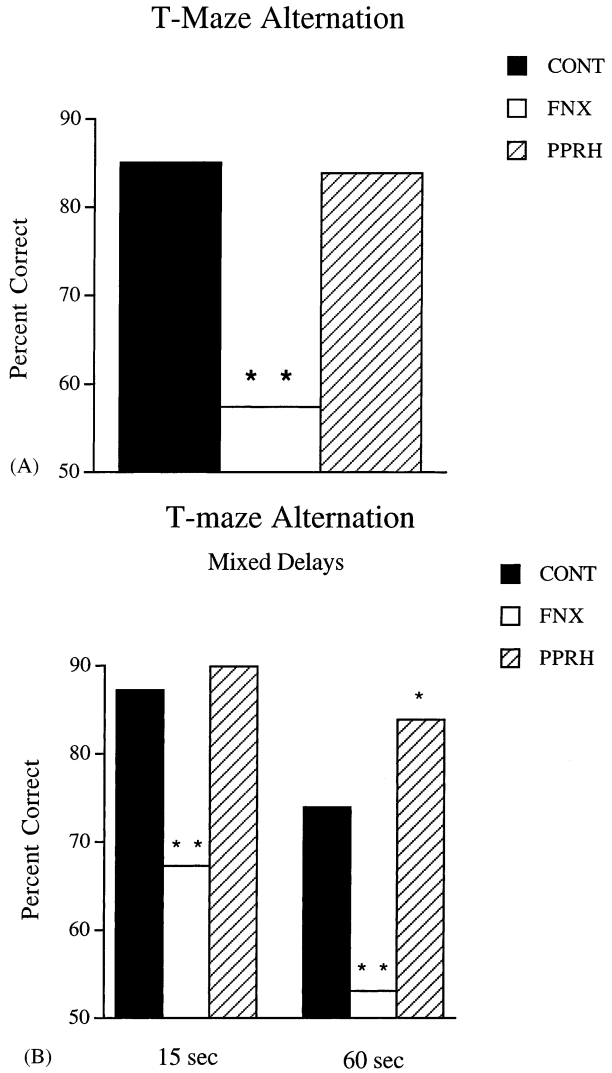

Fig. 5. Performance of PPRH, FNX, and CONT animals on the T-maze alternation task in experiment 1. (A) Basic task with 15 s delay. (B) Mixed delays of 15 and 60 s. Asterisks indicate a significant difference from controls; * $P < 0.0$; 5** $P < 0.01$.

5.3. T-maze alternation

The total percent correct scores over the six training sessions (15 s delay) and the six delay sessions (15 and 60 s delay) are shown in Fig. 5A and B. Analysis of variance using just the data from training sessions revealed a highly significant group difference, $F(2,30) = 62.7$, $P < 0.0001$. Post-hoc Newman–Keuls tests showed that the FNX group differed from both the PPRH and CONT groups (both $P < 0.01$). Similar comparisons for the delay data also revealed the expected group difference, $F(2,30) = 52.8$, $P < 0.0001$. Once again post-hoc Newman–Keuls analysis confirmed that the FNX group performed significantly worse than both of the other groups (both $P < 0.01$). In addition, the same analysis revealed that the PPRH animals also differed from the CONT animals, performing at a higher level overall. There was an overall effect of delay, $F(1,30) = 25.0$, $P < 0.0001$, but no group by delay interaction, $F(2,30) = 1.32$, $P = 0.28$, however analysis of simple effects revealed that the facilitated performance of the PPRH group reached statistical significance at the 60 s delay only.

6. Experiment 2

In experiment 1, it was found that lesions of the fornix and of the perirhinal/postrhinal cortex led to distinct patterns of behavioural impairments. It was found that in general, lesions of the fornix impaired spatial memory, whereas lesions of the perirhinal/postrhinal cortex impaired object recognition. In experiment 2 we sought to investigate whether these lesions would have more similar effects under conditions in which the hippocampus and perirhinal/postrhinal cortex might interact, i.e. in situations where object and spatial information must be integrated. This was tested using two very different paradigms having both 'object' and 'spatial' characteristics. The first was an 'object-in-place' test, carried out in the same apparatus and with the same stimulus material as the object recognition test. Unlike the object recognition test, however, in the object-in-place test rats recognise not that a specific object has been seen before, but that a specific object has exchanged position with another object. We also tested these animals on an 'object location' test in which rats recognise that an object is in a place that had not previously been occupied by any object; thus this task requires the use of spatial information only. In addition, upon completion of the object-in-place test the rats were given a test of spontaneous activity using novel activity cages.

7. Materials and methods

7.1. Object location test

The apparatus and general procedure for both the object-in-place and object location tests was the same as that in experiment 1. Unlike the object recognition test, rats were not tested on the ability to distinguish between objects or to make judgements based on the familiarity of objects. Instead, normal discrimination involved rats recognising that an object had changed location (Fig. 1B). The use of information about the specific identity of the object was thus not required. Two copies of the same object (A) were used in each test. In the sample phase the rat was exposed to objects A1 and A2 which were placed in the two far corners of the arena. The sample phase was terminated when the animal had explored the objects for a total of 25 s.

After a delay of 15 min the test phase began. In the test phase object A3 was placed in the same position as A1 while object A4 was placed in the corner adjacent to the original position of A2, so that the two objects A3 and A4 were now in diagonal corners. Thus both objects in the test phase were equally familiar but one had changed location. All animals received two test sessions separated by 48 h. This ensured that the position of the moved object in the test phase could be counter-balanced for each rat. The objects (A1–4) were identical unopened drink cans that had not been used in any previous test. Testing began one week after completion of the object recognition test.

7.2. Object-in-place test

Unlike the previous two tests, normal performance of the object-in-place test requires the use of information about *both* the location of an object *and* the object's identity. All rats received four test sessions involving the same set of four different glass objects (see Fig. 1C). For the sample phase one object was placed in each of the four corners of the arena (A1, B1, C1, D1). Each rat was then placed in the arena for a total of 5 min. During the retention interval of 6 min the objects were replaced by an identical set (A2, B2, C2, D2) except that the positions of two adjacent objects were exchanged. The time spent exploring the two objects that had changed position was then compared to the time spent exploring to the two objects that remained in the same position. For half of the rats the objects on the left side of the arena changed position, and for the other half the objects on the right changed. All rats were tested 48 h later, counterbalancing the side on which the objects had been exchanged.

7.3. Spontaneous locomotor activity

After completion of the above tests all rats were placed in novel test cages ($56 \times 39 \times 19$ cm) in a novel room. Activity was measured using pairs of photobeams situated 20 cm apart and 18 cm from the end of the cage (Paul Fray Limited, Cambridge, UK). The total number of beam breaks was recorded. Data were gathered in 12 intervals of 10 min each.

8. Results

8.1. Object location test

8.1.1. Exploration during sample period

In this procedure the sample period was held constant at 3 min, and the amount of time spent exploring the objects during that time was recorded and analysed. There was a significant main effect of group, $F(2,30) = 5.10$, $P < 0.05$. Post-hoc Newman–Keuls analysis revealed that animals of the FNX group spent more time exploring the objects during the sample phase than animals of either the CONT or PPRH groups (both $P < 0.05$; MEANS: CONT = 13.0; FNX = 16.5; PPRH = 13.2 s).

8.1.2. Recognition during test period

The analyses took the same form as those used for object recognition in experiment 1. Thus both the d_1 and d_2 scores for 1 min and for all 3 min were compared across the three groups. None of the four ANOVAs showed clear evidence of a group difference, with only the comparison for d_2 (all 3 min) providing any sign of a difference, $F(2,30) = 2.62$, $P = 0.089$. For this measure the FNX group tended to discriminate more poorly than did the other two groups. (MEANS: First minute: CONT $d_1 = 12.5$, $d_2 = 0.48$; FNX $d_1 = 9.78$, $d_2 = 0.23$; PPRH $d_1 = 8.36$, $d_2 = 0.35$. All 3 min: CONT $d_1 = 5.96$, $d_2 = 0.41$; FNX $d_1 = 4.81$, $d_2 = 0.10$; PPRH $d_1 = 5.76$, $d_2 = 0.32$.)

We also examined the confidence limits (95%) of the d_1 and d_2 indices from all 3 min summed across the pair of trials. This analysis showed that for d_1 and d_2 both the CONT and the PPRH animals spent more time exploring the displaced object. In contrast, the FNX group failed to show a significant preference according to both d_1 and d_2 (see Table 1).

8.2. Object-in-place test

8.2.1. Exploration during sample period

In this procedure the sample period was held constant at 5 min, and the amount of time spent exploring the objects during that time was recorded and analysed. There was a significant main effect of group, $F(2,30) = 11.4$, $P < 0.001$. Post-hoc Newman–Keuls analysis revealed that animals of the FNX group spent more time exploring the objects during the sample phase than animals of either the CONT or PPRH groups (both $P < 0.01$; MEANS: CONT = 26.3; FNX = 37.7; PPRH = 28.8 s).

8.2.2. Recognition during test period

Analysis of variance using the difference scores (d_1) for all 3 min of the four test sessions revealed clear evidence of a group effect, $F(2,30) = 4.66$, $P = 0.017$. Newman–Keuls post hoc analysis revealed a significant difference between the PPRH and FNX groups, the former showing the lowest discrimination scores ($P < 0.05$), although neither group differed from controls. A similar analysis using the discrimination index scores (d_2) for all 3 min did not, however, reveal a group effect, $F(2,30) = 1.77$, $P = 0.19$. Similar analyses for the first minute of the object-in-place test sessions, however, revealed clear evidence of group differences: d_1,

$F(2,30) = 7.54$, $P < 0.01$; d_2, $F(2,30) = 4.71$, $P < 0.05$. Post hoc analyses using the Newman–Keuls test showed that for both d_1 and d_2 the differences reflected the poor performance of the PPRH group, which differed significantly from the FNX group (d_1, $P < 0.01$; d_2, $P < 0.05$). In addition, the CONT and FNX groups also differed, with the FNX group achieving the highest scores (MEANS: first minute: CONT $d_1 = 3.11$, $d_2 = 0.10$; FNX $d_1 = 11.7$, $d_2 = 0.30$; PPRH $d_1 = 0.90$, $d_2 = 0.03$. All 3 min: CONT $d_1 = 2.41$, $d_2 = 0.12$; FNX $d_1 = 4.40$, $d_2 = 0.08$; PPRH $d_1 = 0.07$, $d_2 = 0.01$).

Finally, we examined the confidence limits (95%) of the d_1 and d_2 indices from all 3 min summed across all trials. This analysis showed that according to both d_1 and d_2 the CONT animals spent more time exploring the transposed than the static objects. In contrast, the PPRH group failed to show a significant preference according to both d_1 and d_2 (see Table 1). The FNX group showed a significant preference as measured by d1 but failed to discriminate according to d_2. Thus according to this measure FNX and PPRH lesions had similar effects on this task.

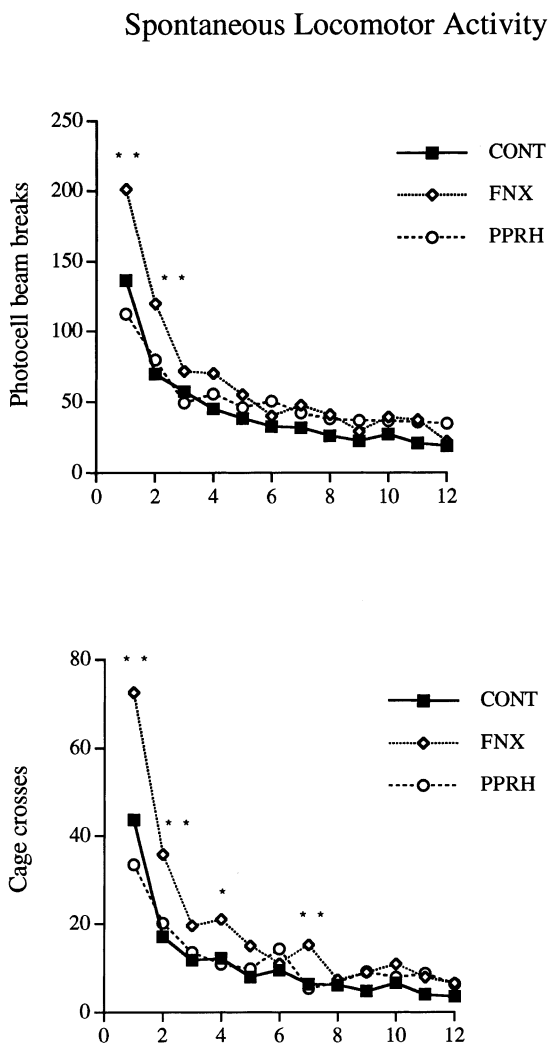

Fig. 6. Spontaneous locomotor activity of PPRH, FNX, and CONT animals in novel cages. Asterisks indicate a significant difference from controls; * $P < 0.05$; ** $P < 0.01$.

8.3. Spontaneous locomotor activity

The beam breaks made by the animals were compared across 12 10-min intervals. A comparison of cage crosses (i.e. breaking one beam followed by breaking the other) revealed clear evidence of a group effect, $F(2, 30) = 6.11$, $P < 0.01$. Post hoc analyses showed that this was due to the higher activity level in the FNX group which differed from both the CONT and PPRH groups (Newman–Keuls, both $P < 0.01$). This difference was most pronounced during the initial 40 min (Fig. 6) as indicated by the highly significant group by interval interaction, $F(22,330) = 7.06$, $P < 0.0001$. A comparison of total beam breaks again revealed a group difference, $F(2,30) = 3.33$, $P < 0.05$, and a highly significant group by interval interaction, $F(22,330) = 4.16$, $P < 0.0001$, that once again reflected the high levels of initial activity by the FNX group.

9. Experiment 3

In experiment 2 evidence was found that in certain situations contributions from the fornix and perirhinal/postrhinal cortex may be integrated. In the object-in-place test PPRH animals failed according to two measures, and FNX animals failed according to one measure, to discriminate objects that remained fixed in place, with those that had exchanged locations with other objects (see Table 1). In experiment 3 we examined a second type of task in which object and place information may need to be integrated. In this visuospatial conditional learning task, carried out in a computerised touchscreen apparatus [11], rats must learn a rule of the type: 'If stimulus A go left; if B go right'. In order to ensure that lesioned rats could discriminate nonspatial and spatial computer graphic stimuli in this apparatus, we first tested the rats on two additional touchscreen tasks: stimulus–reward learning in a discriminative Pavlovian autoshaping paradigm [7], and a pattern discrimination learning task using equiluminant shape stimuli.

10. Materials and methods

10.1. Apparatus

Testing was conducted in an automated apparatus in which a computer video display unit (VDU) presented stimuli to the animal [11]. The VDU was attached to a touch screen so that the animals could select computer

produced stimuli by directly responding toward the VDU with their noses. This apparatus was housed within a wooden sound-attenuating box. The inner chamber measured 48 × 30 × 30 cm, and consisted of a metal frame, clear Perspex walls, and an aluminium floor. Located centrally on the wall at the rear of the chamber was a food magazine attached to a pellet dispenser (Campden Inst., Loughborough), accessed via a hinged perspex panel that was monitored by a microswitch. A pressure-sensitive area of floor measuring 14 × 10 cm and located directly in front of the food magazine made it possible to detect the presence of the rat in this area. The VDU, on which the stimuli were presented, was located at the other end of the chamber. Surrounding the VDU was a 'touchscreen' attachment (Microvitec Touch-tech 501) that monitored when the rats made contact with the screen or came very close. A black perspex 'mask' was attached to the face of the VDU, approximately 2 cm from the surface of the display. This mask served to block access to the VDU display except through response windows each measuring 6 cm high × 8 cm wide. These were positioned 13 cm apart (from centre to centre). A shelf extending 7 cm from the surface of the Perspex mask was positioned just beneath the response windows, approximately 15 cm above the floor of the chamber. The combined effect of the response windows and the shelf was to force the animals to stop, rear up, and stretch toward the stimuli with a head-on approach, thus facilitating the rats' attention to the stimuli.

The pattern discrimination and visuospatial conditional tasks were carried out in the apparatus as described above [10,11].

10.2. Autoshaping

The apparatus for the autoshaping task was a modification of that described above. The food magazine was moved from the rear of the chamber to directly in front of the centre of the screen. The perspex mask was removed thus allowing the use of the entire screen for stimulus presentation. Photocells were installed to monitor rats' entries into the magazine and approaches toward the screen. For a more detailed description and a figure of the modified apparatus, see [7]).

10.3. Procedure

10.3.1. Pretraining

Rats were initially given one 30 min session in which they were allowed to habituate to the testing chamber and collect pellets from the magazine. The houselight was illuminated and pellets were delivered into the magazine on a VI 40 s schedule. Magazine photocell beam breaks were analysed to ensure that all rats were successfully retrieving and consuming pellets. Additional sessions were given as necessary.

10.3.2. Acquisition

On the day following pretraining, rats were trained to associate a stimulus with reward. The two stimuli used were identical vertical white bars (10 × 28 cm), presented on the left or right of the VDU screen. Stimuli were presented for 10 s. One of the stimuli was designated the CS+ and signalled the delivery of a reward pellet immediately following stimulus offset; the other, designated the CS−, was never followed by food delivery. The task is thus 'Pavlovian' in that delivery of reward was not contingent on the rat's response. As rats learn to associate the CS+ with reward, they approach the CS+ with increasing frequency and decreasing latency [7]. The left stimulus was designated the CS+ for half of the animals in each of the experimental groups; for the other half the right stimulus was designated the CS+. Both stimuli were presented on a VI 40 s schedule, and training consisted of 100 presentations of both the CS+ and CS−. When the rat crossed through the photocells in front of a stimulus, it was scored as an approach to that stimulus, and no further approaches were scored during that stimulus presentation.

Presentation of stimuli and collection of response measures were subjected to the following restrictions: (i) stimuli were not presented until the rat was centrally located at the rear of the chamber. This eliminated chance approaches to the stimuli, provided all rats on every trial with an equivalent opportunity for stimulus sampling, and allowed for the accurate calculation of approach latencies based on the time taken for rats to approach the stimuli starting from the same position in the test chamber on each trial; (ii) the minimum time between presentations of the CS+ and CS− was 10 s; (iii) the maximum number of consecutive presentations of either the CS+ or the CS− was two.

Several performance measures were calculated: (i) the number of approaches to the CS+ per ten presentations; (ii) the number of approaches to the CS− per ten presentations; (iii) the mean latency to approach the CS+ (to the nearest 1/100th of a second); (iv) the mean latency to approach the CS− (to the nearest 1/100th of a second).

10.4. Pattern discrimination

10.4.1. Apparatus

The pattern discrimination and visuospatial conditional tasks were carried out in the unmodified version of the apparatus described above [11]. For the pattern discrimination task, two stimuli were used, a white cross (7 cm high, 5 cm wide) and a white rectangle (5 × 4 cm). These stimuli were matched for brightness by ensuring that an equivalent area of the screen was illuminated for each stimulus.

10.4.2. Procedure

The rats were initially trained to nose-poke at the touchscreen and to take food (45 mg food pellet) from the magazine. By the end of pretraining the rats were able to nose-poke at a large yellow square displayed on the VDU. The square was randomly presented in one of the response windows and remained on the screen until the rat responded to it, after which the rat was rewarded with the magazine light, a tone, and a 45 mg pellet. Once a rat was able to obtain 50 rewards within 20 min, it was moved on to the simple discrimination task.

Each discrimination trial began with the simultaneous presentation of the two stimuli, contingent upon the animal being located on the rear floor panel following a 5 s inter-trial interval. The rat was then required to approach the VDU display and select a stimulus by responding to it directly via a nose-poke. Correct responses were followed by the disappearance of the stimuli and the presentation of a 1 s, 4 KHz tone, concomitant with illumination of the magazine light and delivery of a 45 mg food pellet into the magazine. Incorrect responses resulted in the disappearance of the stimuli and the houselight being extinguished for a 'time-out' period of 5 s.

The same pair of stimuli (cross and rectangle) were presented on every trial. For half of the animals in a group the cross was correct (S+), for the other half the rectangle was correct (S+). A nosepoke to the S+ was rewarded with a tone, the magazine light, and a food pellet. A nosepoke to the incorrect stimulus (S−) was followed by extinction of the houselight for a 5 s time-out period. A correction procedure was implemented such that following an incorrect response the trial was repeated, i.e. the S+ remained in the same location. Rats received 100 trials per session.

10.5. Visuospatial conditional discrimination

Rats were required to learn a rule of the type, 'If stimulus A then go left, if stimulus B then go right'. For this task, a three-window mask was used. The three windows were raised the same distance from the floor, one located centrally, the other two located to the right and left of the central window. A trial began with a 5 s inter-trial interval followed by the presentation of one of two discriminative stimuli in the central window. Stimuli were chosen to be easily discriminable and differed on a number of dimensions including size and colour. The rat was required to make a nose-poke to the discriminative stimulus. Immediately following the disappearance of the discriminative stimulus, the choice stimuli (two white squares) appeared in the left and right windows. A nose poke to the appropriate square (left or right, depending on the discriminative stimulus) was rewarded with one pellet; an incorrect response was followed by a 5 s time-out period. Which stimulus was to be associated with which response was counterbalanced across groups; for half of the rats in a group one stimulus-response contingency was correct, for the other half the other contingency was correct. The two discriminative stimuli were presented an equal number of times during a session. If the rat did not respond to the choice stimuli within a 2 s limited-hold period, the choice stimuli disappeared and the house lights were extinguished for a 5 s time-out period. This ensured a consistent response of turning and nose-poking to the left or right while rearing. A correction procedure was administered such that following an incorrect response the trial was repeated, i.e. the same discriminative stimulus was presented and the same response was required. Rats received 100 trials per session.

11. Results

11.1. Autoshaping

11.1.1. Discriminated approach

Difference scores (approaches to the CS+ minus approaches to the CS−) were analysed across the ten blocks of ten stimulus presentations. There was a significant effect of group, $F(2,30) = 3.76$, $P = 0.035$, but no group × block interaction, $F(18,270) = 1.03$, $P = 0.42$. Newman–Keuls post-hoc analysis revealed that the group effect was due to animals of the PPRH group attaining higher levels of discrimination performance than either of the FNX or CONT groups (both $P < 0.05$). There was, however, a significant main effect of block, $F(9,270) = 18.7$, $P < 0.0001$, and analysis of simple interaction effects revealed that the effect of block was significant for all three groups (all Ps < 0.01). Thus animals of the CON, FNX, and PPRH groups were able to acquire discriminative approach in this paradigm, with PPRH animals showing a significant advantage on this task relative to fornix-lesioned animals and controls.

11.1.2. Discriminated magazine approach

There were no differences between groups in discriminated magazine approach, $F(2,30) = 2.99$, $P = 0.065$. There was, however, a significant main effect of block, $F(9,270) = 8.38$, $P < 0.0001$, and analysis of simple interaction effects revealed that the effect of block was significant for all three groups (all $P < 0.01$). There was no significant group × block interaction, $F(18,270) = 0.93$, $P = 0.54$.

11.1.3. Approach latencies

Because animals often made no approaches to the CS− within a block of ten presentations, average approach latencies were calculated by taking the mean

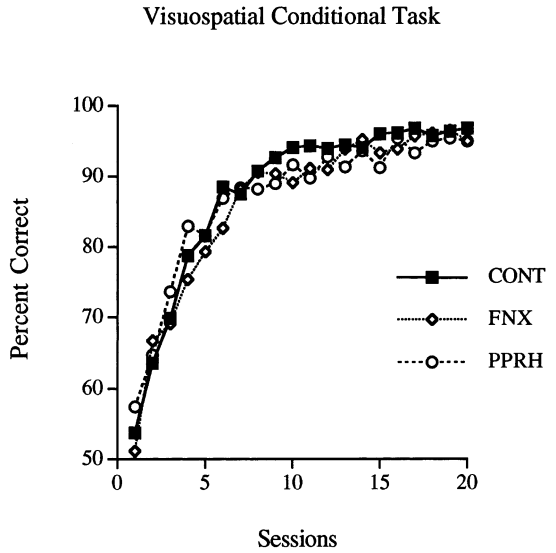

Fig. 7. Acquisition curves for PPRH, FNX, and CONT animals on the visuospatial conditional task in experiment 3. There were no differences between any of the groups.

of the 100 presentations of the CS+ and CS−. There was a significant main effect of group, $F(2,30) = 9.05$, $P < 0.001$, and Newman–Keuls post-hoc comparison revealed that this was due to animals of the FNX group responding faster overall than did control animals ($P < 0.01$) or PPRH animals ($P < 0.05$). There was no significant group × stimulus interaction, $F(2,30) < 1$, $P = 0.61$, and analysis of simple interaction effects revealed a significant effect of stimulus for each of the CON, FNX, and PPRH groups (all Ps < 0.01). Thus, all groups demonstrated discrimination of the CS+ and CS− according to the latency measure, responding faster to the CS+ and slower to the CS−.

11.2. Pattern discrimination

All animals were tested until they reached a criterion of 85% over two consecutive sessions. Comparisons between the three groups using sessions to criterion ($F < 1$) or total errors to criterion, $F(2,30) = 1.23$, $P = 0.31$, revealed no evidence of a group difference (mean sessions to criterion: CONT = 10; FNX = 13.7, PPRH = 13.8).

11.3. Visuospatial conditional task

All three groups acquired the conditional task, and by the end of training were performing above 90% (Fig. 7). The acquisition curves of the three groups were highly similar. Analysis of variance (factors groups and sessions) revealed that there was no group effect ($F < 1$) and no group by session interaction, $F(38,570) = 1.28$, $P = 0.13$, thus confirming the lack of any difference between the three groups. Acquisition performance was also examined by comparing the number of sessions required to reach a criterion of 85%. Once again, there was no evidence of a group difference, $F(2,30) = 1.28$, $P = 0.29$.

12. Discussion

A major aim of the present study was to compare directly the effects of two different disconnections of the hippocampus — fornix transection and excitotoxic lesions of the perirhinal and postrhinal cortices — on tests of object and spatial memory. The two lesions led to distinct patterns of behavioural impairments. Perhaps the most clear comparison was between the object recognition and allocentric T-maze alternation tasks (experiment 1). Animals with perirhinal/postrhinal cortex lesions (PPRH) were impaired relative to control animals (CONT) according to both d_1 and d_2 measures of discrimination, irrespective of whether data were analysed for the first minute only or for all 3 min of the test session. This result confirms previous reports of neurotoxic perirhinal or perirhinal/postrhinal cortex lesion-induced deficits on this task [3,8,17]. In contrast, animals with lesions of the fornix (FNX) were able to discriminate the novel from the familiar object during the first minute and during all 3 min according d_1, and during all 3 min according to d_2. The poor discrimination of the FNX animals according to one analysis (d_2 for the first minute) may have been related to the shorter sample periods of these animals, which might be expected to have a detrimental effect on subsequent discrimination performance. These shorter sample periods were in turn likely to be related to increased spontaneous activity in the FNX animals (experiment 2). PPRH rats showed normal levels of spontaneous locomotor activity, indicating another way in which the effects of FNX and PPRH lesions differ.

Analysis of T-maze performance, however, revealed the opposite pattern of effects. FNX animals were severely impaired in this task relative to both CONT and PPRH animals, whereas PPRH animals were unimpaired. Furthermore, when a 60 s delay was introduced, the PPRH group significantly *outperformed* controls. Thus it appears that a facilitatory effect of PPRH lesions may have been unmasked under this long delay condition by ensuring that the CONT group were not performing at a behavioural ceiling. This finding accords with a recently reported PPRH lesion-induced facilitation on another allocentric spatial task carried out in the radial arm maze [8]. In that study it was also found that PPRH lesions failed to impair performance in the Morris swim task. Performance on all of these tasks — allocentric T-maze alternation, the radial arm maze task, and the Morris swim maze task — is known to be disrupted by both lesions of the fornix and of the

hippocampus [2,4,12,24,30]. These findings thus raise the important question as to the source of visual input to the hippocampus, as it is often assumed that such information is conveyed to the hippocampus via the perirhinal/postrhinal cortex. Not only does this pattern of results suggest that the hippocampus can function without input from either the perirhinal or postrhinal cortices, but also that these regions of cortex have functions of their own, independent of those of the hippocampus.

Several studies have reported that lesions including the perirhinal cortex can spare spatial memory at delays of 60 s [3,17,23,27]. In a recent study, however, it was found that excitotoxic perirhinal cortex lesions could lead to impairments in T-maze performance at longer delays of 120 or 180 s [27]. Although in the present study delays of this length were not used, the observation that PPRH lesions *facilitated* performance at a 60 s delay makes it highly unlikely that an impairment would have been observed at longer delays. Indeed, in a recent study in which we allowed rats to obtain pellets from four arms of an eight-arm radial maze, and then interposed a delay before allowing the rat to search all eight arms for the remaining four pellets, PPRH animals were unimpaired even with a delay of 30 min [8]. The reason for this discrepancy is unclear, although the inconsistencies between research groups points to procedural differences such as lesion method and extent, or type of pretraining. In spite of these factors it remains clear that spatial deficits following joint removal of perirhinal and postrhinal cortices, or perirhinal cortex alone, leads at best to very modest impairments compared to the effects of fornix transection or hippocampectomy.

A second aim of the present study was to test the possibility that these lesions could have similar effects under certain conditions in which the hippocampus and perirhinal/postrhinal cortex might interact, i.e. in situations in which object and spatial information must be integrated. This was tested using two very different paradigms having both 'object' and 'spatial' characteristics: an 'object-in-place' test, carried out in the same apparatus and with the same stimulus material as the object recognition test, and a visuospatial conditional discrimination test carried out in a computerised touchscreen testing apparatus. In the object-in-place test, performance of PPRH animals was significantly worse than that of FNX animals according to d_1 for the first minute and for all three minutes of the test session, and according to d_2 for the first minute of the test session. In contrast, on an object location test performance of FNX animals appeared to be worse than that of controls, but this trend did not reach statistical significance. In a recent study it was reported that fornix-lesioned animals were significantly impaired on the object location test [18]. The failure of the difference between FNX and CONT groups to reach statistical significance in the present study may have been due to the nature of the room cues. In contrast to the study of Ennaceur et al. [18], in the present study the test room was polarised by a large dark screen along one end. It is possible that this reduced the demand on the rats to encode the spatial environment in allocentric coordinates.

Inspection of Table 1, however, sheds additional light on the differences between the lesion groups on these tasks. This table shows the 95% confidence limits of the mean for the d_1 and d_2 measures for all 3 min of the test period for each of the object recognition, object location, and object-in-place tests. This measure is in one sense particularly stringent, as in order to be considered to have *failed* a task a group must show *no* significant discrimination, rather than just differ from another group. During the object location test, both PPRH and the CONT animals spent more time exploring the displaced object according to both d_1 and d_2. FNX animals, in contrast, failed to discriminate according to either measure. This pattern of results is in line with those of Ennaceur et al. [18]. For the object-in-place test, in which the use of both object and location information is necessary for normal performance, PPRH animals failed to discriminate according to either d_1 or d_2. FNX animals showed significant discrimination according to d_1, but failed to discriminate according to d_2. The results of these analyses should not, however, be overinterpreted, because despite the failure of FNX animals to discriminate significantly, d_1 and d_2 scores were in fact highest in this group. The results are, however, broadly consistent with the idea that these regions may cooperate in situations requiring the integration of both object and spatial information [22]. Importantly, they also show that PPRH lesions can affect performance on an object-in-place test that requires the use of object information but which does not require judgements about the familiarity or novelty of objects, as all objects were equally familiar.

The second object/place task we examined was a visuospatial conditional task in which animals learn a rule of the type 'if stimulus A, then go left; if B go right'. Neither FNX nor PPRH lesioned animals were impaired on this task. It has been suggested that the fornix is important for the use of 'idiothetic' information (information concerning the animal's own movements) [20,41]. A prediction following from this view is that fornix-lesioned rats should be impaired on tasks in which a rat learns a relationship between a stimulus and the rat's own spatially guided response. Indeed, it has been reported that monkeys with fornix or hippocampal lesions are impaired in conditional tasks in which the response is spatially directed [34,36,40] but not when the response is nonspatial [21,33]. The present finding that FNX animals were unimpaired in learning such a task appears inconsistent with this view. It has

been pointed out, however, that in two-choice conditional tasks animals can perform exceptionally well by employing strategies such as 'if cue repeats, then repeat the response; if cue changes, then change the response'. Only when the task requires three or more responses can acquisition of the stimulus-response mapping be dissociated from the use of such a strategy [44]. It is therefore conceivable that in the present study FNX rats had adopted such a strategy. Although reconciliation of the foregoing discrepancies will require further investigation, the present results are consistent with the view that whereas fornix lesions often produce impairments in 'allocentric' spatial tasks, the fornix and hippocampus are not required in situations requiring 'egocentric' spatial memory.

The lack of effect of PPRH lesions on any of the visuospatial conditional, pattern discrimination, or Pavlovian autoshaping tasks shows that this region does not have a general role in any of these types of learning and memory. Instead, it has recently been suggested that lesions in this region can lead to deficits in certain types of perceptually demanding tasks [5,32]. Taken together with these previous results, the present findings are consistent with the view that this region is not specialised for any particular type of associative learning, but may be involved in the processing and identification of complex visual stimuli [32].

To summarise, lesions of the fornix and of the perirhinal/postrhinal cortices led to distinct patterns of behavioural impairments. At the same time results were obtained that are consistent with the idea these structures may both be involved under conditions where object and spatial information must be integrated. As the two lesions had similar effects on only one of the two object/place tasks examined, and then only according to one particular analysis, this conclusion must remain tentative. Other reports, however, provide stronger evidence for such polymodal integration in the encoding of complex episodic memories [22]. Thus while these regions are clearly functionally dissociable [1,8,17,19], when complex episodic memories must be encoded these regions may co-operate in what *appears* to be a unitary manner. Under these conditions their activity may resemble more closely that described by prominent neurobiological theories of memory [14,37].

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