The importance of the rat hippocampus for learning the structure of visual arrays

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Abstract

It has been assumed that the integrity of the rodent hippocampus is required for learning the spatial distribution of visual elements in an array. Formally assessing this assumption is, however, far from straightforward as standard tests are amenable to alternative strategies. In order to provide a stringent test of this ability rats were trained on three concurrent visual discriminations in a water tank in which the stimuli in each pair of discriminations contained exactly the same elements but they differed in their spatial arrangement e.g. AB vs. its mirror image BA. Such 'structural' discriminations are a specific subtype of 'configural' or 'nonlinear' tasks. Following acquisition half of the rats received hippocampal lesions and all rats were retrained on the structural discriminations. Hippocampal lesions impaired the ability to relearn these 'structural' discriminations. In contrast, two other groups of rats with similar hippocampal showed no impairment on relearning two non-structural, configural discriminations: transverse patterning and biconditional learning. All three tasks used the same apparatus, the same stimulus elements, and similar training regimes. Superior performance by the rats with hippocampal lesions during a generalization decrement probe showed that hippocampal lesions had diminished sensitivity to 'structural' features on the biconditional task. While the rat hippocampus need not be required for all configural learning, it is important for the special case when the spatial arrangements of the elements are critical. This ability may be a prerequisite for the creation of mental snapshots, which underlie episodic memory.

Keywords: configural associations, discrimination, lesion, rat

Introduction

Consider a biconditional discrimination based on four stimuli, A, B, C and D. Reward might be signalled by the combinations AB and CD, but not by AC and BD. It is not possible to solve this discrimination by selecting individual elements as they are equally often reinforced and nonreinforced. Instead, the solution depends upon an appreciation of the significance of combinations of stimuli. Sutherland & Rudy (1989) proposed that the ability to solve such configural discriminations depends upon the hippocampus. Although this proposal proved highly influential, numerous tests have produced contradictory results so that even modifications to the initial theory (Rudy & Sutherland, 1995) are difficult to support (Gallagher & Holland, 1992; Davidson et al., 1993; Bussey et al., 1998; Han et al., 1998).

The present study tests the proposal by Aggleton & Pearce (2001) that the hippocampus is responsible for solving a particular subset of configural discriminations, namely, spatial–structural discriminations (George et al., 2001; George & Pearce, 2003; Haselgrove et al., 2005). Suppose that the pattern created by two objects A to the left of B signals food, and its mirror image signals the absence of food (A|B+ B|A–). This is a configural discrimination, but it is also a spatial–structural discrimination because the relative position of the two objects indicates the trial outcome. Aggleton & Pearce (2001) argued that a spatial–structural discrimination might be affected by damage to the hippocampus for two reasons. First, the hippocampus is believed to play a fundamental role in spatial learning (O'Keefe & Nadel, 1978; Morris et al., 1982) and, second, hippocampal lesions are known to disrupt the ability to respond to the spatial rearrangement of objects (Save et al., 1992; Mumby et al., 2002).

In experiment 1, two groups of rats were first trained on the spatial–structural discrimination described above. Accurate performance on this simultaneous discrimination would not, however, necessarily require rats to respond on the basis of the spatial relationship between A and B. Instead, they could look towards the extreme left-hand object, say, and solve the simple discrimination A+ B–. Additional trials were therefore included in the discrimination: B|C+ C|B– and C|A+ A|C– (George et al., 2001). Each stimulus occupied each spatial location equally often and was equally reinforced or nonreinforced in these locations (Fig. 1). Thus the solution to the entire problem demands an appreciation of the spatial relationships between the elements within each pattern. Following acquisition, half of the rats received hippocampal lesions and training re-commenced. In experiments 2 and 3 rats received transverse patterning and biconditional discrimination tasks, respectively. These tasks were of similar complexity to the one used for experiment 1, but did not require an appreciation of spatial information for their solution. The biconditional discrimination included test trials to assess the degree to which rats had learned about the spatial relationships between the components in each pattern, even though this information was irrelevant. Rats were also trained concurrently in each experiment on a simple, elemental discrimination to discourage inflexible choice behaviour (Gray & McNaughton, 1983).
Lesion co-ordinates (in mm) were lowered vertically into 17 sites (15 tract sites) bilaterally throughout to minimize the possibility of damage outside the hippocampus. The selected in order to control damage to the overlying parietal cortex and frequency RFG4-A Lesion Maker (Radionics, UK). This method was performed on all rats. Hippocampal lesions were made using a radio- surgery.

Rats were deeply anaesthetized with isofluorane gas and placed in a tank in which rats swam towards suspended stimuli to reach a submerged platform (Alvarado & Rudy, 1992).

All experiments used Dark Agouti rats (Harlan, UK) weighing 220–300 g at the time of surgery. Rats were housed in pairs and tested during the light period. Rats were on ad libitum food and water throughout testing. All procedures were in accordance with the United Kingdom Animal (Scientific Procedures) Act 1986. The behavioural procedures were based on studies of configural learning using a water tank and the next trial commencing after 20 s. If the rat swam to the S+ stimuli for half the animals were the S– stimuli for the other half, and vice versa. If a rat swam to S+ it was allowed to sit on the platform for 10 s before being removed and briefly placed in a dry box and the next trial commencing after 20 s. If the rat swam to the incorrect goal location (S–) it was allowed to swim back around the partition wall to the platform. An incorrect trial occurred if a rat’s snout came within 20 cm of S–. Each trial began with the rat gently lowered into the water facing away from the goal areas and close to the start wall.

Stimuli were attached to goal walls 1 cm above the water’s surface. For the structural and biconditional discriminations one compound stimulus was presented either side of the central partition wall. For transverse patterning the midline of each stimulus pair (e.g. midway between the B and W stimuli; Fig. 1) was slotted behind the protruding partition. Multiple copies of stimuli were used throughout testing to reduce the likelihood of olfactory cues being used to solve the discrimination. An additional safeguard used on the structural discrimination was the fact that by rotating the card 180° the same S+ stimuli could be used as an S– stimulus (and vice versa; Fig. 1). By these means it was possible to exclude the use of olfactory cues and ensure that the rats could not use any unintended visual cues on the test stimuli. All rats were first pretrained to find the hidden platform in the absence of any test stimuli. All sessions contained 30 trials unless otherwise stated. Behavioural testing recommenced at least 10 days after surgery.

### Materials and methods

#### Subjects

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### General training procedures

Throughout discrimination training the escape platform was located underneath the reinforced stimulus (S+). S+ would appear equally often in the right and left goal areas in a random order with the constraint that an S+ could not appear in the same goal location on more than three consecutive trials. Across all experiments and for all discriminations the stimuli were counterbalanced so that the specific S+ stimuli for half the animals were the S– stimuli for the other half, and vice versa. If a rat swam to S+ it was allowed to sit on the platform for 10 s before being removed and briefly placed in a dry box and the next trial commencing after 20 s. If the rat swam to the incorrect goal location (S–) it was allowed to swim back around the partition wall to the platform. An incorrect trial occurred if a rat’s snout came within 20 cm of S–. Each trial began with the rat gently lowered into the water facing away from the goal areas and close to the start wall.

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All rats were trained concurrently on a simple elemental discrimination. The stimuli were in the same location as those used in the configural tasks. Care was taken to select stimuli that did not resemble those in the configural tasks.

**Experiment 1: structural discrimination**

Prior to surgery half of the rats were trained to swim to B|W+, W|H+ and H|B+ (Fig. 1); the remainder were trained on the opposite contingency. The discriminations were introduced progressively until all three were solved concurrently. Stage 1 consisted of five sessions on the B|W+ W|B- discrimination. Stage 2 (six sessions) consisted of 10 trials of B|W+ W|B– followed by 20 trials of W|H+ H|W–. Stage 3 (six sessions) consisted of five trials of B|W+ W|B– then five trials of W|H+ H|W– and 20 trials of H|B+ B|H–. In stage 4 (four sessions) each discrimination was presented for two blocks of five trials. In stage 5 (two sessions) the three discriminations were randomly intermixed, with 10 trials for each one. In stage 6 (three sessions) rats received 12 intermixed trials of the three structural discriminations followed by 18 trials of the simple discrimination (X+, Y–). The simple discrimination was added to determine whether the rats were able to change from side to side in their choices following surgery. Once preoperative testing was completed rats were divided into two groups that were matched for their performance on the structural discrimination. One group received hippocampal lesions (HPC1, n = 6), the other group received surgical sham lesions (Sham1, n = 5).

Following surgery the rats first received six sessions of training on the simple discrimination (X+, Y–; Fig. 1). This was followed by three stages of structural testing, with the simple discrimination given on every fifth trial, i.e. 6 trials per session. In each stage presentations of the component discriminations (i.e. B|W+ W|B–, W|H+ H|W– and H|B+ B|H–) were progressively interleaved until by the final stage discrimination types were presented in a pseudo-random order. This sequence was given to maximize the chances of hippocampal lesioned rats showing normal performance as the gradual interleaving of the sequence was given to maximize the chances of hippocampal lesioned discrimination types were presented in a pseudo-random order. The spatial arrangement of the stimulus features was also counterbalanced, so half the rats were trained with the mirror image of the above configurations (i.e. W|B, H|O, H|B and W|O). The left–right arrangement of individual stimuli then remained fixed throughout initial acquisition. Rats were trained progressively so that stage 1 (five sessions) consisted solely of B|W+ W|B–. Stage 2 (five sessions) consisted of 10 B|W+ W|B– trials followed by 20 trials of O|H+ O|W–. Stage 3 (four sessions) consisted of four blocks of seven trials of the following discriminations: B|W+ B|H–; B|W+ O|W–; O|H+ B|H–; and O|H+ O|W–. In stage 4 (six sessions) the four simultaneous discriminations were presented in a random order with the constraint that the same discrimination could not be consecutive.

In accordance with the other tasks the rats were also trained on a simple discrimination (Fig. 1). Thus in stage 5 (three sessions) rats received three trials of each of the four component discriminations (12 intermixed trials) followed by 18 trials of the simple discrimination (X+, Y–). One group then received hippocampal lesions (HPC3, n = 7), the other group received surgical sham lesions (Sham3, n = 6).

Postoperative testing began with just the simple discrimination (four sessions). Following this training, stage 1 (10 sessions) contained six trials of each of the four component discriminations (B|W+ B|H–; B|W+ O|W–; O|H+ B|H–; and O|H+ O|W–) in a random order. The simple discrimination was presented on every fifth trial.

In stage 2 (six sessions) rats received 12 trials of the original biconditional discrimination and 12 probe trials with the mirror images of the training patterns probe, i.e. W|B+ H|B–; W|B+ W|O–; H|O+ H|B–; and H|O+ W|O– for half the rats and the counterbalanced pairings for the remaining half. A testing constraint was that two trials of the same discrimination could not be presented consecutively and no more than two trials of either the original or probe biconditional discrimination could be presented consecutively. This mirror-image probe condition has the interesting prediction that an animal insensitive to structure will outperform a normal rat as the former will be less aware of the changes while in a normal rat greater generalization decrement effects will reduce performance. Once again, the simple discrimination was given on every fifth trial.

**Histological methods**

Once all behavioural procedures had been completed all animals were deeply anaesthetized with an intraperitoneal injection of pentobarbital (Euthatal, Rhone Merieux) and perfused transcardially with saline followed by 10% formol–saline. The brain was removed and postfixed in formol saline for at least 12 h before being immersed in 25% sucrose solution for at least 24 h. The brain was then cut coronally on a freezing microtome into 40-μm sections and stained with Cresyl Violet, a Nissl stain.
Analyses

Data that met the assumptions of parametric statistics were analysed using *t*-tests for between-subject comparisons and multifactorial analysis of variance for repeated measures. Significant interactions were analysed using simple main effects analysis. All analyses were performed using SPSS software. Mean values are given ± SEM.

Results

Histology results

Animals across the four experiments suffered very similar amounts of tissue loss in the hippocampus and fimbria–fornix, with a tendency for the structural discrimination group (experiment 1) to have slightly less damage (Fig. 2). All hippocampal lesions resulted in substantial damage in the dorsal hippocampus including areas CA1, CA2, CA3, dentate gyrus and dorsal subiculum (Fig. 2). One rat had appreciable unilateral sparing of dorsal CA1 (transverse patterning task) and three rats had some additional unilateral sparing of CA2 and CA3 (Structural Discrimination). There was consistent partial damage to the fimbria–fornix which in some cases was substantial. All rats had damage in the ventral hippocampus, but typically the lesions spared the most posterior regions of the ventral hippocampus which were nevertheless markedly shrunken. In approximately two-thirds of HPC and Sham rats there was minor damage to the overlying cortex as a result of the surgical procedures. The amount of incidental damage to the cortex was matched in the HPC and Sham groups.

Structural discrimination

By the end of preoperative training rats had acquired the structural discrimination (85 ± 2.2% correct, mean ± SEM). Analyses of the average performance of the last three sessions demonstrate that rats were solving each component discrimination significantly above chance: B|W+ W|B−, *t* = 11.6, *P* < 0.001; W|H+ H|W−, *t* = 12.8, *P* < 0.001; H|B+ B|H−, *t* = 7.5, *P* < 0.001. The simple discrimination (X+ Y−) had also been acquired to a level significantly greater than chance: *t* = 17.2, *P* < 0.001. Rats were divided into two groups that were matched for their performance on the structural discrimination. One group received hippocampal lesions (HPC1, *n* = 6), the other served as surgical controls (Sham1, *n* = 5).

Postoperative discrimination training was in three stages that successively removed any possible help from nonstructural information (see Fig. 3). In stage 1, in which each pair of structural discriminations (i.e. B|W+ W|B−, W|H+ H|W−, H|B+ B|H−) was presented in blocks of eight trials, the HPC1 rats were impaired (Fig. 2; *F*1,9 = 14.77, *P* < 0.005) although both groups improved with training (block *F*2,18 = 12.09, *P* < 0.001, group × block *F*2,18 = 2.17, *P* > 0.1). In stage 2 in which each structural discrimination was presented in two blocks of four trials in a counterbalanced order, the HPC1 rats remained impaired (group *F*1,9 = 26.38, *P* < 0.005, block *F*3,27 = 0.98, *P* > 0.4, group × block *F*3,27 = 0.77, *P* > 0.5). For the full test (stage 3), in which each discrimination was presented in a random order, there was a significant group difference (*F*1,9 = 5.64, *P* < 0.05) but no other effects (block *F*4,36 = 2.01, *P* < 0.1; group × block *F*4,36 = 2.62, *P* > 0.05). To test whether the rats had acquired a structural discrimination and had not just learnt two of the three discriminations the scores on stage 3 were compiled for all three concurrent discriminations, when ranked best to worst for each individual animal. The Sham1 rats performed significantly above chance on stage 3 for their worst discrimination (90% correct, *t* = 19.1, *P* < 0.001) and the HPC1 group, even though impaired in comparison to the Sham1 group, were significantly above chance for their worst discrimination (77% correct, *t* = 6.5, *P* < 0.005).

All rats received training on the simple discrimination (X+, Y−) concurrent with the structural discrimination (Fig. 3). By stage I of
The hippocampus and structural learning

Transverse patterning task

By the end of preoperative training the rats were performing the transverse patterning task above chance (77 ± 2.0% correct). Analyses of the overall performance of the last three sessions demonstrate that rats were solving each component discrimination (i.e. B|W + W|B –, W|H + H|W – and H|B + B|H –) significantly above chance: B|W+, t10 = 12.1, P < 0.001; W|H+, t10 = 4.9, P < 0.005; H|B+, t10 = 8.5, P < 0.001. The simple discrimination (X+ Y–) had also been acquired to a level significantly greater than chance: t10 = 9.5, P < 0.001. The rats were then divided into two groups matched for their performance on the transverse patterning task.

After recovery from surgery (HPC2 n = 6, Sham2 n = 5) the groups were trained concurrently on the simple discrimination and transverse patterning. Transverse patterning improved in both groups (Fig. 4) and there was no lesion effect (group F < 1; block F11.99 = 9.75, P < 0.001; group × block interaction F < 1). This significant improvement was found for all three discriminations for both groups when separated into the best, intermediate and worst for each individual animal. This result indicates that increases in performance were not due to the reacquisition of just a subset of the discriminations, thus eliminating the need for configural strategies. Likewise, there was no overall lesion effect across simple discrimination relearning (group F < 1; block F14.126 = 15.34, P < 0.001; group × block F < 1). Relearning of this elemental task was rapid and after Session 10 the mean performance of both groups was > 90% and remained at this level throughout testing.

Biconditional discrimination

At the completion of preoperative training the rats were, overall, performing well above chance (83 ± 2.1% correct). Analyses of the overall performance of the last three sessions also demonstrates that the rats were solving each component discrimination (i.e. B|W+ and O|H+ vs. B|H– O|W–) significantly above chance: B|W+, t12 = 12.0, P < 0.001; O|H+, t12 = 10.1, P < 0.001. The simple discrimination (X+ Y–) had also been acquired to a level significantly greater than chance: t12 = 16.0, P < 0.001. The rats were divided into two groups matched for their performance on the biconditional discrimination and received either hippocampal lesions (HPC3, n = 7) or surgical control procedures (Sham3, n = 6).

After surgery all rats were retrained on both the simple and biconditional discriminations (Fig. 5). Hippocampal lesions had no apparent effect on stage 1 of the biconditional discrimination (F < 1) and both groups improved with training (block F4,44 = 20.67, P < 0.001; group × block F4,44 = 1.18, P > 0.3).

In spite of the null result it would be expected that the HPC3 rats would have learnt less incidentally about the structural relationships of the biconditional stimuli. If structural discrimination learning is automatic it can be predicted that the control animals will be more disrupted when the stimuli are changed to their mirror images (e.g. B|H becomes H|B; see Fig. 1). Probe trials using mirror images of the test stimuli (Fig. 1) comprised 50% of all trials in stage 2 of biconditional training. The Sham3 and the HPC3 groups continued to perform the original biconditional discrimination at a high level (both 79%) but, as expected, the mirror-image stimuli led to a reduction in
performance (Sham3, 60.9%; HPC3, 69.1%). While both groups discriminated the mirror-image stimuli above chance (both $P < 0.05$), group differences emerged when ratio scores [correct choices on the probe biconditional/ (scores for original biconditional + probe biconditional)] were calculated. The HPC3 group (mean $0.47 \pm 0.01$) showed significantly better generalization to the mirror-image stimuli than the Sham3 group (mean $0.43 \pm 0.01$; group $F_{1,11} = 5.07, P < 0.05$).

Finally, the simple discrimination task did not show an overall lesion effect (group $F < 1$). There was, however, an effect of block as the animals improved ($F_{6,66} = 15.92, P < 0.001$) and some indication of a group $\times$ block difference ($F_{5,66} = 2.09, P = 0.066$). After Block 3 the mean performance of both groups remained $>90\%$ correct.

**Discussion**

While hippocampal lesions impaired all stages of relearning three structural discriminations, relearning of two configural tasks, transverse patterning and a biconditional discrimination, appeared normal. These two configural tasks share many features with the structural task. First, the transverse patterning task has three concurrent discriminations that use stimuli identical to those in the structural task (Fig. 1). The key difference is that the solution of the transverse patterning task does not depend on the spatial relationships of the elements within the compounds. Second, the biconditional task used pairs of elements to create compound stimuli that were positioned in exactly the same way as for the structural task. The lack of a relearning deficit on these two matched configural tasks makes it very unlikely that the structural deficit was due to any possible navigational requirements of the task that may be sensitive to hippocampectomy. The generalization decrement probe trials on the biconditional task did, however, show that normal rats automatically encode the structural arrangements of complex stimuli. Rats with hippocampal lesions were significantly less disrupted by this manipulation, presumably because they had failed to learn the spatial arrangements of the individual stimuli.

The selective structural discrimination deficit cannot be linked to task difficulty. Comparisons based on presurgical training showed that the structural and biconditional tasks were closely matched. The transverse patterning task proved the most difficult as normal rats required 41 sessions to reach 77% correct, but only 23 (biconditional) and 26 (structural) sessions to reach 83% and 85% correct, respectively. Nevertheless the HPC3 animals were unimpaired on transverse patterning. Another potential confound is that rats with hippocampal lesions are prone to adopt inflexible patterns of responding (e.g. always go to the right) when confronted by difficult problems (Gray & McNaughton, 1983; Davidson & Jarrard, 2004). This habit was counteracted by training rats on all three tasks prior to surgery. Also, rats were concurrently given a simple elemental discrimination throughout postoperative training. Postoperative accuracy on this elemental task remained $>90\%$ after 10 sessions on all three tasks, so ensuring that the rats with hippocampal lesions could switch flexibly between the goal areas.

Three previous studies have used a similar water tank apparatus to examine the effects of hippocampal lesions on configural learning (Alvarado & Rudy, 1995a, 1995b; Driscoll et al., 2005). Like the present study, all used stepwise procedures to introduce the various discriminations. Unlike the present study all reported hippocampal deficits on transverse patterning. Unfortunately, Alvarado & Rudy (1995b) found that hippocampal-lesioned rats were impaired from the first stage of elemental training. As a consequence, the lesion group were performing worse when first given the full configural task and, hence, final performance can not be safely interpreted. Rats with hippocampal lesions made by kainate and colchicine (Alvarado & Rudy, 1995a) showed exactly the same confound in a second study, although rats with ibotenate lesions in the same study were more closely matched to controls until reaching the full transverse patterning problem, when they were impaired. This study, however, lacked a nonconfigural comparison task in the water tank of similar difficulty. In a third study, intact rats were first trained in a water tank on either transverse patterning or three concurrent elemental discriminations (Driscoll et al., 2005). Postoperative retraining after hippocampal lesions showed a reduction in performance for both the elemental and configural tasks, but this reduction was more permanent for the configural task (Driscoll et al., 2005). This pattern was interpreted as evidence of a hippocampal deficit. However, the study contained no surgical control group (Driscoll et al., 2005) and our results consistently found that sham controls show a clear, initial reduction in performance. In the present experiment radio-frequency lesions were used and these cause damage to fibres of passage. It is possible that the lesion method may account for differences between the present experiment and previous studies which report a hippocampal lesion impairment (Alvarado & Rudy, 1995a, 1995b; Driscoll et al., 2005). However, this argument only makes the present null result more compelling as it would be predicted that radio-frequency lesions would result in greater dysfunction than fibre-sparing lesions. Furthermore, using quite different procedures some other studies of hippocampal system lesions have failed to find deficits in learning transverse patterning tasks in rats (Bussey et al., 1998; Dusek & Eichenbaum, 1998). While the present study cannot resolve this inconsistent literature on its own, the contrast with the structural discrimination deficit suggests that unintended spatial components could create hippocampal deficits in some studies. A further factor is the need to maintain flexible patterns of responding, e.g. by the use of a concurrent simple discrimination.

The lack of a hippocampal lesion deficit on the biconditional task agrees with other studies using a variety of procedures (Whishaw & Tomie, 1991; Marston et al., 1993; Deacon et al., 2001; Good et al., 1998; Coutereau et al., 2002). While deficits have been reported on some biconditional tasks, problems of interpretation have arisen because of different baseline rates of responding between groups (McDonald et al., 1997), associated with difficulties in withholding responses on go/no go tasks (Douglas, 1967; Kimble, 1969; Gray, & McNaughton, 2000; Davidson & Jarrard, 2004). The present study used forced-choice discriminations, and so counteracted problems of withholding responses. While the seemingly normal performances on the biconditional and transverse patterning tasks seem to run counter to existing theories concerning hippocampal function and configural learning (Sutherland & Rudy, 1989; Gluck & Myers, 1993; Rudy & Sutherland, 1995) it is important to determine whether the same results are found when the surgeries are given prior to task acquisition. Even so, a surprising feature of the present study was the length of time it took for control rats to relearn the tasks. It therefore appears that a lot of learning occurred after surgery, presumably reflecting the complexity of the tasks, the interposition of the simple elemental discrimination, and the resultant length of delay between the end of configural learning and its resumption after surgery which was at least 20 days in all cases.

The narrower proposal, that the rat hippocampus supports configural learning when the structure of the elements is critical (Aggleton & Pearce, 2001), finds support from other studies. Hippocampal damage impairs the spontaneous preference for familiar objects in
novel locations, but can spare the spontaneous preference for novel objects (Save et al., 1992; Mumby et al., 2002; Winters et al., 2004; Lee et al., 2005). Fornix lesions can selectively disrupt discriminations that involve spatially rearranged, common stimuli (Gaffan & Harrison, 1989; Hunt et al., 1994). Immediate–early gene expression studies also show changes in hippocampal c-fos activity when rats are confronted by spatial re-arrangements of familiar visual arrays (Wan et al., 1999; Jenkins et al., 2004), but not when confronted by novel objects (Aggleton & Brown, 2005).

The hippocampal lesions did not completely stop reacquisition of the structural discrimination. It is possible other regions involved in this class of task might support relearning. Candidate sites include the parietal cortex and the parahippocampal region. Like the hippocampus, lesions of the parietal cortex leave rats insensitive to the spatial rearrangement of objects (Save et al., 1992; DeCoteau & Kesner, 1998). Brain imaging studies also implicate the parietal cortex in distinguishing mirror images (Alivisatos & Petrides, 1997), and there is clinical evidence that damage to parieto-occipital cortex can lead to a selective discrimination problem for such stimuli (Davidoff & Warrington, 2001). Evidence from c-fos expression studies has also implicated the postrhinal cortex and postsubiculum, as well as the parietal cortex, in responding to changes in structural information (Wan et al., 1999; Jenkins et al., 2004). It is therefore plausible that a parietal–parahippocampal pathway, normally linked to the hippocampus, may support this function. This account fits with computational models that permit retarded learning of configurational tasks by the neocortex in the absence of the hippocampus (O’Reilly & Rudy, 2001). The likelihood that the parietal cortex is involved in the structural task was also the reason why we used radio-frequency lesions plus a full surgical sham group. Although this lesion method damages fibres of passage, it is much easier to control cell loss in the overlying parietal cortex than when making multiple excitotoxic injections. Furthermore, the choice of this surgical technique cannot explain the sparing on the configural tasks (experiments 2 and 3) as damage to fibres of passage would exacerbate any hippocampal dysfunction.

While direct comparisons cannot be made between the three tasks as there are minor procedural differences, both the preoperative acquisition performance and the length of postoperative retraining indicate that for the Sham group the structural discrimination was more rapidly acquired than transverse patterning task but was not necessarily more difficult than the biconditional discrimination. It is therefore unlikely that the selective hippocampal deficit on the structural discrimination was due to task difficulty or the length of time taken to re-acquire the task by control rats. Likewise, the lack of a hippocampal lesion deficit on the two nonstructural tasks is not due to either a ceiling or a floor effect. It may, however, seem surprising that the structural task need not be harder than the nonstructural tasks given the high degree of overlap between the reinforced and nonreinforced cues (Pearce, 1994; George et al., 2005). This result is less surprising if it is assumed that structural information is highly salient. Given that certain spatial information is resistant to overshadowing and blocking (Hayward et al., 2004), and the fact that the biconditional task showed how normal rats acquire structural information even when it is not required, then the present pattern of results seems less surprising. At the same time, the finding that hippocampal-lesioned rats showed significantly superior generalization on the biconditional probe, even though the hippocampal-lesioned rats did not significantly differ from the controls on postoperative reacquisition of the task, shows how the specific structural deficit is present regardless of the ease with which different configurational discriminations are acquired.

The present findings are also relevant for the notion that the hippocampus organizes relationships between disparate items, e.g. sequences of places and events, so that they can be stored and expressed in a flexible manner (Eichenbaum et al., 1996; Eichenbaum, 2000). Our results only support a much narrower version of this ‘relational’ hypothesis, where relational learning must include spatial structural properties. Also, the notion that the hippocampus is required for structural learning provides an explanation for why the hippocampus seems to be critical for the encoding or storage of ‘mental snapshots’ or ‘scenes’ (Tulving, 1983; Gaffan, 1994; Aggleton & Pearce, 2001). Such scenes are unique because of the binding of the component elements, an intrinsic aspect of which is their spatial arrangement. This structural binding might therefore be seen as a prerequisite for the formation of mental snapshots or scenes that comprise episodic memory. While the structural learning task is learnt incrementally over many sessions and is not therefore a measure of episodic-like memory, it taxes an ability likely to be of underlying importance for episodic memory.

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Abbreviations

B, black; H, horizontal bars; HPC, hippocampal-lesioned; O, oval; W, white.

References


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